Advancing Kidney Health

Through Optimal Medication Management

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Medication Therapy Problems in Chronic Kidney Disease

Glossary of Terms

- **ACE inhibitors-** angiotension converting enzyme inhibitors
- **ARBs-** angiotensin receptor blockers
- **CG-** Cockcroft gault
- **CKD** = chronic kidney disease
- **CKD-EPI** = Chronic Kidney Disease Epidemiology Collaboration
- **CrCL** = creatinine clearance
- **eGFR** = estimated glomerular filtration rate, either estimated (e) or measured (m)
- **ESKD-** end stage kidney disease
- **NSAIDs** = nonsteroidal antiinfammatory drugs
- **PPIs**= proton pump inhibitors
- **SGLT-2i**= sodium glucose co-transporter 2 inhibitors

What We’re Going to Cover

- Why this matters
- The solution
- Case study
- Key takeaways

Why Does it Matter?

- Patients with CKD take on average 8- 12 medications per day
- Medication Therapy Problems (MTPs) are very common in CKD
- Pharmacists play a pivotal role in medication management in patients with CKD

Manley HJ, et al. Nephrology Dialysis Transplantation; 2004;19(7);1842–1848.
Pai AB, et al. *Clin Amer Soc Nephrol.* 2013;8(11):1988-1999.

The Solution

1

Medication Reconciliation

- Generate accurate list

2

Medication Review

- Review of list by advanced practitioner to identify MTPs

3

Issue Resolution

- Escalated to prescriber to resolve MTPs

Bluml, BM. J Am Pharm Assoc. 2005;45:566–572.
St Peter WL.*Adv Chronic Kidney Dis.* 2010;17(5):413-419.

Common Medication Therapy Problems in CKD

1. SAFETY- ie. Dosage too high/ Adverse medication Event
    i. Changes in Pharmacokinetic Parameters
    ii. Drug Dosing
    iii. Increased risk of adverse medication events
    iv. Medications causing increased risk of declining kidney function and/or nephrotoxicity
        a. NSAIDs
        b. Herbals
2. INDICATION- unnecessary medication
3. EFFECTIVENESS- ineffective medication
    i. Polypharmacy
4. ADHERENCE

Cardone KE et al. Adv Chronic Kidney Dis. 2010 Sep;17(5):404-12

Case

JP

- HPI
  - 84-year-old female with Stage 4A1 CKD (SrCr 2.1mg/dL; eGFR 23/ml/1.73m^2) secondary to Type 2 Diabetes
- PMH
  - HTN
  - Atrial Fibrillation
  - Dyslipidemia
- Social History
  - Widow – living alone
  - 3 falls last year
  - Sometimes confused and forgets things
  - Children worried about mom

Case

MEDICATIONS

- ASA 81mg po daily
- Dimenhydrinate 50mg po qhs
- Lorazepam 1mg po qhs*
- Apixaban 5mg po bid*
- Metoprolol 50mg po bid*
- Amlodipine 10mg po daily*
- Ramipril 5mg po daily*
- Ginkgo tablets po daily*
- Insulin glargine 15u sc qhs
- Insulin lispro 4-6u sc tid
- Loperamide 2mg po prn
- Furosemide 40mg po bid*
- Atorvastatin 40mg po daily*
- Dextromethorphan syrup po prn
- Lansoprazole 30mg po daily*
- Oxybutynin XL 10mg po daily*
- Vitamin B12 1200mcg po daily*
- Potassium Supplement po daily*
- Calcium/Vitamin D po bid*
- Darbepoietin 10mcg sc q2 weeks
- Ferrous fumarate 100mg po qhs*
- Noni juice -1/2 cup po daily

* Medications dispensed in patient-friendly pack

Common Medication Therapy Problems in CKD: SAFETY

- Changes in Pharmacokinetic (PK) Parameters
  - Absorption
  - Protein Binding
  - Volume Distribution
  - Metabolism
  - Kidney Excretion

- Determination of non-indexed estimated glomerular filtration rate (eGFR) by using non-race based CKD-EPIcr (2021) equation and compare with Cockcroft-Gault eCrCL for drug dosing decisions.

