Optimization of Pharmacotherapy Management: Deprescribing in CKD

Marisa Battistella, Pharm D
Pharmacy Clinician Scientist
Associate Professor
University Health Network-
University of Toronto

Disclosures

- None

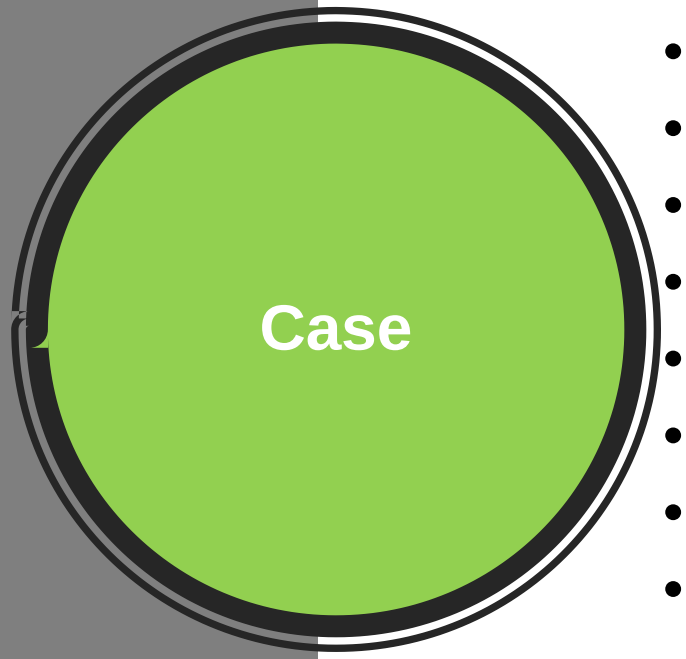
Learning Objectives

- Describe the potential harms of polypharmacy in patients with advanced chronic kidney disease (CKD) and End Stage Kidney Disease (ESKD)
- Identify medications with poor evidence for efficacy and safety in the CKD/ESKD population
- Apply current tools and approaches to medication deprescribing in the CKD/ESKD population

Case of Mrs P

- 84-year-old on HD for the past 6 months secondary to DM
- Widow – living alone
- 3 Falls last year
- Sometimes confused and forgets things
- Children worried about mom

Mrs P's Medications



- ASA 81mg daily
- Dimenhydrinate 50mg qhs
- Lorazepam 1mg qhs*
- Warfarin as directed*
- Metoprolol 50mg bid*
- Amlodipine 10mg daily*
- Ramipril 5mg daily*
- Ginkgo tabs daily*
- Insulin 30/70 12u sc bid
- Furosemide 40mg bid*
- Atorvastatin 40mg daily*
- Dextromethorphan syrup
- Lansoprazole 30mg daily*
- Oxybutynin XL 10mg daily*
- Vitamin B12 1200mcg daily*
- Potassium Supplement daily*
- Calcium/Vitamin D bid*
- Darbepoietin 10mcg iv weekly
- Iron sucrose 100mg iv once monthly

* Medications dispensed in patient-friendly pack

Polypharmacy

Polypharmacy

- Polypharmacy means “many drugs”
  - 5 or more drugs

- Polypharmacy also means inappropriate choices of medications or doses

Patterson et al. Cochrane Database Sys Rev 2012

Polypharmacy

Consequences of Polypharmacy

On people

- decreased adherence, drug-drug interactions, and adverse drug reactions
- 68% report AE after hospital discharge (72% due to medication)

Forster et al CMAJ 2004

Polypharmacy

Consequences of Polypharmacy

On health care utilization

- hospital admissions (preventable, drug-related)

On cost

- 4.4 billion dollars (Canadian) spent from Public Drug Programs on drugs for elderly
- 20% of health care spending

CIHI 2014

Risk Factors for Polypharmacy

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.

