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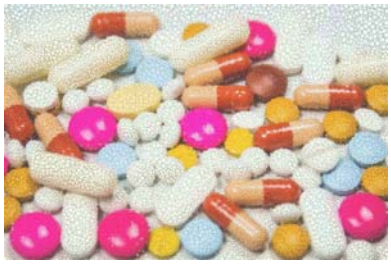

The Medical Impact of Psychiatric Medications

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July 2019

Antipsychotics

- All antipsychotics: *Black Box Warning with use in Dementia-Related Psychosis for which it is not approved; also there is an increased mortality risk in elderly dementia pts on antipsychotics; most deaths are due to cardiovascular or infectious events; it is not clear as to the extent to which the increased mortality is attributable to the antipsychotic vs. some patient characteristic(s)*

Monitoring for all antipsychotics:

- **Monitor weight as weight gain seen with all antipsychotics; lowest with Haldol (haloperidol), Latuda (lurasidone) and Geodon (ziprasidone); highest with Zyprexa (olanzapine) and Clozaril (clozapine); children are particularly vulnerable**
- **Monitor for tardive dyskinesia (TD) via DISCUS (Dyskinesia Identification System: Condensed User Rating Scale) or AIMS (Abnormal Involuntary Movement Scale); rate using either scale initially then every 6 months except > 50 years of age every 3 months; TD rate occurs with conventional antipsychotics at 20% to 50%, and with atypicals from 0.8% (in those younger than 50 yrs) to 5.3% (in those older than 50 yrs)**
- **Periodic CBC due to increase leukopenia/neutropenia**
- **Periodic LFTs due to hepatic effects**
- **Periodic eye exams advised with conventionals and Seroquel due to increased incidence of cataracts, retinopathy (including pigmented) and visual disturbances**
- **Check prolactin if signs of elevation (oligomenorrhea/amenorrhea, decreased libido/sexual dysfunction, galactorrhea, gynecomastia); hyperprolactinemia is due to blockade of D2 receptors in pituitary lactotroph cells which leads to an excess of prolactin secretion (dopamine is AKA PIF or prolactin inhibitory factor); hyperprolactinemia can increase likelihood of fracture, likely related to suppression of sex hormones (hypogonadotropic hypogonadism) as opposed to increase in bone resorption relative to bone formation**

Other concerns for all antipsychotics:

- neuroleptic malignant syndrome (NMS)- occurs in 0.2 to 3.2 % of those on antipsychotics; less in atypicals but almost all of them are reported as causing this, including clozapine (Clozaril)
- other extrapyramidal symptoms (EPS)- are generally dose dependent but not (usually) identified with clozapine (Clozaril) or quetiapine (Seroquel) though I have seen a case with the latter; EPS includes acute dyskinesias and dystonic reactions, tardive dyskinesia, Parkinsonism, akinesia, akathisia, and neuroleptic malignant syndrome.
- antipsychotic-induced sexual dysfunction- this is related to effects on alpha-1 & 2 adrenergic receptors, H1 histamine receptors and dopaminergic receptors orthostatic hypotension (as mentioned previously)

Other concerns for all antipsychotics (2):

- fetal effects: in a cohort study of 1.3 million pregnant women, after accounting for confounding variables including but not limited to psychiatric conditions, there was no increase in risk observed for congenital malformations for typical as well as atypical antipsychotics, except possibly risperidone which appeared to have an increased risk of overall and cardiac malformations. This study took place from Jan 1st of 2000 through Dec 31st of 2010, so does not include newer atypicals that have since come out (including Vraylar, Rexulti, Latuda, Saphris, possibly Fanapt) and this also did not look at other negative outcomes.
- Also during pregnancy some atypicals are known to increase the risk of hyperglycemia; both classes have caution with use in 3rd trimester likely related to a risk of neonatal EPS and withdrawal symptoms; some conventionals still carry a warning of possible risk of embryo toxicity and neonatal death based on animal data; some from both carry a warning about fetal weight as well as incomplete ossification.
- As the data continues to be compiled, prescribers are advised to look at the most recent warnings regarding pregnancy.

Atypical antipsychotics

- ***Black Box Warning*** ***when used for antidepressant effect, regarding increased risk of suicidality for those younger than age 24 years***
- **Monitoring per ADA/APA consensus guidelines for all atypicals:**
  - **medical history at baseline, week 12, then annually**
  - **weight at baseline, week 4/8/12, then every 3 months and annually**
  - **waist circumference at baseline, week 12, then annually**
  - **blood pressure at baseline, week 12, then annually**
  - **fasting glucose/hemoglobin A1c at baseline, week 12, then annually**
  - **fasting lipids at baseline, week 12, then annually**
- **Why monitor? Atypicals increase the risk of having 4 of the 5 components of metabolic myndrome which itself confers a 5-6 fold increased risk of developing type 2 DM and a 3-6 fold increased risk of mortality due to coronary heart disease**
- **Metabolic syndrome is diagnosed when 3 or more of the following found:**
  - **Abdominal obesity (Waist circumference >40 in. in men, >35 in. in women)**
  - **Triglyceride level at or > 150 mg/dL**
  - **HDL cholesterol of < 40 mg/dL in men, < 50 mg/dL in women**
  - **Systolic blood pressure at or > 130 mmHg or diastolic at or > 85 mmHg**
  - **fasting glucose at or > 100 mg/dL**

Clozaril (clozapine):

- Clozaril (clozapine): *In addition to dementia-related psychosis* ***Black Box Warning*** *for all antipsychotics, there are 4 other warnings;*
  - *Severe Neutropenia may occur and lead to serious infection and death; obtain ANC at baseline, then regularly; ANC >1500 for general population or ANC >1000 for benign ethnic neutropenia patients required prior to treatment start; advise patients to report signs and symptoms of severe neutropenia or infection*
  - *Orthostatic Hypotension, Bradycardia, Syncope may occur; risk highest during initial titration period, particularly with rapid dose escalation; reactions can occur even during 1st dose and at doses of 12.5 mg/day; start 12.5 mg PO q Day or BID, then titrate slowly and give in divided doses; use with caution in pts with cardiovascular disease, cerebrovascular disease, or hypotension risk*
  - *Seizures incidence increase with dose; start 12.5 mg PO q Day or BID, then titrate slowly and give in divided doses; caution if seizure history or predisposing factors; advise pts to avoid activities where sudden loss of consciousness would cause serious risk to self or others*
  - *Myocarditis, Cardiomyopathy, Mitral Valve Incompetence including fatal cases have occurred; D/C treatment and obtain cardiac eval. if myocarditis or cardiomyopathy suspected; s/sx incl. chest pain, tachycardia, palpitations, dyspnea, fever, flu-like sx, hypotension, or ECG changes; pts w/ clozapine-related myocarditis/cardiomyopathy generally should not be rechallenged*

