Pharmacists' role in mental health across healthcare settings

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Disclosure

- Ben Chavez has no relevant financial relationships with a commercial interest pertaining to the content of this presentation.

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Objectives

- Identify therapeutic areas in metal health in which pharmacists can make interventions, including counseling opportunities
- Recognize relevancy of drug-drug interactions with psychotropic medications
- Identify opportunities and resources to help patients with mental health concerns

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Use of Antidepressants

- Not just anti "depressants"
- Also clinically useful in anxiety disorders
  - May be even more effective for anxiety!

	NNT / NNH
MDD	10
OCD	6
Non-OCD Anxiety	3
Suicidal Thoughts	143

Bridge et al. JAMA 2007;297:1683-1696.

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Antidepressants and Symptom Response

- Important to talk to patient about what symptoms will actually improve
- Be specific to your patient!
- Depression:
  - Mood, appetite, irritability, sleep, energy, motivation, etc
- Anxiety:
  - Worrying, physical symptoms, panic attacks, sleep, fear of leaving the house, fear of speaking to others, etc.

Response Time

- Within 1st week
  - Improvement in energy, appetite
- 2-4 weeks
  - Improvement in sadness, attention, anhedonia
- 8 weeks or longer
  - Full antidepressant effects

- Sleep can be one of the tougher symptoms to respond

How to Manage Side Effects

- If side effects are not serious/bothersome:
  - Ask patient to wait them out
  - They usually improve in first few weeks
  - Can reduce dose until side effect subsides, then titrate back up
  - Change dosing schedule, if appropriate
  - If necessary, treat with other drug
- If side effect is intolerable or does not go away, change antidepressant
- Re: activation/sedation
  - These can vary widely depending on patient

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Safety Profile of SSRIs

	Fluoxetine (Prozac)	Paroxetine (Paxil)	Sertraline (Zoloft)	Citalopram (Celexa)	Escitalopram (Lexapro)	Fluvoxamine (Luvox)
Half life	**48-72**	21	26	35	27-32	15.6
Adverse effects						
Anticholinergic	0	**1+**	0	0	0	0
Drowsiness	0	**1+**	0	0	0	1+
Insomnia/agitation	**2+**	1+	1+	1+	1+	1+
Orthostatic hypotension	1+	**2+**	1+	1+	1+	1+
QTC prolongation	1+	0 to 1+	0 to 1+	**2+**	1+	0 to 1+
GI side effects	1+	1+	**2+**	1+	1+	1+
Weight gain	1+	**2+**	1+	1+	1+	1+
Sexual dysfunction	3+	4+	3+	3+	3+	3+

Serretti A, Chiesa A. Clin Pharm Ther 2011; 89:142
Wenzel-Seifert K, Wittmann M, Haen E. Dtsch Arztebl Int 2011; 108:687

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Safety Profile of SNRIs

Agents	Venlafaxine (Effexor)	Desvenlafaxine (Pristiq)	Duloxetine (Cymbalta)
Half life	3-7	11	12
Adverse effects			
Anticholinergic	0	0	0
Drowsiness	**1+**	**1+**	0
Insomnia/agitation	2+	2+	2+
Orthostatic hypotension	0	0	0
QTC prolongation	**1+**	0	0
GI toxicity	2+ (IR) 1+ (ER)	2+ (initially) 1+ (after 1 wk)	2+
Weight gain	0	0	0
Sexual dysfunction	3+	3+	3+
Increased blood pressure	ALL; must monitor		

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What About Withdrawal Symptoms?

- Occurs after abrupt discontinuation of drug
- Symptoms:
  - Tingling/numb sensation on skin
  - Tinnitus
  - Vivid dreams
  - Nausea / vomiting
  - Flu-like symptoms*
- More common with short half-life agents
  - Paroxetine, Fluvoxamine, Venlafaxine
- Counsel patients on importance of tapering medications only under supervision

When to Switch or Augment?

