Advancing Kidney Health
Through Optimal Medication Management

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# Depression and Anxiety in CKD: Providing Individualized Care

# How to navigate the module

- Glossary
- Additional Information PDFs
- Quizzes
- Websites
- Evaluation

# Glossary of Terms


- **AKI** = acute kidney injury
- **BDI** = Beck Depression Inventory
- **CBT** = Cognitive Behavioral Therapy
- **CKD** = chronic kidney disease
- **DDI** = drug-drug interactions
- **eCrCL** = estimated creatinine clearance
- **eGFR** = estimated glomerular filtration rate
- **Hgb** = hemoglobin
- **Hgb A1c** = hemoglobin A1c
- **ESKD** = end-stage kidney disease
- **MDD** = Major Depressive Disorder
- **PD** = pharmacodynamics
- **PGx** = pharmacogenomics
- **PK** = pharmacokinetics
- **PHQ-9** = Patient Health Questionnaire 9 item depression scale
- **QOL** = Quality of Life
- **sCr** = serum creatinine
- **SNRI** = serotonin and norepinephrine reuptake inhibitor
- **SRI** = serotonin reuptake inhibitor (SSRI and SNRI)
- **SSRI** = selective serotonin reuptake inhibitor
- **t1/2** = half-life
- **TSH** = thyroid stimulating hormone

# Today’s Roadmap

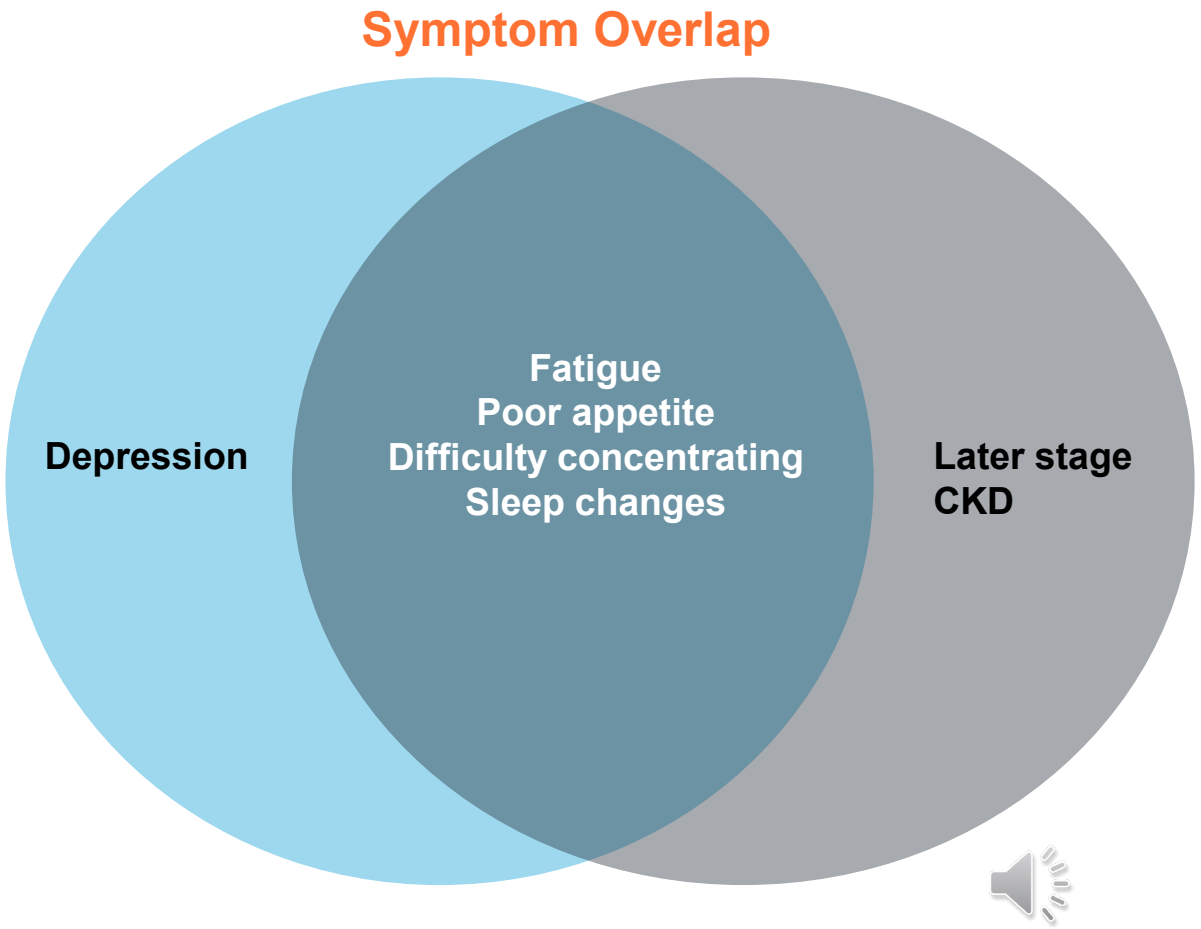
- Review depression and anxiety in CKD: prevalence, risk factors, clinical outcomes
- Review treatment options, clinical considerations, management of side effects
- Follow-up & plan adjustment

