First Line Options: trial two medications	
Sertraline	Good for co-morbid anxiety, trauma history, or prominent neurovegetative symptoms. Well studied in patients with cardiovascular disease and depression post MI. Not ideal for patients with IBS or insomnia. Limited medication interactions, can increase concentrations of statins, tramadol, but effect is weak. No dose adjustments in renal impairment, reduce dosage by 50% in moderate to severe hepatic impairment. Dose range 12.5-200mg daily.

First Line Options: trial two medications (cont)	
Escitalopram	Good for side effect prone individuals, geriatric patients, prominent co-morbid anxiety. More potent than citalopram with better side effect profile and lower risk for QTc prolongation. Fewest drug interactions of all SSRI's, consider with polypharmacy. Dose range 5-30mg daily.

First Line Options: trial two medications (cont)	
Citalopram	Good for patients excessively activated or sedated by other SSRIs. Not as well tolerated as escitalopram, but still among the best for side effect profiles especially in the elderly. Caution in cardiac disease due to risk of QTc prolongation in doses over 40mg, do not exceed 20mg over age 60. May be less effective for anxiety than other SSRIs. No dose adjustment for renal impairment, maximum dose 20mg in hepatic impairment. Dose range 10-40mg daily.

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First Line Options: trial two medications (cont)

Fluoxetine	Good for patients who struggle with missed doses due to long half life and active metabolites. Activating properties can combat lethargy and other neurovegetative symptoms, and cause less weight gain. Caution in patients with anxiety and insomnia. Considerable inhibition at CYP2D6 and CYP3A4, therefore can legitimately increase levels of warfarin, tramadol, simvastatin, atorvastatin, beta blockers, alprazolam. No dose adjustment for renal impairment, lower dose by 50% in moderate to severe hepatic impairment. Dose range 10-80mg daily.

First Line Options: trial two medications (cont)

Paroxetine	Good in patients with co-morbid anxiety disorders and insomnia. Not ideal in non-compliance due to short half life and prominent discontinuation syndrome. CR formulation may be better tolerated. Increased sedation, sexual dysfunction and weight gain due to anticholinergic properties. Can exacerbate confusion in the elderly. Very potent inhibition at CYP2D6, commonly increases levels of warfarin, NSAIDs, beta blockers, as well as interfere with analgesic effects in some opioids. Reduce dosage by 25-50% in renal impairment, 50% in moderate to severe hepatic impairment. Dose range 10-60mg daily.

First Line Options: trial two medications (cont)

Fluvoxamine	Good for patients with OCD, co-morbid anxiety, and need for rapid onset of action. May also have less sexual dysfunction. Caution in IBS due to prominent GI side effects, disadvantage of twice daily dosing. Considerable inhibition at CYP1A2 and CYP3A4, can reduce clearance of caffeine, alprazolam, simvastatin, atorvastatin. Smoking increases the drug clearance and lowers efficacy. Reduce dosage by 25% in renal impairment, 50% in moderate to severe hepatic impairment.

General Pearls

*Trial two SSRI's for 4-8 weeks before moving to second line

*Consider using low dose trazodone for first few weeks for initial insomnia, prn ondansetron for nausea.

*Treat sexual dysfunction with bupropion, sildenafil, tadalafil, buspirone

*Treat night sweats with clonidine 0.1-0.2mg QHS or oxybutinin 5-10mg PO QHS

Second line options

Venlafaxine	Good for low energy, prominent neurovegetative symptoms, somatic symptoms, pain, migraines. Helpful for vasomotor symptoms in menopause. Short half life and prominent discontinuation syndrome, XR formulation is better tolerated. Not ideal for patients with IBS, cardiac disease, or hypertension. Higher doses required for noradrenergic effect, will likely be needed in resistant depression. Very limited drug interactions. Lower dose by 25-50% in renal impairment, 50% in moderate to severe hepatic impairment.

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Second line options (cont)

Bupropion	Good for patients with low energy/motivation, co-morbid ADHD, tobacco use disorder. Also ideal for patients concerned about sexual dysfunction and weight gain. Not ideal with severe co-morbid anxiety, tic disorders, eating disorders, insomnia, or seizure disorder. XL formulation better tolerated in general. Limited drug interactions, but do not combine with nicotine replacement therapy due to risk of hypertension. No dose adjustment necessary with renal impairment, for hepatic impairment maximum dose is 150mg XL every other day. Dose range for XL 150mg-450mg.

Second line options (cont)

Duloxetine	Good for fatigue, somatic symptoms, pain, and co-morbid anxiety. Lower risk of hypertension compared to venlafaxine. Not ideal for patients with liver disease, patients with urologic disorders/prostate enlargement. Moderate inhibition of CYP2D6, may increase levels of beta blockers. Mild CYP1A2 inhibition, tobacco use may reduce drug efficacy. Contraindicated in hepatic insufficiency, no dose adjustment for renal impairment. Dose range 20-120mg daily.

Second line options (cont)

MIrtazapine	Good for patients with insomnia, anxiety, appetite loss, nausea/GI issues. May have less associated sexual dysfunction, and have a faster onset of action. Not ideal in obesity, low energy/fatigue, vulnerability to orthostasis. Weight gain more common in women, occurs within first 6 weeks. Does not affect CYP450 system, minimal drug interactions. Use with caution in hepatic and renal impairment, but no required dose adjustment. Dose range 7.5-45mg daily, dose at night. Sedation occurs mostly at lower doses.

