Psychiatry in Primary Care: What is the Role of Pharmacist?

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Salud

Disclosure Statement

- No financial disclosures

Objectives

- Identify scenarios in which augmenting antidepressant treatment would be safe and appropriate.
- Recommend a treatment plan or medication regimen for a patient presenting with Bipolar Depression.
- Compare and contrast pharmacological options available for the treatment of bipolar depression, as well as treatment options for augmenting treatment of Major Depressive Disorder.

Psychiatry in Primary Care

- Primary care providers (PCPs) are in an ideal setting to capture a vast amount of people with mental health disorder
  - 50% of people will experience a mental disorder in their lifetime
  - Majority of those will see their PCP at one point for some reason
- There is often a stigma to seeing a psychiatrist, but not in seeing a PCP
- Anxiety disorders, mood disorders, and ADHD are the most common mental health diagnoses in primary care

Sansone R, Sansone L. Psychiatry (Edgmont). 2010 Dec; 7(12): 16–19.

How do PCPs manage psychiatric care?

- PCPs only identify about 50% of people who meet a diagnosis
- Only half of those recognized receive treatment
- Only half of those treated receive appropriate treatment
- There is not one solution to this problem, however, pharmacists can play a role in the solution

Wittchen H. Dialogues Clin Neurosci. 2003 Jun; 5(2): 115–128

Outline for Today

- Major Depressive Disorder
  - First-line
  - Second-line (Augment vs Switch)

- Bipolar Depression
  - First-line treatment in primary care

First, some questions…

- Which setting do you work in?
  - A. Inpatient
  - B. Community
  - C. Ambulatory Care
  - D. Other

Which antidepressant has the best tolerability?

- A. Escitalopram
- B. Fluoxetine
- C. Duloxetine
- D. Paroxetine

Which of these has an FDA indication as an augmenting agent for MDD?

- A. Bupropion
- B. Buspirone
- C. Quetiapine
- D. Aripiprazole

Patient Case

- Mary is a 34 year old female who comes to see her PCP for symptoms of depressed mood, low energy, no desire to do any activities other than what she absolutely must do, and becomes tearful easily with minimal stress. She also reports being very irritable with her husband and two young children.
- She reports some mild depressive symptoms in her 20s, but they did not interfere with her life like they are currently.
- PMH: non-contributory
- FH: Mom has depression and diabetes; dad had a recent MI
- Current medications: Ethinyl estradiol/nortethindrone 1/35

What are some questions for Mary?

Questions for Mary (non-inclusive)

- What have you taken before?
  - What happened when you took that medicine?
- Do you have any thoughts of hurting yourself?
- When did this start?
- Are there any side effects that are more undesirable than others?

What is the first step we take with Mary?

First Line Agents

- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Fluoxetine
  - Sertraline
  - Paroxetine
  - Citalopram
  - Escitalopram

Drug name	Pros	Cons	Target Dose (or usual minimum effective dose)
Fluoxetine	Long half-life		20 mg
Sertraline	Good for co-morbid anxiety; slight DA reuptake;	GI side effects	50 mg
Paroxetine	Good for anxiety; slightly more seating	Short half-life Anticholinergic side effects	20 mg
Citalopram	Well tolerated	QT prolongation warning in older adults	20 mg
Escitalopram	Best tolerated		10 mg

Safety Profile of SSRIs

	Fluoxetine (Prozac)	Paroxetine (Paxil)	Sertraline (Zoloft)	Citalopram (Celexa)	Escitalopram (Lexapro)	Fluvoxamine (Luvox)
Generic available	Y	Y	Y	Y	Y	Y
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+

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

Starting SSRIs

- Pick SSRI based on symptoms and tolerability
- Start SSRI at half the target dose
- Titrate to target dose after 1-2 weeks
  - Only exception is escitalopram, where you could start at 10 mg daily
  - This helps increase tolerability

Mary, one year later

- Mary has been on escitalopram 20 mg once daily for the past year. She feels her symptoms have improved, but she does not feel quite herself. While she no longer becomes tearful easily, or rarely becomes as irritable as she used to, she still has very low energy throughout the day and this is impacting her work. She also feels like she has trouble falling asleep most nights, and therefore is not getting restful sleep.

