Psychopharmacology An Overview

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Disclaimer and legal stuff

This presentation is informational only. It does not serve nor substitute for medical decision making. Author is not responsible for any outcomes based on the contents of this presentation.

I am able to answer general questions about medicines. I cannot answer specific questions about patients, situations, or outcomes.

Overview

Depression

Postpartum

Anxiety disorders

PTSD

Special comments on benzodiazipines

Bipolar disorder

Schizophrenia/Schizoaffective Disorders

Sleep Disorders

Attention Deficit Disorders

Special Populations-Pregnancy, Pediatrics, Medically III

Substance Use Disorders Including Medication Assisted Treatment

Working As a Team: Effective Communication

Major Depression

Treatment Categories SSRIs (first and second generation) **SNRIs NDRIs Tricyclics** MAOs "Other" **Augmentation Strategies** Interventional: ECT, rTMS, Spravato/Ketamine

Serotonin

Norepinephrine

Dopamine

GABA

Glutamate

Brain-Derived Neurotropic Factor

Tolerance

Withdrawal

½ life

CYP liver enzymes

Isomer (R vs S) and Enantiomers(L vs D)

Metabolite (Pristiq-Desvenlafaxine)

L vs D and R vs S??

L (laevorotatory)medicines refract light anticlockwise (LEVOTHYROXINE)

D (dextrorotatory) medicines refract light clockwise (DEXEDRINE)

R (rectus) medicines have the relative direction of the priority order clockwise (ARMODAFANIL)

S (sinister) medicines have the relative direction of the priority order counterclockwise (LEXAPRO, SPRAVATO

SSRIs

Fluoxetine (Prozac)

Sertraline (Zoloft)

Paroxetine (Paxil, Paxil CR)

Citalopram Celexa)

Escitalopram (Lexapro)

Fluvoxamine (Luvox, Luvox CR)



SSRIs

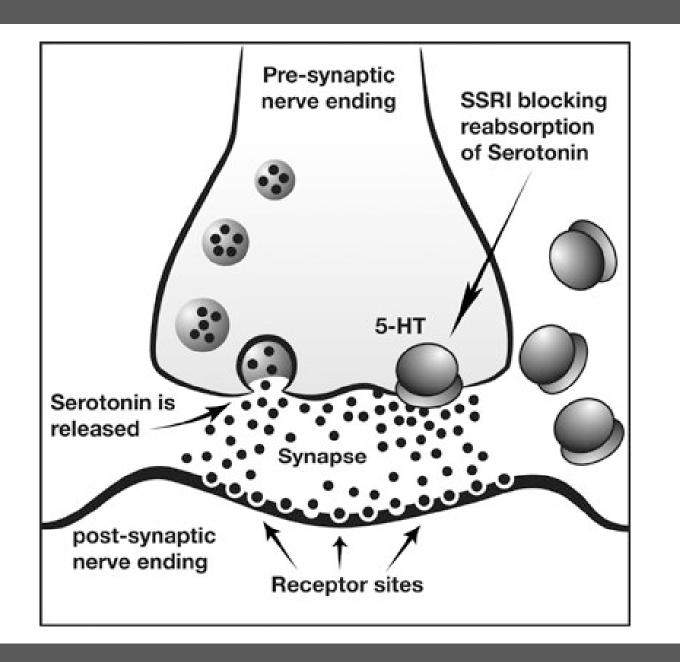
Most commonly prescribed medicines for depression

Very safe—safest class of antidepressants

Safer than but not as efficacious as MAO, TCA, possibly SNRI

Lower doses for major depression, higher doses for anxiety disorders

Long term safety appears certain



SSRIs continued

Some forms relatively safe in pregnancy (favor Zoloft, Lexapro)

Several (Prozac, Zoloft, Lexapro, luvox) FDA indicated for children

Safest antidepressant option for the medically ill and geriatric patients

SSRI Continued

Side effect profile: weight gain, sexual side effects, restless legs, GI side effects, fatigue

Special note that Paxil must be tapered to avoid discontinuation effects (including Paxil CR)

Metabolized by various liver enzymes

SSRI Metabolism

CYP450 2D6—Prozac, Paxil

CYP450 2C19—Zoloft, Lexapro, Celexa

CYP450 1A2--Luvox

Antidepressant Black Box Warning

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. anyone considering the use of xxxxx or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need...

	MDD	GAD	OCD	Bulimia	Panic	Social	PMDD	PTSD
Prozac	X		X	X	X			
Zoloft	Χ		X		X	X	X	X
Paxil	X	X	X		X	X		X
Celexa	X							
Lexapro	X	X						
Luvox			X					
Effexor XR	Χ	X			X	X		
Cymbalta	X	X						
Pristiq	Χ							
Emsam	Χ							
Remeron	X							

Second Generation SSRIs

Viibryd and Trintillix

FDA indicated for Major Depression

Very expensive, may confer superior efficacy but head to head is limited

Trintillix also with FDA indication for improving/maintaining processing speed in the elderly

SNRIs

Venlafaxine (Effexor, Effexor XR), Duloxetine (Cymbalta), Desvenlafaxine (Pristiq)

Dual action on Serotonin and Norepinephrine, with higher serotonin action at lower doses and more norepinephrine activity at higher doses



Serotonin-norepinephrine reuptake inhibitors (SNRIs)

 MOA: Inhibit the reuptake of both 5-HT and NE, Venlafaxine and desvenlavfaxine are potent inhibitor of 5-HT reuptake and, at medium to higher doses, is an inhibitor of NE reuptake

Duloxetine inhibit serotonin and norepinephrine reuptake at all doses.

Uses

- treating depression in patients where SSRIs are ineffective
- Effective against chronic painful symptoms, such as backache and muscle aches (This pain is modulated by 5-HT and NE pathways in the CNS)

SNRI Continued

Discontinuation effects are pronounced (it's like having the flu at 180 MPH); must taper these medicines

Other side effects: sexual side effects, insomnia, dry mouth/eyes, constipation, appetite changes

What Happens During Cymbalta Withdrawal?















Tricyclic Antidepressants

Amitriptyline (Elavil)

Amoxapine (Asendin)

Desipramine (Norpramin)

Doxepin (Sinequan, Silenor)

Imipramine (Tofranil)

Nortriptyline (Pamelor)

Protriptyline (Vivactil)

Trimipramine (Surmontil)

TCA's continued

Work on Serotonin and Norepinephrine

Older class of medicines used primarily for major depression, OCD (clomipramine), and sleep (doxepin especially as Silenor)

Very effective, especially for classic depression

TCA SIDE EFFECTS

Cardiac Arrythmia

High Overdose morbidity/mortality rate

Multiple Interactions

Possible dementia risk (with the exception of Silenor)

Urinary retention

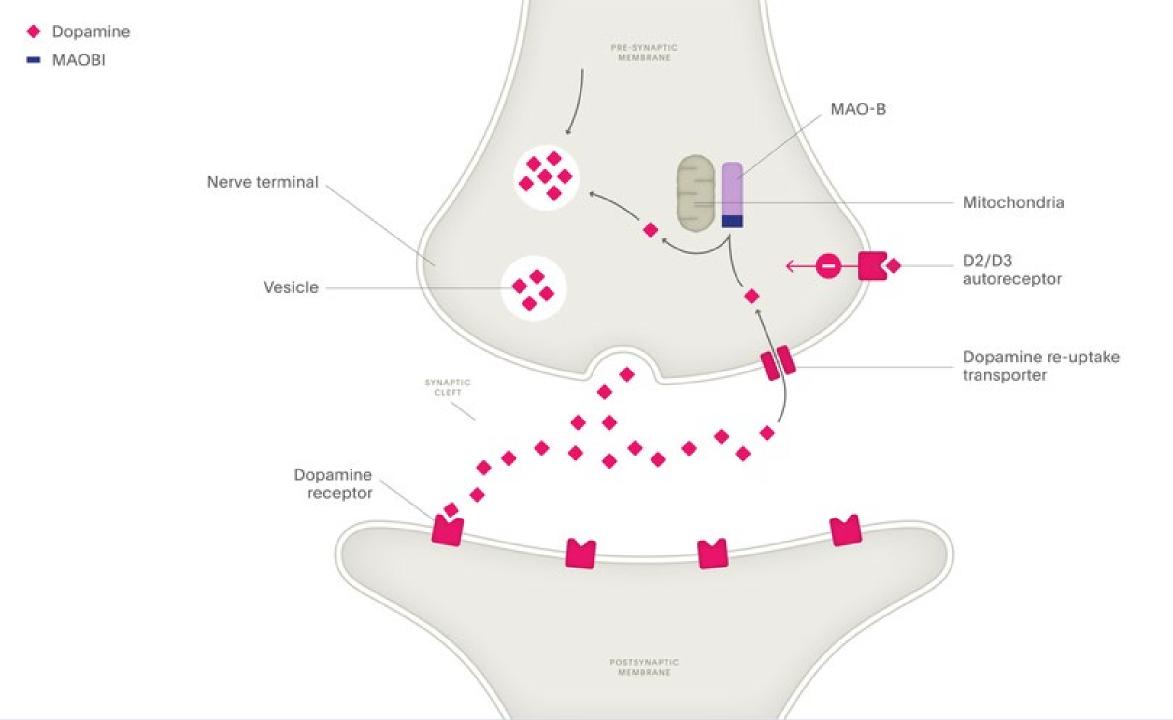
Confusion in the elderly

MAO Inhibitors

Work on Serotonin, Norepinephrine, Dopamine

Gold standard for depression efficacy in a medicine

Probably the most effective class of medicine for major depression, especially atypical depression

