

# Anxiety and Depressive Disorder – The Medication Experience

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# What is polypharmacy?

- Multiple definitions not universally agreed upon
  - Literal: Poly = multiple, Pharmacy = medication
  - “excessive use of medication” or “unnecessary use of medication”
  - CMS Quality Indicator: Nine or more medications
  - Includes Rx, OTC, herbal/dietary supplements
  - Psychiatric Polypharmacy: Use of two or more psychiatric medications

# Polypharmacy



- Patients may take many medications that are all appropriate while others take few but are inappropriate
  - Consider term of “inappropriate medication use” instead
- Caused by a number of factors
  - Multiple providers
  - Transitions of care
  - Provider education
  - Patient expectations
  - Multiple disease states

# Polypharmacy



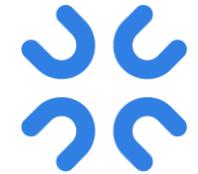
- 10% of the population and more than 30% of older adults take 5 or more drugs simultaneously<sup>2</sup>
- More than two-thirds of older adults concurrently use prescription and OTC/dietary supplements
  - 1 in 6 adults at risk for major drug-drug interaction
- Adverse drug events cause approximately 4 hospitalizations per 1,000 people each year<sup>2</sup>
- High cost (30-180 billion dollars each year)<sup>2</sup>
- 1/3 of patients visiting an outpatient psychiatry department have been found to be on three or more psychotropic drugs

# Why does it matter?



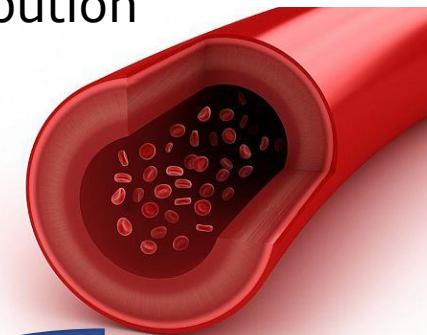
- Increased risk for adverse effects
- Increased risk for drug interactions
- Reduced functional impairment
- Increased hospitalization and institutionalization
- Increased risk for falls in older adults
- Increased mortality
- Increased cost
- Lower medication adherence

