Mind Matters ECHO

Effective Treatments for Depression: Pharmacology

Audience Q&A

Mind Matters ECHO is a monthly learning collaborative which pairs case-based discussion with expert didactics. Below are questions from the audience from our July 2022 meeting which we did not have time to address during the meeting. Answers were provided by Dr. Katie Angelova, MD, Assistant Professor of Psychiatry, Consultation-Liaison Psychiatry Division, Icahn School of Medicine at Mount Sinai.

To watch the meeting recording or view the meeting slides, please visit our Mind Matters webpage.

Does Prozac worsen anxiety due to being more activating?

Prozac, and many other SSRIs, may worsen anxiety in the first few weeks of use. This has to do with a specific subset of serotonin receptors (2C) – there was a recent study published in Nature to further deduce how this happens, but there are still some gaps in understanding of the exact mechanism.

Which are preferred agents for patients with overlapping depression and anxiety? Any need for adjustment if patient reports more depression than anxiety, or vice versa?

Most SSRIs and SNRIs are used for depression and anxiety. Paxil, Effexor, Lexapro are commonly used. Below is a table of FDA approved medications.

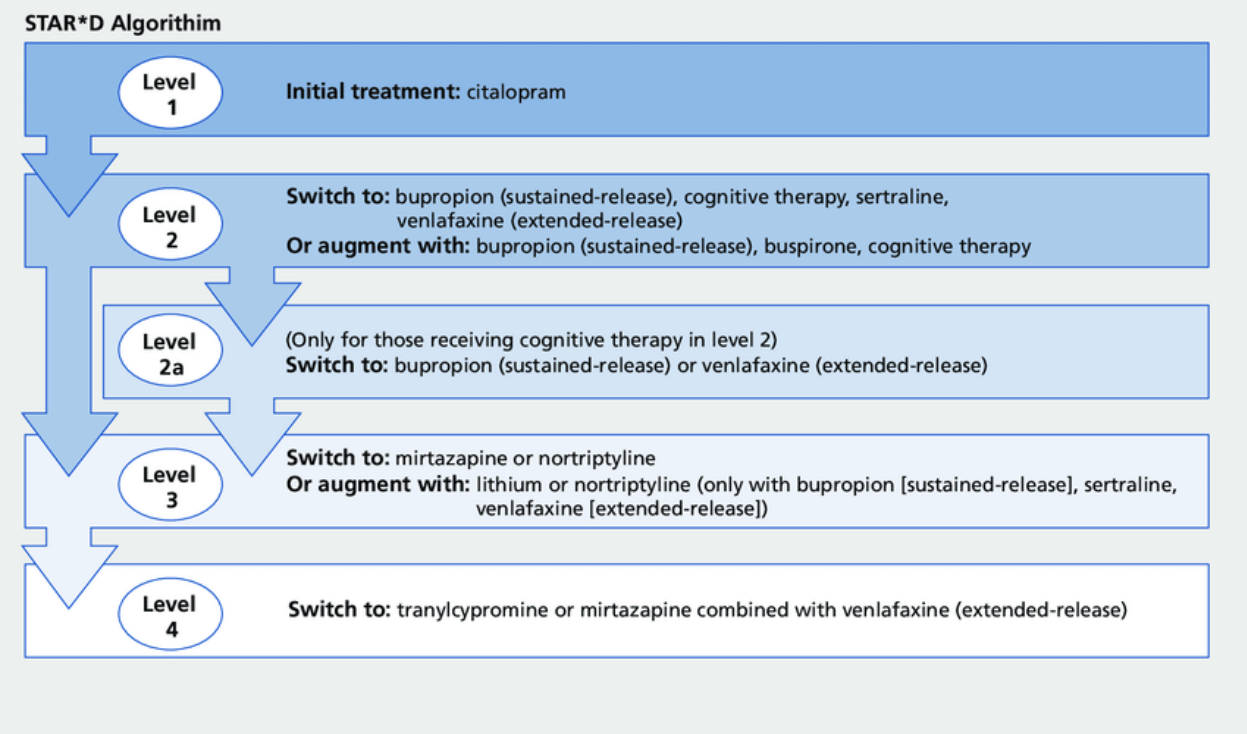
Medication class	Mechanism of action	FDA approvals for anxiety disorder	Off-label uses	Therapeutic dose ranges (mg/day)
SSRIs:				
Fluoxetine	Selective 5-HT reuptake inhibitor (20)	PD	GAD, SAD	20–60
Sertraline		PD, SAD	GAD	50–200
Citalopram		None	GAD, PD, SAD	20–40
Escitalopram		GAD	PD, SAD	10–20
Paroxetine		PD, SAD, GAD	None	20–60
Paroxetine ER		PD, SAD	GAD	27–75
Fluvoxamine		None	GAD, PD, SAD	100–300
SNRIs:				
Duloxetine	5-HT, NE (and DA) reuptake inhibitor (17)	GAD	PD, SAD	30–60
Venlafaxine (XR)		GAD	PD, SAD	75–300
Desvenlafaxine		None	GAD, PD, SAD	50–100
TCAs:				
Clomipramine	NE and 5-HT reuptake inhibitor (20)	None	GAD, PD, SAD	100–250
Imipramine		None	GAD, PD, SAD	100–300
Desipramine		None	GAD, PD, SAD	100–200
Nortriptyline		None	GAD, PD, SAD	50–150
MAOIs:				
Phenelzine	MAO inhibitor (21)	None	GAD, PD, SAD	30–90
Mixed antidepressants:				
Mirtazapine	5-HT_2, 5-HT_3, α_2, H_1 antagonist (27)	None	Anxiety, GAD, PD, SAD	15–45
GABAergic drugs:				
Pregabalin	Unclear, may modulate Ca channels (51)	None	GAD, SAD	150–600
Gabapentin		None	GAD, SAD, PD	600–2,400
Benzodiazepines:				
Clonazepam	GABA-A agonist (44)	PD	Anxiety, GAD, PD, SAD	1–2
Alprazolam		Anxiety, PD	GAD, PD, SAD	1–4
Lorazepam		Anxiety	GAD, PD, SAD	2–6
Chlordiazepoxide		Anxiety	GAD, PD, SAD	20–100
Oxazepam		Anxiety	GAD, PD, SAD	30–60
Antipsychotics:				
Trifluoperazine	D_2 antagonist (84)	Anxiety	GAD, PD, SAD	2–6
Olanzapine	D_2, 5-HT_2 H_1 antagonist (85)	None	Anxiety, GAD	5–15
Quetiapine	D_2, 5-HT_2 H_1 antagonist (85)	None	Anxiety, GAD	50–300
Beta-blockers:				
Propranolol	β-1, β-2 antagonist (77)	None	Anxiety, PD, SAD	60–120
Antihistamines:				
Hydroxyzine	H_1 antagonist (76)	Anxiety	GAD, PD, SAD	25–100
Other anxiolytics:				
Buspirone	5-HT_{1A} partial agonist (22)	Anxiety	GAD	15–60