# Depression in CKD: How Common Is It?

| | Depression Prevalence | |
|---|---|---|
| **Case identification method** | **On Dialysis** | **Not on Dialysis** |
| Clinical Interview | 23% | 21% |
| Screening Questionnaire | 39% | 27% |
| General US Population: 10% | | |

**CKD not on dialysis**
50–60% of those *with* depression report also having anxiety symptoms

Shirazian et al. Kidney Int Rep. 2016 Sep 20;2(1):94-107



# Anxiety: How Common Is It?

## CKD

19% anxiety disorder

43% anxiety symptoms

## General U.S. population

5–12% anxiety disorder

50–60% of those *with* depression report also having anxiety symptoms

Huang et al. General Hospital Psychiatry, 2021 (69) 27-40. Volume 69, 2021
https://pubmed.ncbi.nlm.nih.gov/33516963/

# Risk Factors for Depression

| ESKD on Dialysis | Non-Dialysis CKD |
| --- | --- |
| ☐ White race | ☐ Non-White race |
| ☐ Longer duration of dialysis | ☐ Lower socioeconomic status |
| ☐ Female | ☐ Female |
| ☐ Younger age | ☐ Younger age |
| ☐ Comorbidities | |
| ☐ Frailty | |


Chi CY, Lee SY, Chao CT, Huang JW. Frailty as an Independent Risk Factor for Depression in Patients With End-Stage Renal Disease: A Cross-Sectional Study. Front Med (Lausanne). 2022 Feb 15;9:799544 https://pubmed.ncbi.nlm.nih.gov/35242777/

Shirazian et al. Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management. Kidney Int Rep 2017; (2):94–107 https://pubmed.ncbi.nlm.nih.gov/29318209/

# Why Does it Matter?

## Depression CKD on dialysis

- ↓ QOL; ↑ mortality, ED visits, hospitalizations, CV events, peritonitis, withdrawal from dialysis

## Depression CKD not on dialysis

- ↑ mortality, hospitalization, and progression toward dialysis

## Anxiety CKD

- trend toward ↑ morbidity, mortality; ↓ QOL in all CKD stages

# Treatment Options

## Psychotherapy (e.g., CBT)

- Some people can have their depression or anxiety abate from therapy alone

## Medication

- For those with barriers to psychotherapy, a history of poor response to therapy, or as an initial therapy with therapy added on later