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Monitoring for Clozaril (clozapine):

- **Subsequent to the *Black Box Warning* WBC and absolute neutrophil count (ANC) is monitored weekly for the 1st 6 months, biweekly for the 2nd 6 months, then monthly thereafter**
- **Follow lab algorithm if concerning values found [e.g., Mild Neutropenia (1000 to 1499/µL)- Three times weekly until ANC ≥ 1500/µL; once ANC ≥ 1500/µL, return to patient's last "Normal Range" ANC monitoring interval; for moderate or severe Neutropenia, treatment interrupted with hematology consulted and daily ANCs until improved mild neutropenia]**

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Monitoring for Geodon (ziprasidone):

- **A baseline pre-treatment ECG is indicated if any of the following cardiac risk factors are present:**
  - **known heart disease**
  - **a personal history of syncope**
  - **a family history of sudden death at under age 40 years (especially if both parents had sudden death)**
  - **congenital long QTc syndrome**
- **A subsequent ECG during treatment is indicated if symptoms develop that are associated with a prolonged QTc interval (e.g., syncope).**
- **Note that QTc prolongation may cause torsades de pointes-type arrhythmias and sudden death**

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Concerns with conventional antipsychotics

- **Mellaril (thioridazine) – *Black Box Warning* due to Proarrhythmic Effects; dose-related prolongation of QTc interval may cause torsades de pointes-type arrhythmias and sudden death; restrict use to schizophrenia that is resistant to standard antipsychotic drugs either due to insufficient efficacy or inability to reach effective dose due to intolerable adverse effects**
- **Lactation:**
  - **Haldol (haloperidol)- weigh risk/benefit while breastfeeding; no known risk of infant harm based on limited human data with low doses, though possible drug excretion into milk based on drug properties; no human data available to assess effects on milk production**
  - **Thorazine (chlorpromazine)- consider alternative, though may use short-term while breastfeeding; no known risk of infant harm based on limited human data, though possible risk of infant CNS depression based on drug's mechanism of action; no known adverse effects on milk production based on limited human data**
  - **Stelazine (trifluoperazine)- consider alternative while breastfeeding; no known risk of infant harm based on limited human data; no human data available to assess effects on milk production**
  - **Trilafon (perphenazine)- consider alternative while breastfeeding; no known risk of infant harm based on limited human data; no human data available to assess effects on milk production**
  - **Prolixin (fluphenazine)- use alternative while breastfeeding; no human data available to assess risk of infant harm or effects on milk production**
  - **Loxitane (loxapine)- use alternative while breastfeeding; no human data available to assess risk of infant harm or effects on milk production**
  - **Mellaril (thioridazine)- use alternative while breastfeeding; no human data available to assess risk of infant harm or effects on milk production**

Antiepileptic drugs (AEDs): All AEDs

- **Pregnancy: encourage pregnant patient's on AEDs to enroll in North American Antiepileptic Drug Pregnancy Registry at 1-888-233-2334; additional information can be found at www.aedpregnancyregistry.org**
- **Antiepileptic Drug Hypersensitivity Syndrome (AHS):**
  - **It is an adverse drug reaction associated with the aromatic AEDs phenytoin, carbamazepine, phenobarbital and primidone**
  - **The syndrome is defined by the triad of fever, rash, and internal organ involvement**
  - **Other drugs can also cause the same reaction including sulfonamides, dapsone, minocycline, terbinafine, azathioprine, and allopurinol.**
  - **The diagnosis can be challenging due to the variety of clinical and laboratory abnormalities and manifestations, but also because it may mimic infectious, neoplastic, or collagen vascular disorders**
  - **The incidence is approximately 1 in 3,000 exposures**
  - **It starts with fever, rash and lymphadenopathy generally in the first 2 to 8 weeks after starting the antiepileptic**
  - **Internal manifestations can include but not be limited to agranulocytosis, hepatitis, nephritis, and myositis**
  - **It is associated with excessive amounts of reactive oxidative metabolites of the AED leading to; a possible inadequate detoxification and subsequent cell death, or; a possible contribution to antigen formation that triggers an immune reaction**
  - **Cross-reactivity between phenytoin, carbamazepine and phenobarbital is as high as 70-80%**

Tegretol (carbamazepine):

- *Black Box Warnings including;*
  - *Serious Dermatologic reactions (1.4 out of 10,000 new users) and HLA-B*1502 Allele: serious, sometimes fatal dermatologic reactions reported, incl. toxic epidermal necrolysis and Stevens-Johnson syndrome; the risk is 10x greater in some Asian countries; there is a strong association between risk and HLA-B*1502 allele, which is found almost exclusively in Asian pts; it is advised to screen pts of genetically at-risk ancestry (see package insert) for HLA-B*1502 allele before initiating treatment; pts testing positive should not be treated with carbamazepine unless the benefit clearly outweighs the risk*
  - *Aplastic Anemia/Agranulocytosis risk is 5-8x greater than that of general public; transient or persistent decreases in platelets or WBC is not uncommon with carbamazepine treatment and the majority of leukopenia cases do not progress to aplastic anemia or agranulocytosis; perform baseline and periodic hematological testing; if a low or decreased WBC or platelet count, monitor closely and consider D/C of treatment if evidence of significant bone marrow depression*

Monitoring for Tegretol (carbamazepine):

- **Monitoring Parameters**:
  - CBC with diff, electrolytes, LFTs, BUN/Cr/urinalysis (latter due to risk of SIADH, water intoxication, hyponatremia)
  - ophthalmic exam at baseline, then periodically
  - signs and symptoms depression, behavior changes, suicidality
  - serum drug levels (therapeutic is 4-12 mcg/mL; toxic is >12 mcg/mL) and the timing of the blood draw should be before the morning dose; Time to Steady State is >1mo
  - watch for multiple drug/drug interactions (including with itself via autoinduction of hepatic enzymes) and typically will reduce blood levels of other drugs, sometimes with Tegretol (carbamazepine) levels going up or down as well
- It is contraindicated within 14 days of initiating MAOI (because it has weak serotonergic effects)

Other concerns with Tegretol (carbamazepine):

