NEPHROLOGY EDUCATION SERIES

Antidepressants, Anxiolytics, and ADHD Medications: Blood Pressure and Kidney Effects

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Who this is for. PA and medical students on a nephrology, internal medicine, or psychiatry rotation. You will meet these drugs constantly, because depression, anxiety, and ADHD are common in exactly the patients whose blood pressure and kidney function you are trying to protect. This handout gives you one organizing rule and the handful of interactions that actually change management.

Learning Objectives

After working through this handout you should be able to:

1. Explain **why some psychiatric medications raise blood pressure and others do not**, using transporter pharmacology rather than memorized drug lists.
2. Rank the antidepressant classes by blood-pressure effect and name the safest default class in a hypertensive patient.
3. Identify the **four drug interactions** with antihypertensives that most often cause harm, and state the substitution that fixes each.
4. Recognize **serotonin syndrome** using the Hunter criteria and explain why it matters to the kidney.
5. Adjust the common agents for **CKD stage 4–5 and dialysis**, including the two drugs that are most often dosed wrong.

1. The One Rule That Organizes Everything

Do not memorize which antidepressants raise blood pressure. Memorize **why**, and the list generates itself.

Neurons recycle neurotransmitters using **transporters** — proteins that pull the transmitter back out of the synapse. Two matter here:

- **SERT**, the serotonin transporter. Blocking it treats depression and anxiety. It does *not* meaningfully change blood pressure.
- **NET**, the norepinephrine transporter. Blocking it leaves more norepinephrine in the synapse — including at sympathetic nerve endings on blood vessels and in the brainstem centers that set sympathetic tone. Heart rate rises, vessels constrict, **blood pressure goes up**.

> **THE RULE**
>
> **If the drug blocks norepinephrine reuptake, it raises blood pressure.** If it only blocks serotonin reuptake, it does not. This holds no matter what the drug is marketed as — antidepressant, "non-stimulant" ADHD medication, or stimulant. Class labels mislead; transporter pharmacology does not.

This is not a theory someone asserted. Researchers plotted each drug's reported hypertension signal against its measured NET-versus-SERT binding ratio and found a strong correlation ($R^2 = 0.68$). The more a drug prefers NET, the more hypertension it produces.

The mirror image: some of these drugs make blood pressure *fall*. Older tricyclics block alpha-1 receptors on blood vessels, causing **orthostatic hypotension** — dizziness on standing. And guanfacine and clonidine are alpha-2 *agonists*, the same mechanism clonidine uses as a blood-pressure drug, so they lower pressure on purpose.

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2. Antidepressants and Anxiolytics at a Glance

DRUG / CLASS	EFFECT ON BP	WHAT TO REMEMBER
SSRIs (sertraline, escitalopram, fluoxetine, paroxetine, citalopram)	Neutral	**First-line** in a hypertensive or cardiac patient. Blocks SERT only.
SNRIs (venlafaxine, duloxetine, desvenlafaxine, levomilnacipran)	Raises, dose-dependent	Blocks NET too. Levomilnacipran is worst, duloxetine mildest.
TCAs (nortriptyline, amitriptyline, imipramine, doxepin)	Mixed — up supine, down standing	Nortriptyline raises pressure most; imipramine causes the most orthostatic hypotension.
Bupropion (NDRI)	Raises — and also causes orthostasis	Does both. See Section 3.
Mirtazapine	Neutral	Rarely orthostatic hypotension and falls.
Trazodone	Lowers (orthostatic)	Often given at low "sleep doses" to patients already on 3 BP drugs — additive dizziness.
MAOIs	Usually lowers; crisis if triggered	Orthostatic hypotension is the *common* effect. Hypertensive crisis is the feared one.
Buspirone (anxiolytic)	Neutral	The cleanest anxiolytic in hypertension — but see the diltiazem interaction.

> ⚠ **A CORRECTION TO SOMETHING YOU WILL HEAR REPEATED**
>
> You will be taught that venlafaxine must be avoided in patients whose blood pressure is not controlled. **The original data do not say that.** The meta-analysis of 3,744 patients found the blood-pressure effect became clinically significant **only above 300 mg/day**, and specifically reported that venlafaxine *did not worsen control in patients who already had hypertension*. The real risk factor is **dose**, not baseline blood pressure.