Lea-Henry, TN et al. CJASN Jul 2018, 13 (7) 1085-1095

Stepwise Approach to Adjust Drug Dosages

Kappel et al. CMAJ 2002;166:473-477

Common Medication Therapy Problems in CKD: SAFETY

- Potential for Adverse Medication Events
  - Glucose levels- hypoglycemia
  - Hyperkalemia
  - Blood pressure- hypotension
  - Increased risk of bleeding

Whittaker CF et al. Clin J Am Soc Nephrol. 2018 Nov 7;13(11):1738-1746.

Common Herbal Products That May Cause Kidney Problems

Aristolochic acid	Causes rapidly progressive fibrosing interstitial nephritis and kidney failure. It is also linked to urothelial malignancy. Contained in Virginian and Texas snakeroot or in Chinese herbs like *Stephania tetranda* and *Magnolia officinalis*.
Barberry	Possibly causes interstitial nephritis
Buchu	Causes kidney irritation
Chinese herbal drugs	Contain a variety of herbs, and often aristolochic acid
Juniper	Causes kidney fibrosis
Licorice	Associated with sodium and water retention, hypokalemia and hypertension
Noni juice	Associated with Hyperkalemia Also known as the *Och plant* (India), *Nono* (Tahiti), *Nonu* (Samoa), *Nhau* (Southeast Asia) and *Chinese fruit* (Australia).

Osman NA, et al. J Ren Nutr. 2015;25(6):466-71.
Colson C, De Broe. Advances in Chronic Kidney Disease; 2005; 12 (3): 261-275
Jha V. Nephrology;2010; 15: 10-17

Common Medications That Can Worsen Kidney Disease or Cause Kidney Toxicity

- Potential for worsening of kidney disease and nephrotoxicity
  - Different parts of the kidney are affected by medications
    - Hemodynamics (NSAIDs)
    - Interstitial (Proton Pump Inhibitors-PPIs)
    - Tubular (aminoglycosides)
    - Obstruction – crystallization (acyclovir)

- Nephrotoxicity
  - Sick Days (SADMANS)
  - Other comorbidities – Heart Failure

SADMANS
S- Sulfonylureas
A- ACE Inhibitors
D- Diuretics
M- Metformin
A- ARBs
N- NSAIDs
S- SGLT2 Inhibitors

Perazella MA. et al. CJASN Aug 2022, 17 (8) 1220-1233.
Diabetes Canada Clinical Practice Guidelines 2018

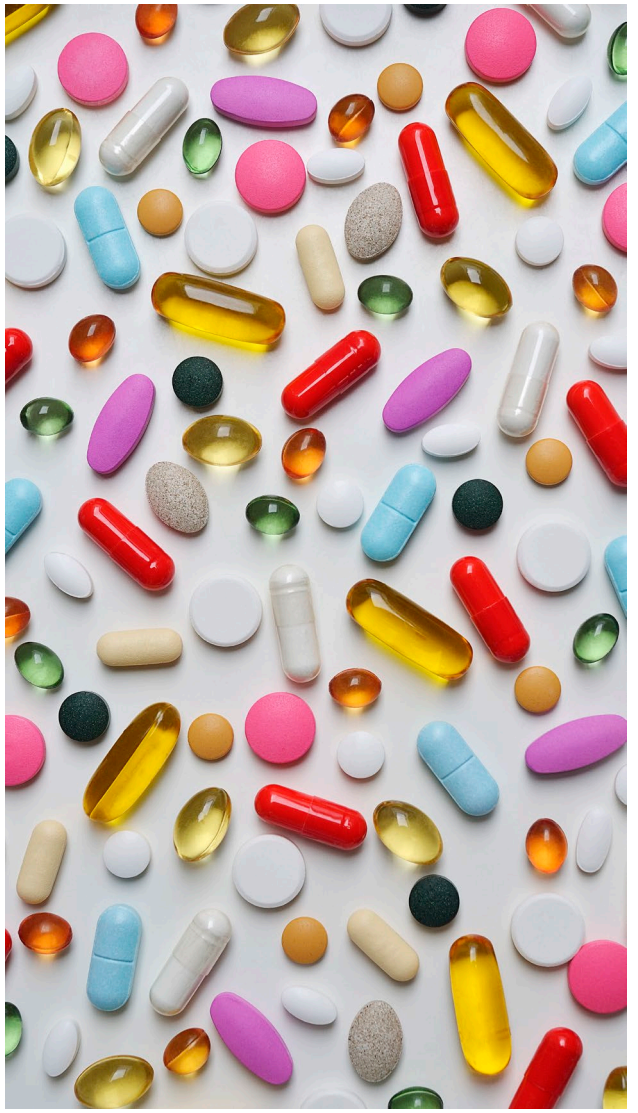
Common Medication Therapy Problems in CKD: INDICATION/EFFECTIVENESS