## Psychotherapy + Medication

- May be more effective than psychotherapy or medication alone

## Exercise, Relaxation, Music

- Generally used as add-on therapy

# Shared Decision-Making

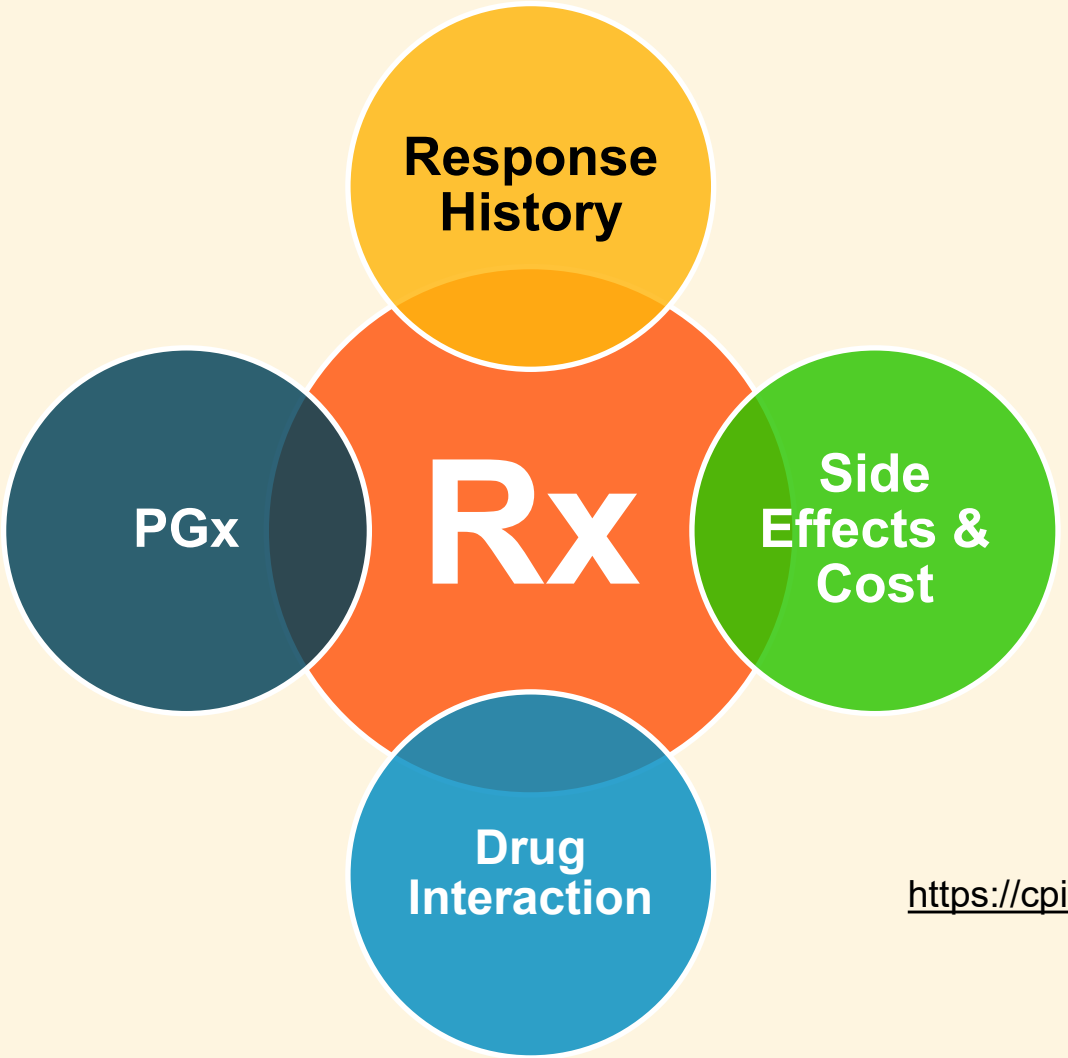