2.1 Buspirone: the anxiolytic worth knowing

Buspirone is a 5-HT1A partial agonist. No meaningful effect on blood pressure, no sedation, no dependence, no withdrawal — which is why it is attractive when a benzodiazepine would be a bad idea.

The catch students always miss: onset takes **2–4 weeks**. Patients expecting benzodiazepine-like relief stop taking it on day five and call it a failure. Tell the patient this at the first visit or the drug will not work.

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3. Bupropion — A Special Case

Bupropion deserves its own section because it behaves unlike the others and because it often arrives through a side door: **smoking cessation**. The prescriber may be treating tobacco use, not depression, and may not be the person managing the blood pressure.

Three things to know:

1. **It moves blood pressure in both directions.** It raises pressure (it blocks norepinephrine *and* dopamine reuptake) but also causes orthostatic hypotension in patients with heart disease. A single sitting blood pressure is a poor way to monitor it — check standing too.
2. **It is a potent CYP2D6 inhibitor.** That puts it in the same danger group as paroxetine and fluoxetine for anyone taking metoprolol or carvedilol (Section 5).
3. **Its kidney behavior is a trap.** In dialysis patients the *parent drug* looks completely normal — but its active metabolites build up and are **not removed by dialysis**.

⚠ THE BUPROPION TRAP IN DIALYSIS

Because the parent drug level looks normal, checking it falsely reassures you. The active metabolite **hydroxybupropion accumulates**, and bupropion's dose-related toxicities — **lowered seizure threshold**, agitation, higher blood pressure — follow total exposure. The one dedicated study in hemodialysis patients concluded that **150 mg every 3 days** is more appropriate than the usual 150 mg daily. A dialysis patient on standard dosing is receiving roughly three times what the evidence supports.

Be honest about the evidence: that study had only 8 patients and used a single dose. It is thin — but it is the only direct evidence, and it points one way.

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4. ADHD Medications

Stimulants raise blood pressure. That part is not surprising. Two findings *are* surprising, and both are commonly gotten wrong on rounds.

4.1 How much do stimulants actually raise blood pressure?

A 2025 Cochrane review pooled 56 randomized trials and 10,583 people:

MEASURE	CHANGE VS PLACEBO	CERTAINTY
Systolic BP	**+1.93 mmHg**	High
Diastolic BP	**+1.84 mmHg**	High
Heart rate	**+3.71 beats/min**	High

These are **small but real and sustained** — still present in trials lasting eight weeks or longer. About 1 in 23 patients stops the drug because of side effects.

4.2 "Non-stimulant" does not mean blood-pressure safe

⚠ THE MOST COMMON MISTAKE WITH THESE DRUGS

A tempting move is to switch a hypertensive patient from methylphenidate to **atomoxetine** because atomoxetine is a "non-stimulant." The evidence does not support this. In a network meta-analysis of 102 trials, stimulants were **not** worse than atomoxetine or viloxazine — and atomoxetine produced the **largest heart-rate increase of any agent studied** in children (+5.58 beats/min).

Go back to Section 1 and this makes sense immediately: **atomoxetine is a pure NET inhibitor.** Blocking norepinephrine reuptake is exactly the mechanism that raises blood pressure. The category name says "non-stimulant"; the pharmacology says otherwise.

4.3 Guanfacine goes the other way

Guanfacine is an alpha-2 agonist — a licensed blood-pressure medication that also treats ADHD. It **lowers** blood pressure: in adults, roughly **10 mmHg systolic** (a wide, uncertain estimate, but clearly downward).

✓ TWO CONDITIONS, ONE DRUG — AND THE TRAP

In an adult with **both ADHD and hypertension**, guanfacine may treat both. But in a patient whose pressure is already at goal, it can cause **low blood pressure, slow heart rate, and dizziness on standing**. If guanfacine is started, the other blood-pressure medications may need to be reduced — not increased.