- **Drug interaction issues: Epocrates lists 10 pages of drug interactions when pulled into a word document; it is advisable to look up this information, especially with psychotropics as many if not most have interactions with this drug**
- **Fetal effects:**
  - **weigh the risk versus benefit with use during pregnancy**
  - **folic acid supplementation is recommended in the 1st trimester**
  - **risk of teratogenicity (major congenital abnormalities mainly including neural tube defects, cardiovascular and urinary tract anomalies, and cleft palate based on human data)**
  - **possible risk of neonatal withdrawal syndrome based on limited human data**
  - **possible risk of neurodevelopmental delay based on conflicting human data**
- **Lactation:**
  - **Seizure Disorder Use: benefits of breastfeeding and AED treatment outweigh risks, though monitor infant closely; risk of infant CNS depression and possible risk of infant hepatic dysfunction based on limited human data; no human data available to assess effects on milk production**
  - **All Other Uses: weigh risk/benefit while breastfeeding otherwise same as for Seizure Disorder Use**

Depakote/Depakene (valproate):

- ***Black Box Warning* including;**
  - ***Hepatotoxicity: serious or fatal hepatic failure has occurred, usually during 1st 6mo of treatment; patients <2 years old at increased of risk fatal hepatotoxicity, especially if multiple anticonvulsant treatment, congenital metabolic disorder, severe seizure disorder with mental retardation, or organic brain disease; in pts <2 years old, weigh benefit versus risk, use with extreme caution and as monotherapy; incidence of fatal hepatotoxicity decreases considerably in progressively older patient groups; hepatotoxicity may be preceded by malaise, weakness, lethargy, facial edema, anorexia, vomiting and loss of seizure control; monitor signs and symptoms including LFTs at baseline, then frequently, especially during 1st 6 months of treatment***
  - ***Increased Hepatotoxicity Risk in Mitochondrial Disease: increased risk of acute liver failure and death in pts with hereditary neurometabolic syndromes caused by mitochondrial DNA polymerase gamma (POLG) gene mutations (e.g. Alpers Huttenlocher Syndrome); contraindicated in patients with POLG-related mitochondrial disorders and in patients <2 years old with suspected hereditary mitochondrial disease; in patients >2 years old with suspected mitochondrial disorder, use only if failed other anticonvulsant treatment and monitor hepatotoxicity signs and symptoms including LFTs regularly; perform POLG mutation screening per current clinical practice***

Depakote/Depakene (valproate;2):

- *Black Box Warning including (continued);*
  - *Fetal Risk: can cause major congenital malformations incl. neural tube defects, decr. IQ scores, neurodevelopmental disorders after in utero exposure; contraindicated for migraine prophylaxis use in pregnancy and women of reproductive potential w/o effective contraception; should not be used for epilepsy or bipolar disorder use in pregnancy and women planning to become pregnant unless other tx options have failed or are unacceptable; women should use effective contraception during treatment*
  - *Pancreatitis: life-threatening pancreatitis, incl. hemorrhagic cases w/ rapid progression from initial sx to death have been reported in both children and adults; cases have been reported shortly after initial use as well as after several years of use; advise pts to promptly report s/sx incl. abdominal pain, nausea, vomiting, and/or anorexia; D/C tx if pancreatitis diagnosis and start alternative tx as clinically indicated*

Monitoring for Depakote/Depakene (valproate):

- Monitoring Parameters:
  - LFTs at baseline, then frequently, especially during 1st 6mo or if suspected hereditary mitochondrial disease
  - CBC with diff, coagulation tests at baseline, then periodically, also before planned surgery, during pregnancy
  - serum drug levels
  - ammonia level periodically but especially with development of any cognitive issues
  - signs and symptoms depression, behavior changes, suicidality
- Therapeutic Drug Levels:
  - Epilepsy: 50-100 mcg/mL (valproic acid)
  - Mania: 50-125 mcg/mL (valproic acid)
  - Toxic Levels: >175 mcg/mL
  - Timing: just before morning dose
  - Time to Steady State: 2-4 days
  - Draw free levels if hypoalbuminemia
- Weight monitoring strongly advisable

Lamictal (lamotrigine):

- **Generally no lab work, but ophthalmic exam may be advisable in prolonged use (per Epocrates; there have been anecdotal reports of permanent vision changes?)**
- ***Black Box Warning for Serious Rash; serious rashes requiring hospitalization and treatment discontinuation include. Stevens-Johnson syndrome, rare cases of toxic epidermal necrolysis, and rash-related deaths; incidence 0.3-0.8% in 2-17 year of age and 0.08%-0.3% in adults; age is only risk factor identified as predictive for risk of rash occurrence or severity; other risk factors may include concurrent valproic acid derivative or exceeding initial lamotrigine dose or dose escalation recommendations; most life-threatening rashes occur in 1st 2 to 8 weeks of treatment with isolated cases after prolonged treatment; though benign rashes may also occur discontinue treatment at 1st sign of rash unless clearly not drug related; treatment discontinuation may not prevent rash from becoming life-threatening or permanently disabling or disfiguring***
- **As per the black box warning, the biggest concern is rash, since this could be indicative of severe cutaneous adverse reaction (SCAR) including Steven's Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) or SJS/TEN overlap; incidence of SCAR is 1 to 2.5 out of 10,000 new users, and higher incidence per the estimates listed above my be presumably due to original initial use without conservative dosing, especially in children; patients advised to stop the medication and seek medical evaluation emergently**

Lamictal (lamotrigine; 2):

- **Mortality estimates vary but range as follows;**
  - **SJS is under 5% to less than 10%; TEN is under 15% to more than 40%; SJS/TEN overlap & for SCAR in general is around 20%**
- **Drug/drug interactions:**
  - **Depakote/Depakene (valproate) can boost blood levels so cut Lamictal (lamotrigine) dosage in half**
  - **Tegretol (carbamazepine) can lower blood levels so double Lamictal (lamotrigine) dosage**
  - **many oral contraceptives have blood levels lowered by Lamictal (lamotrigine), and many can cause lowering of Lamictal (lamotrigine) blood levels**
- **Fetal effects:**
  - **caution advised during pregnancy; consider folic acid supplementation in 1st trimester; possible risk of teratogenicity (especially increased incidence of cleft lip and palate) based on conflicting human data; risk of neurodevelopmental delay not expected based on limited human data**
- **Lactation:**
  - **Seizure Disorder Use: benefits of breastfeeding and AED treatment outweigh risks while breastfeeding, consider monitoring infant lamotrigine levels; low risk of infant harm, incl. CNS depression, apnea, and rash, based on human data; no human data available to assess effects on milk production**
  - **All Other Uses: weigh risk/benefit while breastfeeding, otherwise same as for Seizure Disorder Use**

Trileptal (oxcarbazepine):