Why am I starting this medication?

Benefits? Risks?

What are the alternatives?

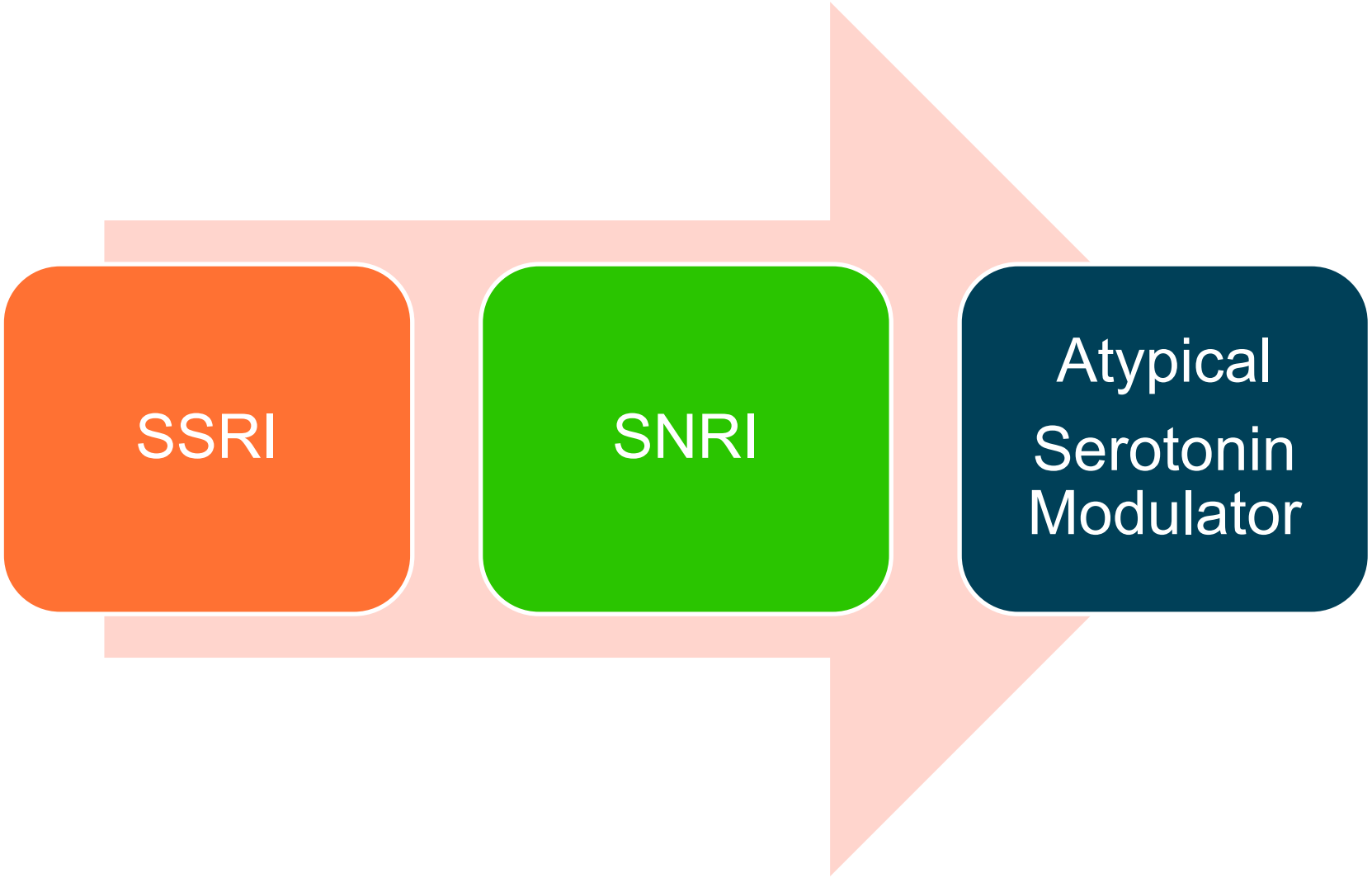
How long will I have to take it? What is the path off?

