Drs. Jonathan Betlinski and Ann Wheeler have nothing to disclose.
Learning Objectives

- Know the four most common anxiety disorders in Primary Care Clinics
- Know at least 3 common medical comorbidities of anxiety
- Be familiar with the GAD-7, PDSR and Mini-SPIN
- Be able to define and apply at least three evidence-based non-pharmacologic treatments for anxiety disorders
- Be familiar with three classes of anxiolytics
Detecting and Treating Anxiety Disorders

- Review the epidemiology of anxiety
- Review medical comorbidities
- Review criteria for GAD, PD, and SAD
- Review GAD-7, PDSR, and Mini-SPIN
- Review non-pharmacologic interventions for Anxiety
- Review pharmacology for GAD, PD, and SAD
Anxiety in the United States of America

**Prevalence**
- **12-month Prevalence:** 18.1% of U.S. adult population
- **Severe:** 22.8% of these cases (e.g., 4.1% of U.S. adult population) are classified as “severe”

**Demographics (for lifetime prevalence)**
- **Sex:** Women are 60% more likely than men to experience an anxiety disorder over their lifetime
- **Race:** Non-Hispanic blacks are 20% less likely, and Hispanics are 30% less likely, than non-Hispanic whites to experience an anxiety disorder during their lifetime
- **Age:**

**Average Age-of-Onset:** 11 years old

Anxiety and Depression are the most common in general medical settings

- Anxiety lags behind Depression
- >30 million Americans have Anxiety
- Anxiety Disorders cost $42 billion/year
- Only 15-36% of those with Anxiety are recognized in Primary Care

http://annals.org/article.aspx?articleid=658879
Anxiety Disorders in DSM-5 (DSM, ICD-10)

Separation Anxiety Disorder (309.21, F93.0)
Selective Mutism (312.23, F94.0)
Specific Phobia (300.29, various)
Social Anxiety Disorder (300.23, F40.10)
Panic Disorder (300.01, F41.0)
Agoraphobia (300.22, F40.00)
Generalized Anxiety Disorder (300.02, F41.1)

https://www.psychiatry.org/psychiatrists/practice/dsm
Anxiety Disorders in DSM-5, continued

Substance/Medication-Induced Anxiety Disorders (291.89 or 292.89, various)

Anxiety Disorder Due to Another Medical Condition (293.84, F06.4)

Other Specified Anxiety Disorder (300.09, F41.8)

Unspecified Anxiety Disorder (300.00, F41.9)

OCD and PTSD get their own chapters now!

https://www.psychiatry.org/psychiatrists/practice/dsm
Anxiety in the Primary Care Setting

• A 2007 study of patients from 15 clinics
  – 19.5% had at least 1 anxiety disorder
  – 8.6% PTSD
  – 7.6% Generalized Anxiety Disorder
  – 6.8% Panic Disorder
  – 6.2% Social Anxiety Disorder
  – 41% of those with Anxiety Disorders had no current treatment

Anxiety and Co-morbid Medical Conditions

- Increased prevalence of Anxiety Disorders
  - Cardiovascular Disease
  - Gastro-intestinal Disease
  - Respiratory Disease
  - Migraines
  - Chronic Pain
  - Cancer

- Odds of an Anxiety Disorder increase with increasing number of CMC's

Those with Anxiety Disorders have

- Higher frequencies of some CMC's
  - Irritable Bowel Syndrome
  - Asthma

- Worse Symptom Severity and Impairment
  - Asthma
  - Cardiovascular Disease
  - Diabetes

- Increased risk for disease progression

Patients with multiple Co-Morbid Medical Conditions can benefit from anxiety treatment as much as those with low medical comorbidity* *(except maybe migraines)*

Generalized Anxiety Disorder

- Excessive anxiety or worry for >6m about a number of events or activities
- Individual finds it difficult to control the worry
- Three or more of the following are present
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle Tension
  - Sleep Disturbance

Panic Attack

Intense fear or discomfort that starts abruptly, peaks in 10 minutes and includes four or more of the following:

- Palpitations, pounding heart or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Paresthesias
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded or faint
- Derealization or depersonalization
- Fear of losing control or going crazy
- Chills or hot flashes
- Fear of dying

https://www.psychiatry.org/psychiatrists/practice/dsm
Panic Attack!!!

