

HIV & The Treatment of Depression III: Antidepressant Selection Part 2

Samuel Jackson, MD (he/him)

Acting Assistant Professor

University of Washington

Department of Psychiatry and Behavioral Science

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I have no conflicts of interest or relationships to disclose

Disclaimer

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Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.



To Learn More:

<https://www.cdc.gov/minorityhealth/racism-disparities>

Objectives

- List the first line FDA approved medications for major depressive disorder
- Discuss relevant drug-drug interactions between common antidepressants and antiretroviral drugs

First Line Antidepressant Agents

SSRIs

- Fluoxetine
- Sertraline
- Paroxetine
- Fluvoxamine
- Escitalopram
- Citalopram

SNRIs

- Venlafaxine
- Desvenlafaxine
- Duloxetine
- Levomilnacipran

Atypicals

- Bupropion
- Mirtazapine
- Buspirone
- Vortioxetine
- Vilazodone

Bupropion

- Wellbutrin[®], Zyban[®], Forfivo[®]
- Dosing Formulation:
IR (TID dosing), SR (BID dosing), XL (daily dosing)
- Dosing Range (XL): 150mg, 300mg, 450mg
- Can be utilized alone or as an augmentation agent
- Can offset the sexual side effect of an SSRI/SNRI
- Targets
 - Atypical Depression
 - ADHD
 - Stimulant Use Disorder
 - Smoking Cessation
 - Weight Loss
 - SSRI/SNRI-induced sexual dysfunction
- Cons
 - Can cause increased anxiety
 - Can cause insomnia
 - Lowers the seizure threshold (IR>SR>XL)
 - Contraindicated in those with h/o seizure, eating disorders, and AUD (if h/o DTs/complicated w/d)
- Pearls
 - SR dosing has long enough t_{1/2} to support daily dosing in augmentation
 - Substituted cathinone which means it is a true stimulant and a relative of the “bath salts”
 - Abusable, can be crushed and snorted
 - Cathinones have a significant risk of lowering seizure threshold and leading to status epilepticus in overdose setting
 - Overdose can be fatal

Bupropion Interactions with Antiretroviral Drugs

- Bupropion is a 2B6 substrate and strong 2D6 inhibitor
- Ritonavir, Lopinavir, Nevirapine, and Efavirenz can all decrease plasma concentration of Bupropion by 50%
 - Dose increases may be required, but still important not to exceed 450mg total daily dose

Mirtazapine

- Remeron®
- Dosing Range: 7.5mg to 45mg; doses up to 60mg to 90mg may be considered
- 7.5mg and 15mg are generally more sedating than doses above 22.5mg; however, it is difficult to predict if 7.5mg will be more sedating than 15mg or vice-versa
- Multiple receptor targets:
 - H1 antagonist – sedation and appetite stimulation
 - 5HT2A – antidepressant effect
 - 5HT2C antagonist – antidepressant effect & weight gain
 - 5HT3 antagonist – antiemetic
 - Alpha-2 antagonist – boosts serotonin and norepinephrine release

Mirtazapine

- **Pros**

- Can be a useful agent for helping medically ill individuals with multi-modal action
 - Think those with hospital insomnia, failure to thrive, chronic nausea, cancer, AIDS
- Few drug-drug interactions
- Oral disintegrating tablet formulation available
- Alpha-2 antagonist activity essentially supercharges SSRIs/SNRIs and making this an ideal augmentation agent for other antidepressants
 - Venlafaxine + Mirtazapine combination may be as effective as tranylcypromine but with less side effects
- Antidepressant least likely to induce hyponatremia
- Can be useful in helping with Cannabis Use Disorder and Stimulant Use Disorder

- **Cons**

- Can be overly sedating with hangover effect possible
 - Mitigate by pushing dose to 30mg
- Weight gain limits use
- Weight gain is more problematic in younger and less so in older patients
 - Up to 15lbs may be common
 - No direct insulin resistance, just increased caloric intake
- May not be as effective as other antidepressants for severe depression in monotherapy

Mirtazapine Interactions with Antiretroviral Drugs

- Likely minimal, though may compound some neuropsychiatric effects of Efavirenz such as ataxia and vivid dreams

Buspirone

- Buspar[®]
- Dosing Range
 - 10mg TID to 20mg TID, OR
 - 15mg BID to 30mg BID
- Uses
 - For generalized anxiety disorder, it may be used as monotherapy and help with symptoms faster than an SSRI; however, it is not a PRN medication
 - Shines as an augmentation agent to other antidepressants (especially 2D6 inhibitors which decrease plasma clearance of Buspirone)
 - Boosts the effect of the antidepressant
 - Can offset sexual side effects of SSRIs/SNRIs
- Cons
 - Short t_{1/2} (2-3hrs) makes dosing adherence problematic
 - TID dosing is ideal and should be utilized in monotherapy
 - Active metabolite has a t_{1/2} of about 6hrs, which supports BID dosing if using it as an augmentation agent
 - Dizziness
 - Sedation

Buspirone Interactions with Antiretroviral Drugs

- Buspirone is a 3A4 substrate
- Boosted regimens may increase plasma concentrations of Buspirone
- This could be a good thing given the short t_{1/2}

Trazodone

- Desyrel[®]
- Dosing Range
 - Insomnia: 25mg – 200mg
 - Depression: 300mg-600mg
- Uses
 - Mainly used as a soporific agent, as better antidepressants exist
 - Can boost the antidepressant effects of other antidepressant agents
- Cons
 - Hangover effect: sedation, ataxia possible
 - Priapism
 - Penile and Clitoral possible
 - Orthostatic hypotension
 - Serotonergic agent: Serotonin Syndrome possible