- Polypharmacy means “many drugs”
  - 5 or more drugs
- Polypharmacy also means inappropriate choices of medications or doses

Patterson SM, et al. Cochrane Database Syst Rev. 2014;(10)

Consequences of Polypharmacy

- Decreased adherence, drug-drug interactions, and adverse drug reactions (ADRs)
- In the USA, ADRs are estimated to claim between 100,000 to 218000 lives annually
- These ADRs cost the healthcare system up to $137–177 billion
- Increased risk of mortality by > 45 % in those taking > 5 medication compared to those taking < 5 medications



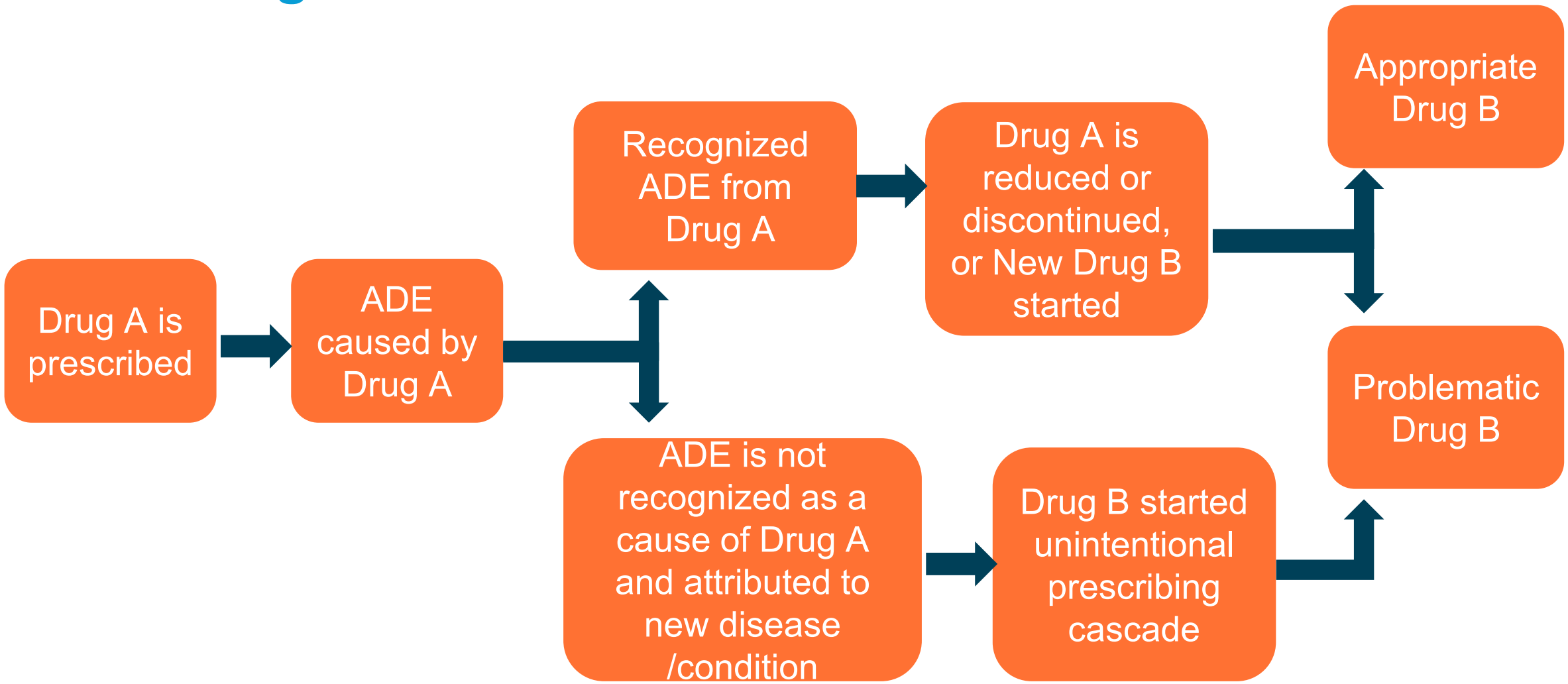
Okpechi IG, et al.. Syst Rev. 2021 Jul 4;10(1):198.