# Choosing a Medication




https://cpicpgx.org/guidelines/

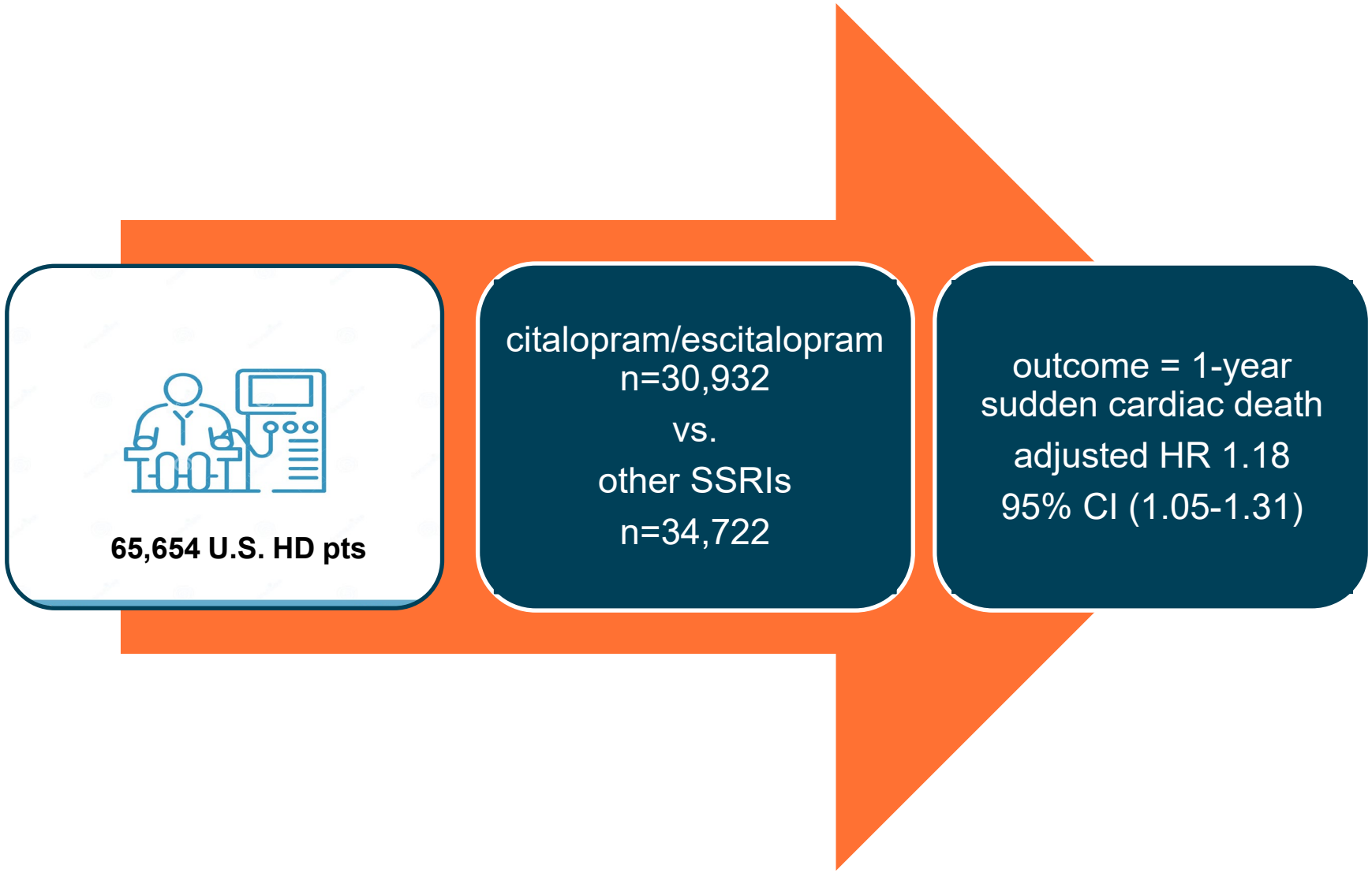
# Usual Selection Order in CKD



# SSRIs in CKD: Usual Dosing & Considerations

| SSRI | Usual dosing/day | CKD dosing<br>GFR/CrCL (ml/min) | Considerations |
|---|---|---|---|
| **Sertraline** | **25–200 mg** | | ➢ **good data in ESKD** |
| Fluoxetine | 10–60 mg | | ➢ weight neutral (or loss), activating, many DDI, long T1/2 |
| Paroxetine | 10–40 mg | **< 60:** ↓ 25–50% | ➢ wt gain, many DDI, short T1/2<br>➢ 2–3x higher exposure in CKD |
| Citalopram<br><br>Escitalopram | 10–40 mg<br><br>5–20 mg | **< 20:**<br>10 mg<br><br>5 mg | ➢ ↑ QTc vs. other SSRIs<br>➢ dialysis: ↑ sudden cardiac death vs. other SSRIs |

# SSRI QT-Prolongation Potential and Sudden Cardiac Death




Assimon et al. Comparative Cardiac Safety of Selective Serotonin Reuptake Inhibitors among Individuals Receiving Maintenance Hemodialysis. J Am Soc Nephrol 2019 Apr;30(4):611-623 https://pubmed.ncbi.nlm.nih.gov/30885935/

# Chronic Kidney Disease Antidepressant Sertraline Trial (CAST)

Does sertraline improve depressive symptoms in CKD?

Randomized, double-blind, placebo-controlled
201 adults MDD +
eGFR < 45 mL/min/1.73m$^2$

Sertraline or placebo x 12 weeks
50 mg/day with titration

150 mg: median achieved dose
12 weeks: median participation time
95-96%: adherence rate, both groups

**Primary Outcome**
Improvement from baseline to 12 weeks using 16-point rating scale

**Results**
No difference between groups!

Hedayati SS et al. Effect of Sertraline on Depressive Symptoms in Patients With Chronic Kidney Disease Without Dialysis Dependence: The CAST Randomized Clinical Trial. JAMA. 2017 Nov 21;318(19):1876-1890 https://pubmed.ncbi.nlm.nih.gov/29101402/

Mills JA et al. Socioeconomic Predictors of Treatment Outcomes Among Adults with Major Depressive Disorder. Pychiatric Serv. 2022 Sep1;73(9):965-969 https://pubmed.ncbi.nlm.nih.gov/35354325/

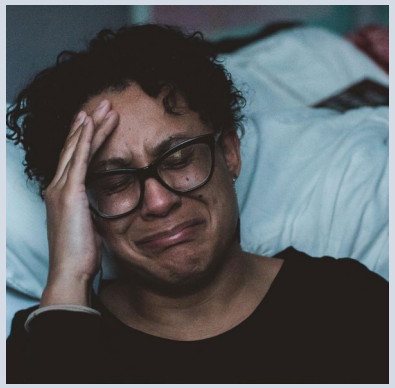
# SNRI – Second Line if SSRI Failure(s)

| SNRI | Usual dosing/day | CKD dosing GFR/CrCl (ml/min) | Considerations |
|---|---|---|---|
| Duloxetine | 30–60 mg | **< 30:** avoid | ➢ CKD 4–5: not recommended<br>➢ 20 mg capsule available |
| Venlafaxine | 37.5–225 mg | **< 30:** 37.5–112.5 mg | ➢ SSRI < 225 mg<br>➢ dose dependent ↑ in BP ≥ 225 mg |
| Desvenlafaxine | 50–100 mg | **30–50:** 50 mg<br>**< 30:** 25 mg daily or 50 mg every other day | ➢ primary active metabolite of venlafaxine<br>➢ higher cost than above options |