Mind racing?

Dizzy, disorientated, light headed?

Vision strange, blurry?

Possible sleep disturbance?

Difficulty in swallowing?

Feeling breathless, breathing fast & shallow?

Heart racing, palpitations?

Nausea / lack of appetite?

Restless?

Jelly-like legs?

Trembling?

Sweating or shivering?

Wanting to run?

http://www.bevaisbettartofanxiety.com/books.html
https://www.amazon.com/Living-Survivors-Guide-Panic-Attacks/dp/0207180407
Panic Disorder

- Recurrent unexpected Panic Attacks
- At least one of the attacks has been followed by 1 month (or more) of one (or more):
  - Persistent concern about having additional attacks
  - Worry about the implications of the attack or its consequences
  - Significant change in behavior related to the attacks
Social Anxiety Disorder

- A persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way that will be embarrassing and humiliating.
- Exposure to the feared situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally pre-disposed Panic Attack.
- The person recognizes that this fear is unreasonable or excessive,
- The feared situations are avoided or else are endured with intense anxiety and distress.
- The avoidance, anxious anticipation or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational functioning, or social activities or relationships, or there is marked distress about having the phobia.

https://socialanxietyinstitute.org/dsm-definition-social-anxiety-disorder
### GAD-7 - Generalized Anxiety Disorder Scale

<table>
<thead>
<tr>
<th>Over the last two weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>Over half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling nervous, anxious, or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Being so restless that it's hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**How difficult have those problems made it for you to do your work, take care of things at home, or get along with other people?**

- Somewhat difficult

**Score:** 14  
**Difficulty Level:** Somewhat difficult  
**Severity Level:** Moderate Anxiety

---

GAD-7, Interpretation

- Score of 5, 10 and 15 are the cut-offs for mild, moderate and severe anxiety
- GAD (10): 89% sensitivity, 82% specificity
- PD (7): 74% sensitivity, 82% specificity
- SAD: 72% sensitivity, 80% specificity
- PTSD: 66% sensitivity, 81% specificity

http://www.ncbi.nlm.nih.gov/books/NBK126694/
Panic Disorder Self Report

1) During the last six months, have you had a panic attack or a sudden rush of intense fear or anxiety? (Circle your answer)  
   YES  NO

   When was the most recent time this occurred?  
   Date ______________________

If NO (you have not experienced a panic attack), please leave the remainder of this form blank. If YES, please continue.

2) Was at least one panic attack unexpected, as if it came out of the blue?  
   YES  NO

3) Did it happen more than once?  
   YES  NO

4) If YES to 3, approximately how many panic attacks have you had in your lifetime?  
   ________________

If YES to 1, 2, and 3, please answer the following questions:
If NO to 1, 2, and 3, please leave the remainder of this form blank.

5) Have you ever worried a lot (for at least one month) about having another panic attack?  
   YES  NO

6) Have you ever worried a lot (at least one month) that having the attacks meant you were losing control, going crazy, having a heart attack, seriously ill, etc.?  
   YES  NO

7) Did you ever change your behavior or do something different (for at least one month) because of the attacks?  
   YES  NO

If YES to 5, 6 OR 7 please answer the following questions:

Think back to your most severe panic attack. Did you experience any of the following symptoms?