# How do medications work?

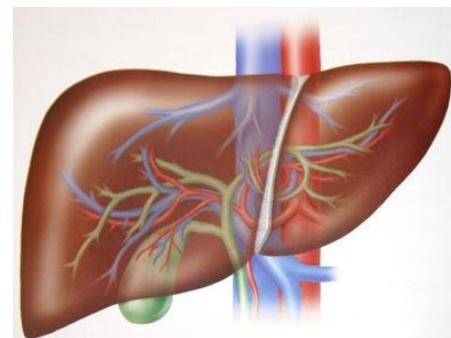


Absorption

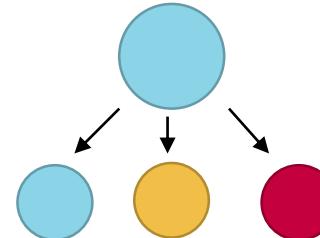
Distribution



Site of Action



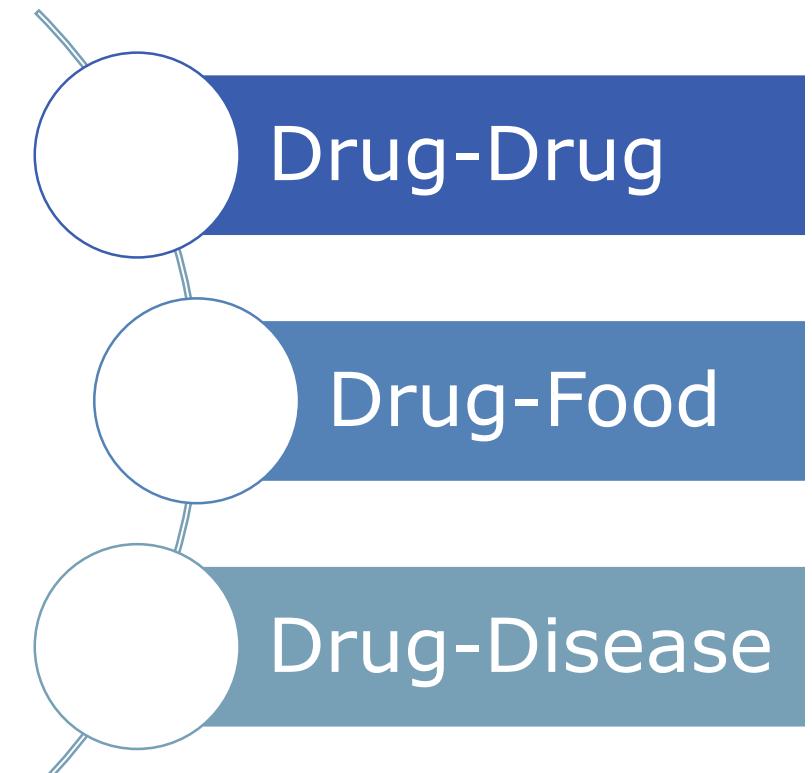
Metabolism

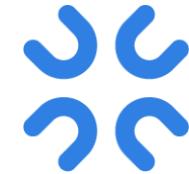


Excretion

# Drug interactions

- What is a Drug Interaction?
  - Pharmacodynamic Interaction:
    - Alters the responsiveness at the site of action
  - Pharmacokinetic Interactions
    - Alters absorption, distribution, binding, metabolism, or excretion of another drug
- Effects can be synergistic, antagonistic, or a completely new effect
- Estimated that 20% of drug adverse effects are related to drug-interactions<sup>2</sup>





# Drug interactions

- **Serotonin Syndrome:** Rare, life-threatening serotonin toxicity related to increased serotonergic activity in the CNS
  - Increased risk with multiple serotonergic medications
  - Sweating, muscle rigidity, tremor, increased body temperature

<b>Common Medications that May Affect Serotonin</b>		
SSRIs (Paxil, Prozac, Zoloft)	Tricyclic Antidepressants (Amitriptyline, Nortriptyline)	St. John's Wort
Illicit Drugs (Cocaine, Ecstasy)	Anti-Parkinson's Drugs	Amphetamines
Metoclopramide	Some Anti-Seizure Drugs	Dextromethorphan
Tramadol	MAOIs	Antipsychotics



# Drug interactions

- **St. John's Wort:**
  - Herbal thought to inhibit reuptake of serotonin, norepinephrine, and dopamine
  - Induction of hepatic metabolism
  - MANY interactions– SSRIs, SNRIs, MAOIs, Benzodiazepines, Warfarin, oral contraceptives, heart medicines, anti-seizure drugs, etc.

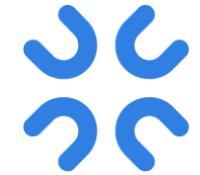


# Drug interactions



- **Opioids and Benzodiazepines (and alcohol)**
  - Common benzodiazepines: Valium (diazepam), Xanax (alprazolam), Ativan (lorazepam), etc.
  - Increased risk for respiratory depression
  - More than 30% of overdoses involving opioids also involve benzodiazepines
- **Monoamine Oxidase Inhibitors (MAOIs)** – Rasagiline, selegiline, etc.
  - Rarely used due to high number of interactions
  - Interact with tyramine-rich food and many other medications





