Prescribing Medications for Anxiety and Depression (without getting anxious and depressed)

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Disclosures

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- None

Learning Objectives

- At the end of this session you will be able to:
  - Use first and second-line treatments for depression and anxiety, including medications for augmentation of partially effective meds.
  - Manage common side effects of medications for depression and anxiety.
  - Develop a differential diagnosis for reasons why treatments are not working as expected for anxiety and depression.

Psychopharmacology ATTACK!

- Lots of info in next 30 minutes!
- We will process more in the breakout session!

Session Structure

- First line treatments for anxiety and depression (15 minutes)
- Augmenting/second line treatments for anxiety and depression (10 minutes)
- Why is my patient not getting better? (5 minutes)

First Line Treatments for Depression and Anxiety

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Anxiety and Depression First Line Treatment

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- Mild-to-Moderate
  - Based on symptoms or PHQ-9/GAD-7 Score
    - PHQ-9 under 10 for Mild, under 20 for Moderate (15-19 Mod-Severe)
    - GAD-7 under 10 for Mild, under 15 for Moderate
  - Cognitive Behavioral Therapy is a good option
  - Medications often are not required for MILD anxiety or depression
- Moderate-to-Severe Medications:
  - SSRIs first line medication treatment
  - Try one at a good dose, give it at least 4-6 weeks
  - Partial response: increase dose and/or Augment
  - No response: go to 2nd SSRI

https://aims.uw.edu/sites/default/files/Exampleprovidertool.pdf

Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006; 166:1092-1097.

Anxiety and Depression First Line Treatment

- KEY RESOURCE:
  - University of Washington AIMS Center
  - https://aims.uw.edu/sites/default/files/ConcisePsychotropicMedicationPrescribingDirections.pdf
- Treat to Target!
  - Value of care management (collaborative care)
  - What is remission?
    - Many use PHQ9<5 for depression as remission.
    - Antidepressant that is partially effective (>25% but <75% reduction on PHQ9/GAD7 score), consider increasing dose or augmenting with another medication.
    - Antidepressant that has not been effective (<25% reduction on PHQ9/GAD7 score) after an adequate dose/time (usually 4-8 weeks), consider changing antidepressants.
    - Ask the patient

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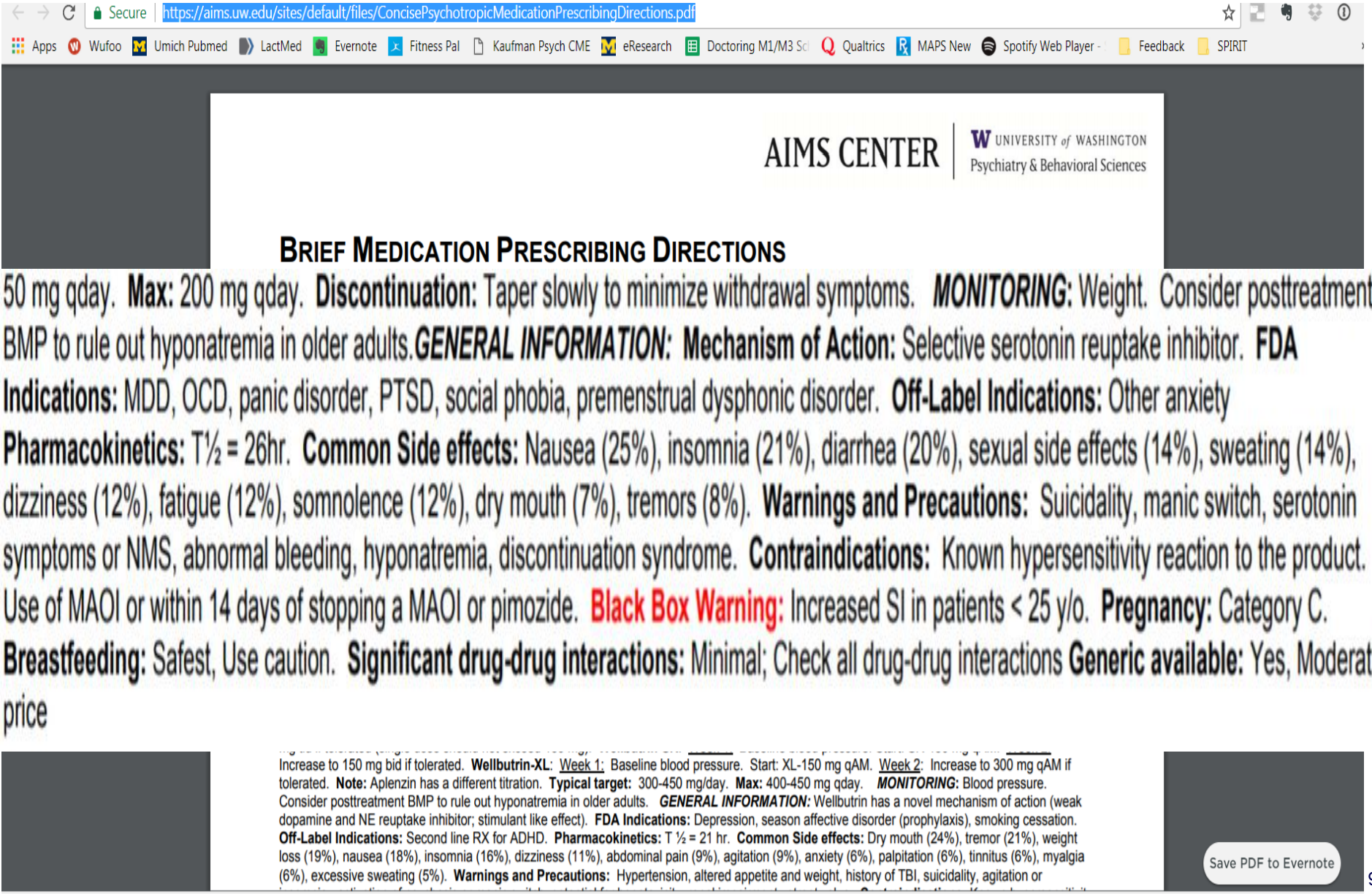
AIMS Primary Care Prescribing Information