Pearls:

* Try 1-2 second line options for 4-8 weeks before moving to augmentation strategies

Augmentation Strategies

Bupropion	Can be added to SSRI or SNRI for potentiation of antidepressant effect, increase energy and improve cognition/concentration. Can also improve sexual dysfunction. Monitor BP when adding to SNRI.

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Augmentation Strategies (cont)

Mirtazapine	Can be added to SSRI or SNRI to potentiate antidepressant effect, improve insomnia, anxiety or appetite. Tends to be more sedating at lower doses (7.5 and 15mg)

Augmentation Strategies (cont)

Buspirone	Can be added in co-morbid generalized anxiety, or for mitigation of sexual side effects.

Augmentation Strategies (cont)

Aripiprazole	Can be added to SSRI or SNRI in cases with low energy/motivation, prominent intrusive or obsessive thinking patterns, and agitation. Has the best evidence of all augmentation strategies. Also a good choice in patients concerned about weight gain. Effective dose range is 2-10mg daily. Common side effects include dizziness, constipation, nausea, and akathisia. No dose adjustment necessary for renal or hepatic impairment. Fluoxetine, fluvoxamine, and paroxetine will increase plasma levels. Check BMI, lipids, A1c at 1,3, and 6 months then yearly.

Augmentation Strategies (cont)

Quetiapine	Can be added to SSRI or SNRI in cases with insomnia, anxiety, agitation, obsessive/intrusive thinking patterns. Not ideal for patients with severe obesity or type II diabetes. Common side effects include sedation, dry mouth, orthostasis, weight gain, akathisia. Very low incidence of extra-pyramidal symptoms. Generally dosed initially at 25-50mg PO QHS, then titrated to 150-300mg for optimal antidepressant effect. Limited drug interactions, can rarely increase warfarin levels. No dose adjustment in renal impairment, reduce dose by 25-50% in hepatic impairment. Check BMI, lipids, A1c at 1,3 and 6 months.

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Augmentation Strategies (cont)

Lithium	Can be added to SSRI or SNRI in cases with prominent emotional dysregulation, chronic suicidal thinking, anxiety, obsessive/intrusive thinking patterns. Used at low doses as adjunct to antidepressant, start at 150mg PO QHS and titrate up to 300-600mg PO QHS. Check level 5-7 days after initiation, and after each dosage increase. Maintain lower blood levels, generally 0.6-0.8. Levels should be checked at 12 hours after last dose to obtain true trough. When stable dose is reached switch to CR formulation and dose at night. Common side effects include nausea, mild tremor, sedation, weight gain, polyuria, polydipsia, and hypothyroidism. Not recommended in renal insufficiency, no dose adjustment necessary for hepatic insufficiency. NSAIDs, thiazide diuretics, COX-2 inhibitors, ACE inhibitors, calcium channel blockers can all increase lithium levels. Monitor levels during GI illness or any condition that involves fluid shifts or dehydration. Check BMP, TSH at baseline then at 1,3, and 6 months.

Augmentation Strategies (cont)

Liothyronine	Can be added to SSRI or SNRI in cases with severe fatigue, weight gain, cognitive slowing. Not ideal in patients with anxiety, eating disorders, hypertension. Low doses 5-25mcg are sufficient, monitor for symptomatic hyperthyroidism. Common side effects include anxiety, insomnia, appetite loss. Studies suggest only mild benefit.

Augmentation Strategies (cont)

Modafinil	Can be added to SSRI or SNRI in cases with co-morbid OSA, fatigue, cognitive difficulties, poor sleep patterns due to shift work. Not ideal in prominent anxiety, insomnia, hypertension. Common side effects include headache, nausea, insomnia, anxiety, palpitations, appetite loss. May increase levels of propranolol, through CYP2C19 inhibition, reduces levels of warfarin, contraceptives. Effect is inhibited by prazosin or other alpha 1 blockers. Less abuse potential compared with stimulants. Dose range is 100-200mg daily. Dose reduction of 50% in both renal and hepatic impairment.

Augmentation Strategies (cont)

Lamotrigine	Can be added to SSRI or SNRI in cases with severe emotional dysregulation, family history of bipolar disorder, impulse control issues. Can be used as mono therapy for depression in patients intolerant of SSRI/SNRI. Very well tolerated without associated weight gain, sedation, or sexual dysfunction. Risk of SJS/TENS is low, just adhere to standard dosing schedule for initiation. Patients missing 5 or more consecutive doses need to be re-titrated. Common side effects include blurred vision, ataxia, nausea. 10% develop a benign rash. Do not administer with valproic acid, this can increase risk of SJS. Dose range is 25-400mg, start 25mg QD x 14 days, then 50mg PO QD x 14 days, then increase to 100mg daily. Dose reduction of 50% in renal impairment, 25% in moderate to severe hepatic impairment.

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Augmentation Strategies (cont)

Methylphenidate	Can be added to SSRI or SNRI in cases with severe fatigue and lack of energy/motivation. Safe and well tolerated in geriatric depression or post stroke depression, generally doses are low 5-20mg daily. Not ideal for patients with substance use disorders, anxiety, insomnia, loss of appetite. Safer and better tolerated than amphetamine preparations. Limited drug interactions, no dose adjustment necessary for renal or hepatic impairment. Caution in patients with coronary artery disease, monitor BP at each visit.

Pearls:

*Treat akathisia with propranolol 10-20mg PO BID

*Can initiate metformin with atypical antipsychotics, which will likely prevent associated metabolic effects

*Treat lithium induced hypothyroidism with levothyroxine, polyuria can be treated with amiloride

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