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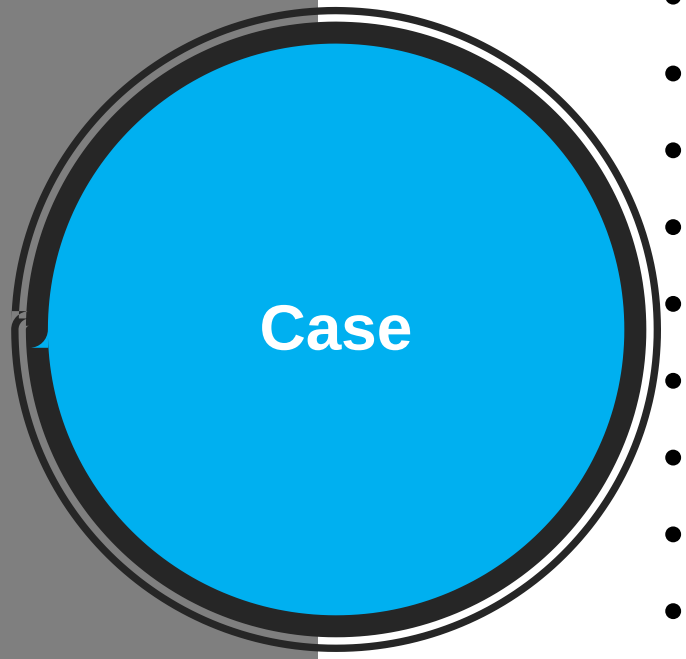

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Prescribing Cascade

Polypharmacy

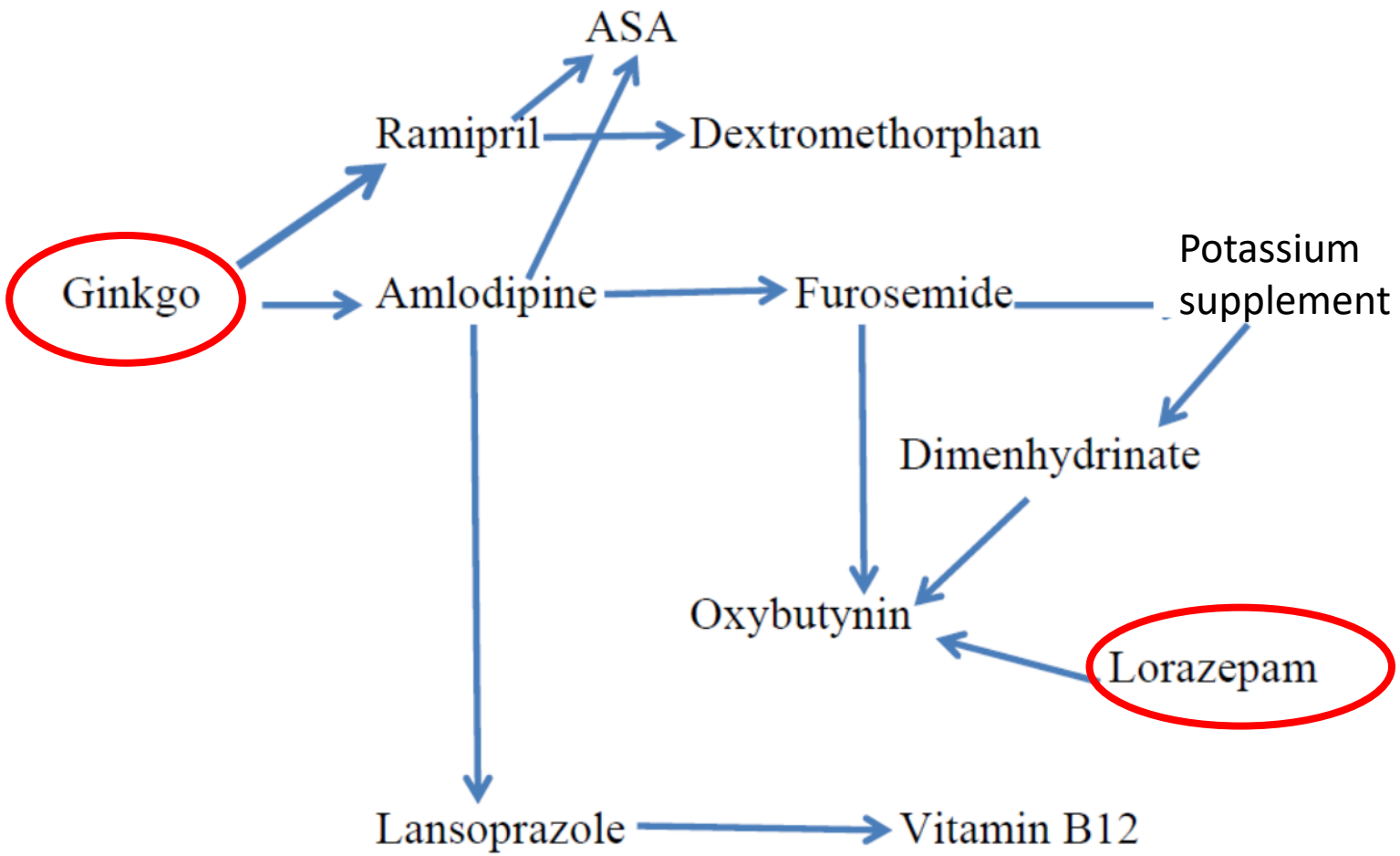
An adverse reaction is interpreted as a new disease so new medication is added