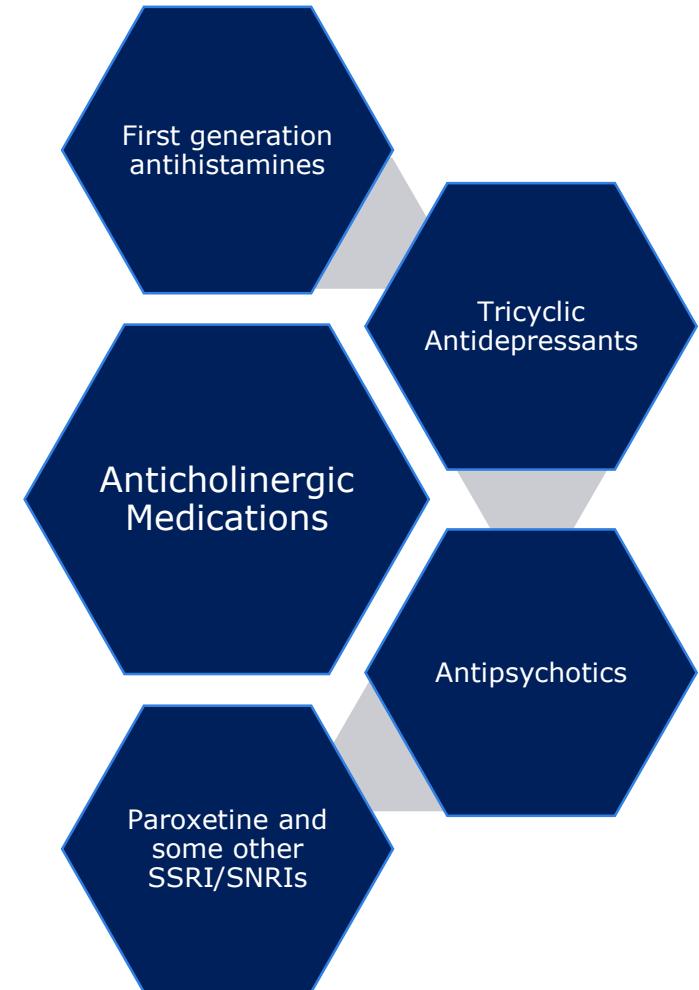
# Drug interactions

- **Alcohol**
  - Bupropion
  - Most anxiety/depression treatment options
  - Sedating medications
- **Grapefruit** - blocks major drug metabolism enzyme and boosts drug effects
  - Valium, Midazolam, Buspirone, Sertraline (Zoloft), Carbamazepine (Tegretol)

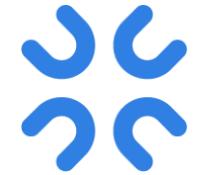


# Adverse effects

- Multiple medications with similar adverse effect profile can potentiate adverse effects
- Anticholinergic Medications:
  - Inhibit binding of acetylcholine to receptors
  - Dizziness, dry mouth, dry eyes, constipation, urinary incontinence
- Falls
  - Dizziness and/or sedation may precipitate falls. Common side effect for most anxiety/depression treatment options
  - Higher risk with anticholinergic medications



# Drug interactions & adverse effects



- Interaction Checkers
- What do I do if I suspect a problem?

UpToDate®

Lexicomp® Drug Interactions

Add items to your list by searching below.

Enter item name

ITEM LIST

Clear List      Analyze

8 Results

Risk Rating	Description	Action
D	AmLODIPine (CYP3A4 Substrates (High risk with Inducers)) St John's Wort	Avoid combination
D	Ortho-Cyclen (28) (CYP3A4 Substrates (High risk with Inducers)) St John's Wort	Consider therapy modification
D	Ortho-Cyclen (28) (Estrogen Derivatives (Contraceptive)) St John's Wort	No action needed
D	Ortho-Cyclen (28) (Progestins (Contraceptive)) St John's Wort	No known interaction
D	Simvastatin AmLODIPine	Monitor therapy
D	Simvastatin (CYP3A4 Substrates (High risk with Inducers)) St John's Wort	Consider therapy modification
D	Simvastatin (HMG-CoA Reductase Inhibitors (Statins)) St John's Wort	No action needed
C	FLUoxetine (Serotonin Modulators) St John's Wort (Serotonin Modulators)	No known interaction

Display complete list of interactions for an individual item by clicking item name.