Do we switch drugs or augment?

Why Augment vs Switching?

- Augment when:
  - A patient is on a maximum dose and having partial response
  - Patient has failed multiple monotherapy trials
  - Switching presents a logistical problem (such as tapering)
- Switch when:
  - Pill burden / complexity of regimen is a concern
  - Not obtaining any response (or minimal)
  - Having intolerable side effects to antidepressant

Augmentation Options

- 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 2 mg 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 Guidelines
Risk of Metabolic Abnormalities

Drug	Weight Gain	DM risk	↑ Lipids
Clozapine	+++	++	++
Olanzapine	+++	++	++
Risperidone	++	+	+
Quetiapine	++	+	+
Ziprasidone	+/-	+/-	+/-
Aripiprazole	+/-	+/-	+/-
Lurasidone	-	-	-

ADA/APA. Diabetes Care 2004 Feb; 27(2): 596-601

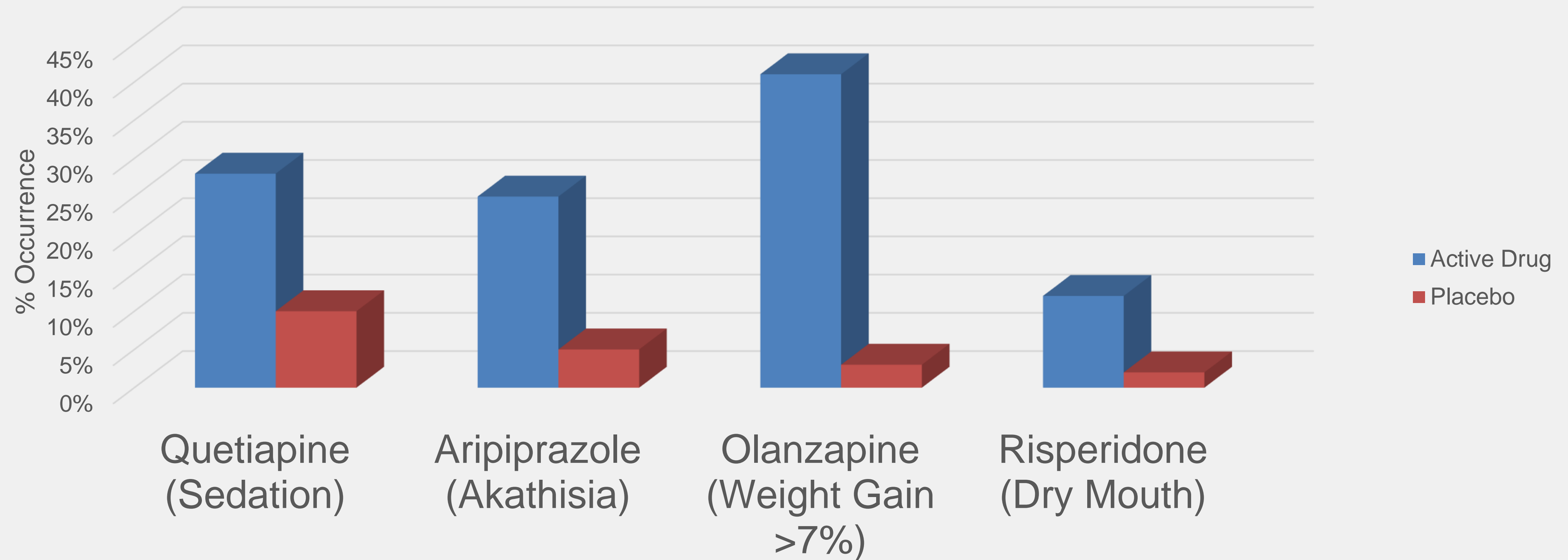
Quetiapine - Dosing

- 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

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

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.

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.