An adverse reaction is interpreted as a new disease so another medication is added

An adverse reaction is interpreted as new disease and yet another new medication is started

Mrs P's Prescribing Cascade

Polypharmacy



Question

What is the average number of medications a dialysis patient takes daily?

A. 3-5 medications

B. 6-10 medications

C. 11-15 medications

D. > 15 medications

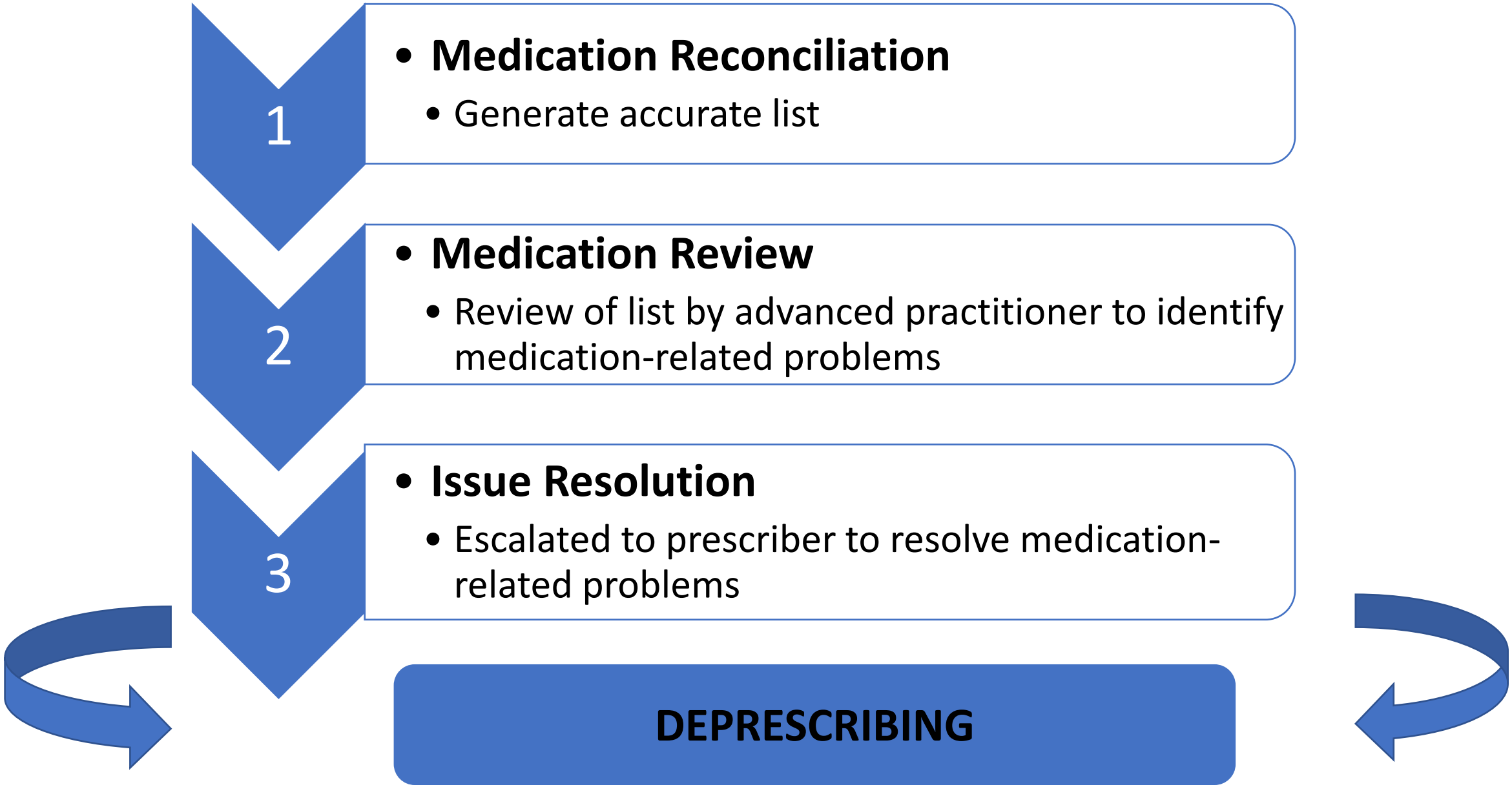
Polypharmacy In CKD

Polypharmacy

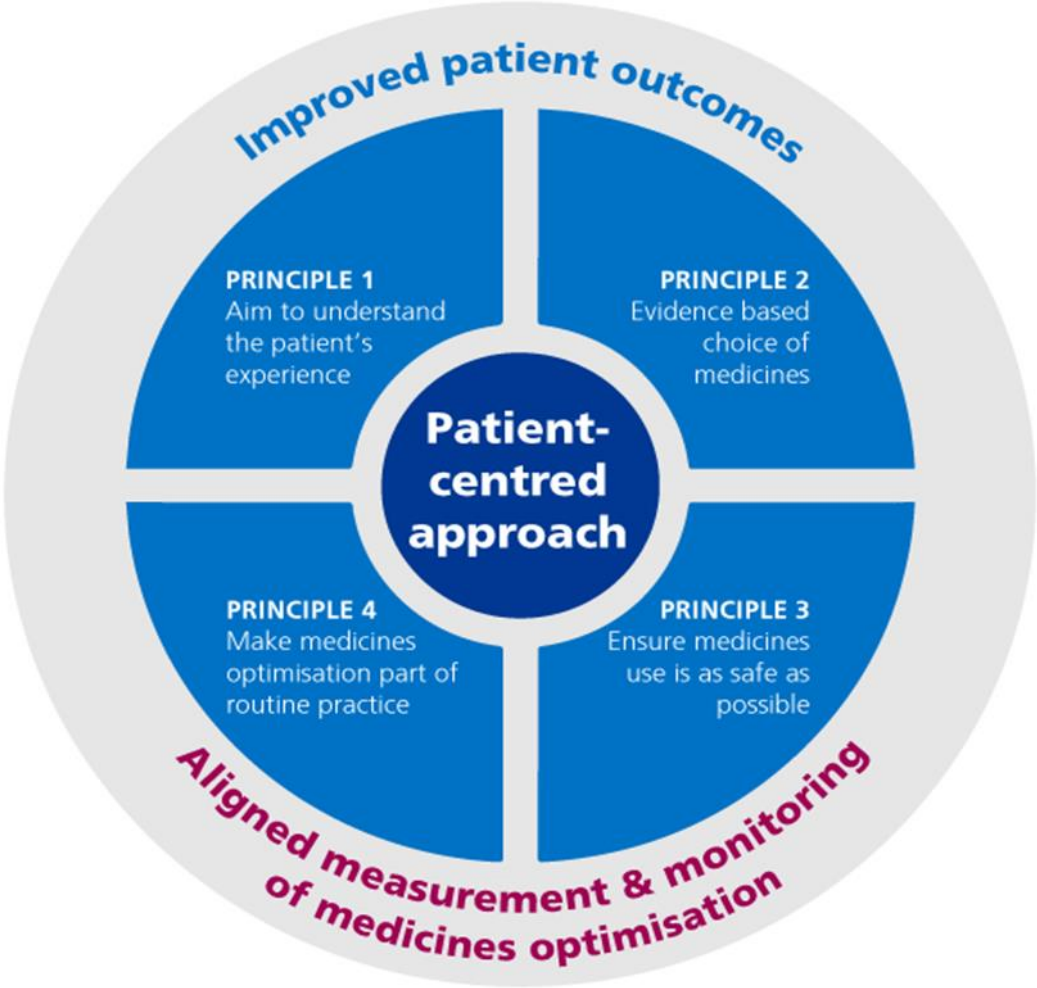
- USRDS 1998- HD pts were taking a median of 9 medications/day
- USRDS -redone in 2004- 12 median medications/day
- University Health Network (Toronto) HD unit (2015):
  - Median of 12 medications/day