8) Shortness of breath or smothering sensations?  
   YES  NO

9) Feeling dizzy, unsteady, lightheaded, or faint?  
   YES  NO

10) Palpitations, pounding heart, or rapid heart rate?  
    YES  NO

11) Trembling or shaking?  
    YES  NO

12) Sweating?  
    YES  NO

13) Feelings of choking?  
    YES  NO

14) Nausea or abdominal distress?  
    YES  NO

15) Numbness or tingling sensations?  
    YES  NO

16) Flashes (hot flashes) or chills  
    YES  NO

17) Chest pain or discomfort?  
    YES  NO

18) Fear of dying?  
    YES  NO

19) Fear of going crazy or doing something uncontrolled?  
    YES  NO

20) How much do these symptoms interfere with your daily functioning? (Circle one)
    
    0 1 2 3 4
    No  Mild Interference  Moderate Interference  Severe Interference  Very Severe Interference

21) How distressing do you find these symptoms? (Circle one)
    
    0 1 2 3 4
    No  Mild Interference  Moderate Interference  Severe Interference  Very Severe Interference

22) When you have had bad panic attacks, does it often take less than ten minutes from the point at which the attack begins, to the point at which it reaches a peak or becomes most intense?  
    YES  NO

23) Just before you began having panic attacks, were you taking any drugs or excessive amounts (more than 4 cups daily) of stimulants (e.g., coffee, tea, or cola with caffeine)?  
    YES  NO

   a) If YES, what was it that you were taking?  
      __________________________

   b) How much of it were you taking (in cups, etc.)?  
      __________________________

24) Have you ever been diagnosed with a medical problem (hyperthyroidism, a seizure or cardiac condition, etc.) that could have caused your panic symptoms?  
    YES  NO
24 questions related to panic disorder

- Items 1-3 must all be Yes
- Items 1-3, 5-19, and 22 are 1 point each
- Items 20 and 21 are each divided by 2
- Items 4, 23 and 24 are not scored

- Cut off score is 8.75
- 89% Sensitivity, 100% Specificity

Mini-SPIN Screening Tool for Social Phobia

Score of 6 or more
Sensitivity 89%
Specificity 90%
PPV 53% NPV 98%


Shorter version of the 17-question SPIN

http://serene.me.uk/tests/spin.pdf

<table>
<thead>
<tr>
<th>Mini-SPIN Screener for Social Anxiety (Phobia) Disorder</th>
<th>Not at all</th>
<th>A little bit</th>
<th>Somewhat</th>
<th>Very much</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does fear of embarrassment cause you to avoid doing things or speaking to people?</td>
<td></td>
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<tr>
<td>2. Do you avoid activities in which you are the center of attention?</td>
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<tr>
<td>3. Is being embarrassed or looking stupid among your worst fears</td>
<td></td>
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</tr>
</tbody>
</table>

http://primarycare.ementalhealth.ca/download.php?encodedName=y4PmRf6fa5zuueT7shOCTabViQve-slash-Ths8VWd50Ja6TIEquals-&folder=diagnosticTools&fileName=Social%20anxiety%20-%20Mini%20SPIN%20dcg_o15.pdf
Non-Pharmacologic Interventions for Anxiety

Non-Pharmacologic Interventions for Anxiety

- Thorough Work-up
- Education
- Lifestyle Modification
- Behavioral Techniques
Treating Anxiety

- Start with a thorough medical work up
  - Neurologic
  - Endocrine (thyroid, pheo, carcinoid)
  - Mitral valve prolapse

- Evaluate for Substance Abuse
  - Both intoxication and withdrawal
  - Don't forget alcohol, caffeine and nicotine

- Evaluate for other psychiatric disorders

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC427612/
Organic Anxiety

Features of Anxiety Secondary to Organic Causes

- Onset of anxiety symptoms after age 35 years
- Lack of personal or family history of an anxiety disorder
- Lack of childhood history of significant anxiety
- Absence of significant life events generating anxiety symptoms
- Lack of avoidance behavior
- Poor response to psychiatric treatment

Differential Diagnosis: Anxiety Secondary to Organic Factors

- Medical Illness
  - Brucellosis
  - Carcinoid syndrome
  - Cerebral arteriosclerosis
  - Chronic obstructive pulmonary disease
  - Coronary insufficiency
  - Diabetes mellitus
  - Drug withdrawal: anxiolytic agents, caffeine, alcohol, sedatives, opiates
  - Pancreatic tumor
  - Pheochromocytoma
  - Psychomotor epilepsy, complex partial seizures
  - Pulmonary emboli
  - Thyroid disease (hypo- and hyperthyroidism, thyroiditis)