4.4 Do these drugs cause heart attacks and strokes?

Short answer: no clear evidence of that. Two very large studies (1.2 million children and young adults; 150,000 adults) found no increase in heart attack, stroke, or sudden death.

But over years, blood pressure is a different question. A study of 278,027 people found the risk of being diagnosed with **hypertension** rose with how long the medication was taken — about **1.8 times higher after more than 5 years** of use.

HOW TO HOLD BOTH FACTS AT ONCE

These findings do not contradict each other; they measure different things. A drug that adds about 2 mmHg and 4 beats per minute will **not** rupture a plaque this year — but over a decade it shifts a population's blood pressure upward. That is precisely what the data show. For a patient who also has CKD, years of slightly higher pressure is the outcome that matters most.

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5. Drug Interactions with Blood Pressure Medications

This is the highest-yield section. These interactions cause more harm than any 2 mmHg average effect.

5.1 Never combine

COMBINATION	WHAT HAPPENS
MAOI + any SSRI, SNRI, buspirone, or stimulant	Hypertensive crisis and/or serotonin syndrome. Requires a **14-day washout** in each direction.
Linezolid + any serotonergic drug or stimulant	Linezolid *is* a reversible MAOI — most people forget this. Documented hypertensive crisis with serotonin syndrome.
Methylene blue + serotonergic drug	Same mechanism as linezolid.

⚠ LINEZOLID IS THE ONE YOU WILL ACTUALLY SEE

The classic MAOI interaction is mostly historical. **Linezolid is not.** It is used for VRE and resistant MRSA — infections common in dialysis patients — and a large share of those patients are already on an SSRI or buspirone that nobody reconciles when the antibiotic is ordered. **Check the psychiatric medication list before the antibiotic starts**, not after the blood pressure hits 220.

5.2 The four that change management

IF THE PATIENT TAKES...	AVOID	BECAUSE	DO THIS INSTEAD
Metoprolol or carvedilol	Paroxetine, fluoxetine, bupropion, duloxetine	These block CYP2D6, raising metoprolol levels **3–5 fold**; causes bradycardia and heart block	Use **sertraline or escitalopram**
Diltiazem or verapamil	Standard-dose buspirone	These block CYP3A4; diltiazem raises buspirone levels **5.5-fold**	Start buspirone at **2.5–5 mg twice daily**
A thiazide diuretic	Unmonitored SSRIs, especially citalopram	Additive water retention causes **severe low sodium**	Check sodium at **2 and 4 weeks**
Clonidine or guanfacine	TCAs, mirtazapine	They block the alpha-2 receptor the BP drug is trying to stimulate	Use an **SSRI**

THE SINGLE HIGHEST-YIELD SUBSTITUTION

If you remember one interaction from this handout: a patient on **metoprolol or carvedilol** who needs an SSRI should get **sertraline or escitalopram**, never paroxetine or fluoxetine. That one swap prevents the most common clinically significant interaction between psychiatric and blood-pressure medications.

Good news: ACE inhibitors, ARBs, amlodipine, and spironolactone are essentially **interaction-free** with all of these drugs. The trouble concentrates in beta-blockers, diltiazem/verapamil, thiazides, and clonidine/guanfacine.

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6. Serotonin Syndrome — Recognize It Fast

This is the acute emergency in this drug group. It matters to the kidney because severe cases cause **muscle breakdown (rhabdomyolysis) leading to acute kidney injury**.

Use the **Hunter criteria**, which are more accurate than the older Sternbach criteria (84% vs 75% sensitivity; 97% vs 96% specificity). Seven features matter:

- **Clonus** — inducible, spontaneous, or ocular
- Agitation
- Diaphoresis (sweating)
- Tremor
- Hyperreflexia
- Hypertonicity (muscle rigidity)
- Temperature above 38 °C

CLONUS IS THE FINDING THAT MAKES THE DIAGNOSIS

Dorsiflex the ankle. Clonus is the single most useful sign, and it is characteristically **worse in the legs than the arms**. Use it to separate three look-alike syndromes:

- **Serotonin syndrome** — hyperreflexia and clonus, onset usually **under 24 hours**
- **Neuroleptic malignant syndrome** — **lead-pipe rigidity** and slowed movement, onset over **days to weeks**, after a dopamine blocker
- **Anticholinergic toxicity** — dry skin, absent bowel sounds, **normal reflexes**

All three can produce fever. The reflex exam tells them apart.