Manley et al NDT 2004 ; Battistella et al JRC 2015

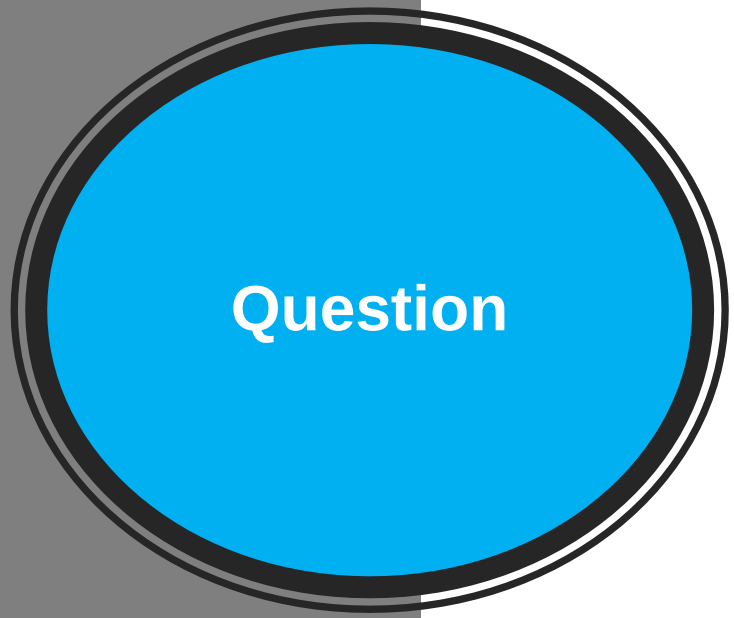
Medication Therapy Management



Optimization of Medications



https://www.england.nhs.uk/medicines-2/medicines-optimisation/



Question

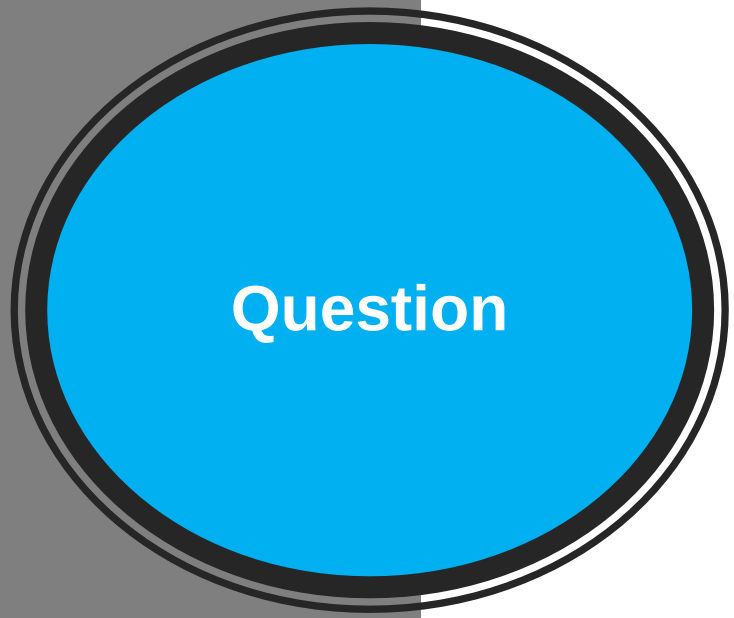
What is the most common medication used by dialysis patients?

A. Proton Pump Inhibitors

B. Benzodiazepines

C. Statins

D. Opioids



Question

What is the most expensive drug used by dialysis patients?

A. Proton Pump Inhibitors
B. Insulin
C. Statins
D. Opioids

Polypharmacy

A Province-Wide, Cross-Sectional Study Of Demographics And Medication Use Of Patients In Hemodialysis Units Across Ontario

Battistella et al CJKHD 2018;5:1-10

Table 1. Baseline Characteristics of Patients Receiving a Study Medication (N = 3094).