Risk Factors for Polypharmacy

- Age
- Multi-morbidity
- Acute hospitalization
- Health care visits
- Multiple providers

Hajjar ER, Am J Geriatr Pharmacother. 2007;5(4):345-51.
Betteridge TM, et al. Int Med J 2012;42(2):208-11.
Jorgensen T et al. Ann Pharmacother. 2001;35:1004-1009.

Prescribing Cascades



Rochon PA, Gurwitz JH. Lancet. 2017;389(10081):1778–80.

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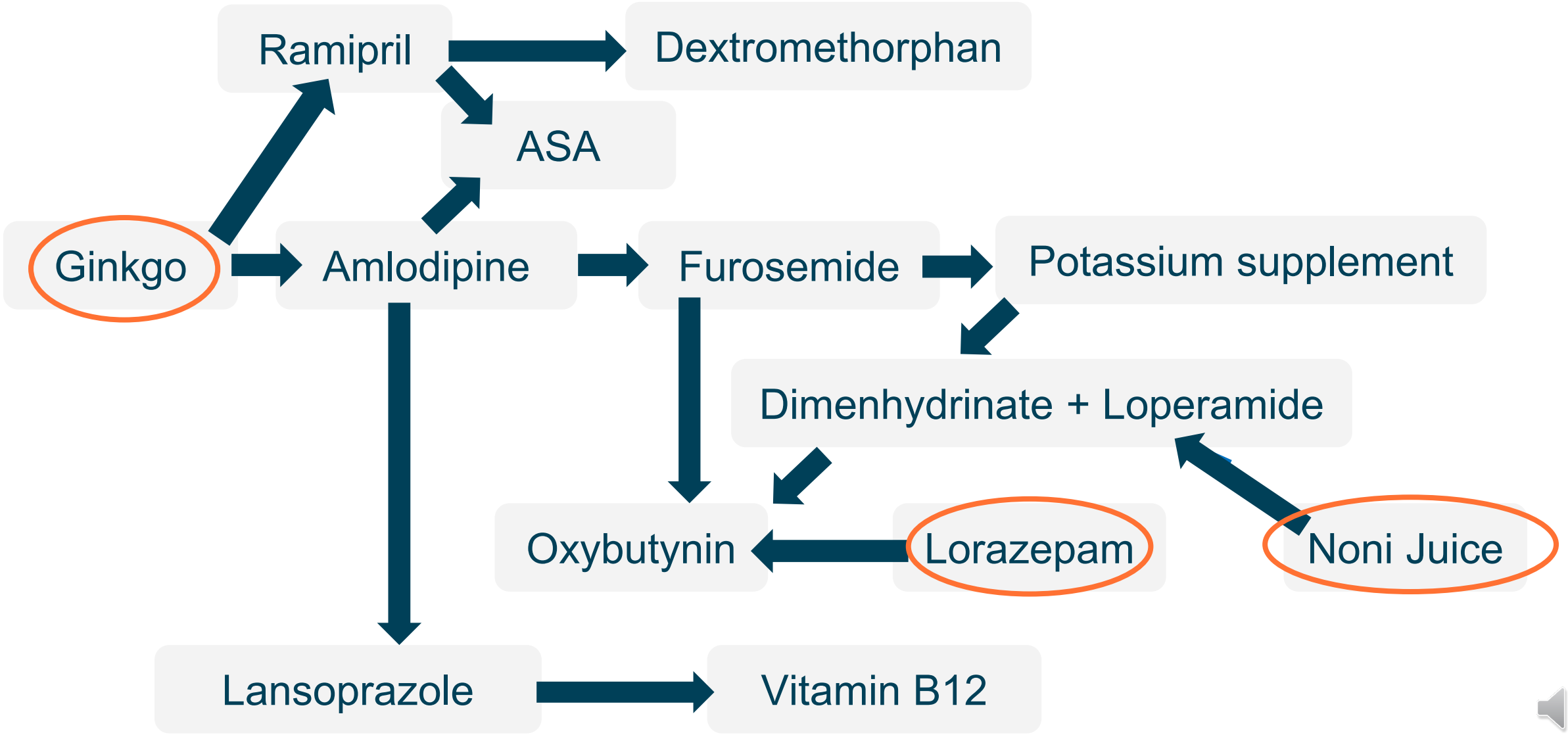
JP's Prescribing Cascade



