Mind Matters ECHO

Module: Depression
Session 3: Effective Treatments for Depression: Pharmacology

July 14, 2021

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Mount Sinai Health Partners

Welcome!

- Pre-survey: bitly.com/mindmatters3
- Hub team introductions
- Disclosures
- Questions during presentations

Case Presentation

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Mount Sinai Doctors, General Medicine Associates

Patient Information

Demographic Information	• 34 year old cis-female • Lives with spouse/partner • Commercial insurance • Employed full time (shipping company)
Medical History	• Cervical radiculopathy • Chronic low back pain • Shoulder impingement • Diabetes • Migraine • Morbid obesity • IBS
Current Medications	• Buproprion XL 300 mg • Metformin • Topamax 50 mg • Gabapentin 300 mg TID • Labetalol 100 mg • Cyclobenzaprine

Patient Information

Current Psychiatric Diagnoses	• Major depression
History of treatment	• Sadness, anhedonia, poor sleep, difficulty with concentration, diffuse pain and IBS symptoms after mother passed in 2018 • Started on Buproprion XL with improvement in sadness, anhedonia and concentration • Increasing pain symptoms starting a year ago, but denied depression • Poor adherence to follow up and treatment recommendations • Leave of absence from work for 3 months then requested urgent appointment 4/2021 to obtain letter for work
Current Symptoms	• Palpitations • Sweating • Chest pain • Shortness of breath • Dizziness • Paresthesia Reports feelings of depression only related to worsening overall health
Current Treatment Plan for Psychiatric Conditions	Attempting to switch from Wellbutrin to Duloxetine but patient is reluctant

Patient & Case Information

Areas of Support and Consultation Being Sought	• Diagnostic uncertainty • Pharmacological consultation • Psychotherapeutic consultation • Identify appropriate behavioral health referrals • Strategies for engaging the patient • Managing countertransference (strong feelings about the patient that may interfere with the treatment alliance)
Main Question	In a patient who continues to deny depression and anxiety, but symptoms are not otherwise explained, how do I help her make the connection? It has been difficult to engage and build rapport as she feels I am writing off her symptoms.

Effective Treatments for Depression: Pharmacology

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Outline

- Antidepressant efficacy
- Major classes of antidepressants
- First line medications for treatment of depression
- How to chose antidepressant medication for your patient
- When to refer to a specialist

Do Antidepressants Work?

- Depression is a treatable illness
  - Approximately 80% of people receiving treatment for depression experience some relief from symptoms
    - Mild depression: psychotherapy and medications have similar efficacy
    - Moderate to severe depression: pharmacotherapy and combination treatments are most effective
- Relative to placebo, all antidepressants are associated with higher rates of remission (Cipriani et al 2018)
  - Antidepressant efficacy ranges from 40-70% in clinical trials
  - Placebo response rate = 30%
  - More severe depression = higher response/remission rates
- In head to head trials, antidepressants have similar efficacy but varying tolerability
- Antidepressants reduce risk of relapse by up to 70% (Geddes et al 2003)

www.psychiatry.org/patients-families/depression/what-is-depression

Major Classes of Antidepressants

- Monoamine Oxidase Inhibitors (MAOIs)
- Tricyclic Antidepressants (TCA)
- **Selective Serotonin Reuptake Inhibitors (SSRIs)**
- **Antidepressants with multiple receptor targets (SNRIs, NDRIs, Atypical)**
- NMDA Glutamate Receptor Antagonists
  - Esketamine

Antidepressants by Class

Table 3

ANTIDEPRESSANTS				
Atypical Antidepressants	**MAOIs**	**SNRIs**	**SSRIs**	**Tricyclic Antidepressants**
bupropion nefazodone mirtazapine trazodone	isocarboxazid phenelzine tranylcypromine	venlafaxine desvenlafaxine duloxetine	fluoxetine paroxetine sertraline fluvoxamine citalopram escitalopram	amitriptyline nortriptyline desipramine clomipramine amoxapine doxepin protriptyline trimipramine imipramine