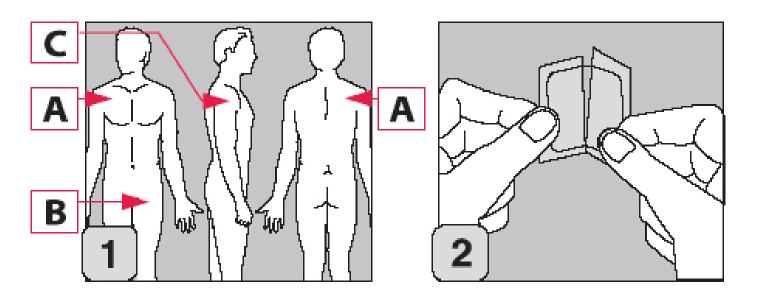


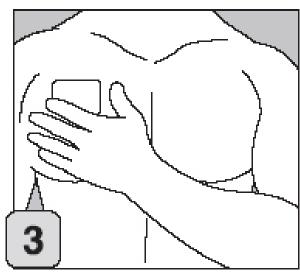
MAO Inhibitors Continued

Multiple medicine interactions

Food interactions, especially with oral forms

Newer MAO, Emsam, patch with fewer medicine and food interactions; highly effective but expensive





Norepinephrine Agents

Buproprion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Forfivo, Aplenzin), Levomilnacipran (Fetzima),

Most effective for atypical depression, can cause anxiety

Side effects: insomnia, weight loss

Buproprion has a seizure warning

Buproprion metabolizes at 2B6 and inhibits 2D6

Other Antidepressants

Mirtazapine (Remeron) works on serotonin, histamine, and low binding on dopamine, muscarinic cholinergic receptors

Unique binding profile makes it one of the safer options for older patients

Helps with sleep, has weight gain as a side effect

Metabolized at 2D6, 1A2, 3A4)

Augmentation Strategies for Major Depression

Antipsychotics

Antiseizure Medicines

Deplin/Vitamins

Multiple antidepressants (most commonly SSRI with Wellbutrin)

Controversial: dopamine agents— Stimulants, wake promoting agents

A Word on Genetic Testing for Meds

There is NO genetic test that will reveal what antidepressants will work

Genetic tests indicate metabolism patterns

Emerging data regarding serotonin receptor morphology

Insurance prohibitions, 23andMe

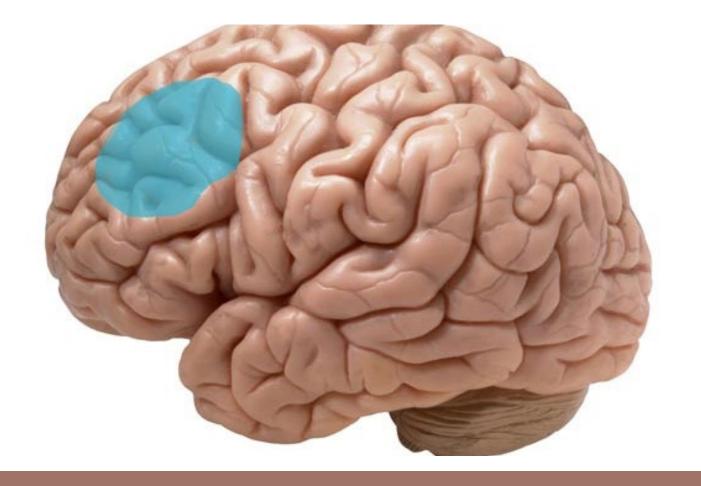


Interventional PsychiatryrTMS

Repetitive Transcranial Magnetic Stimulation

Designed to address major depression

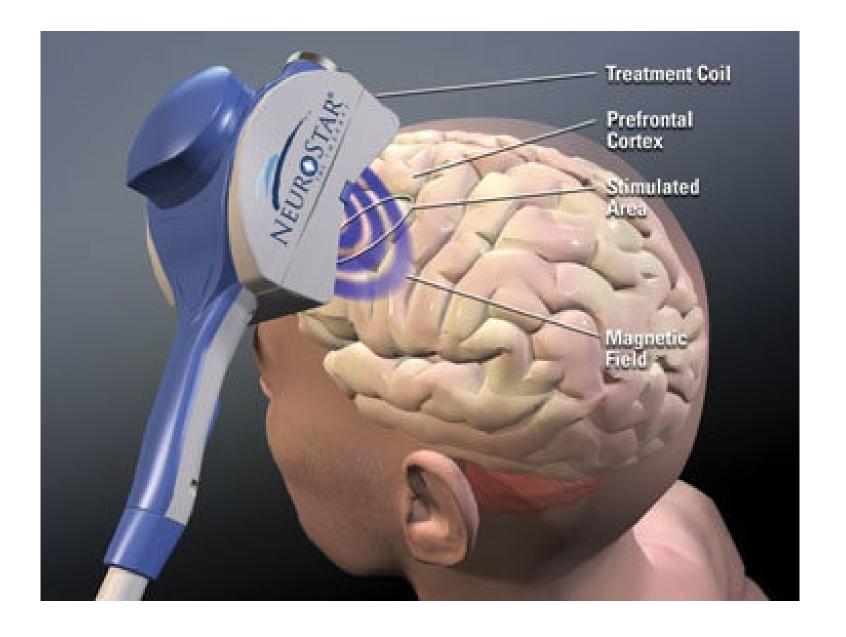
Creates neuroplasticity leading to enduring changes in the left dorsolateral prefrontal cortex



Dorsolateral Prefrontal Cortex

- Responsible for:
- Decision making
- Novelty detection
- Working memory
- Conflict management
- Mood regulation
- Mind processing
- Timing

rTMS coil
targeting
Dorsolateral
Prefrontal
Cortex



rTMS

Roughly 30-36 treatments over 6-8 weeks, treatments about 20 minutes long

Side effects: headache during/after treatment (tension type), scalp tenderness

rTMS Contraindications

Seizures

Pacemakers (possible to do with VNS pacemakers for depression)

metal in head/neck area

of stroke or other neuro-anatomical or neurovascular compromise



rTMS

Safe

Effective

Relatively convenient

Covered by most insurances

New protocol: 17-18 minute treatments



ECT

Electroconvulsive Therapy

Current treatment is applied to right hemisphere

Series of treatments, generally 6-12 over 3-4 weeks

Induces a controlled series of seizures to alter neural communication and plasticity

Enduring efficacy for depression

ECT Continued

Side effects: Transient confusion, memory loss for the time around the treatment, nausea, headache, jaw pain, muscle ache

Logistics are challenging as must involve anesthesia, performed at a hospital setting

ECT is significantly underutilized. It has a stigma based on historical application as well as misconceptions regarding its mechanism of action and side effects

Who is ECT For?

Severe depression with psychosis, suicidal risk or refusal to eat

Treatment-resistant depression

Severe mania

Catatonia

Agitation and aggression in people with dementia

ECT Continued

Safe in pregnancy

Safe in older adults who cannot tolerate drug side effects

Utilized by patients who prefer ECT to medicines

Utilized when ECT has been successful in the past

Relative ContraIndications for ECT

Recent MI or stroke (w/I 30 days)

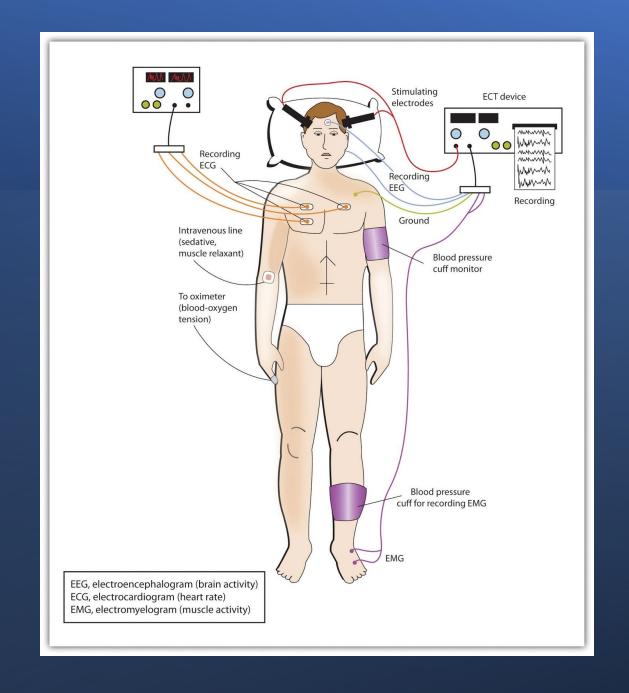
Increased intracranial pressure

Aneurysms, active CNS bleeding

Retinal detachment

Unstable dentition

Pheochromocytoma (absolute contraindication until resolved)





Still the gold standard

Primarily reserved for refractory cases

Underutilized

ECT



Ketamine/Spravato

Utilized for treatment-refractory major depression

Possible applications for PTSD, anxiety and substance concerns but this is off-label and there is NO FORMAL INDICATION FOR THIS

Ideally administered with observation in a physician's office (and a word on this...if depression is the thing being addressed, probably best that a psychiatrist is monitoring the treatment)..i mean, I can go out and do knee surgeries, but should I?

Side effects: elevated blood pressure, dissociation, nausea

It is widely held that there is no respiratory arrest risk at the doses used for depression; nonetheless the physician's office must be prepared to navigate any medical eventuality, including respiratory arrest

Contra-indications for Spravato/Ketamine

- Aneurysms
- Arteriovenous malformations
- History of cerebral hemorrhage
- Some heart diseases
- Increased intracranial pressure
- Pregnancy
- History of psychosis

Spravato/ketamine Administration

- Spravato is administered under a REMS protocol
 - Blood pressure is closely monitored
 - Patients are not allowed to drive after treatment
 - Storage and administration requirements as Spravato is controlled
 - Strongest evidence is for intranasal and IV ketamine. Insufficient evidence for oral, subcutaneous, or intramuscular ketamine for treatment resstent depression



APA guidelines on Ketamine Use for Depression

Patient selection-for appropriateness and to exclude contra-indications

Physical exam and monitoring vital signs during and immediately after treatment

Clinic equipped with appropriate cardiorespiratory monitoring

Patient has reliable transportation to/from treatments

APA Guidelines Continued

Ketamine is administered only in settings with multidisciplinary personnel, including professionals with expertise in assessing mood disorders and suicidal ideation

The APA does NOT support take-home ketamine treatment

The APA believes Ketamine should be managed solely by professionals who are equipped to navigate psychiatric emergencies

Special Consideration— Seasonal Affective Disorder

Typical presentation is fall/winter

Phototherapy is a powerful modality—10,000 lux broad spectrum light used about 1½ feet away in the morning time (using too late in the day will risk insomnia)—a tanning bed WILL NOT WORK as the eyes must perceive the light. NO UV in a SAD phototherapy light.