# Other Options to Consider or Avoid

| Atypical agents | Usual dosing/day | CKD dosing GFR/CrCL (ml/min) | Considerations |
|---|---|---|---|
| Bupropion | 150–450 mg | **15–60:** max 150 mg daily<br>**< 15:** 100 mg q48h/150 mg q72h | ➢ consider avoiding in anxiety<br>➢ useful if sexual dysfunction with SSRI/SNRI |
| Mirtazapine | 7.5–45 mg | **< 30:** 7.5–30 mg at bedtime | ➢ ↑ dose = ↓ sedation |
| **Serotonin modulators** | | | |
| Vortioxetine | 5–10 mg, ↑ weekly to target of 20 mg | | ➢ expensive |
| Gepirone | complicated | **< 50:** 18.2 mg daily; may ↑ to max 36.3 mg on day 7 | ➢ QTc prolongation<br>➢ no more effective than other choices |

# Case Study



## Patient

L.D. is a 63 yo female who self-identifies as Black, referred for initiation of an antidepressant

PMH: T2DM, HTN, CKD stage 4, adopted, does not know her family history.
Allergies: none

L.D. describes low mood and loss of interest in cooking and visiting her grandchildren, activities she used to enjoy. She reports poor concentration, fatigue, and difficulty falling and staying asleep due to worrying about needing dialysis soon. During the day, she often stays in bed and has missed medical appointments. These symptoms have been present for the past 6 months. Cognitive behavioral therapy helped a little, but she had to stop due to high co-pays. She has never used a medication to help with mood, but she feels ready to do so. She finds her current medications affordable.

## Labs/Vitals

| **Vital** | **Today** |
|---|---|
| BP | 107/62 |
| HR | 62 |
| Weight (lbs) | 186 |
| Height (in) | 64 |
| **Labs** | **Today** |
| TSH | 2.98 mIU/L |
| Hgb | 10.6 g/dL |
| eGFR | 25 ml/min/1.73m$^2$ |
| Hgb A1c | 6.9% |

## Medications

Losartan 50 mg daily
Empagliflozin 10 mg daily
Carvedilol 25 mg bid
Torsemide 40 mg daily

# Managing Common SRI Side Effects

**Gastrointestinal**
- Nausea, diarrhea

- Take with food
- Start low, gradual dose titration

**Activation**
- Anxiety, restlessness, insomnia

- Start (very) low
- Choose less activating agent

# Managing Common SRI Side Effects

**Sexual**
- ↓ libido and sensation
- delayed ejaculation/anorgasmia

- Reduce dose
- Switch/add: bupropion, mirtazapine, buspirone, PDE inhibitor

**Withdrawal**
- With d/c or intermittent adherence

- Pay attention to $t_{1/2}$
- Gradual taper

Patients who are prepared for potential side effects are less likely to discontinue their medication prematurely and may be more proactive in seeking help from their healthcare provider if side effects occur.