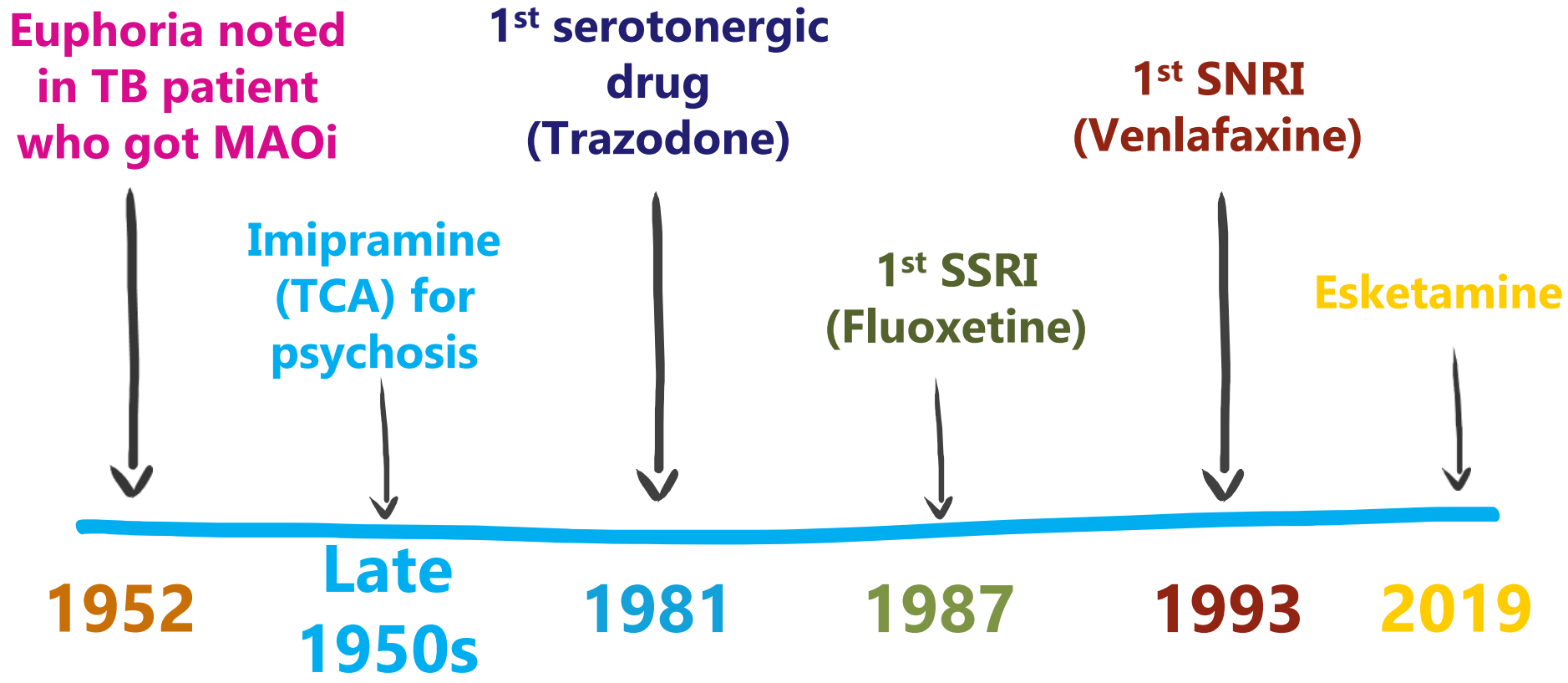
Newer antidepressants:

vortioxetine (Trintellix) – most like SSRI

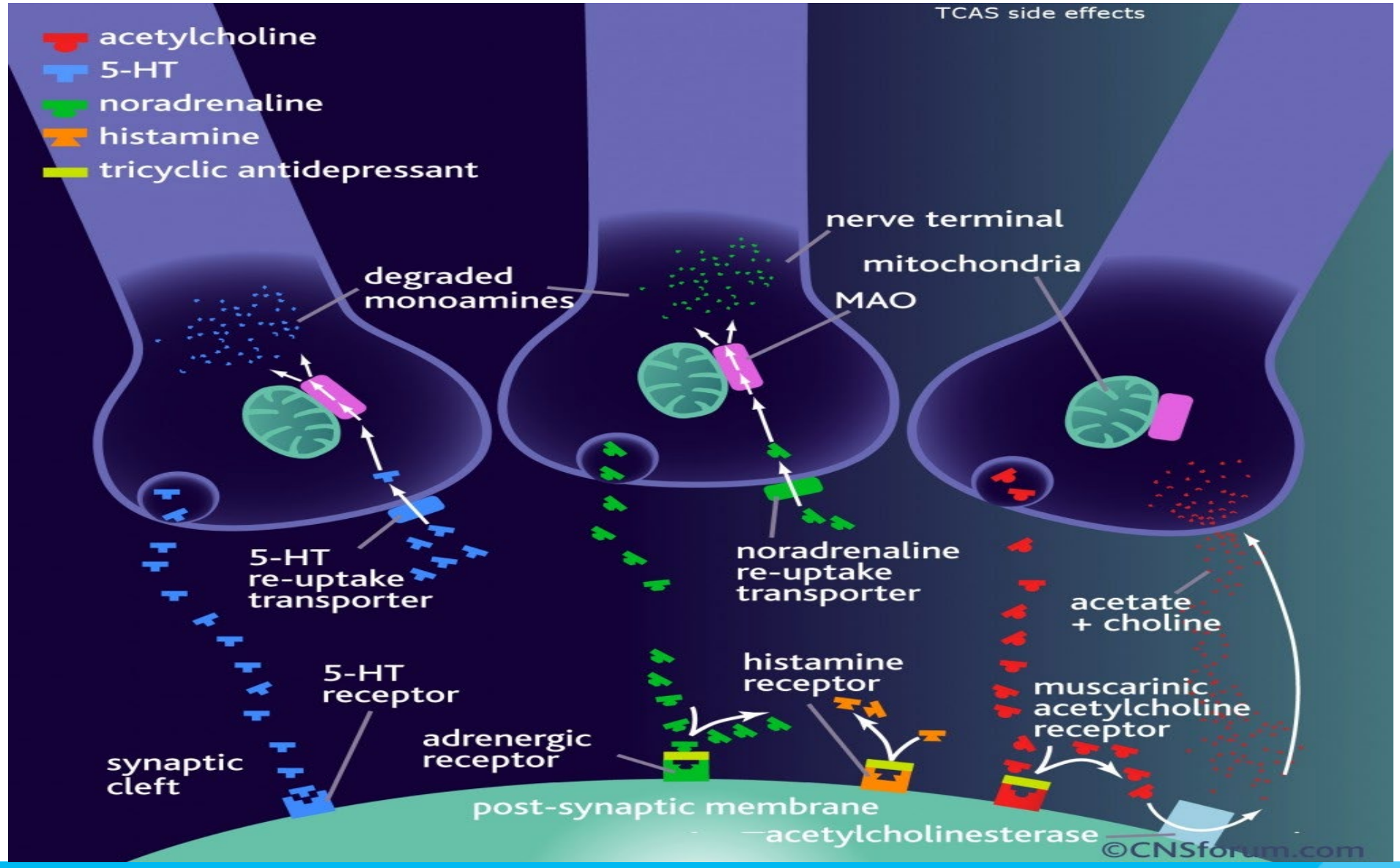
vilazadone (Viibryd) – most like SSRI

levomilnacipran (Fetzima) – most like SNRI

History of Antidepressant Treatment



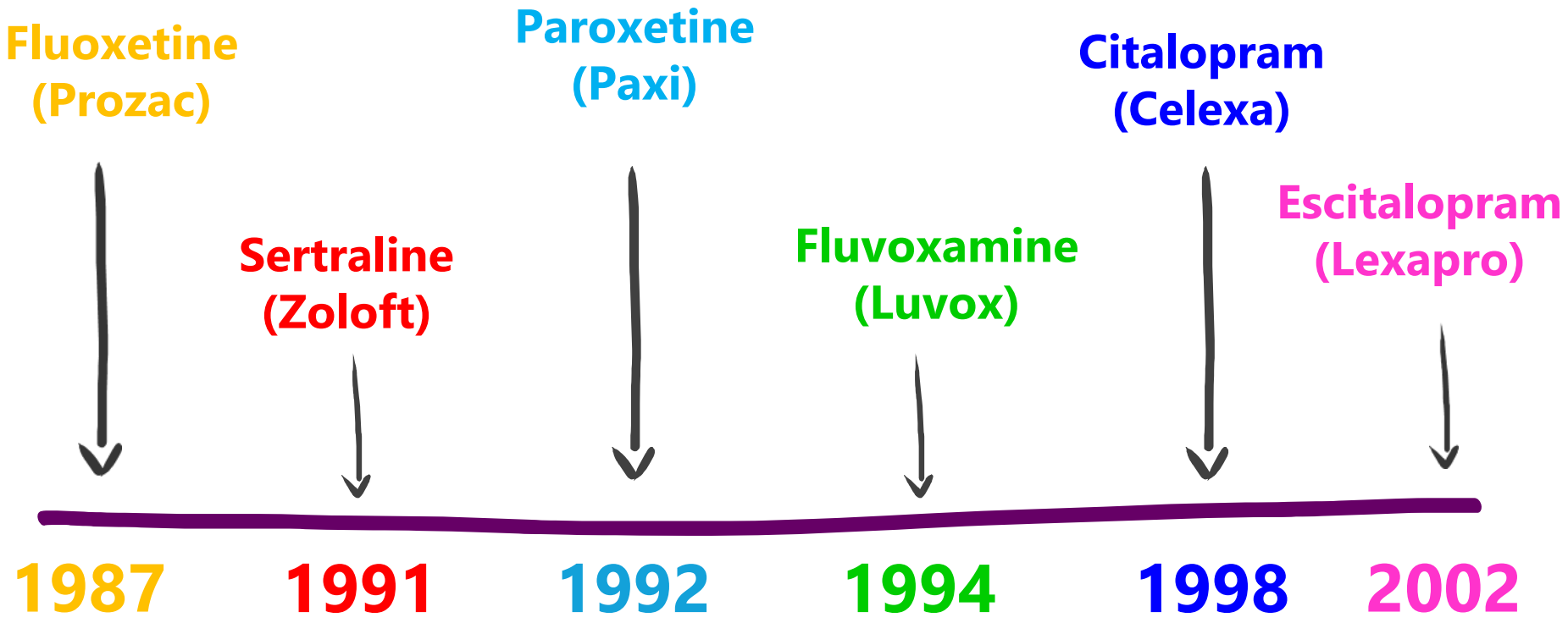
Antidepressant Mechanism of Action



Which Antidepressant Class to Choose?

- All antidepressants have similar efficacies
- MAOIs and TCAs have low tolerability
- MAOIs require dietary restrictions
- MAOIs and TCAs are toxic in overdose
- American Psychiatric Association (APA)
  - Prior to 2018>>SSRIs were recommended as 1st line treatment
  - New guidelines recommend both SSRIs and mixed receptor antidepressants as 1st line treatment for depression of any severity
- National Institute for Health Care Excellence (NICE)
  - Guidelines recommend SSRIs as 1st line treatment for moderate to severe depression
- SSRIs/mixed receptor antidepressants
  - Less side effects than their predecessors
  - Less drug-drug interactions
  - Most medications not dangerous in overdose
  - Many different options to try

Selective Serotonin Reuptake Inhibitors (SSRIs)



(New drugs: SSRI +: vortioxetine, vilazodone)

Antidepressants with Multiple Receptor Targets

- Medications target more than one type of neurotransmitter
- Medications bind to more than one type of transporter or receptor
- Types:
  - SNRIs
    - e.g. venlafaxine, desvenlafaxine, duloxetine
    - serotonin and norepinephrine reuptake inhibition
  - NDRIs
    - e.g. bupropion
    - norepinephrine and dopamine reuptake inhibition
  - Other/atypical
    - e.g. mirtazapine
    - primarily increases norepinephrine and serotonin by targeting pre and postsynaptic receptors