Key: 5-HT, Serotonin; AGP, Agoraphobia; DA, Dopamine; D_2, dopamine-2 receptor; ER, XR, Extended Release; FDA, Food and Drug Administration; GAD, Generalized Anxiety Disorder; GABA, Gamma Aminobutyric Acid; H_1, Histamine 1 receptor; MAO, Monoamine Oxidase; MAOI, Monoamine Oxidase Inhibitors; NE, Norepinephrine; PD, Panic Disorder; SSRI, Selective Serotonin Reuptake Inhibitor; SNRI, Serotonin Norepinephrine Reuptake Inhibitor; SAD, Social Anxiety Disorder; TCA, Tricyclic Antidepressants.

Instead of switching agents, when do you consider adding a second agent in a nonresponder?

In terms of switching versus using an adjunct, there is no hard rule, but generally, if there is partial response to the agent the patient is already on, but a few remaining symptoms linger (for example, depression improved but sleep remains poor), I may add

an agent to target those specific symptoms. If side effects outweigh benefits on a particular agent, I may prefer to switch. The Star*D study made some general suggestions (see below).



How often do SSRIs start a manic episode?

There have been very few conclusive studies regarding the risk for "switching" to mania on antidepressant. According to a literature review by Dr. Goldberg, "antidepressant induced manias have been reported with all major antidepressant classes in a subgroup of 20-40% of bipolar patients." With that said, bipolarity is a spectrum, there are many confounding factors, including what other medications patients are on, and the "switch" is often not as dramatic as one expects.

What do you think of genetic testing through Genomind? Do you use that avenue when having trouble finding a medication?

I have found Genetic testing with Genomind helpful in patients who you suspect are not metabolizing certain medications as usual (need much higher or much lower doses).

The testing sheds light on CYP450 enzymes and other metabolism factors, but does not replace clinical judgment in selecting an agent.

Have you seen any differences between brand and generic medications?

Regarding brand vs generic, studies will say there is no difference in clinical outcomes, but patients have repeatedly experienced decompensation following a switch from brand to generic in my experience and anecdotal evidence. As a matter of fact, a significant difference is allowed in the “inactive ingredients” between the two. I personally usually start with generic to avoid later issues.