Trazodone Interactions with Antiretroviral Drugs

- Trazodone is a 3A4 and 2D6 substrate
- Increased sedation, fatigue, hypotension, and syncope reported when co-administered with Ritonavir and Cobicistat
- Use with Saquinavir is not recommended given risk of cardiac arrhythmia

Newer Antidepressants

Vortioxetine (Trintellix)

- Dosing Range: 5mg to 20mg
- Pros
 - May have less sexual side effects than SSRIs at low doses
 - Pro-cognitive, can increase focus and concentration
 - Somewhat activating
- Cons
 - \$\$\$
 - Not very good for anxiety
 - Significant nausea as side effect

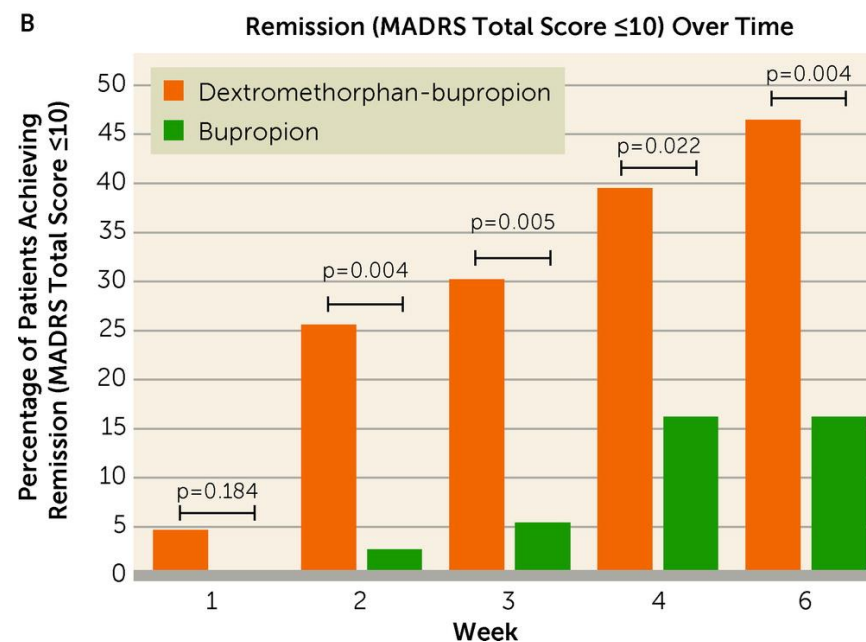
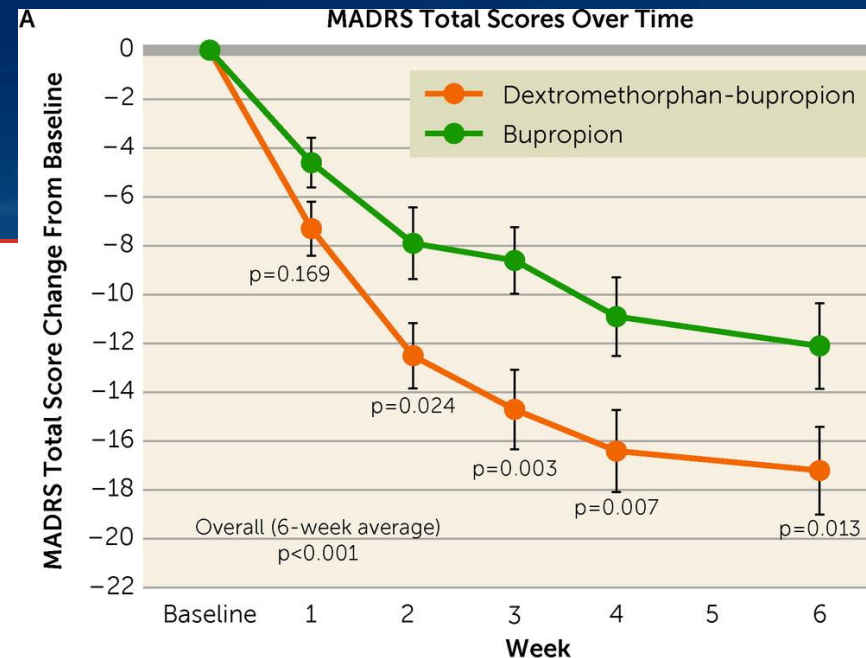
Vilazodone (Viibryd)

- Dosing Range: 10mg to 40mg
- Pros
 - May have less sexual side effects than SSRIs at low doses
 - Maybe better for anxiety than Vortioxetine
- Cons
 - \$\$\$
 - Must be taken with food
 - Can cause nausea (less so than Vortioxetine)

Newer Antidepressants

Bupropion-Dextromethorphan (Auvelity)

- Typical Dose: Dextromethorphan 45 mg/Bupropion 105 mg twice daily
 - Start at once daily in the morning then increase to BID
- Pearls
 - Mixed activity of both Bupropion and Dextromethorphan results in rapid reduction in depressive symptoms
 - Not associated with psychotomimetic effects
- Cons
 - \$\$\$ - Approved 2022
 - Dizziness, nausea, dry mouth, decreased appetite, and anxiety



Newer Antidepressants Interactions with Antiretroviral Drugs

- Vortioxetine & Vilazodone
 - No significant interactions expected
- Bupropion/Dextromethorphan
 - Protease Inhibitors will decrease reduction of Bupropion by inducing 2B6

Questions?

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