Antidepressants: How to Choose

- All antidepressants have similar efficacy and onset of action
- Side effects can vary greatly
- Thus, choice is often based on pharmacokinetics, pharmacodynamics and other clinical considerations
- When choosing an antidepressant consider:
  - Symptoms (e.g.. agitated vs. retarded depression)
  - Comorbidities (e.g.. anxiety, pain)
  - Tolerability
  - Previous response
  - Genetics
  - Drug-drug interactions (CYP450 effects)
  - Patient preference (placebo response)
  - Cost

Consider SSRIs

SSRIs treat both depression and anxiety and are generally well tolerated

- **Fluoxetine**
  - Most commonly prescribed antidepressant in the US
  - Activating
  - Longest half life of all the SSRIs
    - Least likely to cause withdrawal
    - Avoid in elderly
  - Has good evidence in eating disorders
- **Paxil**
  - Great for anxiety
  - Avoid in patients on multiple medications (high rates of drug-drug interactions)
  - Significant withdrawal syndrome
- **Escitalopram, sertraline, citalopram**
  - Well tolerated
  - Moderate risk of withdrawal syndrome
  - Citalopram – risk of QT prolongation with doses over 40mg
- **Fluvoxamine**
  - Good evidence in patients with OCD
  - Prone to drug-drug interactions
  - Sedating
  - Dosed BID

Consider SNRIs

- SNRIs treat both depression and anxiety and are generally well tolerated

- Venlafaxine, Desvenlafaxine
  - Good evidence in adults and elderly
  - Noradrenergic inhibition occurs at doses over 150mg (venlafaxine)
  - Monitor for hypertension at higher doses
  - Good for co-morbid depression and migraine

- Duloxetine
  - Monitor for hypertension at all doses
  - Very activating
  - Also indicated for neuropathic pain and fibromyalgia

Consider Bupropion

- Primarily for depression
- May worsen anxiety
- Risk of seizures?
- Very activating
- Good side effect profile
- Used on combination to treat SSRI side effects
- Other indications: smoking cessation, ETOH abuse, weight loss
- May have some benefit in mild ADD

Consider Mirtazapine

- Greater benefit for depression than anxiety
- Very sedating
- More sedating at lower dosages
- More rapid onset of action?
- Increases appetite and promotes weight gain
  - Good for use in oncology patients
  - Good for use in patients with nausea/vomiting

Initiating Antidepressant Treatment

- Start low, go slow
- Increase every 2 weeks if tolerating
- Monitor closely for initial side effects including suicidal ideation (under age 25)
- Conduct an adequate trial
  - At least 4-8 weeks duration
  - Effective dose of medication (proven efficacy)
- Use minimum effective dose to minimize side effects
- If symptoms improve but don't remit, try going higher
- If symptoms fully remit, treat for at least 6-12 months for a first episode of depression
- Taper meds over weeks when stopping
- If no improvement seen
  - Assess adequacy of medication dose and duration
  - Assess compliance
  - Reassess diagnosis
  - Assess comorbidities (e.g.. substance use)
  - Trial another antidepressant

Talking to Patients About Antidepressants

- Set expectations with patients before starting
  - Up to 2/3 of patients may not achieve full remission with the first antidepressant trial (Trivedi et al 2006)
  - Medications will take up to 4-6 weeks to show benefit
- Discuss most common side effects expected
  - Avoid exhaustive list
  - Encourage patients to both report and then wait out common side effects
- Remind patients that medications must be taken daily to work
- Once remission achieved, remind patients that antidepressants help prevent relapse
- Be positive >> placebo effect is very real!

When to Refer Patients Out

- Suicidality
- Psychosis
- No improvement after 2 adequate antidepressant trials
- History of bipolar disorder
- Medication induced hypomania
- Treatment in pregnancy or postpartum
- Significant comorbidities (e.g. substance abuse)
- Patient overly sensitive to medication side effects

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