Buproprion is also used for this

Vitamin D needs to be checked to ensure good space



Postpartum Depression COMMON SYMPTOMS



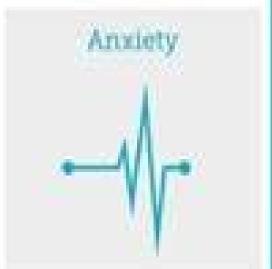












Postpartum Disorder

May present during pregnancy or after delivery

Most often treated with SSRIs

Of special note, Zoloft specifically has been studied and safe in breastfeeding

Postpartum esp new onset: screen carefully for bipolar disorder. In the literature there is an association of post-partum depression and bipolar disorder.

Zulresso for Post-Partum Depression

IV treatment, 60 hours, for refractory post-partum depression

Works through GABA(a) receptors

Prescribed under a REMS authority due to risk of excessive sedation or sudden loss of consciousness

Continuous pulse oximetry monitoring, cannot care for children unsupervised

Post-Partum
Depression is
the Most
Common
Complication
of Pregnancy



Table 2. Distinguishing Between "Baby Blues" and Postpartum Major Depression

Characteristic	Baby blues	Postpartum major depression
Duration	Less than 10 days	More than two weeks
Onset	Within two to three days postpartum	Often within first month; may be up to one year
Prevalence	80 percent	5 to 7 percent
Severity	Mild dysfunction	Moderate to severe dysfunction
Suicidal ideation	Not present	May be present

Anxiety disorders

Generalized Anxiety Disorder, Panic Disorder, Social Anxiety Disorder, Phobias

First line medicine: anti-depressant therapy, typically SSRI/SNRI

Buspirone is also indicated for generalized anxiety disorder

Benzodiazipines were used in the past but are falling out of favor due to concerns about long-term usage and cognitive side effects

Other agents used: gabapentin, Vistaril, low dose beta blockers, magnesium, Remeron

Special advice on HOW to use Buspirone

Buspirone (Buspar) is an easily dismissed, harder-than-average medicine to use. It gets a bad rap primarily because it is often not used efficaciously

Buspar is a very short ½ life medicine. It must be dosed frequently to work...think 3-4 times a day.

I initiate buspirone at 15 mg tabs, 1/3 three times a day for a week, then 2/3 three times a day for a week, then 1 three times a day

Set the expectations: buspirone does not work like Xanax...it takes awhile for it to build up and create an effect

Buspar absorbs better when it is dosed with food...several times higher effect

The package insert dose range for buspar is up to (?45 or 60) mg a day, but it has safety data much higher than this; nausea and dizziness are the limiting factors

The metabolization of buspar is impacted adversely by grapefruit and other potent CYP3A4 inhibitors; avoid grapefruit. Buspirone can potentiate some benzodiazipines, like xanax

93 1003

5 5 5 5

PTSD

Antidepressant therapy is first line for PTSD

However, compelling data for prazosin, doxazosin, lamotrigine for PTSD

These are not FDA-indicated, but prazosin in fact has a larger effect size for PTSD than the antidepressants

There is not a place for long-term benzodiazepine usage in PTSD. There is an especially high risk of addition with benzodiazepines and PTSD

Many of the most commonly prescribed benzos are those which are most readily abused, including: ALPRAZOLAM (Xanax)



CLONAZEPAM (Klonopin)



(Librium)



DIAZEPAM (Valium)



LORAZEPAM (Ativan)



TEMAZEPAM (Restoril)



TRIAZOLAM (Halcion)





Special comment on benzos

Long term benzodiazepine usage is associated with cognitive dulling

Long ½ life benzos may be more implicated than short ½ life benzos, but the long shot is not positive for the class in general

Tapering may be prolonged

Benzos continued

WHAT DOES THIS MEAN FOR PATIENT CARE?

- Don't start patients on benzos especially long-term benzos.
 The data no longer supports this
- When appropriate (which is almost always), attempt to taper patients off benzos

Long-term usage of benzos

Defined as greater than 3 mo use

Tolerance can develop more quickly than this

Controversial: changes in MRIs that may be temporary or permanent

Standardized tapers but some patients benefit from "Ashton protocol"

Benzos reserved for intermittent, urgent or truly refractory

Replacement Options Include

gapapentin

maximized antidepressants

beta-blockers

buspirone

Patients Who Will Require Prolonged Tapers

Elderly

Female

Daily use especially over a month and especially over 3 months

Highly anxious

Somatic

Bipolar Disorder

Antiseizure Agents

Antipsychotics

Lithium

ECT

Lamotrigine

FDA indicated in Bipolar I, to delay time to occurrence of mood disorders in patients treated for acute episodes with standard therapy

Often used off label for bipolar II as well

Is not indicated for bringing patients to remission, but rather, for keeping patients in remission

Side effects: nausea, discontinuation seizure risk, B vitamin deficiencies, Steven-Johnson Syndrome/toxic epidermal necrolysis

Steven-Johnson Syndrome

Flu-like symptoms followed by

Painful rash that spreads and blisters

Rash involves skin and mucous membranes

Typical onset is at beginning of treatment or at dose titration

Treated by stopping offending agent and possible systemic treatment up to and including intensive care treatment; can be fatal

Valproic Acid/Depakote

FDA indicated for manic episodes associated with bipolar disorder

FDA indicated for mixed episodes associated with bipolar disorder (ER version only)

Risks: pancreatitis, liver impairment, teratogenesis

Many psychiatrists will not use this with reproductive aged women, even if birth control

Carbamazepine

Carbamazepine (Tegretol XR, Tegretol, Epitol, Carbitrol, Equitro)

Used for bipolar mania

Must be titrated

Side effect profile

Rash including Steven-Johnson rash

Aplastic Anemia

Agranulocytosis

Sodium depletion

Dizziness, loss of coordination, nausea, vomiting, drowsiness

Carbemazepine/oxcarbazepine

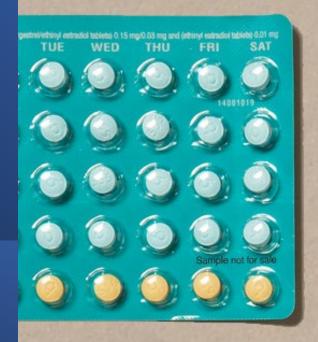
Trileptal, Oxtellar XR

Not FDA indicated for any psychiatry usage

May help with bipolar mania, impulse control disorder

Same risk profile as carbamazepine formulations

Both Carbemazepine and Oxcarbazepine reduce the efficacy of oral hormone contraception













Atypical Antipsychotics

Risperone (Risperdal)

Olanzepine (Zyprexa)

Quetiapine (Seroquel, Seroquel XR)

Aripiprazole (Abilify)

Ziprasidone (Geodon)

Clozapine (Clozaril)—only available via REMS

Paliperidone (Invega)

Atypicals Continued

Cariprazine (Vraylar)

Lurasidone (Latuda)

Asenapine (Saphris)

Brexpiprazole (Rexulti)

Lumateperone (Caplyta)

Risperdal	Schizophrenia 13+; short-term acute manic or mixed bipolar I 10+
Zyprexa	Acute/maintenance schizophrenia, acute manic/mixed bipolar I and maintenance in adults; acute bipolar I depression in adults (with Prozac), treatment-resistant depression (with Prozac)
Seroquel	Schizophrenia 13+; bipolar mania 10+; bipolar depression adults
Abilify	Schizophrenia 13+; acute mania/mixed bipolar I 10+; adjunct depression adults; agitation-schizophrenia, bipolar mania
Invega	Acute/maintenance schizophrenia; acute schizoaffective
Geodon	Bipolar maintenance;
Clozaril	Treatment-resistant schizophrenia; reducing SI in patients with schizophrenia or schizoaffective
Latuda	Schizophrenia; Bipolar I depression;
Vraylar	Schizophrenia; acute manic/mixed bipolar
Rexulti	Schizophrenia; adjunct for major depression in adults
Saphris	Schizophrenia in adults; acute manic/mixed bipolar I 10+; bipolar I maintenance in adults
Caplyta	Schizophrenia in adults

Atypical antipsychotics, continued

They work on dopamine, serotonin

Varying impact on histamine, acytylcholine

It is important to check blood sugar, weight and cholesterol periodically

One of the downfalls of telemedicine: harder to get accurate weights and timely labs for patients

Side Effect Profile



Weight Gain

Mean weight gain in patients receiving standard doses of antipsychotics over a 10-week period: 4.45 kg with clozapine, 4.15 kg with olanzapine, 2.92 kg with sertindole, 2.10 kg with risperidone, and 0.04 kg with ziprasidone.



Some drugs may be associated with an increased risk of ocular lens opacities. Also, patients with schizophrenia often have risk factors for lens opacities, such as Diabetes, hypertension and poor nutrition.



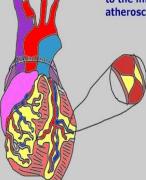
Sexual side effects

Antipsychotic-induced sexual dysfunction is related to the effects of the drugs on alpha-1 and alpha-2 adrenergic, H1 histamine and dopaminergic receptors, in particular to the blockade of D2 receptors in pituitary lactotroph cells, which leads to an excess of prolactin secretion



Diabetes Mellitus

The prevalence of type-2 DM in people with schizophrenia is more than twice higher than in the general population. Most of these studies indicate that drugs associated with greater weight gain.