- Initially no lab work was reportedly necessary
- Currently Na level monitoring strongly advised, especially at higher dosages (my experience has been almost inevitable hyponatremia when finally at effective dosing); Cr at baseline also advised
- Other concerns:
  - fetal effects: weigh risk/benefit during pregnancy; folic acid supplementation recommended in 1st trimester; possible risk of teratogenicity and low birth weight based on conflicting human data; risk of teratogenicity and developmental toxicity based on animal data
  - lactation: caution advised while breastfeeding; inadequate human data available to assess risk of infant harm; no human data available to assess effects on milk production
  - similar drug/drug interactions as compared to Tegretol (carbamazepine)

Topamax (topiramate):

- **Monitoring:**
  - **Creatinine at baseline**
  - **Bicarbonate at baseline due to metabolic acidosis risk, then periodically**
  - **Signs and symptoms of depression, behavior changes, suicidality**
  - **Symptoms of pain in or around the eye and/or vision change of any kind (especially bilateral) and/or headache during tx indicates possible onset of secondary angle closure glaucoma; the pt should emergently have eye exam and IOP measured; risk typically occurs within 1 month of treatment**
- **Other concerns:**
  - **Cognition (sometimes referred to as "stupamax") - typically problems with word finding, possible cognitive slowing**
  - **fetal effects: weigh risk/benefit during pregnancy; risk of teratogenicity, incl. oral clefts, and low birth weight based on human data; possible risk of neonatal metabolic acidosis based on drug's mechanism of action and transfer to fetus; risk of neurodevelopmental delay inconclusive**
  - **lactation: weigh risk/benefit while breastfeeding; inadequate human data available to assess risk of infant harm, though possible drug excretion into milk based on drug properties; no human data available to assess effects on milk production**

Neurontin (gabapentin):

- Cr at baseline only advised as it is primarily renally excreted
- Other issues:
  - fetal effects: caution advised during pregnancy; risk of teratogenicity not expected based on limited human data; risk of embryo-fetal toxicity and death based on animal data at 1-4x maximum recommended human dosage (MRHD)
  - lactation: may use while breastfeeding; no known risk of infant harm based on limited human data; no human data available to assess effects on milk production

Lithium:

- ***Black Box Warnings**: Lithium Toxicity which is closely related to serum lithium levels and can occur at doses close to therapeutic levels; start treatment only if facility available for prompt accurate serum lithium determinations (lithium toxicity symptoms when mild can include weakness, worsening tremor, mild ataxia, poor concentration and diarrhea; with worsening toxicity symptoms include vomiting, onset of gross tremor, slurred speech, confusion and lethargy)*
- **Monitoring for lithium:**
  - **Weight and pregnancy test at baseline**
  - **Baseline Ca (parathyroid dz), Cr, urinalysis, TSH (because of thyroid suppression leading to hypothyroidism), then recheck these at least q6-12mo**
  - **Serum drug levels 2x/wk until stable, then q2mo until chronic steady dose, then q6-12mo**
  - **ECG at baseline in pts >40 years of age if cardiovascular disease (arrhythmogenic potential), then q6-12mo**
  - **Consider CBC at baseline**
  - **Therapeutic Drug Levels:**
    - **Acute Mania: 0.8-1.2 mEq/L**
    - **Bipolar Disorder: 0.6-1.2 mEq/L**
    - **Toxic Levels: >1.5 mEq/L (adult/child), >0.8 mEq/L (elderly)**
    - **Timing: 12h after PM dose, holding AM dose if necessary; Time to Steady State: 3-6 days (adult), 3-5 days (child), 4-8 days (elderly)**

Other concerns with lithium:

- **Pregnancy: consider avoiding use in 1st trimester or monitor fetal ECHO; caution advised near-term; possible risk of teratogenicity and risk of fetal and neonatal harm, incl. lithium toxicity, based on human data (the risk for fetal heart defects, including Ebstein's anomaly*, at dosages below 900mg may be much lower than previous estimates and possibly negligible)**
- ***Ebstein's anomaly is a congenital heart defect in which the (septal and posterior) leaflets of the tricuspid valve (between the 2 right chambers) sit lower than normal and are malformed, which can cause leakage of blood back through the valve from the right ventricle to the right atrium. Half of the time there is an atrial septal defect in these cases as well.***
- **Lactation: use alternative while breastfeeding, or consider monitoring infant lithium levels, BUN/Cr, TSH; possible risk of infant harm based on human data; no human data available to assess effects on milk production**
- **Typical drug/drug interactions:**
  - **NSAIDs can boost lithium blood levels**
  - **antihypertensive drugs (such as diuretics and renin-aldosterone system inhibitors) can boost lithium blood levels**
  - **medications with serotonergic activity can increase risk of serotonin syndrome**

Antidepressants: all classes

- ***Black Box Warning for increased suicidality risk in those younger than age 24 esp. during 1st month of treatment with antidepressants vs. placebo; weigh risk vs. benefit; in short-term studies of antidepressants vs. placebo, suicidality risk not incr. in pts >24 yo, and risk decreased in pts 65 yo and older; observe all pts for clinical worsening, suicidality, or unusual behavior changes; not approved for pediatric use***
- **Monitoring: weight monitoring advisable with long term use due to weight gain risk with all antidepressants**
- **Abrupt discontinuation is inadvisable; cross-taper to mitigate antidepressant discontinuation syndrome and/or relapse risk; discontinuation syndrome can be divided into six clusters of symptoms:**
  - **Sensory symptoms (paresthesia, numbness, electric shock-like sensations, rushing noise " in head" and palinopsia, or visual trails)**
  - **Disequilibrium (light-headedness, dizziness and vertigo)**
  - **General somatic symptoms (flu-like syndrome which includes lethargy, headache, tremor, sweating and anorexia)**
  - **Affective symptoms (irritability, anxiety, low mood and tearfulness)**
  - **Gastrointestinal symptoms (nausea, vomiting and diarrhea)**
  - **Sleep disturbance (insomnia, nightmares and excessive dreaming)**

Antidepressants: all classes (2)

- **Encourage pts to enroll in National Pregnancy Registry for Antidepressants at 1-844-405-6185; additional info at www.womensmentalhealth.org/clinical-and -research-programs/pregnancyregistry/antidepressants**
- **Per Quebec Pregnancy Cohort; paroxetine increased the risk of cardiac defects and ventricular/atrial septal defects; citalopram increased the risk of musculoskeletal defects and craniosynostosis; TCA was associated with eye, ear, face and neck defects; and venlafaxine was associated with respiratory defects**
- **Lactation: generally Zoloft (sertraline) is the antidepressant of choice due to low risk of harm on human data but TCAs may be generally safe with breastfeeding**
- **There is a risk of liver damage which may take place within days or up to six months after beginning an antidepressant**
- **The highest risk of liver damage appears to be monoamine oxidase inhibitors (MAOIs), tricyclic/tetracyclic antidepressants, nefazodone, bupropion, duloxetine and agomelatine (European/Australian melatonin and serotonin receptor acting antidepressant)**

