THIS IS WHY with Dr. Busti

ANTIDEPRESSANTS: SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)

BASIC DRUG CLASS SUMMARY

Drugs	Common Indications & Uses	Targeted Neurotransmitter	Mechanism of Action	Common Side Effects	Clinical Pearls
Citalopram (Celexa) **Escitalopram** (Lexapro) **Fluoxetine** (Prozac) **Fluvoxamine** (Luvox) **Paroxetine** (Paxil) **Sertraline** (Zoloft)	▪ Bipolar depression (augmentation) ▪ Bulimia nervosa ▪ Generalized anxiety disorder ▪ Major depressive disorder ▪ Obsessive-compulsive disorder ▪ Panic disorder ▪ Post-traumatic stress disorder ▪ Premenstrual dysphoric disorder ▪ Social anxiety disorder ▪ Treatment-resistant depression ▪ Vasomotor symptoms of menopause	5-HT (Serotonin) **Other Targets** Cardiac Nav1.5 (VGSC) & Kv11.1 (hERG K+ channels (only Citalopram & Escitalopram) Sigma-1 (Sertraline) Muscarinic-1 (M1) (Paroxetine) NE reuptake inhibition (Fluoxetine)	Selective inhibition of the reuptake of serotonin (5-HT) by the 5-HT transporter, prolonging serotonergic neurotransmission	▪ GI side effects (N/V especially in the acute phase of starting the SSRI) & insomnia (also greater with sertraline) ▪ Sexual dysfunction (the most common side effect, which includes decreased libido, delayed or inhibited ejaculation) ▪ SSRIs have been associated with SIADH and hyponatremia, especially in geriatric patients (at rates of 1% to 32%) ▪ Concentration-dependent QT prolongation with citalopram & escitalopram. ▪ SSRIs (paroxetine historical) have been linked with Persistent Pulmonary Hypertension of the Newborn (PPHN) if used during 2nd half of pregnancy.	▪ SSRIs will take about 6-8 weeks for the full effect of that drug & dose. ▪ Rule out the presence of bipolar disorder before starting (may need a mood stabilizer first) ▪ Sertraline is considered the preferred SSRI in pregnancy ▪ Fluoxetine has the longest half-life (4 to 6 days). Missing a dose or abrupt discontinuation can allow for some forgiveness. ▪ Paroxetine may cause more sedation & weight gain. ▪ Escitalopram is the S-enantiomer (active form) of citalopram, which is both the R- & S-enantiomer. ▪ Fluoxetine and paroxetine are strong inhibitors of CYP2D6 and are associated with relevant DDI. ▪ If used for anxiety, start at lower doses and titrate slowly to avoid worsening anxiety. ▪ Citalopram 20 mg = escitalopram 10 mg = fluoxetine 20 mg = fluvoxamine 75 mg = paroxetine 20mg = sertraline 50 mg

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ANTIDEPRESSANTS
GENERAL CLINICAL KNOWLEDGE

Medication Class	Efficacy (OR)*	Side effects	Cost	Notes
Selective Serotonin Reuptake Inhibitors (SSRIs)	1.52-1.75	Mild	$	Considered most tolerable class & safest (except in overdoses with citalopram/escitalopram)
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)	1.49-1.85	Moderate	$$	Additional treatment effects for pain, & energy
Atypical Antidepressants				
Mirtazapine	1.89	Mild	$	Helps with sleep and appetite
Bupropion	-	Moderate	$$	Helps with fatigue and is an alternative to SSRI-induced sexual dysfunction. Higher risk of seizures in overdose.
Vortioxetine	1.66	Moderate	$$$	May help with neuropsychological performance
Vilazodone	-	Mild	$$$	Less sexual side effects
Tricyclic Antidepressants (TCAs)	1.49-2.13	High	$	Helps with pain (including migraine prevention), insomnia
Monoamine Oxidase Inhibitors (MAOIs)	-	High	$-$$	Reserved/last line; high efficacy but side effects and drug-food interactions limit use

*Efficacy based on Cipriani A et al. Lancet 2018;391:1357-66. The summary represents the editor's best effort to compile information from reputable sources of information and reported clinical trial data. It is also meant to be for educational purposes only and is not intended to replace medical decision-making or clinical judgment.

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SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI) ANTIDEPRESSANTS

OVERVIEW OF SIDE EFFECTS

Drugs	Anticholinergic Effects	GI Effects	Hypotension	Insomnia & Agitation	Sedation	Sexual Dysfunction	Weight Gain	Other
Citalopram (Celexa)	-	+	+	+	+	++/+++	+	▪ Higher risk of dose-dependent QT prolongation ▪ Requires a lower max dose in geriatric patients, those with hepatic impairment, or poor 2C19 metabolizers
Escitalopram (Lexapro)	-	+	+	+	+	++/+++	+	▪ S-enantiomer of citalopram ▪ Few side effects, except for dose-dependent QT prolongation
Fluoxetine (Prozac)	-	+	+	++	-	++/+++	-	▪ Most prolonged half-life; consider in those who forget to take doses or have limited adherence ▪ Strong inhibitor of CYP2D6 and risk of drug interactions
Fluvoxamine (Luvox)	-	+	+	+	+	++/+++	+	▪ Most drug-drug interactions in SSRI class which limit use
Paroxetine (Paxil)	+	+	++	+	++	+++	++	▪ Strong inhibitor of CYP2D6 and risk of drug interactions ▪ Some evidence to support vasomotor symptoms of menopause, but most don't tolerate weight gain, sedation, & constipation
Sertraline (Zoloft)	-	++	+	++	+	++/+++	+	▪ Best documented cardiovascular safety ▪ Preferred agent for pregnant patients

The summary represents the editor's best effort to compile information from reputable sources of information and reported clinical trial data. It is also meant to be for educational purposes only and is not intended to replace medical decision-making or clinical judgment. Mann JJ. N Engl J Med 2005.

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