- Medications
  - Analgesics
  - Anticholinergics
  - Antihistamines
  - Antihypertensives
  - Antimicrobials
  - Calcium channel blockers
  - Estrogen
  - Insulin
  - Muscle relaxants
  - Non-steroid anti-inflammatory drugs
  - Sedatives
  - Sympathomimetics
  - Theophylline

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC427612/
Educate about the Cycle of Anxiety

http://www.jabfm.org/content/22/2/175.full.pdf+html
Education about the Cycle of Anxiety

• Educate about the cycle of anxiety
  – Address behavioral avoidance with gradual exposure
  – Address cognitive distortions with evidence
  – Address physical symptoms with DB and PMR

http://www.jabfm.org/content/22/2/175.full.pdf+html

• Goal: Manage anxiety, not erase it

Lifestyle Modification

- Regular exercise counteracts anxiety

- Avoid caffeine and alcohol
  [http://www.jabfm.org/content/22/2/175.full.pdf+html](http://www.jabfm.org/content/22/2/175.full.pdf+html)

- Improve sleep hygiene

Diaphragmatic Breathing

• Increases parasympathetic tone
  – Slows heart rate
  – Decreases blood pressure
  – Increases oxygen
  – Decreases carbon dioxide

• Practice for five minutes twice daily
• Use as needed

Belly Breathe!

https://www.youtube.com/watch?v=_mZbzDOpylA
Progressive Muscle Relaxation

• Deliberately ordered tensing and relaxation of muscle groups

• 65% Panic-free at 12 weeks, 82% at 1 year (vs. 74% and 89% with CBT)

• Keys for use:
  – Often helpful for bedtime relaxation
  – Practice the same system
  – Use a tape or video to help

Cognitive Behavioral Therapy

- Effects persist at least 6-12 months
- Cognitive component may be more effective
- More effective than Supportive Therapy and Psychodynamic Therapy
- May outperform pharmacotherapy*
  - Response rates of 56%
  - Highly motivated problem solvers
  - Cost-effective

http://www.uptodate.com/contents/psychotherapy-for-generalized-anxiety-disorder
Cognitive Behavioral Therapy

- Usually lasts 6-15 sessions
- Addresses the **cognitive, physical and behavioral** symptoms of anxiety
  - Education
  - Self-Monitoring
  - Relaxation Training
  - Cognitive Restructuring
  - Imagery Exposure
  - Situational Exposure
  - Relapse Prevention

http://www.uptodate.com/contents/psychotherapy-for-generalized-anxiety-disorder

https://www.amazon.com/Mastery-Your-Anxiety-Panic-Treatments/dp/0195311345
Pharmacologic Treatment Recommendations
General Treatment Recommendations

- Recommendations from:
  - *World Federation of Biological Psychiatry*
  - Complement to diagnostic guidelines prepared by the World Health Organization (WHO) and American Psychiatric Association (APA)
  - *Agency for Healthcare Research and Quality*
  - *National Institute for Health and Clinical Excellence*
General Treatment Recommendations

Treatment selection is based upon:

- patient preference
- severity of illness
- co-morbidity
- concomitant medical illnesses
- complications like substance abuse or suicide risk
- history of previous treatments
- cost/coverage
- availability of types of treatment in a given area

General Treatment Recommendations

Treatment options include both pharmacologic and non-pharmacologic approaches

- Prior to initiating pharmacologic treatment, it is recommended that patients are informed of advantages and disadvantages
- Treatment should continue for at least 6 – 24 months after remission has occurred, in order to reduce the risk of relapse, and may be stopped only if all, or almost all, symptoms disappear.