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Augment vs Switch

When to Augment?	When to Switch?
- Patient is on maximum tolerated dose and having partial response - Patient has failed multiple monotherapy trials - Switching presents a logistical problem	- Patient is obtaining very minimal or no response - Patient having intolerable side effects - Pill burden / complexity of regimen is a concern - Has only had had one or two trials of antidepressants

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Options for Augmenting

- At least 50% of people will not achieve adequate response with first treatment option
- Second-generation antipsychotics
  - Aripiprazole
  - Quetiapine
  - These have an FDA indication as augmenting agent
- Bupropion
- Buspirone

Aripiprazole - Dosing

- Range: 2-15 mg
- Start at 2-5 mg/day
  - Increase by 5 mg intervals every 1-2 weeks
- One trial suggests if patient does not respond at 2mg in 30-60 days, they may not respond at higher doses

Aripiprazole - Safety

- Don’t forget about risk of metabolic syndrome!
  - This is NOT a dose-dependent side effect
  - Monitor per ADA/APA guideline (see next slide)
- Akathisia also common!
  - Up to 20% incidence
  - Dose-dependent side effect

ADA/APA MONITORING PROTOCOL

	Baseline	4 wks	8 wks	12 wks	Quarterly	Annually	Every 5 yrs
Family History	X					X	
Weight / BMI	X	X	X	X	X		
Waist Circ.	X					X	
Blood Pressure	X			X		X	
Fasting Glucose	X			X		X	
Lipid	X			X			X

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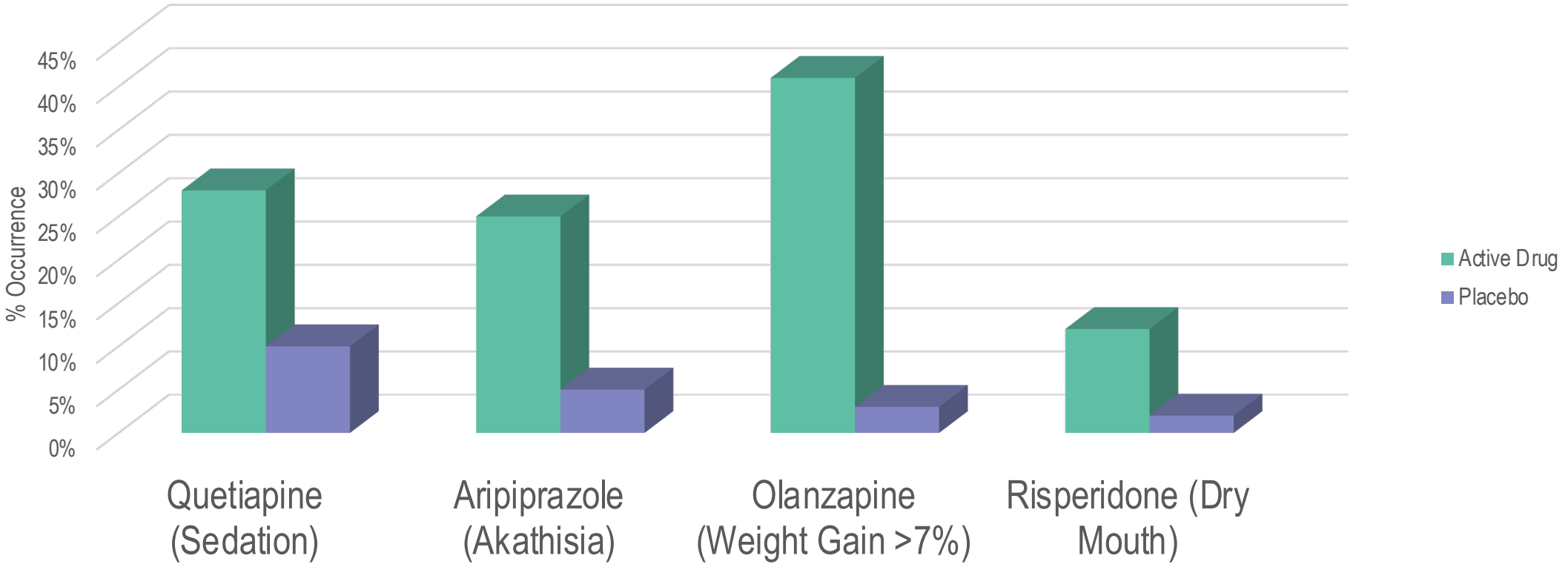
Quetiapine - Dosing