Screening/Assessment Tools

American Geriatric Society- Beers Criteria

- Beers List is a consensus list of potentially inappropriate medications
- Limitations
  - Drug-nutrient interactions
  - Medication Underuse
  - OTC
  - Medication Adherence

Cardiovascular	
Peripheral alpha-1 blockers for treatment of hypertension ■ Doxazosin ■ Prazosin ■ Terazosin	**Avoid use as an antihypertensive** High risk of orthostatic hypotension and associated harms, especially in older adults; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile QE = Moderate; SR = Strong
Central-alpha agonists Clonidine for first-line treatment of hypertension Other CNS alpha-agonists ■ Guanabenz ■ Guanfacine ■ Methyldopa ■ Reserpine (>0.1 mg/d)	**Avoid clonidine as first-line antihypertensive. Avoid other CNS alpha-agonists as listed** High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension QE = Low; SR = Strong

J Am Geriatr Soc. 2019 Apr;67(4):674-694

START/STOPP Criteria

- **STOPP** – **S**creening **T**ool of **O**lder **P**erson's **P**rescriptions
  - inappropriate combinations of medicines and disease
- **START** – **S**creening **T**ool to **A**lert doctors to **R**ight **T**reatment
  - a set of recommended treatments for given conditions

Gallagher P, et al. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. Int J Clin Pharmacol Ther. 2008 Feb;46(2):72-83

What about Deprescribing?

"the process of tapering, stopping, discontinuing, or withdrawing drugs, with the goal of managing polypharmacy and improving outcomes"