### Drug Classes Studied in Anxiety Disorders

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Panic</th>
<th>GAD</th>
<th>SAD</th>
<th>OCD</th>
<th>PTSD</th>
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<td>X</td>
<td>X</td>
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<tr>
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<td>X</td>
<td>X</td>
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<td>Ca Channel Modulators</td>
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<td>Gabapentin</td>
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<td>Benzodiazepines</td>
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<td>Atypical Antipsychotics</td>
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<td>Risperdal</td>
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<td>Other</td>
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<td>Mirtazapine</td>
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<td></td>
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<tr>
<td>Hydroxyzine</td>
<td></td>
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</table>
## Guideline Recommendation Grade

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Panic</th>
<th>GAD</th>
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<td><strong>SSRIs</strong></td>
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<td>Citalopram</td>
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</tr>
</tbody>
</table>

**Grade Key:**
1 = Category A evidence and good risk-benefit ratio  
2 = Category A evidence and moderate risk-benefit ratio  
3 = Category B evidence (limited positive evidence)  
4 = Category C evidence (evidence from uncontrolled studies or case reports)  
5 = Category D evidence (inconsistent results)
SSRIs

- Generally well tolerated
- Restlessness, jitteriness, increase in anxiety symptoms, insomnia or headache in the first few days/weeks of treatment may jeopardize compliance
- Use low starting doses to minimize overstimulation
- Anxiolytic effect may start with a delay of 2 to 4 weeks (in some cases up to 6 to 8 weeks)
## Guideline Recommendation Grade

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<tr>
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<tbody>
<tr>
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<td>Venlafaxine</td>
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<td>Duloxetine</td>
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5=Category D evidence (inconsistent results)
SNRIs

- Generally well tolerated
- Similar to SSRIs, use low starting doses to minimize overstimulation
- Anxiolytic effect may start with a delay of 2 to 4 weeks
- Unclear evidence does not support use in OCD
# Guideline Recommendation Grade

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Panic</th>
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<tr>
<td><strong>TCAs</strong></td>
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<td>Amitriptyline</td>
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<td>Clomipramine</td>
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<td>Imipramine</td>
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<tr>
<td><strong>MAOIs</strong></td>
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<td>2</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

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4 = Category C evidence (evidence from uncontrolled studies or case reports)
5 = Category D evidence (inconsistent results)
TCAs

- Well proven efficacy, however compliance may be reduced due to adverse effects
- Concern with drug interactions and potential for toxicity/lethality
- SSRIs and SNRIs are typically tried first
## Guideline Recommendation Grade

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<thead>
<tr>
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<td><strong>Ca Channel Modulators</strong></td>
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<td>Pregabalin</td>
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<td>Gabapentin</td>
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</table>

**Grade Key:**

1 = Category A evidence and good risk-benefit ratio
2 = Category A evidence and moderate risk-benefit ratio
3 = Category B evidence (limited positive evidence)
4 = Category C evidence (evidence from uncontrolled studies or case reports)
5 = Category D evidence (inconsistent results)
Pregabalin

- Anxiolytic effects are attributed to its binding at the α2-δ-subunit protein of voltage-gated calcium channels in CNS tissues
- Binding reduces calcium influx at nerve terminal and modulates the release of neurotransmitters
- Anxiolytic effect starts in first days of treatment
## Guideline Recommendation Grade

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Panic</th>
<th>GAD</th>
<th>SAD</th>
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<td>Risperidone</td>
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<td>Mirtazapine</td>
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<td>Hydroxyzine</td>
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<td>Clonazepam</td>
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<td>Lorazepam</td>
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<td><strong>Tricyclic Anxiolytic</strong></td>
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<td>Buspirone</td>
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Buspirone

How does it work?