Extrapyramidal symptoms Move-

ments disorders, kinesia (inability to initiate movement) and akathisia (inability to remain motionless)

Prolongation QTC Interval

An increase in the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. A prolonged QTC interval is a biomarker for ventricular tachyarrhythmias and a risk factor for sudden death

A high concentration of lipid

in the blood, an increased risl for cardiovascular disease due to the influence on atherosclerosis

Hyperlipidemia

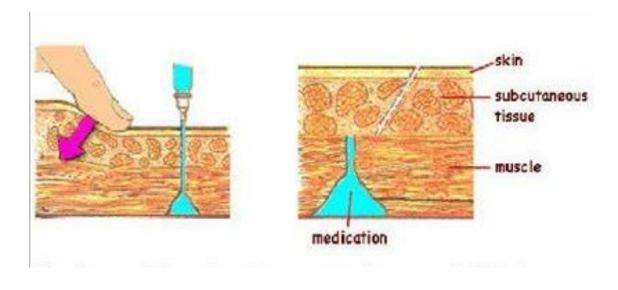
Myocarditis

Inflammation of heart muscle. It can cause a mild disease without any symptoms that resolves itself, or it may cause chest pain, heart failure, or sudden

Depos

- Once every few weeks to once every 3 mo shots
- Improve compliance
- Allows the prescriber to monitor compliance
- Smoother modality with fewer peaks/troughs
- Insurance coverage can be a barrier
- Test oral dose for tolerability
- May need to continue oral dose until depot kicks in





Lithium

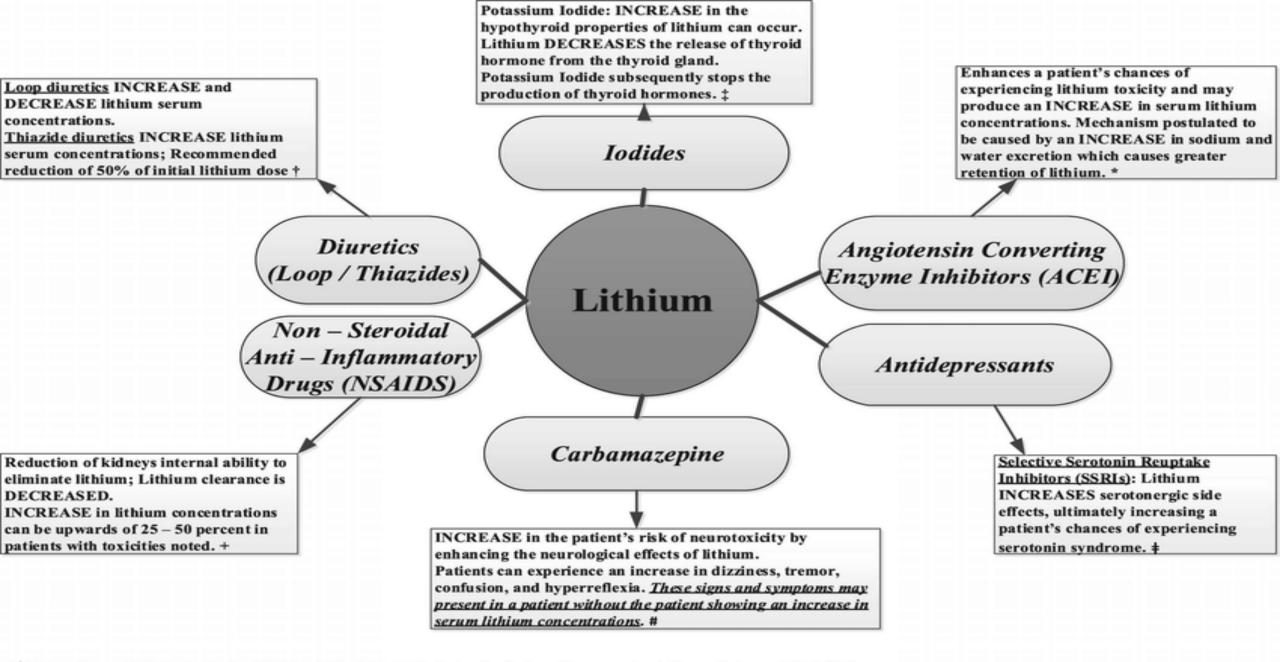
Gold standard for bipolar disorder

Challenging medicine to use, with a narrow therapeutic index

Levels must be done periodically

Hard on kidneys, thyroid, parathyroid, rarely on sodium, blood cell production

Lab will often reflect and elevated wbc which is NOT indictive of infection



^{†#‡}Lithium. Dynamed Web site. Last updated 2013 July 24. Available at: http://web.a.ebscohost.com.libproxy.presby.edu/dynamed/. Accessed July 9, 2015. ‡Lithium and Potassium Iodide. Drug Interaction Report. Available at: http://online.lexi.com.libproxy.presby.edu/lco/action/interact. Accessed July 9, 2015. *Douste-Blazy PH, Rostin M, Livarek B, et al. Angiotensin-Converting Enzyme Inhibitors and Lithium Treatment. Lancet, 1986, i:1448.

⁺Phelan KM, Mosholder AD, and Lu S. Lithium Interaction With the Cyclooxygenase 2 Inhibitors Rofecoxib and Other Nonsteroidal Anti-Inflammatory Drugs. J Clin Psychiatry, 2003, 64(11):1328-34

Target Lithium Levels

Recommended Labs & Monitoring

Acute Mania: 0.8-1.2 mEq/L

Maintenance: 0.6-1.0 mEq/L

•Baseline: CBC, CMP, Cr, BUN, TSH

+1 week*: Li level, TSH, BUN/Cr, Electrolytes

+1-2 months*: Li level, TSH, BUN/Cr, Electrolytes

+6-12 months*: Li level, TSH, BUN/Cr, Electrolytes

Every 6-12 months: Li level, TSH, BUN/Cr, Electrolytes

Consider baseline EKG in pts >50yo

Monitor weight

•Check Li levels after 4-5 half lives (blood should be collected prior to next dose)

•Recheck Li levels after dose changes, addition of other drugs, or if suspecting toxicity

*After initiating Lithium

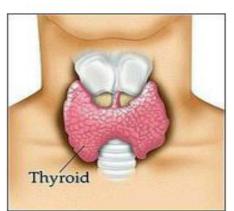
Lithium Side Effects

- Acute effects
 - Nausea, Diarrhea
 - Lethargy
 - Impaired Cognitive Functioning
 - Hand Tremor





- Long Term Side Effects
 - Hypothyroidism
 - Cardiac Effects
 - Weight Gain
 - Leukocytosis
 - Dermatological Effects
 - · Acne, Psoriasis









Definitions are important: schizoaffective is a psychotic disorder, and a mood disorder, where the two do not necessarily coincide in timing, and tends to have a less severe course than schizophrenia

Both disorders are treated with antipsychotics. Schizoaffective also requires the mood component to be treated. Schizophrenia may have co-occurring mood disorder that also merits treatment. The treatment for psychosis and mood can be with one med that covers both (ie the atypical antipsychotics)

Medicines to treat psychosis

Typical antipsychotics

- Pill and depot versions available
- High risk of extrapyramidal side effects
- Rarely used and reserved for emergencies or highly refractory cases

Atypical antipsychotics

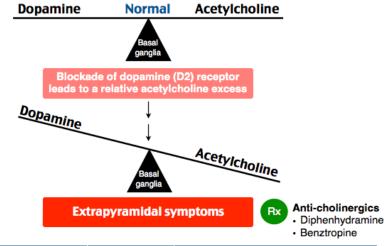
- Pill and depot versions available
- Lower but still present risk of extrapyramidal side effects
- High risk of weight gain, cholesterol elevation, hyperglycemia, and possible association with strokes in the elderly
- Should NOT be used in the elderly unless the benefits clearly outweigh the risks, especially for "behavior control"

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Typical
Antipsychotics
(First
Generation)

Chlorpromazine Fluphenazine Haloperidol Loxapine Pimozide Perphenazine Prochlorperazine Thioridazine **Thiothixine** Trifluoperazine

Extrapyramidal symptoms



Reaction	Onset	Features
Acute dystonia	Hours to days	Spasm of tongue, neck, face and back
Parkinsonism	5 to 30 days	TremorShuffling gaitDroolingStooped postureInstability
Akathisia	5 to 60 days	Compulsive, repetitive motionsAgitation
Tardive dyskinesia	Months to years	Lip smackingWorm-like tongue movements"Fly-catching"



A. Dystonia—spasms of the tongue, neck, back, and legs. Spasms may cause unnatural positioning of the neck, abnormal eye movements, excessive salivation.



B. Akathisia—continuous restlessness, inability to sit still. Constant moving, foot tapping, hand movements may be seen.



 Pseudoparkinsonism—muscle tremors, cogwheel rigidity, drooling, shuffling gait, slow movements.



D. Tardive dyskinesia—abnormal muscle movements such as lip smacking, tongue darting, chewing movements, slow and aimless arm and leg movements.