# When Will it Work? How Long do I Take It?

## Acute
## 6–12 weeks

- Phone call 1 week
- Office visit 1 month, 3 months

## Continuation
## 4–5 months

- Maintain improvement
- Adjust PRN
- Regular follow-up

## Maintenance

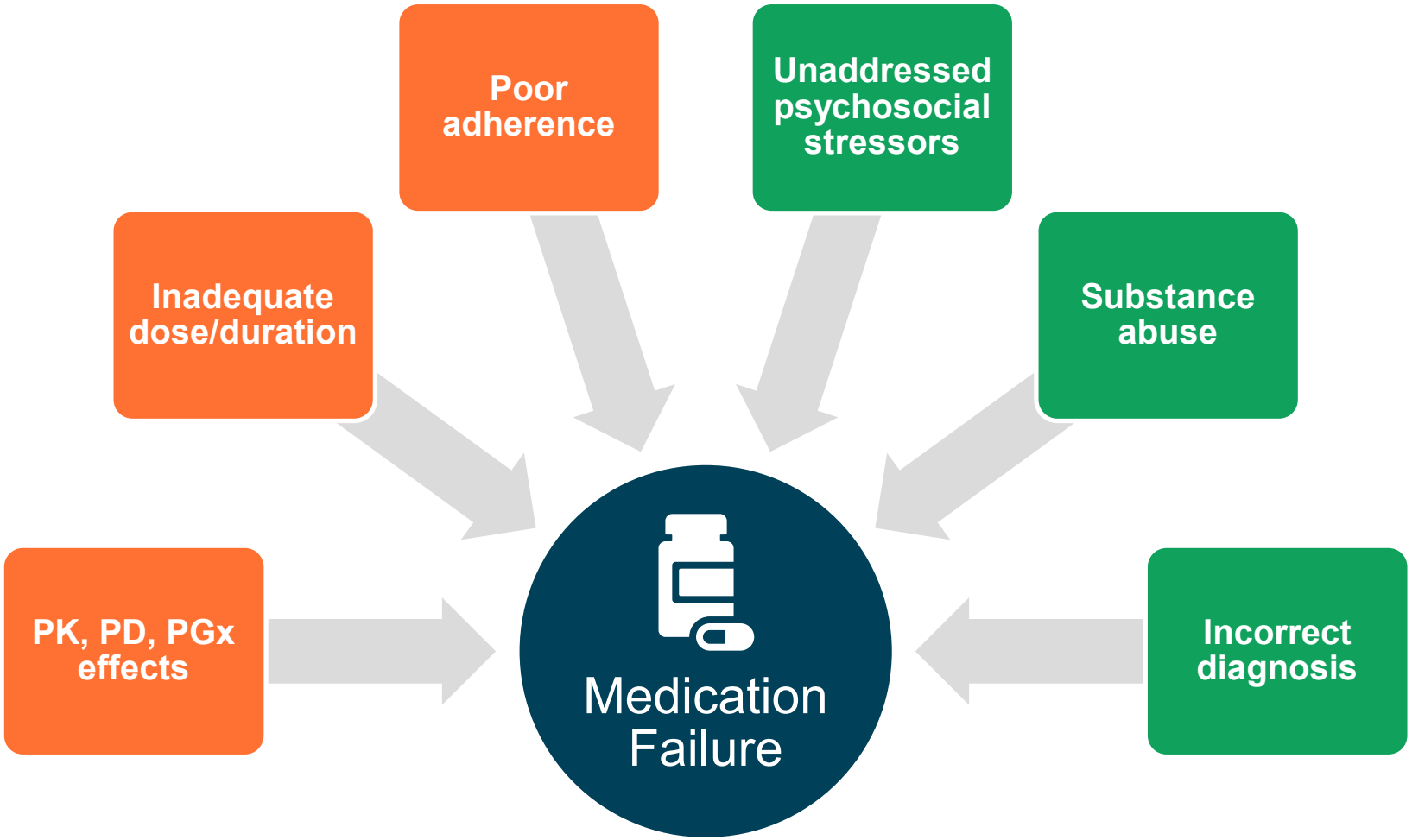
- Prevent relapse
- Consider taper at 1 year
- Continued regular follow-up

# My SSRI is Not Helping. What Next?

| | |
|---|---|
| Good but incomplete response | • Ensure 6–12 wks on optimized dose<br>• Consider adding psychotherapy or med from a different class |
| Minimal or no response after adequate trial | • Assess adherence<br>• Switch |

Ensure adequate dose and duration before considering medication a failure!

# Medication Failure Complexities



# Case Study

## Patient

L.D. is a 63 yo female who self-identifies as Black, referred for initiation of an antidepressant

PMH: T2DM, HTN, CKD stage 4, adopted, does not know her family history.
Allergies:  none

You see L.D. back in clinic three months later. She looks brighter and reports feeling more energetic and motivated, however, she is complaining of continued poor sleep and concentration which is reducing her quality of life. Her prescription dispensing history is regular, and she reports no side effects to her medications and very few missed doses.

## Labs/Vitals

| **Vital** | **Today** |
|---|---|
| BP | 116/68 |
| HR | 66 |
| Weight (lbs) | 181 |
| Height (in) | 64 |
| **Labs** | **Today** |
| TSH | 2.98 mIU/L |
| Hgb | 10.6 g/dL |
| eGFR | 25 ml/min/1.73m$^2$ |
| Hgb A1c | 6.9% |

## Medications

Losartan 50 mg daily
Empagliflozin 10 mg daily
Carvedilol 25 mg bid
Torsemide 40 mg daily
Sertraline 50 mg daily

# Doing Our Best for All Patients

- Know their healthcare and medication-related goals
- Obtain an accurate medical, social, & medication history
  - Learn about the patient, and listen
- Explain options: shared decision-making is key!
  - Educate to allow her to make an informed decision
- Create a sound follow-up plan

# Summary

Depression is a complex medical problem

In CKD, depression is associated with many negative outcomes

Care must be taken in selecting, dosing, and adjusting antidepressants

Patient education and shared decision-making are the keys to success!