Characteristic	N	%
Age, years		
Mean (SD)	76.5 (7.3)	
Median (IQR)	76 (70-82)	
≤65 years	121	3.9
66-69 years	536	17.3
70-74 years	646	20.9
75-79 years	697	22.5
80-84 years	622	20.1
85-89 years	335	10.8
90+ years	137	4.4
Sex		
Women	1373	44.4
Men	1721	55.6
Location[c]		
Urban	2885	93.2
Rural	209	6.8
Long-term care residence	277	9.0
Neighborhood income quintile[d]		
1 (lowest)	779	25.2
2	690	22.4
3	592	19.2
4	536	17.4
5 (highest)	489	15.8
Comorbidities		
Coronary artery disease (including angina)	1911	61.8
Diabetes mellitus	1628	52.6
Heart failure	1592	51.5
Chronic lung disease	1298	42.0
Arrhythmia (bradyarrhythmia and tachyarrhythmia)	907	29.3
Atrial fibrillation/flutter	667	21.6
Myocardial infarction	519	16.8
Peripheral vascular disease	474	15.3
Chronic liver disease	344	11.1
Stroke or transient ischemic attack	226	7.3
Coronary revascularization	152	4.9
Aortic aneurysm repair or bypass	33	1.1
Renal transplant	11	0.4

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Median Dialysis Vintage- 4.2 years (2-5)

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Number of unique drug names		
Mean (SD)	11.3 (5.0)	
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9-12 drug names	984	31.8
13-16 drug names	680	22.0
17+ drug names	466	15.1
Study medication use (of 28 study medications only)		
Number of unique drug names		
Mean (SD)	5.4 (2.3)	
Median (IQR)	5 (4-7)	
Health care use (prior 365 days)		
Primary care visits		
Mean (SD)	12.0 (14.8)	
Median (IQR)	7 (3-15)	
0 visits	202	6.5
1-3 visits	712	23.0
4-6 visits	541	17.5
7-9 visits	369	11.9
≥10 visits	1270	41.0
Prescriber information		
Number of prescriber specialties[b]		
Mean (SD)	2.8 (1.3)	
Median (IQR)	3 (2-4)	
1 specialty	391	12.7
2 specialties	1031	33.4
3+ specialties	1672	54.0
Prescribing physician specialty[a]		
General practitioner	1312	49.40
Nephrologist	1189	44.80
Cardiologist	60	2.30
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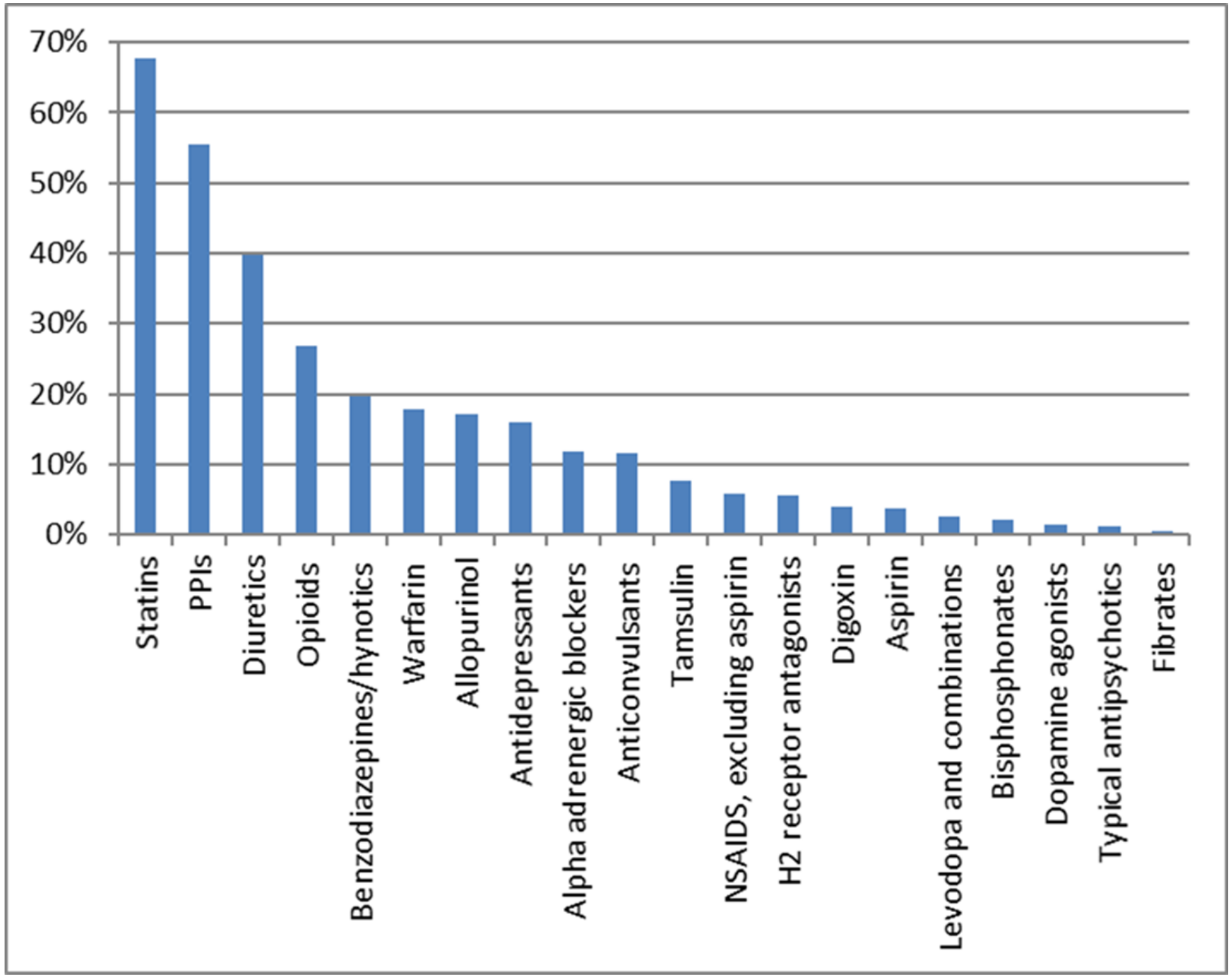
Percentage of Medication Use in HD Patients