Sleep disorders

Divided into sleep onset, sleep maintenance, and combined

Emphasis on sleep hygiene is paramount

Sleep Disorders continued

Cognitive platforms like CBT-Icoach or Calm are helpful for both sleep onset and sleep maintenance

Rule out medical disorders like restless leg syndrome or sleep apnea

Sleep diary

Pharmacology for sleep disorder-Sleep Onset

Melatonin—specific instructions on use

Sonata, Ambien, Ambien CR, Lunesta

Belsomra, Dayvigo

Rozerem

Pharmacology for sleep disorder-Sleep Maintenance Silenor (3-6 mg doxepin, NOT higher)

Belsomra, Dayvigo

Ambien CR, Lunesta

Combined Sleep Difficulties Belsomra, Dayvigo

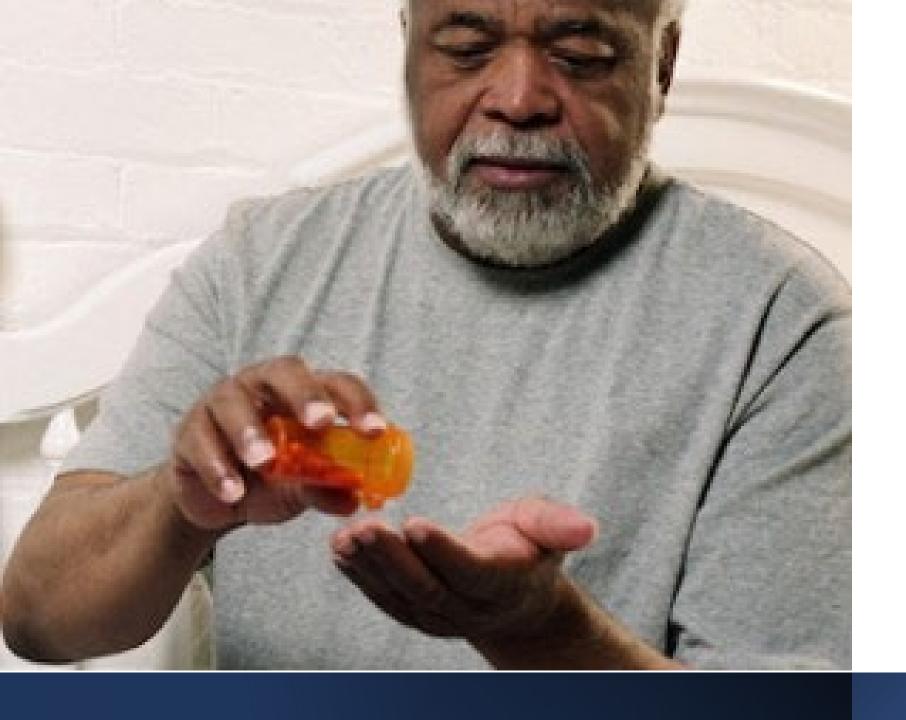
Trazodone

Z-drugs: Ambien CR,Lunesta

Benedryl

Not a great longterm option

Robustly anticholinergic



Medicine and the Elderly and Vulnerable

- These patients are more vulnerable to medicine side effects, due to:
- Decreased clearance
- Increased number of meds/interactions
- Decreased physical and cognitive resilience

BEERS



What are the Beers Criteria?

The Beers Criteria (or the 'Beers Criteria for Potentially Inappropriate Medication Use in Older Adults) are, as it's longer description suggests, guidelines for healthcare professionals – guidelines that improve the risk-benefit ratio of medicine use in older adults.

The Beers Criteria...

- ✓ Serve as guidelines
- ✓ Are not a substitute for professional judgement
- ✓ And are used alongside other prescribing criteria



The Beers Criteria was first created in 1991 by the geriatrician, Mark H. Beers.

The list is categorised according to the risk of negative outcomes.

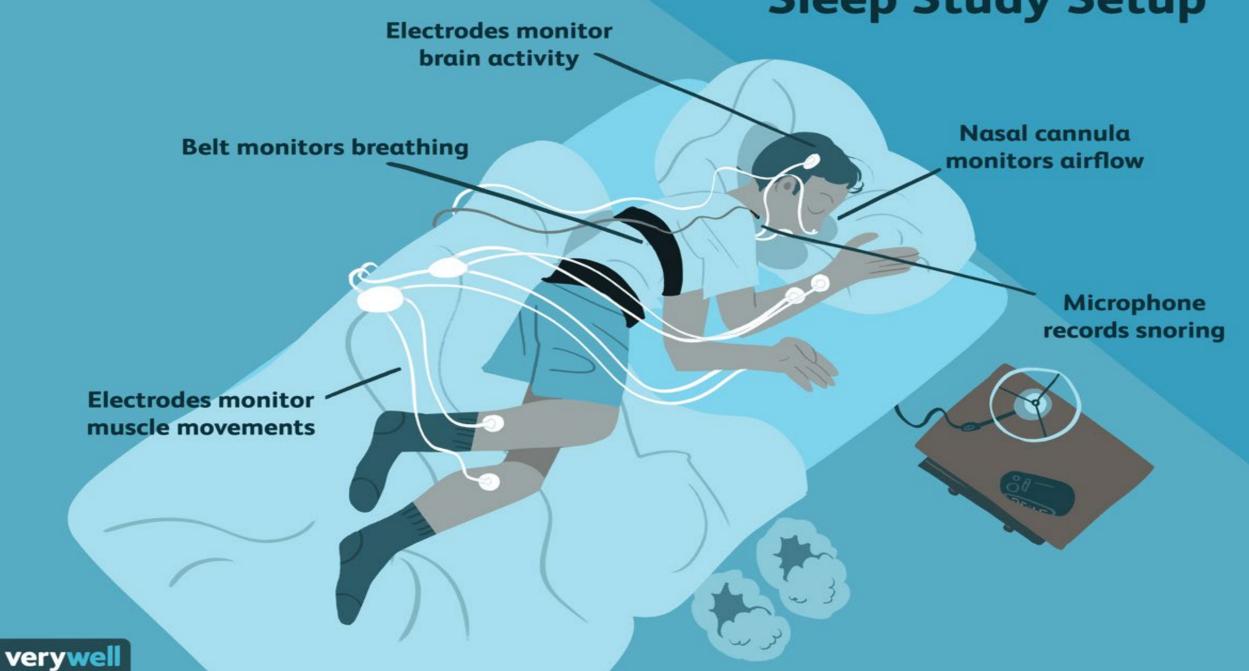
Example: Diphenhydramine, a H_1 receptor antagonist, may increase sedation and increase the risk of confusion and/or falls.







Sleep Study Setup







Wake-Promoting Agents for Sleep Apnea, Narcolepsy Modafanil (Provigil), Armodafanil (Nuvigil), and Solriamfetol (Sunosi)

Improve utilization of dopamine in the brain; promote wakefulness when compliant sleep apnea treatment is inadequate

Promote increased daytime wakefulness in narcolepsy

Provigil and Nuvigil invalidate oral contraception

Provigil and Nuvigil don't work with these!



Difficulties associated with ADHD in adults



- Difficulties with maintaining attention
- Difficulties with completing tasks
- Unable to prioritize or manage thoughts and actions
- Forgetting important things
- Difficulties with day-to-day responsibilities
- Inconsistent performance at work or in their careers
- Feelings of frustration, guilt or blame
- Relationship problems









Attention Deficit Disorder Three types: inattentive, hyperactive, impulsive

Onset in childhood

Onset of primarily inattentive attention deficit disorder in adulthood-work up for alternate or comorbid

Differential for ADD

Anxiety disorders

Sleep disorders

Mood disorders

Substance Use Disorders

Learning disorders

Oppositional Defiant Disorder

Narcolepsy

Dx ADD/ ADHD continued

Attention disorders are

The side effect burden for many of the treatments for attention disorders is high

Some sort of psychometric screening or evaluation is important to clarify the diagnosis and exclude confounding or co-occurring illnesses

Formal testing, parent/teacher questionaires, performance-based assessments all have a role

Nonstimulant Medicines for Attention Disorders Norepinephrine agents: Atomoxetine (Strattera) Viloxazine (Qelbree)

Alpha adrenergic agents: Guanfacine ER (Intuniv), Clonidine ER (Kapvay)

Off-label Medicines Used to Treat Attention Disorders

Wake-promoting agents: Modafanil, Armodafanil, Solriamfetol

- efficacy in ped population specifically
- risk of rash in studies
- invalidate some hormone contraception

Buproprion, SNRI's, Tricyclic antidepressants, MAOs

- Not especially powerful
- Same side effects and risk/benefits as when used for depression

Methylphenidates: Intermediate Duration Ritalin LA

Ritalin SR

Metadate CD

Cotempla XR-ODT

Cotempla CR

Methylphenidates: Extended Duration

Aptensio XR Concerta Daytrana (patch) Adhansia XR Jornay PM Metadate CD Quillivant XR Quillichew ER

Dexmethylphenidates

Focalin—about 4-6 hours duration

Focalin XR—about 8 hours duration

Azstarys – a dexmethylphenidate prodrug, serdexmethylphenidate, combined with an immediate release dexmethylphenidate—about 12 hours duration

Amphetamines: Intermediate Duration Adderall XR (mixed amphetamines)

Adzenys ER/XR-ODT (pure amphetamine)

Dyanavvel XR(mixed amphetamines, liquid)

Amphetamines: Extended Duration

Mydayis

Dexedrine—4-6 hours

Dexedrine SR--6-8 hours

Zenzedi—4-6 hours

Vyvanse—is actually a prodrug, lisdexamphetamine, very long acting

Dexamphetamines

Stimulants: risks

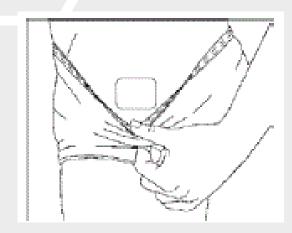
These are highly controlled medicines. Addiction risk is high. That being said, ASAM states treating attention deficit disorders, even with stimulant medicines, likely reduces the risk of substance abuse. However, if the patient has a history of recent substance struggle, treatment with an efficacious, non-controlled medicine is prefere

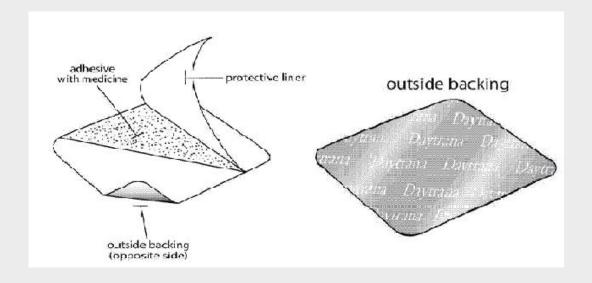
Controlled substance contract with the patient. In our clinic...cannot replace if lost stolen or destroyed. If filled in another clinic or by another provider, we will no longer fill controlled medicines

PMP interrogation to ensure medicines filled properly

Blood pressure and pulse elevation, cardiovascular risks like stroke, heart attack.