Common triggers on a hospital service: linezolid, methylene blue, fentanyl, tramadol, methadone, ondansetron — each added to a patient already taking an SSRI.

Management: stop all serotonergic drugs, give **benzodiazepines** for agitation, cool the patient actively, and consider **cyproheptadine** in moderate-to-severe cases. Dantrolene and bromocriptine treat other syndromes and have no role here.

TWO THINGS NOT TO DO

1. Do not use physical restraints. A patient straining against restraints generates isometric muscle contraction, which worsens the fever, the acidosis, and the muscle breakdown — the exact process that injures the kidney. Sedate chemically instead.

2. Do not reflexively give large-volume fluids to a dialysis patient. In rhabdomyolysis you were taught to give aggressive IV fluids to protect the kidneys. In a patient who makes no urine, there is no kidney function left to protect and nowhere for the fluid to go — you will cause pulmonary edema. Those patients need **urgent dialysis** for potassium and acid, not volume.

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7. Dosing in Kidney Disease

DRUG	CKD STAGE 3–4	DIALYSIS / EGFR UNDER 30
Sertraline	No change	No change — the usual default choice
Escitalopram	No change	Maximum 10 mg/day
Citalopram	Maximum 20 mg/day	Maximum 20 mg/day (QT prolongation)
Venlafaxine	Reduce 25–50%	Clearance falls about 55%; poorly dialyzed
Duloxetine	No change if eGFR 30 or above	**Not recommended below 30**
Bupropion	Reduce	**150 mg every 3 days** — not daily
Buspirone	5 mg twice daily in stage 4–5	Not dialyzed; no extra dose after HD
Guanfacine	**No major change**	**No major change** — non-kidney clearance compensates
Amphetamines	Caution; reduce	Excreted by the kidney; avoid in dialysis
Methylphenidate	No change expected	Broken down by the liver

THE NEPHROLOGY DETAIL ALMOST NOBODY KNOWS

Amphetamine clearance depends on urine pH. Amphetamine is a weak base: **alkaline urine** means more is reabsorbed and blood levels rise; **acidic urine** means more is excreted and levels fall.

Why this matters in nephrology: many CKD patients take **sodium bicarbonate** for metabolic acidosis, which alkalinizes the urine. If a patient tells you their ADHD medication "stopped working" or suddenly became intolerable after a bicarbonate dose change, this is a real and under-recognized explanation.

BE HONEST ABOUT WHAT IS NOT KNOWN

There are **no studies of ADHD medications in CKD or dialysis populations**. The recommendations above are inferred from how each drug is eliminated, not from trials in kidney patients. Say so when you present — a confident-sounding number you cannot source is worse than an acknowledged gap.

8. Clinical Pearls and Common Pitfalls

PITFALL	WHAT TO DO INSTEAD
Starting paroxetine in a patient on metoprolol	Use sertraline or escitalopram
Switching to atomoxetine to "protect" the blood pressure	It is a pure NET inhibitor — no advantage; reconsider guanfacine
Standard buspirone dosing on diltiazem	Start 2.5–5 mg twice daily
Checking only a sitting blood pressure on bupropion or a TCA	Check standing too — these cause orthostasis

PITFALL	WHAT TO DO INSTEAD
Adding linezolid without reviewing psychiatric medications	Reconcile *before* the antibiotic is ordered
Giving standard-dose bupropion to a dialysis patient	150 mg every 3 days
Assuming buspirone failed at day 5	Onset is 2–4 weeks — counsel the patient upfront
Physical restraints in serotonin syndrome	Benzodiazepines; restraints worsen rhabdomyolysis