Battistella et al CJKHD 2018;5:1-10

Annual Costs for Most Costly Study Medications

Study Medication	Total Prescriptions	Total Annual Cost [a]
Insulin	6320	$ 662,112
Proton pump inhibitors	31,847	$ 433,093
Calcitriol	18,710	$ 404,305
Statins	35,771	$ 384,073
Calcium channel blockers	24,865	$ 312,209
Beta blockers	29,789	$ 228,950
Opioids	8989	$ 201,132
Oral antiglycemics	7937	$ 164,476
Diuretics	20,230	$ 141,529
ACE inhibitors	10,014	$ 131,530

[a]- calculated over one year

Battistella et al CJKHD 2018;5:1-10

A Province-Wide, Cross-Sectional Study Of Demographics And Medication Use Of Patients In Hemodialysis Units Across Ontario

Polypharmacy

- Polypharmacy is frequent in HD patients.
- Strategies to improve prescribing and deprescribing ineffective medications warrant testing for better patient outcomes and reduced healthcare costs.

Battistella et al CJKHD 2018;5:1-10

Deprescribing

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

Thompson and Farrell *Can J Hosp Pharm*. (2013); 66(3): 201–202

Why Deprescribe in Dialysis?

- Dialysis patients have high pill burden
  - Median of 12 medications per patient
- Evidence for efficacy of many therapies is lacking in this population
- Safety concerns for medications that are cleared by the kidney and not removed by dialysis
- No tools for deprescribing available for this population

Chiu *et al. Clin J Am SocNephrol*. (2009);4(6):1089-96

Question

What medication would you most likely Deprescribe in your patients?