Other side effects: insomnia, headache, appetite decrease, anxiety, agitation, psychosis, manid induction





UDS for stimulant compliance

Performed to ensure patient is taking what they are supposed to be taking

Also to ensure they are not taking things that are not helpful

Methylphenidates will NOT test positive on a point-of-care UDS

ADD and Substance Abuse

ASAM guidelines: Treat the ADD! Improves outcome of the SUD

Noncontrolleds when possible

Controlleds with adequately treated ADD better than inadequately treated

Monitor, pill counts, UDS, more frequent visits

Even if the substance abused was a stimulant (this is new, controversial)

Elements of a controlled substance contract

Acknowledgement of controlled nature of the medicine

Pledge to take as directed and not share

Agree to notify prescriber before taking other controlled medicines

Allow PMP reviews

Agree to submit to random urine drug screens as a part of treatment

Allow prescriber to communicate with other providers

Comply with pill counts when requested

Acknowledge failure to comply may lead to no controlled medicines being prescribed

Special populations: pregnancy, peds, elderly, medically compromised



Pregnancy

Treating two patients

Many medicines cross placenta; fetal clearance is not the same

Highest risk for birth defects is first trimester medicine use (especially heart, midline deficits)

Highest risk for perinatal onset difficulties is third trimester medicine use (especially neonatal abstinence syndromes, perinatal sedation)

Altered medicine metabolism in pregnancy



Medicines for the Pediatric Population

Kids are not "small adults"

Some medicines can impact development

Different medicine metabolism rate

Different volume of distribution (water vs lipid higher in young kids)



Geriatric Considerations

Slowed medicine metabolism

Burden of additional illnesses, medicines

Loss of physical resiliency, cognitive resiliency and neuroplasticity

Risk of significant side effects



Significant Cooccurring Illnesses

Risk of interactions with other medicines

Risk of exacerbating significant medical illness

Risk of masking underlying illness



THE NEXT SECTION HAS DISCUSSION AND IMAGES OF CONTROLLED AND ADDICTIVE SUBSTANCES





Substance d/o

Alcohol

Opioids

Nicotine

Benzodiazepines

Stimulants

Cocaine

Marijuana



Alcohol

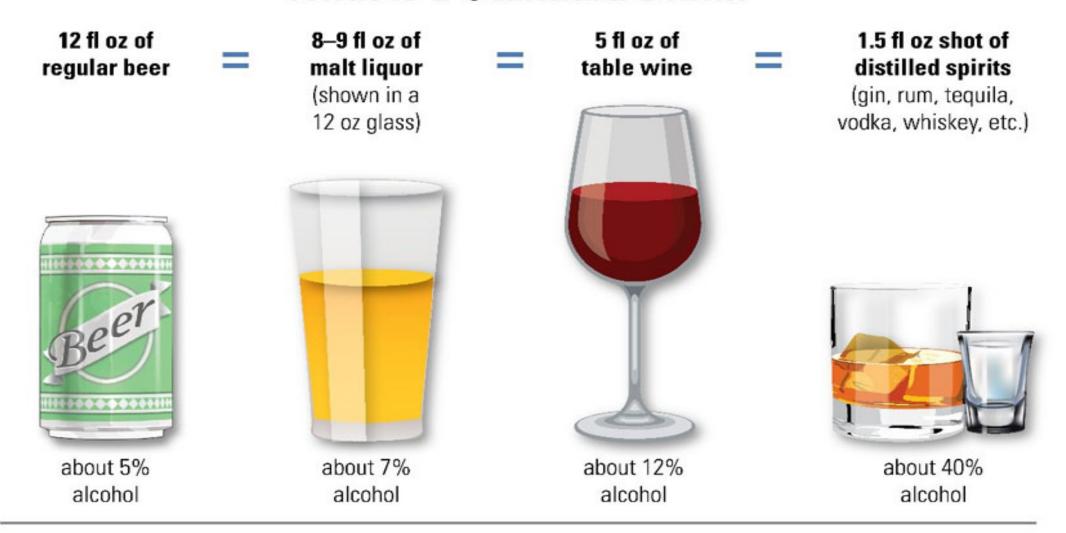
Detoxification

Relapse Prevention

Medical Complications

- Acute
- Prolonged

What Is a Standard Drink?



Each beverage portrayed above represents one standard drink (or one alcoholic drink equivalent), defined in the United States as any beverage containing .6 fl oz or 14 grams of pure alcohol. The percentage of pure alcohol, expressed here as alcohol by volume (alc/vol), varies within and across beverage types. Although the standard drink amounts are helpful for following health guidelines, they may not reflect customary serving sizes.

DETOX-ALCOHOL

Level of detox determined by CIWA score

Benzodiazepines (Librium or Ativan)

Thiamine

CIWA— Clinical Institute Withdrawal Assessment Scale for Alcohol

Clinical Institute Withdrawal Assessment Scale for Alcohol, Revised (CIWA-Ar)

Nausea and Vomiting

0 - No nausea or vomiting

2

3

4 - Intermittent nausea with dry heaves

5

7 - Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats

- 0 No sweat visible
- 1 Barely perceptible sweating, palms moist

2

4 - Beads of sweat obvious on forehead

5

7 - Drenching sweats

Agitation

- 0 Normal activity
- 1 Somewhat more than normal activity

3

4 - Moderate fidgety and restless

6

7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances

- 0 Not present
- 1 Very mild photosensitivity
- 2 Mild photosensitivity
- 3 Moderate photosensitivity
- 4 Moderately severe visual hallucinations
- 5 Severe visual hallucinations
- 6 Extreme severe visual hallucinations
- 7 Continuous visual hallucinations

Tremor

- 0 No trem
- 1 Not visible, but can be felt at finger tips

4 - Moderate when patient's hands extended

-

7 - Severe, even with arms not extended

Tactile Disturbances

- 0 None
- 1 Very mild paraesthesias
- 2 Mild paraesthesias
- 3 Moderate paraesthesias
- 4 Moderately severe hallucinations
- 5 Severe hallucinations
- 6 Extremely severe hallucinations
- 7 Continuous hallucinations

Headache

- 0 Not present
- 1-Very mild
- 2 Mild
- 3 Moderate
- 4 Moderately severe
- 5 Severe
- 6 Very severe
- 7 Extremely severe

Auditory Disturbances

- 0 Not present
- 1 Very mild harshness or ability to frighten
- 2 Mild harshness or ability to frighten
- 3 Moderate harshness or ability to frighten
- 4 Moderately severe hallucinations
- 5 Severe hallucinations
- 6 Extremely severe hallucinations
- 7 Continuous hallucinations

Orientation and Clouding of the Sensorium

- 0 Oriented and can do serial additions
- 1 Cannot do serial additions
- 2 Disoriented for date but not more than 2 calendar days
- 3 Disoriented for date by more than 2 calendar days
- 4 Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0-8	No medication needed
9-14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

Relapse Prevention-Alcohol

Naltrexone/Vivitrol

Campral

Topamax

Antabuse



Opioids

Prescriptions

- Presriptions for chronic pain
- Prescriptions from multiple providers
- Scripts are checked now via PMP

Diverted prescriptions

- Relatives
- Scripts obtained/sold

Illicit Substances

• Heroin

Over the counter legal substances

Kratom

Bad effects of OPIATES

dilation of the blood vessels causing increased pressure in the brain

drowsiness confusion memory loss fatigue hallucinations convulsions

respiratory depression

pupil constriction Slurred speech

nausea vomiting weight loss

sexual dysfunction



constipation

effects of using OPIATES non-sterile needles OPIATES and adulterants mixed with

skin abscesses

infected and collapsed veins

lung abscesses

brain abscesses

endocarditis (heart lining inflammation)