# References


- Assimon et al. Comparative Cardiac Safety of Selective Serotonin Reuptake Inhibitors among Individuals Receiving Maintenance Hemodialysis. J Am Soc Nephrol 2019 Apr;30(4):611–623 https://pubmed.ncbi.nlm.nih.gov/30885935/
- Burrai F et al. Effects of Listening to Live Singing in Patients Undergoing Hemodialysis: A Randomized Controlled Crossover Study. Biol Res Nurs. 2019 Jan;21(1):30-38 https://pubmed.ncbi.nlm.nih.gov/30249121/
- Chi CY et al. Frailty as an Independent Risk Factor for Depression in Patients With End-Stage Renal Disease: A Cross-Sectional Study. Front Med (Lausanne). 2022 Feb 15;9:799544 https://pubmed.ncbi.nlm.nih.gov/35242777/
- Cukor D, et al. Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. J Am Soc Nephrol. 2014 Jan;25(1):196-206 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3871769/
- Hedayati SS et al. Effect of Sertraline on Depressive Symptoms in Patients With Chronic Kidney Disease Without Dialysis Dependence: The CAST Randomized Clinical Trial. JAMA. 2017 Nov 21;318(19):1876-1890 https://pubmed.ncbi.nlm.nih.gov/29101402/


# References


- Huang et al. Prevalence and risk factors for elevated anxiety symptoms and anxiety disorders in chronic kidney disease: A systematic review and meta-analysis. General Hospital Psychiatry, 2021;(69) 27–40. Volume 69, 2021 https://pubmed.ncbi.nlm.nih.gov/33516963/
- Martin et al. The Experience of Symptoms of Depression in Men vs Women: Analysis of the National Comorbidity Survey Replication. JAMA Psychiatry. 2013;70(10):1100–1106 https://pubmed.ncbi.nlm.nih.gov/23986338/
- Mehrotra et al. Comparative Efficacy of Therapies for Treatment of Depression for Patients Undergoing Maintenance Hemodialysis: A Randomized Clinical Trial. Ann Intern Med. 2019 Mar 19;170(6):369-379 (ASCEND) https://pubmed.ncbi.nlm.nih.gov/30802897/
- Mills JA, Suresh V, Chang L, Mayes T, Croarkin PE, Trivedi MH, Strawn JR. Socioeconomic Predictors of Treatment Outcomes Among Adults With Major Depressive Disorder. Psychiatr Serv. 2022 Sep 1;73(9):965-969 https://pubmed.ncbi.nlm.nih.gov/35354325/
- Natale P et al. Psychosocial interventions for preventing and treating depression in dialysis patients. Cochrane Database Syst Rev. 2019;12:CD004542. Epub 2019 Dec 2 https://pubmed.ncbi.nlm.nih.gov/31789430/


# References


- Palmer et al. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. Kidney Int 2013;(84):179–191 https://pubmed.ncbi.nlm.nih.gov/23486521/
- Shirazian et al. Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management. Kidney Int Rep 2017; (2):94–107 https://pubmed.ncbi.nlm.nih.gov/29318209/
- Shirazian S. Depression in CKD: Understanding the Mechanisms of Disease. Kidney Int Rep. 2018 Nov 28;4(2):189–190 https://pubmed.ncbi.nlm.nih.gov/30775614/
- Soliva MS et al. Intervention study to verify the effect of live classic music during hemodialysis on the quality of life of patients with chronic kidney disease. Nefrologia (Engl Ed). 2022 Sep-Oct;42(5):559-567 https://pubmed.ncbi.nlm.nih.gov/36739245/
- Swetlitz N. Depression's Problem with Men. AMA J Ethics. 2021;23(7):E586–589 https://journalofethics.ama-assn.org/article/depressions-problem-men/2021-07
- Tsai YC et al. Association of symptoms of depression with progression of CKD. Am J Kidney Dis. 2012 Jul;60(1):54-61 https://pubmed.ncbi.nlm.nih.gov/22495469/


# Advancing Kidney Health

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**Thank you!**