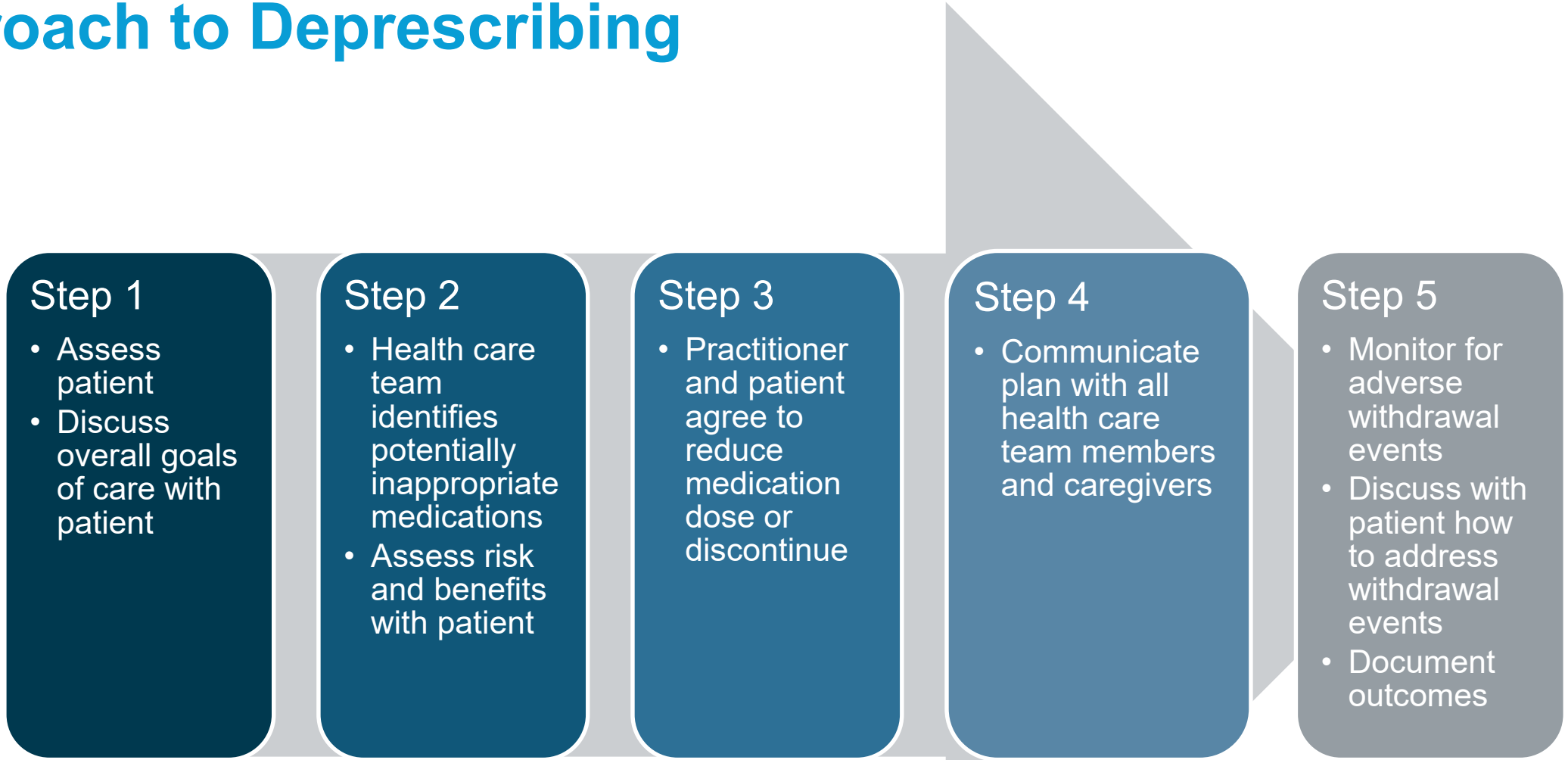
Scott IA, et al. JAMA Intern Med 2015;175:827-34

How to Stop? Or Deprescribe?

- Reduce or stop one medication at a time
- Start with medications where there is:
  - Risk of harm with no known benefit
  - Little chance drug withdrawal
  - Unclear or no indication
  - Indication but unknown or minimal benefit
  - Benefit but side effect or safety issues