- Range: 150– 300 mg daily
- Start at 50 mg once daily, and titrate by 50 mg as quickly as every 3 days
- Note: only XR formulation is FDA approved as an augmenting agent

Quetiapine - Safety

- Sedation is most common side effects (~22%)
  - Less occurrence with XR formulation
- Higher risk of weight gain than aripiprazole
- Lower risk of extrapyramidal symptoms
- Also has anti-anxiety properties

Incidence of Most Common Side Effect



NNT	9	8	13	6
NNH (DC vs AE)	11/6	38/6	12/3	24/11

Kato M, Chang C. CNS Drugs 2013;27(S1):S11-S19.

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Bupropion

- Off-label use
- Usual Dose: 150-300 mg daily
  - Split as BID for SR formulation
- STAR*D trial showed this to a better augmenting option that buspirone
- Good addition when low energy and sexual dysfunction is a concern

Ehret M. J Pharm Pract 2006;19(6):353-60.

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Buspirone

- Off-label use
- Dose: Start at 10 mg BID, and increase by 10 mg/day every 1-2 weeks, max 60 mg/day.
- Generally well-tolerated
- Good choice if a patient has residual anxiety symptoms

Options for Switching Drugs

- Switch to another drug in same class
  - Particularly if only has tried one SSRI
- Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)
- Bupropion
- Mirtazapine

Drug Interactions!

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QT Prolongation – Citalopram

- FDA issued warning of dose-dependent QT prolongation
  - Doses > 40 mg/day are not recommended for any patients
  - Doses > 20 mg/day not recommended for patients > 60 years old

What about escitalopram?

- Technically, FDA did not issue any recommendations against escitalopram
- British MHRA does recommend a max dose of 10 mg/day in patients > 65 years old

Is this concern real?

- Average QT prolongation with citalopram:
  - 20 mg = 8.5 milliseconds
  - 40 mg = 12.6 milliseconds
  - 60 mg = 18.5 milliseconds
- Average QT prolongation with escitalopram:
  - 10 mg = 11.0 milliseconds
  - 20 mg = 15.7 milliseconds

FDA states that medications that increase QT interval by more than 20 ms show an increase risk of torsades de pointes.
They also state that a clinically relevant change from baseline is at least 30 ms.
For more perspective, sotalol increases QT interval by 25-54 ms from baseline

Hutton LMJ. J Pharm Practice 2017;30(3):353-58.

So when should I be worried?

- In all cases where citalopram has been associated with an increased QT interval or TdP, there was at least one identifiable risk factor
- Risk factors:
  - Female gender - Bradycardia
  - Advanced age - Hypokalemia
  - Hypomagnesemia - Severe medical illness
  - Use of other QT prolonging drugs (or drug interactions)

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SSRIs and QT Prolongation - Conclusion

- If a patient has risk factors, stick to the dosing recommendations if citalopram/escitalopram must be used
  - If patient is starting a new SSRI, and other options are feasible, fluoxetine and paroxetine are safer choices.
- If a patient is psychiatrically stable on citalopram/escitalopram, it may be ok for them to stay on current medication. Assess for risk.

Funk KA. Ann Pharmacother 2013;47(10):1330-41.
Gerlach LB. Am J Geriatr Psych 2017;25(4):407-14.

Patient Case

- 35 year old female has been stable on citalopram 20 mg daily for MDD over the last year
- She goes to her PCP c/o of frequent migraines. She is prescribed sumatriptan 25 mg daily.
- What do we do?

Patient case, cont.

- Patient's citalopram is stopped due to concerns of serotonin syndrome; replaced with bupropion
- Sumatriptan is effective for her migraines, but her depressive symptoms return

More Drug Interactions!

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How likely is serotonin syndrome to occur?