# Polypharmacy– What can we do about it?

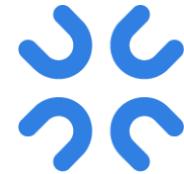
- For Prescribers: If multiple medications are needed, select drugs with different mechanisms of action and side effect profiles
- Reach out to a physician or pharmacist
  - De-prescribing or changes in therapy
  - Comprehensive Medication Management (CMM)
  - Pharmacogenomic testing
- Education
- Encourage member to use just one pharmacy

# Comprehensive Medication Management (CMM)



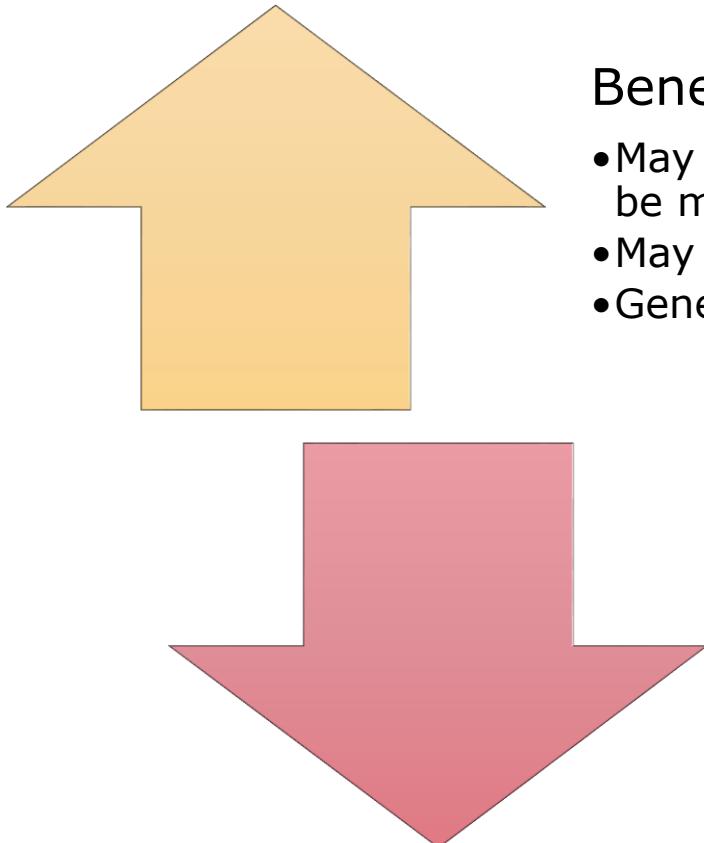
- AKA Medication Therapy Management (MTM)
- Complete Medication Review (CMR) with a pharmacist to go over medications to ensure that they are indicated, safe, effective, and convenient to use
- Some MTM pharmacists work under collaborative practice agreements and can change therapies directly, otherwise, they reach out and collaborate with prescribing provider(s)
- Available in multiple settings: Clinics, Hospitals, Retail Pharmacies, Telephonic medicine, Long-term Care settings, etc.

# UCare CMM coverage



- **Medicare (CMS)**
  - ≥3 chronic health conditions AND/OR
  - ≥8 medications AND/OR
  - Cost of medications ≥\$4,044 per year
- **Medicaid (DHS)**
  - Not eligible for Medicare Part D
  - Taking 1 or more prescription medication
  - 1 or more chronic condition(s)
  - Telephonic, Email, or SNF visits are not covered

# Pharmacogenomic testing



## Benefits

- May be able to determine up-front if a medication will be more effective or more likely to have side effects
- May help guide dosing
- Genes do not change over time

## Limitations

- Not necessarily inclusive of all medications
- Does not preclude possibility of adverse effects or treatment improvements unrelated to genetic influences
- Studies remain somewhat limited
- Can be costly