SSRI Pearls

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- Higher than FDA-recommended may be needed
  - Maximum benefit up to 250 mg equivalents of imipramine in metanalysis[1]
  - 250 mg of imipramine=300 mg of sertraline=250mg of fluvoxamine=50 mg of paroxetine or fluoxetine=83.25 mg of citalopram=41.75 mg of escitalopram
- Anxiety disorders – start really low dose
- Blunting of affect at higher doses
- Bruising (platelets have 5HT receptors!), hyponatremia in elderly
- STAR-D trial showed maximum benefit after TWELVE weeks!
- Celexa over 40 mg (20 mg for geriatrics)
  - VA demonstrated worse outcomes when celexa doses lowered[2]
  - UM study showing higher healthcare utilization and higher sedatives when dose changed[3]
  - Baseline EKG if going over these doses and recheck EKG, keep K/Mg stable

1. Jakubovski E et al. Systematic review and meta-analysis; Dose-response relationship of Selective Serotonin Reuptake Inhibitors in Major Depressive Disorder. Am J Psych. 2016 Feb 1; 173(2):174-183
2.. Rector et al. Outcomes of citalopram dosage risk mitigation in a veteran population. Am J Psychiatry. 2016 Sept 1;173(9):896-902.
3. Gerlach et al. Unintended Consequences of Adjusting Citalopram Prescriptions Following the 2011 FDA Warning. Am J Geriatr Psychiatry. 2017 Apr;25(4):407-414.

SNRIs

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- Co-morbid pain and anxiety/depression – consider 1st line
- Cymbalta to 120 mg
  - Better outcomes with pain at 120 mg[1]
- Effexor to 300 mg in XR, 375 in IR
  - Effexor does not hit NE until 150 mg and above (SSRI like before 150mg)
- Same time course as SSRIs
- May increase BP
- May be more effective for severe depression[2]

1. Ney JP et al. (2013), Comparative Efficacy of Oral Pharmaceuticals for the Treatment of Chronic Peripheral Neuropathic Pain: Meta-Analysis and Indirect Treatment Comparisons. Pain Med 2013;14: 706–719.
2. Bradley AJ, Lenox-Smith AJ. Does adding noradrenaline reuptake inhibition to selective serotonin reuptake inhibition improve efficacy in patients with depression? A systematic review of meta-analyses and large randomized pragmatic trials. J Psychopharmacol. 2013 Aug;27(8):740-58.