- Selective 5HT1A partial agonist, with activity at both presynaptic and postsynaptic 5-HT1A receptors
- Appears to block presynaptic dopamine receptors selectively and produces an increased firing of midbrain dopamine neurons
- Thus, buspirone produces anxiolytic effects via postsynaptic receptor activity, while its activity at autoreceptors initially suppresses neuronal firing but gradually restores serotonergic neurotransmission
Use in Generalized Anxiety Disorder:

- **Initial dose is 7.5mg BID.**
  - May be increased every 2-3 days in increments of 2.5 mg twice daily to a maximum of 30 mg twice daily.
  - There is a significant delay in the onset of clinical activity, which can vary from 2 weeks to much longer.
  - Role: treating GAD in patients who cannot tolerate, or fail to respond to, an SSRI or SNRI.
Benzodiazepines

- Act as positive allosteric modulators on GABA-A receptors (potentiates GABA)
- Associated with sedation, dizziness, and prolonged reaction time
- After a couple of weeks or months of continuous use, dependency may occur in a substantial number of patients
- Can be helpful in first days/weeks of initiating antidepressant treatment
- Anxiolytic effect starts within minutes
## Agent Comparison

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of Action</th>
<th>Peak Onset (hrs)</th>
<th>Half-life (hrs)</th>
<th>Elimination</th>
<th>Dose Equivalent</th>
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</thead>
<tbody>
<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
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<tr>
<td>Chlordiazepoxide (Librium)</td>
<td>Int</td>
<td>2-4</td>
<td>5-30 (parent)</td>
<td>Oxidation</td>
<td>10mg</td>
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<td>3-100 (metab)</td>
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<tr>
<td>Diazepam (Valium)</td>
<td>Rapid</td>
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<td>20-50 (parent)</td>
<td>Oxidation</td>
<td>5mg</td>
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<td></td>
<td></td>
<td></td>
<td>3-100 (metab)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurazepam (Dalmame)</td>
<td>Rapid</td>
<td>0.5-2</td>
<td>47-100 (metab)</td>
<td>Oxidation</td>
<td>30mg</td>
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<tr>
<td><strong>Intermediate Acting</strong></td>
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<tr>
<td>Alprazolam (Xanax)</td>
<td>Int</td>
<td>0.7-1.6</td>
<td>6-20 (parent)</td>
<td>Oxidation</td>
<td>0.5mg</td>
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<tr>
<td>Clonazepam (Klonopin)</td>
<td>Int</td>
<td>1-4</td>
<td>18-39 (parent)</td>
<td>Oxidation</td>
<td>0.25mg</td>
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<tr>
<td>Lorazepam (Ativan)</td>
<td>Int</td>
<td>1-1.5</td>
<td>10-20 (parent)</td>
<td>Conjugation</td>
<td>1mg</td>
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<tr>
<td>Oxazepam (Serax)</td>
<td>Slow</td>
<td>2-3</td>
<td>3-21 (parent)</td>
<td>Conjugation</td>
<td>15mg</td>
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<tr>
<td>Temazepam (Restoril)</td>
<td>Slow</td>
<td>0.75-1.5</td>
<td>10-20 (parent)</td>
<td>Conjugation</td>
<td>30mg</td>
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<tr>
<td><strong>Short Acting</strong></td>
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<tr>
<td>Triazolam (Halcion)</td>
<td>Int</td>
<td>0.75-2</td>
<td>1.6-5.5 (parent)</td>
<td>Oxidation</td>
<td>0.5mg</td>
</tr>
</tbody>
</table>

Onset of Action:  Rapid=within 15 min; Intermediate=15-30min; Slow=30-60min
Clinical Considerations

- Use lowest dose for shortest period of time
- Benefit has been seen with short-term use (2-4 weeks)
- Consider alternative agents for long-term needs
  - Consider both non-pharmacologic and pharmacologic alternatives
- Avoid use with benzodiazepines (black box warning)
- Dependence can be a significant issue for patients taking benzodiazepines for >1 month
  - All patients should be made aware of the risks of dependence with ongoing use
  - Periodic trials of dose reduction and cessation are recommended
  - High potency, short half-life agents more likely to cause dependence
Reasons for discontinuation of BZs

- Tolerance -- no longer effective for the condition for which they were prescribed.
- Dependence -- stopping will result in withdrawal symptoms, and the end result is long-term continuation in order to avoid withdrawal syndromes.
- Prevention of adverse effects such as cognitive and psychomotor impairment, depression, irritability, loss of concentration and emotional blunting.
- Reduce risk of falls in the elderly.
- Reduce risk of accidents while driving.
- Avoid potential interaction with other medications and with alcohol.