diseases such as hepatitis and HIV



Kratom

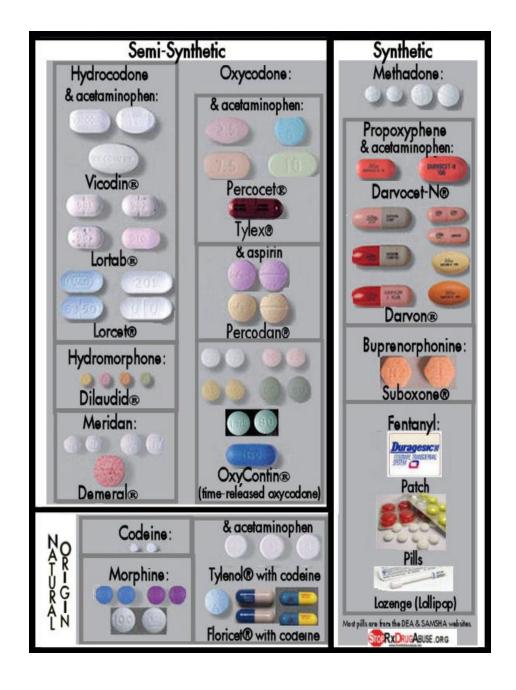
Kratom Dosage Chart



Withdrawal Symptoms



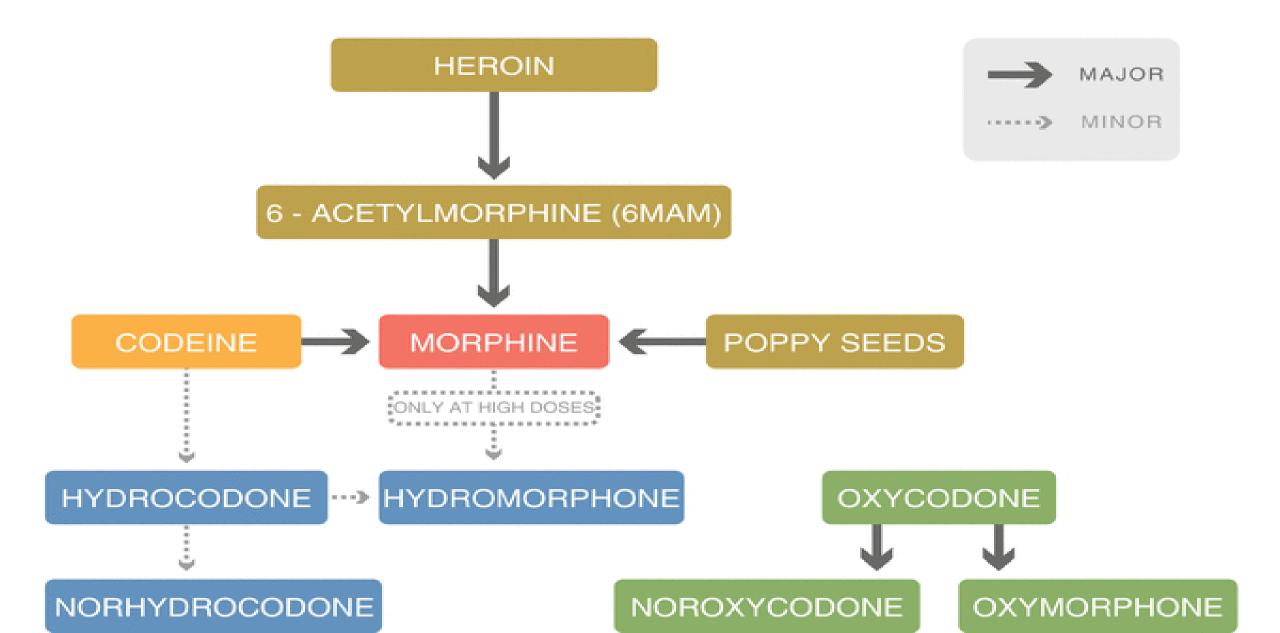
Narcotic and Opiate Prescription Drugs



Testing-Opiates

- Standard point of care UDS will pick up many but not always all opiates
- Must look specifically to find synthetic opiates
- Buprenorphine

OPIOID METABOLITES



UDS:Opiates

Detection time: 1-3 days

False Positives: some antibiotics (fluoroquinolones), Seroquel, rifampicin, tramadol, verapamil

We send all unsupported positives (unless the patient attests the result) and all unexpected and/or unattested negatives for confirmation, for all urine drug screens, for any class

Treatment for Opiate abuse (opiate vs opiod)

Replacement therapy: buprenorphine, methadone

Supportive therapy: clonidine, Vistaril

Receptor blockade: naltrexone, vivitrol

Medication-Assisted Treatment

- Replacement therapy with Buprenorphine
 - Single agent sublingual—buprenorphine,
 Subutex
 - Single agent subcutaneous—Sublocade
 - Combination agent transmucosal—Suboxone, Zubsolv, buprenorphine-naltrexone

Medication-Assisted Treatment cont.

- Replacement therapy with Methadone
 - Only available in supervised administration clinics
 - Take-home doses ultimately achieved
 - New development of electronic medical dispensing devices may change the landscape
 - Methadone with similar risks to buprenorphine, but higher risks of medicine interactions and overdose

Medicated Assisted Treatment (MAT) for opioid use disorder

Behavioral support



therapy
12-step fellowship
care management
peer supports





buprenorphine methadone

mortality
overdose
hepatitis C + HIV

survival birth outcomes treatment retention NIDC 12496-1202-3

2 mg/0.5 mg @

30 gosches each containing 1 sublingual film.

Suboxone (buprenorphine and naloxone) sublingual film 2 mg/0.5 mg

Buprenorphine

Partial agonist

binds very tightly to mu receptors but only partially stimulates them

Very high affinity for mu receptors

Will displace other opioids (heroin, morphine, etc) and precipitate withdrawal If bound, not displaced by heroin, morphine

Analgesic

Can divide patient's typical dose into more frequent (e.g BID) dosing for acute pain





known liver failure or LFTs >5x
normal limit
known active significant
polysubstance abuse (benzos use
controversial)



methadone use in 36-48 hrs, not in withdrawal, on chronic pain meds

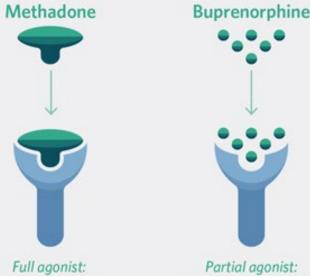




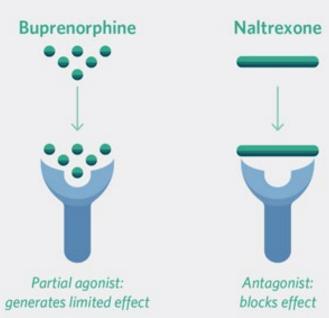
safe in pregnant patients and lactation but recommend OB consult



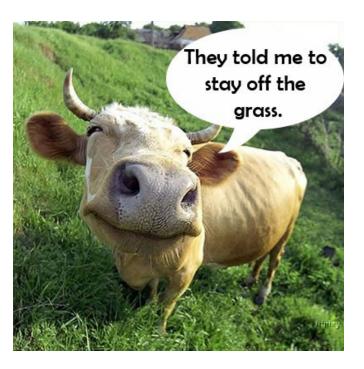




generates effect



MAT guided by COWS



Appendix A - Clinical Opioid Withdrawal Score (COWS)

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

Clinical Opioid Withdrawal Score (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. For example: if heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

	ïrst dose, 2 hours after first dose, etc.	Time:	Time:	Time:	Time:
Resting Pulse Rate: Record beats per minute aft	er patient is sitting or lying down for one minute				
0 - pulse rate 80 or below 1 - pulse rate 81–100	2 - pulse rate 101–120 4 - pulse rate greater than 120				
Sweating: Over past 1/2 hour not accounted for b	y room temperature or activity				
O - no chills or flushing 1 - subjective chills or flushing 2 - flushed or observable moistness on face	3 - beads of sweat on brow or face 4 - sweat streaming off face				
Restlessness: Observation during assessment • 0 - able to sit still	• 3 - frequent shifting or extraneous movement of legs/arms				
• 1 - reports difficulty sitting still, but is able to do so	5 - unable to sit still for more than a few seconds				
Pupil size					
0 - pupils pinned or normal size for light 1 - pupils possibly larger than normal for light	2 - pupils moderately dilated 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: If patient was having pain p attributed to opiate withdrawal is scored	reviously, only the additional component				
0 - not present 1 - mild/diffuse discomfort 2 - patient reports severe diffuse aching of ioints/muscles	4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: Not accounted for by col					
0 - none present 1 - nasal stuffiness or unusually moist eyes	2 - nose running or tearing 4 - nose constantly running or tears streaming down cheeks				
Gl upset: Over last ½ hour	2 - nausea or loose stool				
0 - no Gl symptoms 1 - stomach cramps	3 - vomiting or diarrhea 5 - multiple episodes of diarrhea or vomiting				
Tremor: Observation of outstretched hands					
0 - no tremor 1 - tremor can be felt, but not observed	2 - slight tremor observable 4 - gross tremor or muscle twitching				
Yawning: Observation during assessment O - no yawning 1 - yawning once or twice during assessment	2 - yawning three or more times during assessment 4 - yawning several times/minute				
Anxiety or irritability	2 - patient obviously irritable or anxious				
0 - none 1 - patient reports increasing irritability or anxiousness	4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin	3 - piloerrection of skin can be felt or hairs standing up on arms				
0 - skin is smooth	5 - prominent piloerrection				
5—12 = mild;					
13—24 = moderate;	TOTAL				
25—36 = moderately severe;	OBSERVER INITIALS				
> 36 = severe withdrawal					

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003Source: Wesson, D. R., & Ling, W. (2003), The Clinical Opiate Withdrawal Scale (COWS), J. Psychoactive Drugs, 39(2), 253-9.