Mirtazapine

- Sedating
  - More sedating at lower dose (higher dose NE kicks in)
- Increased appetite
  - Weight gain will not be subtle unlike atypical antipsychotics

Buspirone

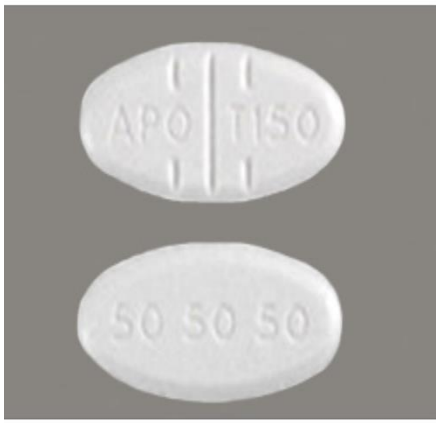
- Can augment SSRI for depression and anxiety
- If it works, it works!
- Does not work well for people who have BDZ exposure already[1]

1. Chessick CA et al. Azapirones for generalized anxiety disorder. Cochrane Database of Systematic Reviews 2006, Issue 3

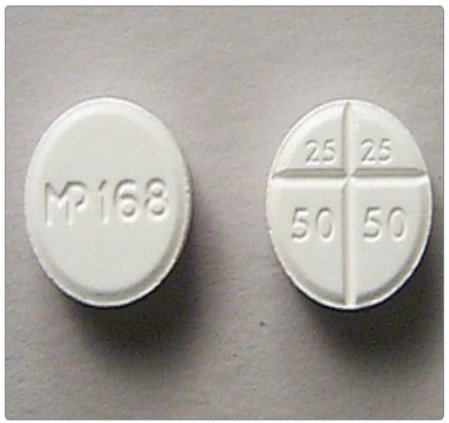
Trazodone

- Approved for depression (higher doses)
- Mostly used for sleep
- SE: sedation, orthostatic hypotension/dizziness, priapism
- PEARL: 150 mg often scored in half one side, in thirds on other side (makes flexible dosing easy)

trazodone tablet
150 mg



trazodone tablet
150 mg



trazodone tablet
150 mg

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New(er) Agents

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- Vilazodone
  - SSRI and 5HT1A partial agonist (Like Buspar and SSRI in one)
  - GI SE most common, headache
- Levomilnacipran
  - SNRI (enantiomer of milnacipran which is approved for fibromyalgia)
  - More heavy on norepinephrine, so more HR/BP/urinary hesitancy issues
- Vortioxetine
  - Trade name changed from Brintellix to Trintellix
  - SSRI, 5HT1A full agonist, 5HT3 antagonist
  - Increases dopamine, NE, Ach in prefrontal cortex
    - Could this be good for improved cognition in depression? 3 RCTs say so[1]
    - Studied in geriatric patients and shows effect

1.McIntyre RS et al. The effects of vortioxetine on cognitive function in patients with major depressive disorder: A meta-analysis of three randomized controlled trials. Int J Neuropsychopharmacol. 2016 Aug 24. pii:pyw055.

Bupropion

- Great for low energy, smoking cessation, low concentration
- Off-label use for ADHD
- Does NOT help out generalized anxiety and may make anxiety worse
- THREE FORMULATIONS:
  - Immediate release (TID)
  - Sustained release (SR – BID)
  - Extended release (XR – qday)
  - When dosing TID or BID, do not dose too close to bed
    - BID= qam and qdinner (9AM, 5 PM)

Tricyclic Antidepressants

- Effective – dirtier drugs re: receptor affinities
- More SE than SSRI and SNRI
  - Dry mouth, sedation, constipation, urinary retention, blurry vision, orthostasis
- Lethal in overdose (as few as 10 day supply can be lethal)
- Benefit with chronic pain
- Nortriptyline often tolerated better than amitriptyline
- Lower doses for pain; higher doses for depression
- EKG at baseline and annually if over 65 yo, cardiac diseases
- Can test blood levels!

Complementary and Herbals

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- We are in Ann Arbor after all!
- Carlat Report Psychiatry July/August 2013 still one of best resources
- Depression effective and safe: Rhodiola rosea (300-900 mg), SAMe (200-800 mg BID)
  - St. John's Wort as well, but interacts with SSRI/serotonin agents
  - 5-HTP may help but TID-QID
  - Methylfolate may help depression as adjunct
  - Fatty acids possible; 1-2 grams
- Kava helps anxiety but not safe (hepatotoxic)
- Valerian may help insomnia but poor studies

Augmenting Agents for Depression and Anxiety

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Benzodiazepines

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- Lipophilic- diazepam, alprazolam
- Hydrophilic – lorazepam, clonazepam
- Oxazepam, temazepam, lorazepam safer in liver disease
- Risk Assessment for BDZ Abuse:
  - Higher risk if h/o alcohol use DO, FH of alcohol use DO
  - Risk of accidental OD with Opioids
- Red Flags
  - Unwilling to try other treatments
- Urine GCS will catch alcohol metabolites!
- BDZ in depression may help patient stick with other meds short term[1]
  - Lower risk if using PRN; Some patients use as back-up coping mechanism
- UK NICE guidelines recommend 2-4 week treatment, not for mild GAD

1. Furukawa TA et al. Antidepressant plus benzodiazepines for major Depression. Cochrane Database of Systematic Reviews 2001, Issue 3.