Antidepressants: all classes (3)

- **Cross taper versus "wash out"**
  - **generally, medication "wash out" is generally indicated for clinical trials; cross-tapering seems to be the least disruptive means to switch medication, with an exception being for MAOI use, which is generally a 7 day wash out when switching to an MAOI from another antidepressant except for the follow;**
    - **after stopping Prozac (fluoxetine) wait 5 to 6 weeks to start MAOI, and if Prozac dosage greater than 20mg you will need to gradually reduce instead of stopping abruptly**
    - **after stopping Trintellix (vortioxetine) wait 14 to 21 days to start MAOI, and if Trintellix dosage greater than 10mg you will also need to gradually reduce instead of stopping abruptly**
    - **after stopping TCAs and mirtazapine wait 14 days to start MAOI (except wait 21 days after stopping imipramine and clomipramine)**
    - **after stopping an MAOI wait 14 days to start any other antidepressant (except wait 21 days before starting clomipramine)**
  - **why need for "wash out" where MAOIs are concerned?**
    - **depending on the agent, there is a risk of hypertensive crisis, serotonin syndrome, and dopaminergic excess (the latter can manifest as psychosis, hypomanic/manic symptoms, aggression, and/or compulsive behaviors)**

Selective Serotonin Reuptake Inhibitors (SSRIs): entire class

- There is a risk for Serotonin Syndrome (SS), especially when used with other serotonergic agents and SS is characterized by:
  - Agitation or restlessness
  - Confusion
  - Rapid heart rate and high blood pressure
  - Dilated pupils
  - Loss of muscle coordination or twitching muscles
  - Muscle rigidity
  - Heavy sweating
  - Diarrhea
  - Headache
  - Shivering
  - Goose bumps
- Severe serotonin syndrome can be life-threatening. Signs and symptoms include:
  - High fever
  - Seizures
  - Irregular heartbeat
  - Unconsciousness

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SSRIs: entire class (2)

- **Mnemonic: SHIVERS**
  - **Shivering- unique to Serotonin Syndrome, helps to distinguish it from other hyperthermic syndromes**
  - **Hyperreflexia and myoclonus- frequently seen in mild to moderate cases; are especially notable in the lower extremities; muscular rigidity occurs only in more severe cases**
  - **Increased temperature- although variable in SS and usually observed in severe cases, is likely caused by muscular hypertonicity**
  - **Vital sign instability- can present as tachycardia, tachypnea, and/or labile blood pressure**
  - **Encephalopathy (mental status changes such as agitation, delirium, confusion, and to a lesser extent obtundation)- can develop from hyperthermia**
  - **Restlessness and incoordination- common because of excess serotonin activity**
  - **Sweating (diaphoresis)- autonomic response to excessive serotonin stimulation; anticholinergic toxicity will instead typically manifest with hot, dry skin**

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SSRIs: entire class (3)

- **Fetal effects:**
  - **Paxil (paroxetine): weigh risk/benefit during pregnancy, consider alternate SSRI; risk of teratogenicity in 1st trimester (has an increased risk of cardiac defects; ultrasound advised with exposure) and neonatal withdrawal symptoms or serotonin syndrome in 3rd trimester based on human data; risk of neonatal persistent pulmonary HTN or autism is inconclusive**
  - **Celexa (citalopram): has an increased risk of musculoskeletal defects and craniosynostosis per Quebec Pregnancy Cohort**
  - **Otherwise, caution advised during pregnancy, esp. in 3rd trimester; risk of fetal harm low, though risk of neonatal withdrawal symptoms or serotonin syndrome based on human data; risk of neonatal persistent pulmonary HTN inconclusive**
  - **A recent study Canadian study showed increased incidence of autism with SSRI exposure in 3rd trimester, but does not directly causally link antidepressants to the increased incidence of autism; the study did not control for severity of depression, making it difficult to asses if the underlying depressive illness may have been causative; given that combination antidepressant exposure in 2nd or 3rd trimester quadrupled the incidence, this may suggest severity of illness was more of a factor; dosages of antidepressants were also not accounted.**

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Monitoring with SSRIs: specific agents

- Prozac (fluoxetine):
  - ECG at baseline if QT prolongation and ventricular arrhythmia risk, then periodically
- Lexapro (escitalopram):
  - ECG if QT prolongation risk
- Celexa (citalopram):
  - K (potassium), Mg (magnesium) at baseline if electrolyte disturbance risk, then periodically; ECG if QT prolongation risk; should not be used beyond 40mg due to QTc prolongation potential substantially increasing

Serotonin-Noradrenergic Reuptake Inhibitors (SNRIs):

- **Includes:**
  - **Pristiq (desvenlafaxine)**
  - **Cymbalta (duloxetine)**
  - **Fetzima (levomilnacipran)**
  - **Savella (milnacipran)**
  - **Effexor (venlafaxine)**
- **Monitoring:**
  - **All SNRs: baseline and periodic blood pressure due to noradrenergic action; class associated with liver failure risk but LFT monitoring not useful due to unpredictable and abrupt onset**
  - **All SNRIs: risk of Serotonin Syndrome when combined with other serotonergic agents**
  - **Effexor (venlafaxine) and Pristiq (desvenlafaxine): baseline and periodic lipid monitoring if using long term**
- **Fetal effects:**
  - **Effexor (venlafaxine) and Pristiq (desvenlafaxine) caution advised during pregnancy, esp. in 3rd trimester; risk of fetal harm low, though risk of neonatal withdrawal sx or serotonin syndrome based on limited human data (primarily based on venlafaxine data regarding Pristiq, as limited to no human data available); increased risk of respiratory defects per Quebec Pregnancy Cohort**
  - **Savella (milnacipran) and Fetzima (levomilnacipran) caution advised during pregnancy, esp. in 3rd trimester; no human data available, though risk of neonatal withdrawal sx or serotonin syndrome based on human data with other SNRIs; possible risk of embryo-fetal toxicity, incl. skeletal variation, based on conflicting animal data at up to 1.5x MRHD (maximum recommended human dosage)**
  - **Cymbalta (duloxetine) caution advised during pregnancy, esp. in 3rd trimester; risk of fetal harm low, though risk of neonatal withdrawal sx or serotonin syndrome based on limited human data**

Wellbutrin (bupropion):