9. Monitoring Checklist

WHEN	CHECK
Baseline	BP sitting **and** standing, heart rate, sodium; ECG if starting citalopram/escitalopram with risk factors
2 weeks	BP, orthostatics, sodium if on a thiazide or if elderly
4 weeks	BP, heart rate, sodium, symptom response
8–12 weeks	BP, heart rate, metabolic panel
After every dose increase	BP and heart rate within 2 weeks — these effects are dose-dependent
Yearly on long-term ADHD medication	BP, and reconsider whether the drug is still needed

DO NOT SKIP STANDING BLOOD PRESSURES

In the hypertension clinic you watch for pressure going *up*. In the elderly or dialysis patient, the event that causes a hospital admission is pressure going *down* on standing. Check orthostatics in anyone over 70, on three or more blood-pressure drugs, or on dialysis. **The sitting pressure you record in clinic tells you nothing about the pressure at 3 a.m. on the way to the bathroom.**

10. Check Your Understanding

1. A 58-year-old on **metoprolol 50 mg twice daily** for hypertension needs treatment for major depression. The resident writes for paroxetine. What is the problem, and what would you suggest?

   Answer: Paroxetine strongly inhibits CYP2D6, which metabolizes metoprolol, raising metoprolol exposure 3–5 fold and risking bradycardia or heart block. Substitute **sertraline or escitalopram** (weak CYP2D6 inhibitors), or change the beta-blocker to atenolol or bisoprolol.

2. A 34-year-old with ADHD and newly diagnosed hypertension is on lisdexamfetamine. A colleague suggests switching to atomoxetine "because it is not a stimulant." Is that reasoning sound?

   Answer: No. Atomoxetine is a pure **NET inhibitor** — the mechanism that raises blood pressure. Head-to-head data show non-stimulants are not gentler, and atomoxetine caused the largest heart-rate rise of any agent studied. A better option is **guanfacine**, which lowers blood pressure and treats ADHD.

3. A hemodialysis patient on sertraline is started on **linezolid** for VRE bacteremia. Two days later: agitated, sweating, temperature 38.9 °C, and clonus at both ankles. What is happening and what must you avoid?

   Answer: **Serotonin syndrome** — linezolid is a reversible MAOI. Stop the serotonergic drugs, give benzodiazepines, cool actively, consider cyproheptadine. **Avoid physical**

restraints (worsens rhabdomyolysis) and **avoid reflexive large-volume fluids** in an anuric patient — manage potassium and acidosis with dialysis.

4. A dialysis patient is on bupropion 150 mg daily for smoking cessation. A level of the parent drug is normal. Is the dose appropriate?

   Answer: Probably not. The parent drug appears normal in dialysis, but the **active metabolites accumulate and are not dialyzed**. The only dedicated study supports **150 mg every 3 days**. A normal parent level is falsely reassuring, and the risk is a lowered seizure threshold.

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11. Summary — What to Remember

1. **NET blockade raises blood pressure; SERT blockade does not.** One rule generates the whole list.
2. **SSRIs are the safe default** in a hypertensive patient.
3. **SNRIs raise pressure with dose**; venlafaxine's real threshold is above 300 mg/day.
4. **Paroxetine/fluoxetine + metoprolol is the interaction to know.** Swap to sertraline or escitalopram.
5. **Diltiazem raises buspirone levels 5.5-fold** — start low.
6. **"Non-stimulant" is not blood-pressure safe.** Atomoxetine is a NET inhibitor.
7. **Guanfacine lowers blood pressure** and can treat both conditions.
8. **Clonus diagnoses serotonin syndrome**; no restraints, and no volume loading in an anuric patient.
9. **Bupropion in dialysis: 150 mg every 3 days**, because metabolites accumulate invisibly.
10. **Sertraline and guanfacine are the safest defaults in advanced CKD.**

Key References

1. Pillinger T, et al. The effects of antidepressants on cardiometabolic and other physiological parameters: a systematic review and network meta-analysis. *Lancet*. 2025;406(10515):2063-2077. PMID 41135546

2. Montastruc JL, et al. Role of serotonin and norepinephrine transporters in antidepressant-induced arterial hypertension. *Eur J Clin Pharmacol*. 2020;76(9). PMID 32483650