Atypical Antipsychotics

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- FDA approved for augmenting depression (as of 7/2017):
  - Aripiprazole
  - Brexpiprazole
  - Olanzapine
  - Quetiapine XR
- None FDA approved for augmenting anxiety
  - Off-label use for quetiapine doses from qhs to even TID dosing
    - May be similar to SSRI effect BUT HIGHER SE PROFILE!

1.Depping AM et al. Second-generation antipsychotics for anxiety disorders. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.CD008120.

Atypical Antipsychotic Pearls

- High Metabolic Risk: Olanzapine, Clozapine
- Medium Metabolic Risk: Quetiapine, risperidone, asenapine, iloperidone
- Low Metabolic Risk: Aripiprazole, Brexpiprazole
- Lowest Metabolic Risk: Ziprasidone, Lurasidone
- Ziprasidone and Lurasidone need to be taken with food (300 cal)
- Augmenting doses are on lower end of spectrum; bipolar doses mid-range; schizophrenia doses highest

Atypical Antipsychotic Pearls

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- Most Sedating: Quetiapine, Olanzapine, Clozapine
- Don’t forget Akathesia (looking at you aripiprazole)
  - Reduce dose, add low dose BDZ or propranolol, switch agents
- METABOLIC MONITORING FOR ALL

Atypical Antipsychotic Metabolic Monitoring

Diabetes Care February 2004 vol. 27 no. 2 596-601

Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes

Table 3—

Monitoring protocol for patients on SGAs*

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

- *

* More frequent assessments may be warranted based on clinical status

Other Augmenting Agents

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- Can mix and match MOST groups of antidepressants
  - SSRI/SNRI/TCA together to not make much sense (maybe low dose TCA)
  - We didn't discuss MAOIs – do NOT mix serotonin meds with MAOIs!
- Mirtazapine for depression/anxiety
- Bupropion for depression (can worsen anxiety)
- Buspirone for depression/anxiety
- Low dose stimulants for geriatric depression[1]
  - 5-10 mg of methylphenidate; up to 40 mg
- Gabapentin for Anxiety (off label use)
- Hydroxyzine for PRN use anxiety
- Lithium for unipolar depression (per STAR*D)
- Cytomel (T3)for depression (per STAR*D)
- STAR-D: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/allmedicationlevels.shtml

1. Lavretsky H et al. Citalopram, methylphenidate, or their combination in geriatric depression: A randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2015 Jun;172(6):561-9

Why is My Patient Not Getting Better?

Reasons for Treatment Failure

- Is the dose high enough?
- Has the treatment been long enough?
  - Instant gratification does not work with SSRI/SNRIs
- Do you have the correct diagnosis?
  - Could this be bipolar depression? Hypomania often undiagnosed and unrecognized. Bipolar depression notoriously difficult to treat.
  - What are the refractory symptoms?
    - Attention? Irritability? Consider co-morbid ADHD
    - Irritability? Mood Swings? “0 to 60 in seconds”? Consider Personality DO
    - Trauma? Irritability? Avoidances? Nightmares? Consider PTSD

Reasons for Treatment Failure

- Chronic Pain
- Is there a medical cause?
  - Thyroid? Brain tumor?
  - Revisit your review of systems
- Are they taking their meds?
- Are meds affordable? (Donut Hole, loss of insurance)
- Culture – is mental illness accepted?
  - LARGE placebo effect in psychiatric medications
  - If you undersell meds, they will not work as well

Tools to Help

- PHQ-9 (depression)
- GAD-7 (anxiety)
- Mood Disorder Questionnaire (bipolar– not good universal screen)
- CIDI (Structured bipolar screening)
- PC-PTSD (Primary Care PTSD screen)
- PCL-5 (PTSD symptom scale – LONG)
- Adult ADHD Self-Report Scale
- AUDIT and AUDIT-C (alcohol screening)
- DAST-10 and DAST-20 (Drug abuse screening)
- https://www.integration.samhsa.gov/clinical-practice/screening-tools

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- Lavretsky H et al. Citalopram, methylphenidate, or their combination in geriatric depression: A randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2015 Jun;172(6):561-9
- STAR*D Summary Site: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/allmedicationlevels.shtml
- https://www.integration.samhsa.gov/clinical-practice/screening-tools

Thank you!

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