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

Safety Profile of SNRIs

Agents	Venlafaxine (Effexor)	Desvenlafaxine (Pristiq)	Duloxetine (Cymbalta)
Generic	Y	**N**	Y
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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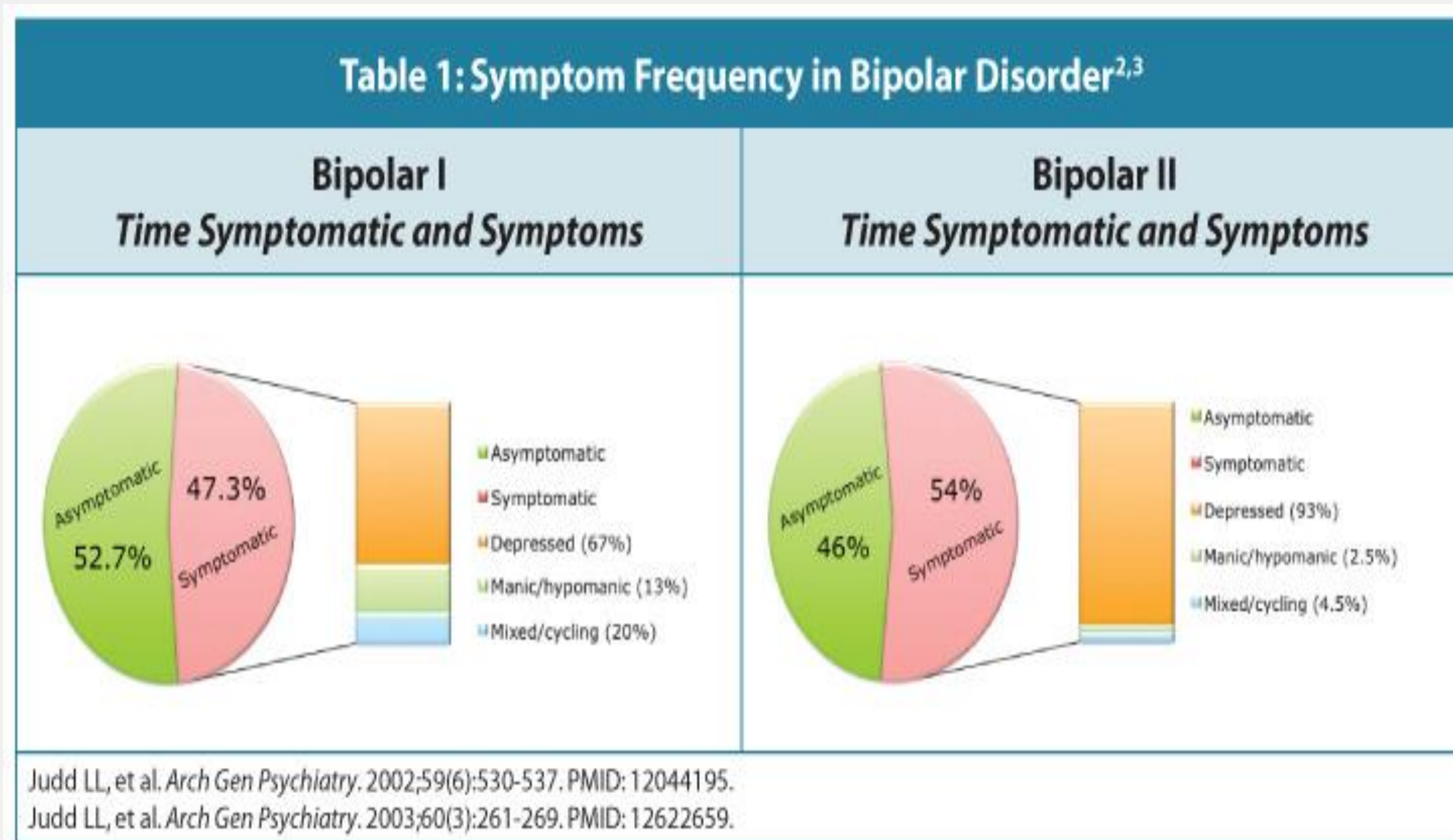
Treatment of Bipolar Depression

Bipolar Depression vs Unipolar Depression

- How do we tell the difference?
- Assess for depression symptoms (SIGECAPS)
- Ask about prior manic symptoms
  - Ask in multiple ways!
  - Have you had periods where you felt you didn't need sleep?
  - Have you had periods where people said you were reckless or impulsive?
  - Have you ever been hospitalized for a psychiatric reason?
- Patient may not know!
- Mood Disorder Questionnaire – good simple screening tool!