Nicotine dependence

Chantix

Zyban (Buproprion)

Replacement: Nicotrol, nicotine gum and patches

1-800-quitnow with free resources for many of these medicines

Common Symptoms of Nicotine Withdrawal







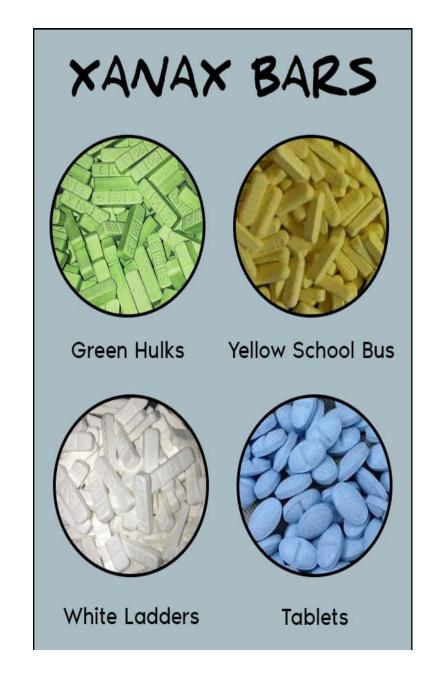
Oklahoma Tobacco Helpline

1 800 QUITNOW

1-800-784-8669

OKhelpline.com

Street names for Xanax



benzodiazipines

Dependence comes through prescriptions or diversion

When this class of medicine launched, it was felt to be safe as it had better safety profile than barbituates

Even long term prescription usage can lead to dependence, with cognitive impairment

Avoid starting these medicines

Controversy on whether/how to discontinue benzodiazepine treatment for patients who are on long-term treatment

benzos

Long ½ life

- Klonopin, Valium
- Less risk of inter-dose withdrawal
- Higher risk of build-up and significant cognitive impairment

Vs short ½ life

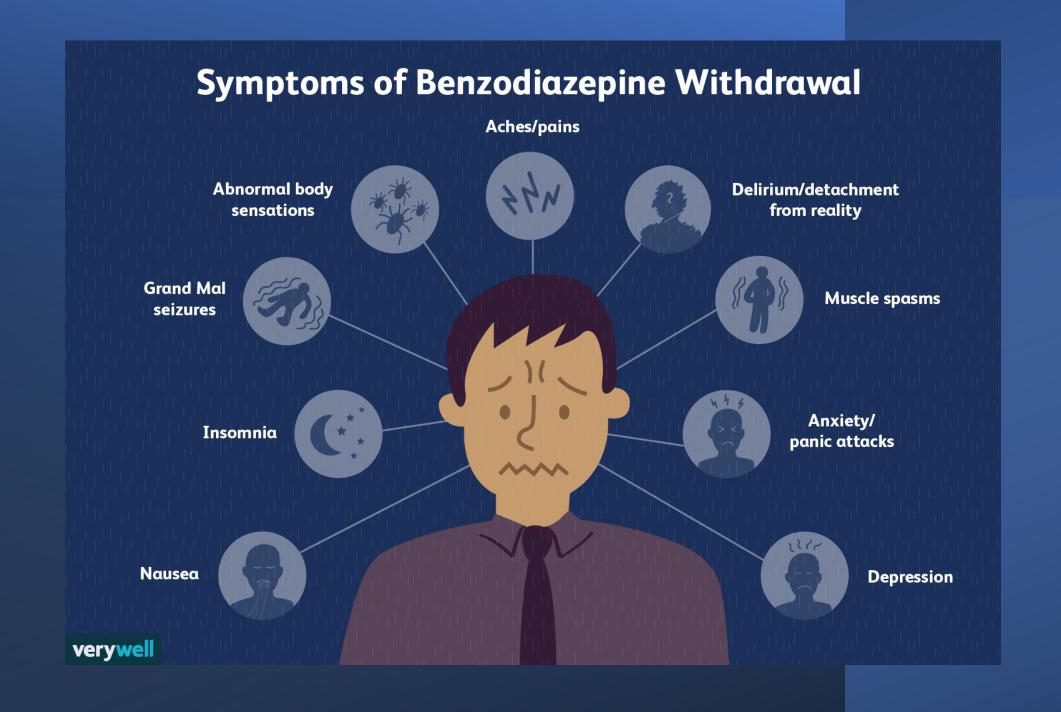
- Ativan, Xanax, Restoril, serax, tranxene
- Increased risk of inter-dose withdrawal
- Arguably less risk of cognitive impairment, dosing notwithstanding



BENZODIAZEPINE OVERDOSE SYMPTOMS

- DIFFICULTY BREATHING
- BLUISH TINGE TO THE LIPS
- CONFUSION OR DISORIENTATION
- EXTREME DIZZINESS
- COORDINATION ISSUES

- BLURRED VISION
- SEVERE WEAKNESS
- SEVERE TREMORS
- STUPOR
- COMA



Benzo taper

Dependence can happen in the space of a few months

Taper can take months to years

Cognitive decline may or may not improve

Benzodiazepine Metabolism Diazepam Temazepam Chlordiazepoxide Nordiazepam^a Oxazepam Chlorazepate 7-aminoclonazepam Clonazepam α-hydroxyalprazolam Alprazolam Lorazepam-glucuronide Lorazepam

Benzodiazepine UDS

Positive for 1-10 days

False Positives: Zoloft, Oxaprozin

Stimulant Abuse

Methamphetamine

Prescription Diversion

Stimulant Abuse Treatment

- No FDA-indicated treatment
- Evidence that treating co-morbid ADD, if present, reduces relapse
 - Treatment often requires higher doses of stimulants
 - Preference for using extended-release versions
 - This data is most compelling for adolescent-young adult males

UDS-Stimulants

Positive: 1-5 days

False Positives: Atenolol, Wellbutrin, Ephedrine, Labetalol, Propranolol, Pseudoephedrine, Ranitidine, Trazodone



Psychological Effects



Memory of Euphoria (Risk for Addiction)

Physical Effects



Full-Body Stimulation





Angry / Anxious / Paranoid

Intense Pleasure

Talkative / Confident

Cocaine High





Extreme Use



Heart Problems*



Seizures



Death



Addiction



Cocaine Abuse Treatment

No medicines FDA-indicated

Dopamine agonists, like Adderall, show promise but are controversial

Antabuse MAY have a role; also controversial

Possibly Topamax; also off-label

Cocaine UDS

Positive for 1-3 days

False Positives: not much...





Live Resin





Shatter Bubble Hash



Crumble





Budder Sugar Wax

Marijuana UDS

Positive for 1-3 days (acute single use) OR up to 30 days (heavy daily use)

False positive: Efavarinz, ibuprofen, naproxen, pantoprazole

Treatment for Marijuana Abuse

No FDA-Indicated Treatment

Treat comorbidities including Attention Deficit Disorder

NAC (N-acetyl-cysteine) has some evidence for reducing marijuana cravings in adolescents

Marijuana as Medicine-Interactions and Medical Concerns

THC: metabolized by CYP450 3A4 2C9 and inhibits 1A2, 2B6 2C9 2D6

CBD: metabolized by CYP450 3A4, 2C9, and 2C19 and inhibits 3A4, 2B6, 2C9, 2D6, 2E1

Data is evolving but likely multiple interactions; must be utilized with care

Use is associated with upregulation of CB1 receptors: metabolic syndrome

Upregulation of CB1 receptors also associated with increased compulsive behavior including alcohol use, drug addiction, increased smoking and compulsive eating

Working together as a team

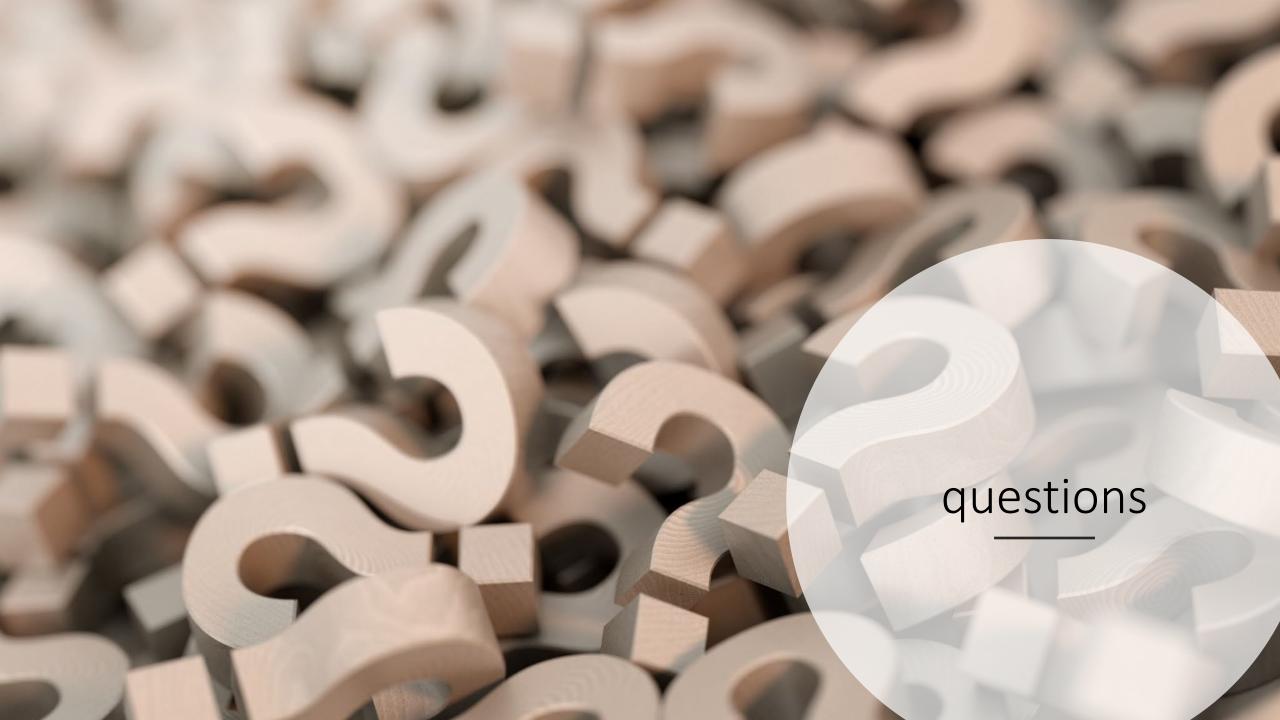
Medicine is very collaborative, with multiple people filling multiple roles

Ideal ways to collaborate—avoid triangulation!

- Sharing findings, observations—medicine effects, impacts, side effects with the prescriber
- Presenting diagnostic queries directly to the provider (avoid triangulation)
- Asking questions about medicines directly to the prescriber

Less helpful/harmful ways to collaborate:

- Questioning medicine choices, diagnoses with the patient
- Suggesting medicines to the patient to try. Especially controlled medicines. Especially benzos. No really. No, really.



Can't get enough?

Questions: I would love to answer your general medicine questions. I am not able to answer specific questions about specific patients.

Please let me know if you have questions about what was presented today.

I also crave feedback about this presentation. If there is constructive actionable feedback, please let me know!

Jenn Morris, (405)245-1721

Please note this is my personal cell; please do not release this to clients