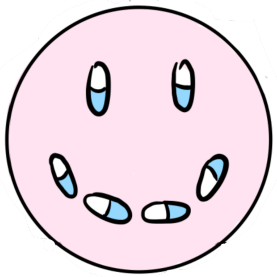

Antidepressant Medications

Contributor: Amin Hajamohideen
Reviewer: Shefani Perera

Class	Drug	Indications	MoA	Contraindications / precaution	Side Effects	Other
SSRIs (Selective Serotonin Reuptake Inhibitors) 	**Fluoxetine** (Prozac): young person, longest half-life, 7 days (less withdrawal effects) **Sertraline** (Zoloft): Safe in pregnancy, post-MI **Escitalopram** (Lexapro): elderly, well-tolerated, less nauseous **Citalopram** (Celexa) **Paroxetine** (Paxil) **Fluvoxamine** (Luvox)	1st line for depression and anxiety (GAD, OCD, PTSD)* PMDD*	Selectively inhibits reuptake of 5HT	Hx of mania or suspicion of BPAD* Risk of serotonin syndrome (↑5HT: SNRI, MAOI, TCA, triptans, cocaine, St John's wort) Warfarin Fluoxetine contraindicated in hepatic impairment and breastfeeding Fluoxetine and paroxetine contraindicated with TCA due to CYP enzyme **Paroxetine** contraindicated in pregnancy (teratogenic, risk of cardiac abnormalities, persistent pulmonary HTN) 	**General** • **Initiation syndrome**: short-term increased suicide risk (highest in first 1-2 weeks, improves after 10 days, requires close monitoring). Symptoms include: (psychiatric/ behavioural) increased suicidal thoughts, anxiety, agitation, insomnia, irritability, (other) nausea, diarrhoea, weight/appetite loss, sweating/flushing/tremour, headache, dizziness, sedation • **Discontinuation syndrome**: **FINISH** (**F**lu-like sx, **I**nsomnia, **N**ausea, **I**mbalance, **S**ensory disturbance, **H**yperarousal) • **Serotonin syndrome**: **SHIVERS** (**S**hiver, **H**yperreflexia, **I**ncreased T, **V**ital signs unstable, **E**ncephalopathy, **R**estlessness, **S**weating) • Sexual dysfunction • SIADH hyponatremia • Stroke and bleeding risk **Specific** • **Fluoxetine**: anorexia, initial weight loss, persistent pulmonary HTN • **Escitalopram**: long QT, less weight gain, agitation, insomnia • **Citalopram**: long QT • **Paroxetine**: Birth defects, hyponatremia, bone fracture, acute closed angle glaucoma, shortest half-life, seizure • **Sertraline**: GIT bleeds, Sedation or change HR, cause high BP, glaucoma, lower threshold for seizures, unstable BSLs (diabetes) • **Fluvoxamine**: Highly sedative, taken in PM	Takes 4-6 weeks to reach therapeutic effect At 6 weeks, monitor sodium levels Monitor LFTs due to hepatic metabolism If on fluoxetine and switching to another SSRI, allow 7-day washout period due to long-half life of fluoxetine Add bupropion if sexual dysfunction Taper over several weeks to prevent withdrawal syndrome

NARIs (Noradrenaline Reuptake Inhibitors) 	**Reboxetine** (Edronax) **Atomoxetine** - (Used in ADHD)	1st line for depression *Atomoxetine not recommended as 1st line	Inhibits reuptake of noradrenaline & adrenaline		**General** Insomnia, sweating, headache, fatigue, nausea, dry mouth, and constipation Increases noradrenaline and adrenaline - increased HR & BP	
NaSSA (Noradrenergic and Specific Serotonergic Antidepressant) 	**Mirtazapine** (Avanza) **Mianserin**	1st line for depression Buzzword: elderly, insomnia, loss of appetite and weight loss	Inhibits α2 (Alpha-2) - adrenoceptors, resulting in increase of NA/5HT without anticholinergic effects or cardiotoxicity		**General** • Sedation (taken in PM) • Dry mouth, weight gain • Sexual dysfunction (uncommon) • Associated with less nausea (due to 5HT3 blockage) • hypertensive urgency with MOAI **Rare** Blood dyscrasias **Specific** Mianserin: Agranulocytosis	Do not cease abruptly - risk of discontinuation syndrome Safe for patients with heart disease. But it is not first line because it is associated with weight gain
Melatonergic Agonist 	Agomelatine	1st line Can be considered for major depression, used to treat insomnia, sexual dysfunction in some cases	Unclear. Melatonin receptor (M1 and M2) agonist and 5HT2C receptor antagonist	Inhibitors of CYP1A2 (Fluvoxamine) – increases agomelatine concentration and side effects Avoid in people with liver disease	Serotonergic: Similar to SSRI Does not appear to have any abuse potential or withdrawal effect	High risk of hepatotoxicity LFTs need to be monitored regularly at the start of treatment 
NDRIs (Noradrenaline Dopamine Reuptake Inhibitors) 	Bupropion *Not commonly used in Australia for depression	Only indicated in Australia for smoking cessation	Blocks the action of the noradrenaline transporter and dopamine transporter	contraindicated in patients with bulimia or anorexia nervosa	Risk of seizures (lowers seizure threshold) Tachycardia, palpitations, dry mouth, weight loss, insomnia, agitation, and headache. Advantages: No sexual dysfunction, weight gain or orthostatic hypotension	Can be used as an adjunct to SSRI to improve sexual function

SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors) 	**Duloxetine** (Cymbalta): also for neuropathic and chronic pain **Desvenlafaxine** (Pristiq): for post-menopausal women with hot flushes **Venlafaxine** (Effexor) **Milnacipran** (Joncia)	2nd line for depression Useful for severe depression, melancholia Useful for chronic or neuropathic pain (Duloxetine) Venlafaxine is good for rx-resistant depression	Inhibits reuptake of serotonin (5HT) and noradrenaline (NA)	cardiovascular disease (CVD) Hx of mania or suspicion of BPAD Risk of serotonin syndrome (↑5HT: SNRI, MAOI, TCA, triptans, cocaine, St John's wort) Duloxetine contraindicated in hepatic impairment	**General** • Initiation and discontinuation syndrome similar to SSRIs • Additional NA effects: HTN, palpitations, Takotsubo cardiomyopathy, constipation, dry mouth, headache, sweating • Insomnia, strange dreams, nightmares **Specific** • Desvenlafaxine/Venlafaxine: hypersensitivity rash • Venlafaxine: short half-life - withdrawal symptoms with missed doses. Increased risk of seizures	Hepatic metabolization - monitor LFTs Venlafaxine dangerous in overdose (more so than SSRIs) - increased mortality, cardiac complications, seizure risk
TCAs (Tricyclic Antidepressants) 	**Desipramine** **Amitriptyline** **Doxepin** – also Tx for itch **Imipramine** **Clomipramine** - also Tx for OCD **Dothiepin** **Nortriptyline** **Trimipramine**	2nd line for depression (role in severe or melancholic depression)	Blocks NA reuptake Some can block 5HT reuptake Inhibit H1, a1, M1 receptors. Some also block 5HT2C, 5HT receptors and voltage-sensitive Na channels.	BPH (urinary retention) CVD High risk of suicide (fatal OD) Hx of mania Driving/heavy machinery (due to sedation)	Lethal in overdose Serotonergic: Similar to SSRI Blockade of α1-adrenoceptors: postural hypotension Antihistaminergic: sedation, weight gain Anticholinergic: anti-SLUDGE (dry mouth, dry eyes and blurry vision, urinary retention, constipation + GIT disturbances, emesis), glaucoma Blockade of cardiac fast sodium channels: cardio toxic in overdose e.g. arrhythmias, regular broad complex tachycardia, long QT, may lead to VT/VF especially if QT prolongation, mydriasis, dry skin and urinary retention. CNS toxicity: seizures, mental state changes  Sexual dysfunction Amitriptyline exacerbates closed-angle glaucoma	4-6 weeks to reach therapeutic effect Baseline ECG before starting Treatment of overdose: IV sodium bicarbonate

SM (Serotonin Modulator)	Vortioxetine	2nd line Can be considered for severe depression	Acts as an agonist at some serotonergic subtypes and antagonist at others	MAOIs – may contribute to serotonin syndrome	Serotonergic: Similar to SSRI	Given at PM Enhanced cognition
MAOIs (Monoamine Oxidase Inhibitors)	**Nonselective (5-HT, DA, NE)** Tranylcypromine phenelzine Isocarboxazid (irreversible) **MAO-A (5HT, NA)** Moclobemide Clorgyline (reversible) **MAO-B (DA)** Selegiline (irreversible)	Moclobemide & nonselectives 3rd line for depression 1st line for atypical depression Moclobemide useful for mild/mod depression with anxiety Nonselective useful for melancholia, atypical depression, and treatment resistant depression MAO-B useful in Parkinsons	Nonselective inhibitors of MAO-A and MAO-B: inhibits breakdown of adrenaline, NA, 5HT, DA - increase these levels Reversible MAOIs selectively and reversibly inhibit MAO-A Selegiline: selective MAO-B inhibitor → inhibit breakdown of DA → increases DA	Risk of serotonin syndrome (↑5HT: SNRI, MAOI, TCA, triptans, cocaine, St John's wort) Cheese, alcohol, aged foods High risk of suicide (increased risk of death) 	Hypertensive crisis (MAO-A only): cheese reaction due to interaction of MAOI and tyramine Serotonergic: Similar to SSRI Noradrenergic (α1-adrenoceptors): postural hypotension Anticholinergic: anti-SLUDGE (dry mouth, dry eyes and blurry vision, urinary retention, constipation + GIT disturbances, emesis)	Avoid foods with tyramine while on medication, and for 2 weeks after ceasing Can see response in a few days
SARI (Serotonin Antagonist and Reuptake Inhibitors)	Trazodone	Adjunctive	Serotonin antagonist and reuptake inhibitor. At lower doses, has hypnotic action		Trazodone causes priapism, sedation, orthostatic hypotension, nausea	