# Pharmacogenomic testing

- Drug-Gene testing – how your body responds to medications

Antidepressants		
USE AS DIRECTED	USE WITH CAUTION	USE WITH CAUTION AND WITH MORE FREQUENT MONITORING
desvenlafaxine (Pristiq®) selegiline (Emsam®)	citalopram (Celexa®) [4] escitalopram (Lexapro®) [4] sertraline (Zoloft®) [4] trazodone (Desyrel®) [1]	amitriptyline (Elavil®) [6] bupropion (Wellbutrin®) [6] clomipramine (Anafranil®) [6] desipramine (Norpramin®) [6] duloxetine (Cymbalta®) [7] fluoxetine (Prozac®) [6] fluvoxamine (Luvox®) [7] imipramine (Tofranil®) [6] mirtazapine (Remeron®) [3] nortriptyline (Pamelor®) [6] paroxetine (Paxil®) [6] venlafaxine (Effexor®) [6]

Antipsychotics		
USE AS DIRECTED	USE WITH CAUTION	USE WITH CAUTION AND WITH MORE FREQUENT MONITORING
quetiapine (Seroquel®) ziprasidone (Geodon®)	clozapine (Clozaril®) [3] olanzapine (Zyprexa®) [3] perphenazine (Trilafon®) [3] risperidone (Risperdal®) [1]	aripiprazole (Abilify®) [6] haloperidol (Haldol®) [6]

[1]: Serum level may be too high, lower doses may be required.

[2]: Serum level may be too low, higher doses may be required.

[3]: Difficult to predict response because of multiple gene variations.

[4]: Genotype suggests less than optimal response.

[5]: Blood levels may be outside of optimal range.

[6]: Use of this drug is associated with an increased risk of side effects.

[7]: Serum level may be too low in the presence of CYP1A2 inducers. See page three for additional information.

# Medication adherence

- “The degree to which the person’s behavior corresponds with the agreed recommendations from a health provider”
- Poor adherence is associated with increased health care utilization, cost, and decreased quality of life
- Increased risk of mortality and increased risk of hospitalization
- Medication adherence rates in chronic disease range from 20-80%<sup>12</sup>
- Depressed patients are 1.8 times more likely to be non-adherent than non-depressed patients<sup>12</sup>

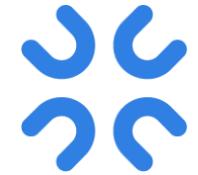
*“Drugs don’t work in patients who don’t take them.”*  
—C. Everett Koop, MD

# Adherence and Star Measures



- **STAR Measures:** CMS' way to evaluate health plans
- Part D Measures
- Adherence rates for diabetes medications, Statin Medication, Anti-hypertensives
- Statin use in persons with diabetes
- 2021:
  - Polypharmacy of Multiple Anticholinergic Medications in Older Adults
  - Polypharmacy Use of Multiple CNS-Active Medications in Older adults

# Factors that relate to adherence



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Poor Health Literacy

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Perceived Risk of Disease

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Understanding Medications

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Language Barriers

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Cultural Beliefs

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Physical Barriers (vision, hearing)

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Housing/Environmental Factors

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Cost of Medications

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Provider-Patient Relationship

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Mental Health

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Complexity of treatment

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Side Effects

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Time to Achieve Therapeutic Effect

# Medication adherence

- **Figure out what the barrier is and tailor adherence attempts to that specific barrier**
- Reduce polypharmacy – prescribing cascade
- 90-day refills or mail order
- Med sync programs
- Bubble Packs
- Pill boxes
- Alarms
- Smart Phone Apps
- Involve Family Members
- Motivational Interviewing



# Medication disposal

- Hennepin County Disposal Sites:  
<https://www.hennepin.us/-/media/hennepinus/residents/recycling/documents/meds-disp-flyer.pdf>
- Ramsey County Disposal Sites:  
<https://www.ramseycounty.us/residents/recycling-waste/collection-sites/medicine-collection>
- Deterra Bags



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