http://www.patient.co.uk/doctor/benzodiazepine-dependence
Benzodiazepine Withdrawal

Dependence

- Associated with use >4 weeks
- Prevalence estimate:
  - 40% general practice pts; 63% psychiatric pts

Factors associated with long-term use:

- Psychiatric comorbidity, older age, less educated, living alone and those who use avoidance coping behavior

Benzodiazepine Withdrawal

Advantages of withdrawal in long-time users

Study reviewed changes in elderly patients’ cognitive function, quality of life, mood and sleep

Findings:

- 60% of pts had been taking the bz for >10yrs
- 27% of pts had been taking the bz for >20yrs
- Those that tapered off of the bz showed improvement on several cognitive and psychomotor tasks
- Withdrawers vs. control did not differ in sleep or benzodiazepine withdrawal symptoms

Benzodiazepine Withdrawal

Signs and Symptoms

- Tremors
- Anxiety
- Perceptual disturbances
- Dysphoria
- Psychosis
- Seizures

Abrupt withdrawal can be dangerous
Withdrawal Strategies

Taper schedules

Early stages of withdrawal are easier to tolerate than the later and final stages

Even short-term use may require a tapering regimen (e.g. 2 weeks at lower doses)

Optimal duration is not clear and may vary from patient to patient

In most patients, a brisk schedule (8-12 weeks) is possible. Longer-term users may require longer tapers (up to several months).

4 week taper at 25% per week—51% require slower d/c
Beta Blockers

- It is proposed that propranolol’s anxiolytics properties may result from its peripheral (autonomic) rather than central activity
- Works best to break the cycle of anxiety where bodily sensations (increase ventilation or palpitations) trigger panic
- In general, there is a lack of well-designed clinical trials which limits conclusions in favor or against the use of propranolol in the treatment of anxiety disorders
- Early adjuvant therapy with propranolol may be recommended instead of benzodiazepines while waiting for effect of SSRIs to be established
- Reported side effects: sleeping disturbances, nightmares, transient fatigue, and cold extremities

J Psychopharm 2016; 30(2):128-139
## Dosing Ranges of Grade 1 Agents

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<td>Pregabalin</td>
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</table>
Treatment Considerations

• Most patients will respond to low dose antidepressants
  • OCD is the exception where higher doses are often needed
• Start low and go slow
• Single daily doses enhance treatment adherence
• In patients with hepatic impairment, consider medications that are primarily renally cleared
Treatment Considerations

- Unless poorly tolerated, maintain an **adequate** dose for 4-6 weeks (8-12 weeks in OCD or PTSD) before switching agents.

- Consider non-pharmacologic treatment alternatives or enhancements.
Treatment Considerations

- **Panic disorder and agoraphobia**
  - Severe attacks may require short-acting benzodiazepines
  - SSRIs and venlafaxine are first-line treatment options
  - After remission, treatment should continue for at least several months in order to prevent relapses
  - Combination CBT and medication has been shown to have the best treatment outcomes
Generalized Anxiety Disorder (GAD)

- First-line treatment options are SSRIs, SNRIs and pregabalin
- Benzodiazepines should only be used when other drugs or CBT have failed (or short-term only)
• **Social Anxiety Disorder (SAD)**
  - SSRIs and venlafaxine are first-line treatment options
  - Benzodiazepines not extensively studied
  - No evidence for use of TCAs
  - Performance anxiety—beta blockers are an acceptable alternative
  - Propranolol 20 to 60 mg taken 30 to 60 minutes prior to the anxiety-inducing situation
Treatment of Anxiety in Primary Care

- Anxiety Disorders are very common
- Anxiety Disorders commonly improve
- Treatment starts with
  - Thorough medical workup
  - Education and lifestyle modification
  - Behavioral management
- CBT, DB, PMR can be just as effective as medications—sometimes better!
The End!