3. Thase ME. Effects of venlafaxine on blood pressure: a meta-analysis of original data from 3744 depressed patients. *J Clin Psychiatry*. 1998;59(10). PMID 9818630

4. Chan M, Musini VM, Wright JM. Effect of amphetamines on blood pressure. *Cochrane Database Syst Rev*. 2025;3:CD007896. PMID 40152309

5. Farhat LC, et al. Comparative cardiovascular safety of medications for ADHD in children, adolescents, and adults. *Lancet Psychiatry*. 2025;12(5). PMID 40203844

6. Zhang L, et al. ADHD medications and long-term risk of cardiovascular diseases. *JAMA Psychiatry*. 2024;81(2). PMID 37991787

7. Cooper WO, et al. ADHD drugs and serious cardiovascular events in children and young adults. *N Engl J Med*. 2011;365(20). PMID 22043968

8. Habel LA, et al. ADHD medications and risk of serious cardiovascular events in young and middle-aged adults. *JAMA*. 2011;306(24). PMID 22161946

9. Bahar MA, et al. The impact of CYP2D6 mediated drug-drug interaction: metoprolol and paroxetine/fluoxetine. *Br J Clin Pharmacol*. 2018;84(12). PMID 30248178

10. Lamberg TS, Kivistö KT, Neuvonen PJ. Effects of verapamil and diltiazem on the pharmacokinetics and pharmacodynamics of buspirone. *Clin Pharmacol Ther*. 1998;63(6):640-645. PMID 9663178

11. Dunkley EJ, et al. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM*. 2003;96(9). PMID 12925718

12. Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med*. 2005;352(11). PMID 15784664

13. Shahbazi F, et al. Hypertensive crisis associated with serotonin syndrome following linezolid administration. *Curr Drug Saf*. 2025;20(1). PMID 38847376

14. Worrall SP, Almond MK, Dhillon S. Pharmacokinetics of bupropion and its metabolites in haemodialysis patients who smoke. *Nephron Clin Pract*. 2004;97(3). PMID 15292684

15. Nagler EV, et al. Antidepressants for depression in stage 3-5 chronic kidney disease: ERBP systematic review. *Nephrol Dial Transplant*. 2012;27(10). PMID 22859791

16. Troy SM, et al. The effect of renal disease on the disposition of venlafaxine. *Clin Pharmacol Ther*. 1994;56(1). PMID 8033490

17. Lobo ED, et al. Effects of varying degrees of renal impairment on the pharmacokinetics of duloxetine. *Clin Pharmacokinet*. 2010;49(5). PMID 20384393

18. Kirch W, Köhler H, Braun W. Elimination of guanfacine in patients with normal and impaired renal function. *Br J Clin Pharmacol*. 1980;10 Suppl 1:33S-35S. PMID 6994776

19. Huang W, Isoherranen N. Mechanistic PBPK modeling of urine pH effect on renal and systemic disposition of methamphetamine and amphetamine. *J Pharmacol Exp Ther*. 2020;373(3). PMID 32198137

20. Hedayati SS, et al. Effect of sertraline on depressive symptoms in patients with CKD without dialysis dependence: the CAST randomized clinical trial. *JAMA*. 2017;318(19). PMID 29101402

21. Slee A, et al. Pharmacological treatments for generalised anxiety disorder: a systematic review and network meta-analysis. *Lancet*. 2019;393(10173):768-777. PMID 30712879

22. Rosner MH. Severe hyponatremia associated with the combined use of thiazide diuretics and selective serotonin reuptake inhibitors. *Am J Med Sci*. 2004;327(2). PMID 14770031

Related Resources

- Clinical Mastery: Psychotropic and ADHD Medications in Hypertension and CKD — the physician-level version, with full evidence appraisal and 49 references
- Lecture: Psychiatric and ADHD Medications and Blood Pressure — the interactive teaching version

- Drug Dosing in CKD: Quick Reference
- RAAS Inhibitors Student Handout
- Hypertension Advanced Module