- Bottom line: with most drugs, very unlikely
- With triptans, one study found 2 cases in 14 years and 19,000 patients
- Individual risk with each agent is unknown, however, MAOIs and tramadol seem to have highest risk
  - Cocaine also increases risk significantly

Orlova Y. JAMA Neurol 2018;75(5):566-72.

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So what do we do?

- Counsel patient on signs and symptoms
  - (see next slide)
- Be more mindful when MAOIs or tramadol is involved
- Do not withhold medication, as missing doses of SSRI will increase risk of withdrawal symptoms and possible psychiatric symptom relapse

Symptoms

Severity	Neuromuscular hyperactivity	Altered mental status	Autonomic dysfunction
Mild	Hyperreflexia Tremor Myoclonus	Anxiety Restlessness Insomnia	Diaphoresis Mydriasis Tachycardia
Moderate	Spontaneous or inducible muscle spasms	Agitation	Hypertension (occipital headache) Hyperthermia (< 40° C, < 104° F) Hyperactive bowel sounds Diarrhea, nausea, vomiting
Severe	Rigidity Respiratory failure Tonic-clonic seizure	Coma Delirium Confusion	Severe hyperthermia (≥ 40° C, ≥ 104° F) Dynamic blood pressure

What about tramadol and SSRIs?

- Mechanism: 5-HT and NE reuptake inhibitor, along with weak agonism at mu-opioid receptors

- Significant concerns with increased seizures and serotonin syndrome

Hassamal S. Am J Med 2018;131:1382e1-e6.

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Tramadol and Serotonin Syndrome

- 968 cases reported in 10 year period (3% of all ADRs reported for tramadol)
  - 98 resulted in mortality
  - Most reports were in combination with antidepressants
  - Fluoxetine and paroxetine may have higher risk due to CYP2D6 inhibition

Tramadol and seizures

- ~2000 cases reported over 10 years (7% of all ADRs reported for tramadol

- Risk is great with higher doses of tramadol, when combined with other 5-HT drugs, and 2D6 inhibitors

Tramadol, seizures, and characteristics

- 50-75% of tramadol-seizures occur in patients taking antidepressants or 2D6 inhibitors
- Patient abusing tramadol are 5x more likely to have a seizure
  - Most occur in younger patients abusing tramadol at doses > 1000 mg/day
- Chronic tramadol users are 4x more likely to have a seizure

Tramadol: Bottom Line

- Avoid in patients taking antidepressants or 2D6 inhibitors
- Avoid in patients with any history, or risk, of seizures
- If tramadol must be used, use lowest possible doses for short period of time
  - And educate on s/s of serotonin syndrome

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Resources for Pharmacists!

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What can a pharmacist do for a person in a mental health crisis?

- Be empathic
- Listen to their concerns
- Do not dismiss them as “crazy”
- Offer to help by being a liaison to their PCP
- Offer resources for them to call

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Mental Health Resources

- Available statewide 24/7/365
- Free, confidential, and immediate professional help to anyone who needs it
- Provide immediate support, information, referrals, and connections
- The person in need, or someone else (ie. pharmacist) can make the call
- Have walk-in centers available and mobile care
- www.coloradocrisisservices.org

COLORADO CRISIS SERVICES | 844-493-TALK (8255) OR TEXT TALK TO 38255

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Mental Health Resources

- Place where students, teachers, parents, and community members can report safety concerns
  - Good option for school safety issues, bullying, suicidal thoughts, gun safety, etc.
- People can call, use website, or app
- Completely anonymous

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Mental Health Resources

mantherapy.org

Therapy. The way a man does it.

- Web-bases resources tailored for men
- Also offer resources to connect people over the phone or chat online
- Has veteran crisis line as well

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Mental Health First Aid - Colorado

- www.mhfaco.org
- Offer classes across the state – check out website!
  - Majority are no cost, some are $20
- Classes teach signs and symptoms of mental health, what do in emergencies, and where to get help

MENTAL HEALTH FIRST AID COLORADO
Be a lifeline.

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Questions?

Thank you!

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