- *Carries an additional Black Box Warning; Neuropsychiatric Symptoms and Suicidality: monitor for serious neuropsychiatric events incl. behavior change, hostility, agitation, depression, and suicidality as well as worsening of pre-existing psychiatric illness which have occurred in pts taking bupropion and after discontinuation; some cases were possibly complicated by nicotine withdrawal sx, but were also reported in pts who continued to smoke while taking bupropion; weigh bupropion risks vs. benefits of smoking cessation*
- Should not be typically used in seizure disorder or ED with vomiting component (anorexia nervosa or bulimia nervosa) due to lowering of seizure threshold
- Maximum safe dosage appears to be 450mg per day
- Fetal effects: caution advised during pregnancy; risk of congenital heart defects inconclusive, though no known risk of other teratogenicity based on human data

Serzone (brand discontinued in US; nefazodone):

- *Black Box Warning regarding life-threatening hepatic failure; in US there has been an incidence of 1 per 250,000-300,000 patient-yr of cases of hepatic failure resulting in death or transplant; avoid in active hepatic disease or elevated baseline LFT; advise pts to monitor for hepatic impairment signs and symptoms; D/C if clinical signs and symptoms of hepatic failure or AST or ALT >3x ULN and do not restart treatment*
- Monitoring: LFTs at baseline, then periodically; signs and symptoms hepatic impairment; sx suicidality, clinical worsening, and/or unusual behavior changes, especially during initial treatment or after dose changes
- Fetal effects: caution advised during pregnancy, esp. in 3rd trimester; inadequate human data available to assess risk, though risk of teratogenicity not expected based on limited human data; risk of neonatal withdrawal sx or serotonin syndrome based on human data with SSRIs; risk of decreased fetal weight based on animal data at >1.3x MRHD (maximum recommended human dosage), though no known risk of teratogenicity at 5x and 6x MRHD

Trintellix (vortioxetine) and Tricyclic Antidepressants:

Trintellix (vortioxetine)- the antidepressant formerly known as Brintellix:

- Fetal effects: caution is advised during pregnancy, esp. in the 3rd trimester; no human data available, though there is a risk of neonatal withdrawal symptoms or Serotonin Syndrome based on human data with SSRIs; the risk of neonatal persistent pulmonary HTN or autism is inconclusive based on human data; no known risk of teratogenicity based on animal data
- monitoring can include; serum drug levels; ECG if cardiovascular disease; symptoms of suicidality, clinical worsening, and/or unusual behavior changes, especially during initial treatment or after dosage changes

Tricyclic antidepressants:

- 1 gram generally considered lethal in adults
- Monitoring can include; serum drug levels if indicated (mainly when hepatic inhibition a concern since it is infrequently used as primary antidepressant; typically they are currently used adjunctively for insomnia); ECG if cardiovascular disease; symptoms of suicidality, clinical worsening, and/or unusual behavior changes, especially during initial treatment or after dose changes
- Pregnancy: caution generally advised related to possible neonatal withdrawal, teratogenicity (per Quebec Pregnancy Cohort associated with eye, ear, face and neck defects) and post partum hemorrhage

MAOIs (mono-amine oxidase inhibitors):

Examples include;

- **selegiline (Eldepryl)**
- **isocarboxazid (Marplan)**
- **phenelzine (Nardil)**
- **tranylcypromine (Parnate)**
- **rasagiline (Azilect- in Isreal)**

Except potentially with lower dosage of Emsam (selegiline) patch, avoid high tyramine foods to prevent build up of this amino acid with pressor activity, to avoid hypertensive crisis; examples of foods high in tyramine include:

- **Strong or aged cheeses, e.g; aged cheddar, Swiss and parmesan; blue cheeses (Stilton and Gorgonzola); Camembert. Cheeses made from pasteurized milk (American cheese, cottage cheese, ricotta, farmer cheese and cream cheese) are less likely to contain high levels of tyramine**
- **Cured meats e.g. those treated with salt and nitrate or nitrite (dry-type summer sausages, pepperoni and salami)**
- **Smoked or processed meats e.g. hot dogs, bologna, bacon, corned beef or smoked fish.**
- **Pickled or fermented foods e.g. sauerkraut, kimchee, caviar, tofu or pickles**
- **Sauces e.g. soy sauce, shrimp sauce, fish sauce, miso and teriyaki sauce.**
- **Soybeans (and soybean products)**
- **Snow peas, broad beans (fava beans) and their pods**
- **Dried or overripe fruits e.g. raisins or prunes, overripe bananas or avocados**
- **Meat tenderizers (or meat prepared with tenderizers)**
- **Yeast-extract spreads e.g. Marmite, brewer's yeast or sour dough bread**
- **Alcoholic beverages e.g. beer (especially tap or homebrewed beer), red wine, sherry and liqueurs**
- **Combination foods (that contain any of the above ingredients(**
- **Improperly stored foods or spoiled foods meaning that recommendations to eat only fresh foods (and no leftovers or foods past their freshness dates)**

Fetal effects: caution advised since teratogenicity risk not clear; more related to risk of decreased uteroplacental blood flow and/or vasoconstriction based on mechanism of action

Medication Assisted Treatment (MAT):

- Antabuse (disulfiram)
  - ***Black Box Warning*** *Alcohol Contraindicated: never administer if alcohol intoxication or without patient's full knowledge, instruct relatives accordingly*
  - With alcohol, leads to the "disulfiram" reaction, including flushing, fast heartbeats, nausea, thirst, chest pain, vertigo, and low blood pressure; do not take it for at least 12 hours after drinking alcohol; reactions may still happen with drinking alcohol several weeks after stopping it
  - requires periodic LFTs
  - Pregnancy: caution advised during pregnancy; inadequate human data available to assess risk; risk of embryo-fetal toxicity based on animal data at recommended human dose
  - Lactation: use alternative while breastfeeding; no human data available to assess risk of infant harm or effects on milk production
- ReVia (brand discontinued- oral naltrexone) and Vivitrol (LAI naltrexone)
  - s/sx of depression and suicidality
  - LFTs previously advised, but may not be necessary (and not listed as needing monitoring in Epocrates)
  - Data showing safety even with stable or compensated cirrhosis, but is not recommended in acute liver failure
  - Pregnancy: caution advised during pregnancy; risk of teratogenicity is not expected based on limited human data; risk of embryo-fetal death based on animal data at 2-18x recommended human dose
  - Lactation: may use while breastfeeding; no known risk of infant harm based on limited human data and drug properties; no human data available to assess effects on milk production

MAT: Buprenorphine containing medications (Subutex, Suboxone, Zubsolv, etc.) and methadone (Methadose, Dolophine)