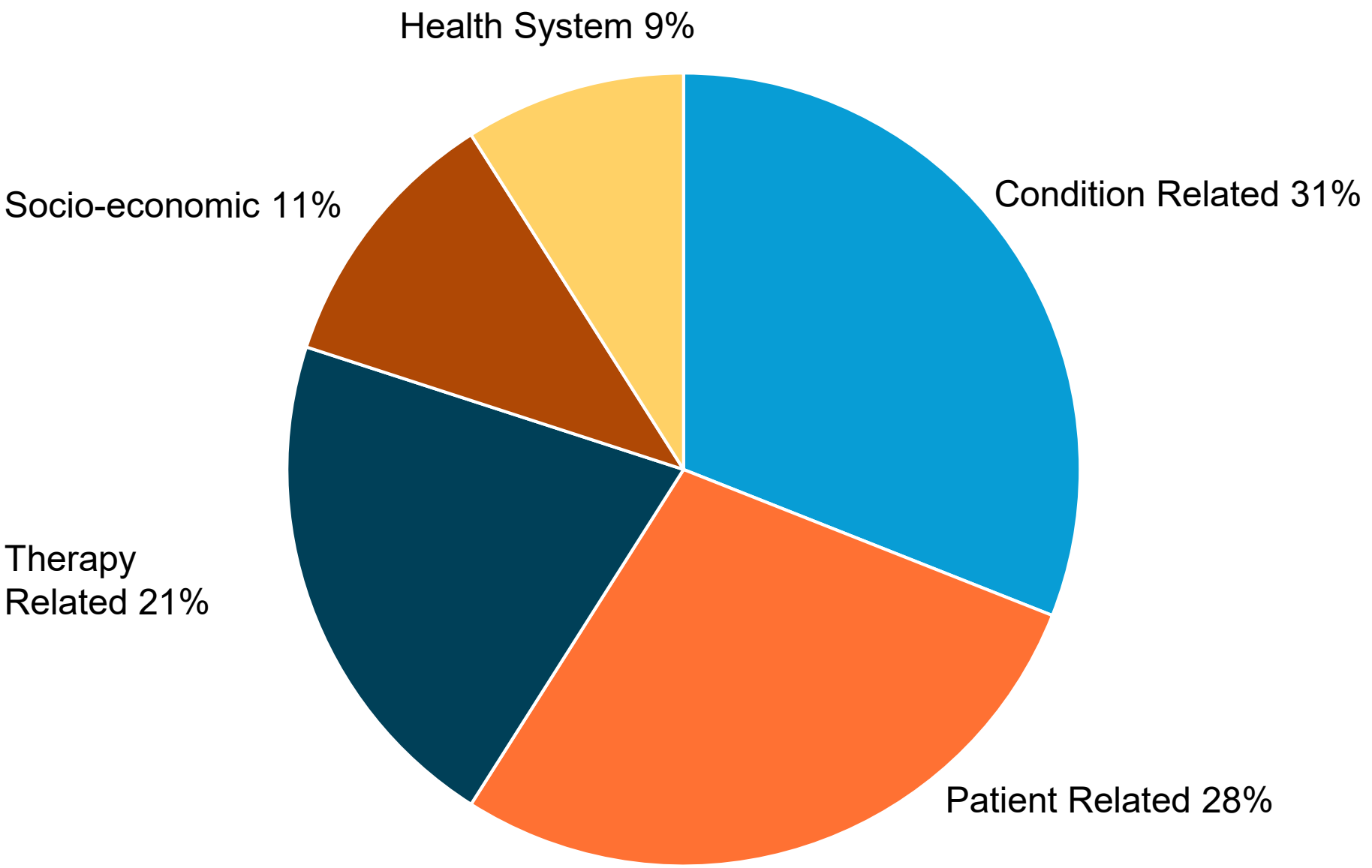
Scott IA, et al. Evid Based Med. 2013; 18(4):121-124.

Approach to Deprescribing



Reeve E, et al. Eur J Intern Med. 2017;38:3-11.

Common Medication Therapy Problems in CKD: ADHERENCE



Seng JJB et al. Int Urol Nephrol. 2020 May;52(5):903-916.

Medication Adherence- socioeconomic factors

- Discount cards for those with commercial insurance
  - America's Pharmacy, GoodRx, WellRx
- Low cost generic medication programs (active in 2022)
  - HEB, Hyvee, Walgreens, Walmart, Winn-Dixie
  - Mark Cuban CostPlus Drug Company
- Pharmaceutical company prescription assistance programs
  - Focus is on tradename (non-generic) medications
- Federal and state assistance programs
  - Medicare Part D Extra help program

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How can we do our best for this patient?

Know her healthcare and medication-related goals

Improve her medication literacy

- Encourage to speak to her health care team about her medication use in CKD

Assess Prescribing Cascades and Deprescribing

- Medication Reconciliation and Review

Shared decision-making is key!

Summary

Medication Therapy Problems are common in CKD/ESKD

Appropriate & Problematic Prescribing Cascades are also common

Polypharmacy, a main issue in CKD/ESKD leads to serious complications

Medication Reconciliation and Review are key to resolution of problems

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Thank you!

Additional Helpful References

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