Symptom Distribution



TL:DR Relatively small amount of time is spent in mania!

Depression Symptoms

- Sleep, can be insomnia or hypersomnia
- Interest, loss of
- Guilt, feeling of
- Energy, lack of
- Concentration, problems with
- Appetite, usually decrease, but can be increase
- Psychomotor retardation or agitation
- Suicide

Treatment Options – Bipolar Depression

- Lamotrigine
- Second-Generation Antipsychotics
  - Quetiapine
  - Lurasidone
- Antidepressants
- Lithium
  - Role in primary care is limited
- Guidelines by CANMAT and ISBD 2018

Yatham L et al. Bipolar Disorders 2018;20:97-170.

Lamotrigine

- Positive data for bipolar depression and bipolar maintenance
- Start dose at 25 mg daily x 2 weeks
  - Target dose: 50 mg – 200 mg daily
- Must follow titration schedule due to risk of Stephens-Johnson Syndrome
  - If patient misses more than 5 days, must re-start titration schedule

Lamotrigine – Clinical Pearls

- Slow titration may lead to a delay in response
  - Not ideal for patients who require rapid response
- Well-tolerated
  - Weight neutral
  - Nausea is only ADR > 10% (7-14%)
- Ideal for primary care
  - No monitoring required

SGA and Bipolar FDA Indications

	Acute Mania	Bipolar Depression	Bipolar Maintenance
Olanzapine	√		√
Risperidone	√		* LAI Only
Quetiapine	√	√	√
Ziprasidone	√		√
Aripiprazole	√		√
Asenapine	√		
Lurasidone		√	
OLZ/FLX		√	

SGAs in Bipolar Depression

- Quetiapine:
  - Target dose: 300 mg/daily
  - Both IR and XR are FDA approved
- Lurasidone:
  - Initial dose: 20 mg once daily
  - Maximum effective dose: 60 mg once daily
  - Must be taken with >350 calorie meal
  - Akathisia rates ~20% and dose-dependent

SGAs – Clinical Pearls

- Preferable when rapid response is needed
  - Some improvement may be seen as early as one week
- Will also address any psychotic symptoms that may be present
- Quetiapine also has anti-anxiety properties
- Be mindful of weight gain and worsening diabetes with all SGAs

What about antidepressants?

What did we all learn to fear about them?

What about using antidepressants?

- Common to see used during depression or maintenance phase of bipolar disorder
  - As high as 40% in some studies!
  - Could be due to poor tolerability of mood stabilizers and old methods of practice
- More than likely patient will have minimal benefit and experience side effects from SSRIs
  - However, some subset of patients may have benefit

Liu B et al. J Affect Dis 2017 Dec 1;223:41-48.

What about switching to mania?

- Actual risk is low!
  - 4-8% depending on which trial you examine
  - No differences compared to placebo switch rate
- Patients can experience a switch regardless of AD treatment
- Risk may be higher with SNRIs and TCAs (10%-15%)
  - Risk may be lowest with bupropion

Sidoor MM. J Clin Psychiatry. 2011;72(2):156.
Gijsman HJ et al. Am J Psychiatry. 2004;161(9):1537.

Antidepressants Role in Bipolar Depression

- If used, should be used in conjunction with mood stabilizer
- May have a larger role in patients with comorbid anxiety
- Or patients with prior response to antidepressant

Conclusion

- Pharmacists can have an impact in psychiatric care in primary care
- Major depressive disorder and bipolar depression are common presentations in primary care
- Think about appropriate times to switch vs augment in MDD
- Bipolar depression can be treated in primary care!
- Don’t be afraid of SGAs!

Questions?

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