- ***Black Box Warning (for both agents)****:*
  - *Addiction, Abuse, and Misuse; Schedule III controlled substance with risk of addiction, abuse, and misuse, which can lead to overdose and death; assess opioid abuse or addiction risk prior to prescribing; regularly monitor all pts for misuse, abuse, and addiction*
  - *Respiratory Depression; serious, life-threatening, or fatal cases may occur even with recommended use; monitor for resp. depression esp. during treatment start or after dosage incr.*
  - *Neonatal Opioid Withdrawal Syndrome; prolonged maternal use of opioid treatment during pregnancy can lead to potentially life-threatening neonatal opioid withdrawal syndrome; infants may require treatment according to neonatology protocols; advise pregnant pts of risks and ensure appropriate treatment avail. if prolonged opioid use required*
  - *Risks from Concomitant Use with Benzodiazepines, CNS Depressants; concomitant opioid use with benzodiazepines or other CNS depressants, incl. alcohol, may result in profound sedation, resp. depression, coma, and death; reserve concomitant use for pts with inadequate alternative treatment options; limit to minimum required dosage and duration; monitor pts for signs and symptoms of resp. depression and sedation*

MAT: Buprenorphine containing medications (Subutex, Suboxone, Zubsolv, etc.) and methadone (Methadose, Dolophine) 2

Black Box Warning (for methadone only)*:*

- *Appropriate Use: should only be prescribed by healthcare professionals knowledgeable in use of methadone for chronic pain management or detoxification and maintenance treatment of opioid use disorder; reserve extended-release and long-acting formulations for pts without any treatment alternatives; not indicated for prn analgesic use; proper dosing and titration essential to decrease respiratory depression risk*
- *Opioid Analgesic REMS: FDA required risk evaluation and mitigation strategy (REMS) program to ensure benefits outweigh risks; REMS-compliant education program must be available to healthcare providers; providers are strongly encouraged to complete REMS-compliant program, counsel pts and/or caregivers with each Rx on safe use, serious risks, storage, and disposal, emphasize importance of reading med guide, and consider other tools to improve pt, household, and community safety*
- *Accidental Ingestion: accidental ingestion of even one dose, esp. by children, can result in fatal methadone overdose*
- *QT Prolongation: life-threatening QT prolongation and serious arrhythmias incl. torsades de pointes have occurred; most cases involve pain treatment with large and /or multiple daily doses, but also reported with doses commonly used for opioid use disorder maintenance treatment; monitor for ECG changes during treatment start or after dose incr. in pts with QT prolongation risk factors, pts with history of cardiac conduction abnormalities, and pts taking medications affecting cardiac rhythm*
- *CYP450 Interactions: concomitant use with CYP450 3A4, 2B6, 2C19, 2C9, or 2D6 inhibitors or D/C of concomitant CYP450 3A4, 2B6, 2C19, or 2C9 inducers may incr. methadone levels and may cause potentially fatal resp. depression; monitor pts receiving any concomitant CYP450 inhibitor or inducer, and consider decreased dose with any changes to concomitant medications that may result in incr. methadone levels*
- *Opioid Addiction Treatment: methadone used for detoxification and maintenance of opioid dependence should be administered in accordance with treatment standards cited in 42 CFR Section 8, incl. limitations on unsupervised administration*

MAT: Buprenorphine containing medications (Subutex, Suboxone, Zubsolv, etc.) and methadone (Methadose, Dolophine) 3

- Monitoring:
  - buprenorphine containing agents: LFTs at baseline, then periodically
  - methadone: Cr at baseline; signs and symptoms respiratory depression, esp. 24-72h after treatment start or incr. dose; ECG during treatment start and after dose incr. if QT prolongation risk
  - Both agents: consider random drug screens
- Pregnancy (for both agents):
  - Opioid Dependence Use: caution advised during pregnancy; low risk of fetal harm based on limited human data; risk of neonatal opioid withdrawal syndrome based on human data and drug's mechanism of action
  - Pain Use: caution advised during pregnancy, esp. with prolonged use in 3rd trimester; use alternative immediately before and during labor; otherwise same as Opioid Dependence Use
- Individuals of Reproductive Potential (for both agents):
  - caution advised in pts trying to conceive if long-term use; long-term opioid use may result in androgen deficiency based on limited human data and drug's mechanism of action
- Lactation (for both agents):
  - may use while breastfeeding; no known risk of infant harm based on limited human data and drug properties; possible decreased milk production based on conflicting human data

Benzodiazepines:

- ***Black Box Warning*** *from Risks from Concomitant Opioid Use: concomitant benzodiazepine use with opioids may result in profound sedation, respiratory depression, coma, and death; reserve concomitant use for pts with inadequate alternative treatment options; limit to minimum required dosage and duration; monitor pts for signs and symptoms of respiratory depression and sedation*
- Examples include: Xanax (alprazolam); Onfi (clobazam); Klonopin (clonazepam); Tranxene (clorazepate); Librium (chlordiazepoxide); Valium (diazepam); Prosom (estazolam); Ativan (lorazepam); Serax (oxazepam); Restoril (temazepam); Halcion (triazolam)
- monitoring:
  - LFTS if prolonged use
  - drug screens reasonable especially if suspicion of abuse/misuse/diversion
- other concerns:
  - risk of seizure and withdrawal delirium with abrupt discontinuation or excessive lowering of dosage; will require long term tapering at higher dosages, or detox if part of a SUD
  - in dementia there is risk of disinhibition but this does not seem to deter many prescribers
  - in elderly there is increased fall risk
  - in pediatric population there is a risk of disinhibition
  - there is a general risk of iatrogenic substance use disorder, with evidence of long term changes to nervous system making it increasingly difficult to taper off successfully
  - increased risk of dementia associated with long term use

Cognitive related medications:

- Memory/cognitive enhancers:
  - include:
    - Aricept (donepezil)
    - Exelon (rivastigmine)
    - Namenda (memantine)
    - Razadyne/Reminyl (galantamine; not used as frequently, possibly due to bradycardia and orthostasis warning?)
  - Monitoring: only Namenda with possible lab work indicated which is Cr at baseline (primarily renally excreted)
- ADHD medication/stimulants and related:
  - ***Black Box Warning*** *regarding Abuse and Dependence; CNS stimulants have high potential for abuse and dependence; assess abuse risk before prescribing; monitor for signs of abuse and dependence during treatment*
  - include:
    - amphetamine (Adzenys XR ODT, Evekeo)
    - amphetamine/Dextroamphetamine(Adderall and Adderall XR)
    - dextroamphetamine (Dexedrine, ProCentra, Zenzedi)
    - dexmethylphenidate (Focalin and Focalin XR)
    - lisdexamfetamine (Vyvanse)
    - methylphenidate (Concerta, Daytrana, Metadate CD and Metadate ER, Methylin and Methylin ER, Ritalin, Ritalin SR, Ritalin LA, Quillivant XR)
  - Monitoring: includes baseline cardiac evaluation in patients with risk factors; blood pressure and heart rate at baseline, after dose increase, then periodically; height and weight in pediatric patients at baseline, then periodically

Cognitive related medications (2):

- ADHD medication/stimulants and related, cont'd.
  - Strattera (atomoxetine):
    - ***Black Box Warning*** *regarding Suicidality: increase risk of suicidality in children/adolescents with ADHD, especially during 1st months of treatment; weigh risk vs. benefit; co-morbidities occurring with ADHD may be associated with increased risk of suicidal ideation or behavior; observe closely for clinical worsening, suicidality, or unusual behavior changes; not approved for major depression; average risk 0.4% with atomoxetine versus none with placebo in pooled analyses of short-term use, no suicides in these trials*
    - Monitoring: baseline cardiac evaluation in patients with risk factors; blood pressure, heart rate at baseline, after dose increase, then periodically; height, weight in pediatric patients at baseline, then periodically; symptoms of suicidality, clinical worsening, and/or unusual behavior changes in pediatric patients, especially during initial treatment or after dose changes
    - Pregnancy; caution advised during pregnancy, esp. in poor CYP2D6 metabolizers; inadequate human data available to assess risk, though risk of teratogenicity not expected based on limited human data; no known risk of fetal harm based on animal data at 2-2.5x MRHD
    - Lactation; caution advised while breastfeeding; no human data available to assess risk of infant harm or effects on milk production
  - Provigil (modafinil) and Nuvigil (armodafinil):
    - monitoring includes initial than periodic blood pressure for both, and additionally for heart rate with Nuvigil (armodafinil)

Other agents:

- Buspirone
  - risk of serotonin syndrome with other serotonergic medications
  - fetal effects: may use during pregnancy; risk of teratogenicity not expected based on limited human data; no known risk of fetal harm based on animal data at 30x MRHD
  - caution advised while breastfeeding; no known risk of infant harm based on limited human data and drug properties; no human data available to assess effects on milk production
- Anticholinergics:
  - watch in use in dementia as it counteracts acetylcholinesterase inhibitors and may directly exacerbate dementia symptoms; also concerns with use in elderly in general as they are more sensitive to anticholinergic effects due to physiological and pathophysiological changes that often accompany the aging process; central anticholinergic effects range from sedation, mild confusion and inability to concentration to frank delirium.
  - increased risk of dementia with long term anticholinergic exposure
  - examples include Cogentin (benztropine), Artane (trihexyphenidyl), Vistaril/Atarax (hydroxyzine), Benadryl (diphenhydramine);
  - fetal effects and lactation vary from agent to agent so look up latest data

Other agents (2):

Alpha adrenergic tone reducers:
- Catapres, Kapvay (clonidine):
  - Monitoring: Cr at baseline; vital signs frequently if cardiac conduction disturbance; HR, BP at baseline in ADHD pts, after dose increases, then periodically; periodic fasting blood sugar may be advisable
  - ***Black Box Warning*** *regarding Obstetrical, Postpartum, or Perioperative Use: weigh risk/benefit; epidural clonidine generally not recommended for obstetrical, postpartum, or perioperative pain management due to risk of hemodynamic instability, esp. hypotension and bradycardia*
  - Fetal effects: caution advised during pregnancy; risk of teratogenicity not expected, though possible risk of decreased birth wt based on limited human data; risk of embryo-fetal death based on animal data at 0.067x to 8x MRHD
  - lactation: consider alternative while breastfeeding; inadequate human data available to assess risk of infant harm or effects on milk production
- Minipres (prazosin):
  - monitor BP
  - fetal effects: caution advised during pregnancy; risk of fetal harm not expected based on limited human data; no known risk of fetal harm based on animal data at up to 225x greater than MRHD
  - lactation: consider alternative while breastfeeding; no human data available to assess risk of infant harm or effects on milk production

Beta blockers:
- ***Black Box Warning****: Avoid Abrupt Cessation in pts with CAD may cause angina exacerbation, MI, and ventricular arrhythmias; taper gradually and monitor when D/C chronic treatment; restart treatment if angina worsens or acute coronary insufficiency develops; avoid abrupt D/C in all pts in case unrecognized CAD*
- examples include: acebutolol (Sectral), atenolol (Tenormin), bisoprolol (Zebeta), metoprolol (Lopressor, Toprol-XL), nadolol (Corgard), nebivolol (Bystolic), propranolol (Inderal LA, InnoPran XL)
- Periodic fasting blood sugar may be advisable
- fetal effects and lactation vary from agent to agent so look up latest data

Does mental health treatment with psychotropics help with physical illness?

- Severe mental illness (SMI), including schizophrenia, bipolar disorder, schizoaffective disorder and major depressive disorder mortality, leads to increase in mortality, with those with these conditions having two or three times as high as that in the general population, translating to a 13-30 year shortened life expectancy.
- This shortened life span has widened in recent decades even in countries with relatively "good" healthcare.
- 60% of this excess mortality is felt to be due to physical illness (obesity, unhealthy lifestyles, disparities in healthcare access and utilization, and psychotropic effects- these all increase risk of CAD, CVA, as well as cancer and respiratory disease).
- In Bipolar Disorder for example, cardiovascular disease risk nearly doubles, and the rate of premature death from cardiovascular disease is doubled in those with schizophrenia (all compared to those without either mental health condition).
- Also in schizophrenia, there is triple the risk of death from respiratory disease.
- As a whole, it is unclear if, broadly, psychotropics have a protective effect with physical illness in those with SMI.

Does mental health treatment with psychotropics help with physical illness? (2)

- Some data actually showing that in general, when used in the SMI population they may be associated with an increased risk of physical illnesses.
- However, with depression and CAD and CVA incidence, studies of those with moderate to severe depression found treatment with antidepressants alone lowered the risk by up to 50% of; dying; developing coronary artery disease; or having a stroke (when compared to those who didn't take antidepressants or statins).
- This may be related to being motivated/able to make heart-healthy lifestyle choices as well as seek and follow through with medical interventions, but also related to a reduction in cortisol levels.
- Serious mental illness increases cancer risk, with some estimates saying 2.6 times more likely than the general population.
- Overall, treatment with conventional antipsychotics was not related to a reduced risk of cancer, but for cancers of the rectum, colon and prostate there were suggestive decreases in risk. An increased risk of breast cancer in SMI patients may be related to medications that increase prolactin, which is a risk factor for breast cancer