A. ACE inhibitors
B. Proton Pump Inhibitors
C. Insulin
D. Antidepressants

Targeted Deprescribing in an Outpatient Hemodialysis Unit: A Quality Improvement Study to Decrease Polypharmacy

AJKD 2017; 70(5):611-618

Methods

Phase 1: Development of Deprescribing Tool

- Focus groups were conducted
- Literature search performed
- Reviewed 50 charts- medication lists
- Five target medications were selected based on:
  - 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

AJKD 2017; 70(5):611-618

Five Targeted Medications

- Diuretics*
- PPIs
- Quinine
- Alpha-blockers
- Statins**

* Only for anuric patients

** Primary Prevention in patients greater than 80 years of age

Medication specific algorithms were developed

AJKD 2017; 70(5):611-618

Methods

Phase 2: Validation of Deprescribing Tool

- Face and content validity
  - Tool revised and retested on an iterative basis- total of 3 cycles
  - In consultation with 5 different nephrology team members, (15 different team members; 12 nephrologists, 2 pharmacists, 1 nurse practitioner).

AJKD 2017; 70(5):611-618

Methods

Phase 3: Implementation of Deprescribing Tool

- Prospective Observational Pilot Study
- Patients receiving HD at Toronto General Hospital between May 2014 and March 2015 were included

AJKD 2017; 70(5):611-618

Methods

Phase 3: Implementation of Deprescribing Tool

Collect BPMH*, Identify Target Medication, Apply Algorithm, Inform Team, Consent Patient

Communicate with patient the plan, monitor as per algorithm

Follow up 6 months later

BPMH- Best Possible Medication History

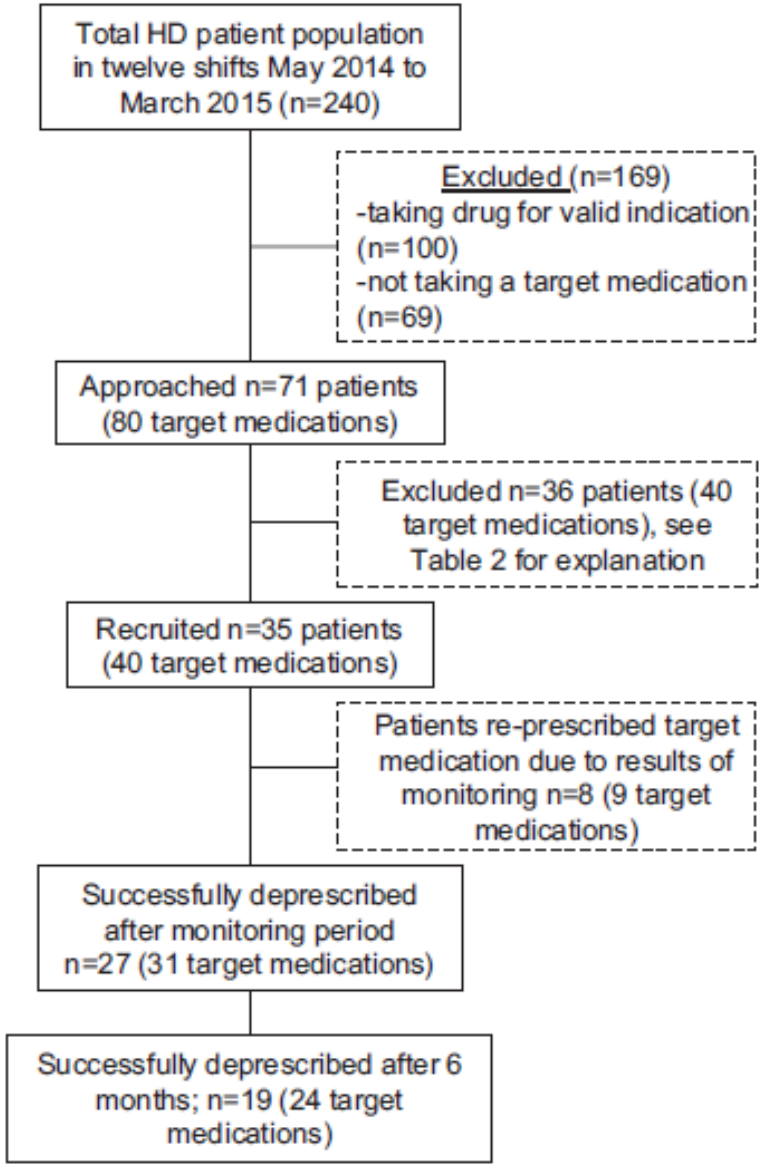
AJKD 2017; 70(5):611-618

Deprescribing

RESULTS

AJKD 2017; 70(5):611-618

Selection of Patients



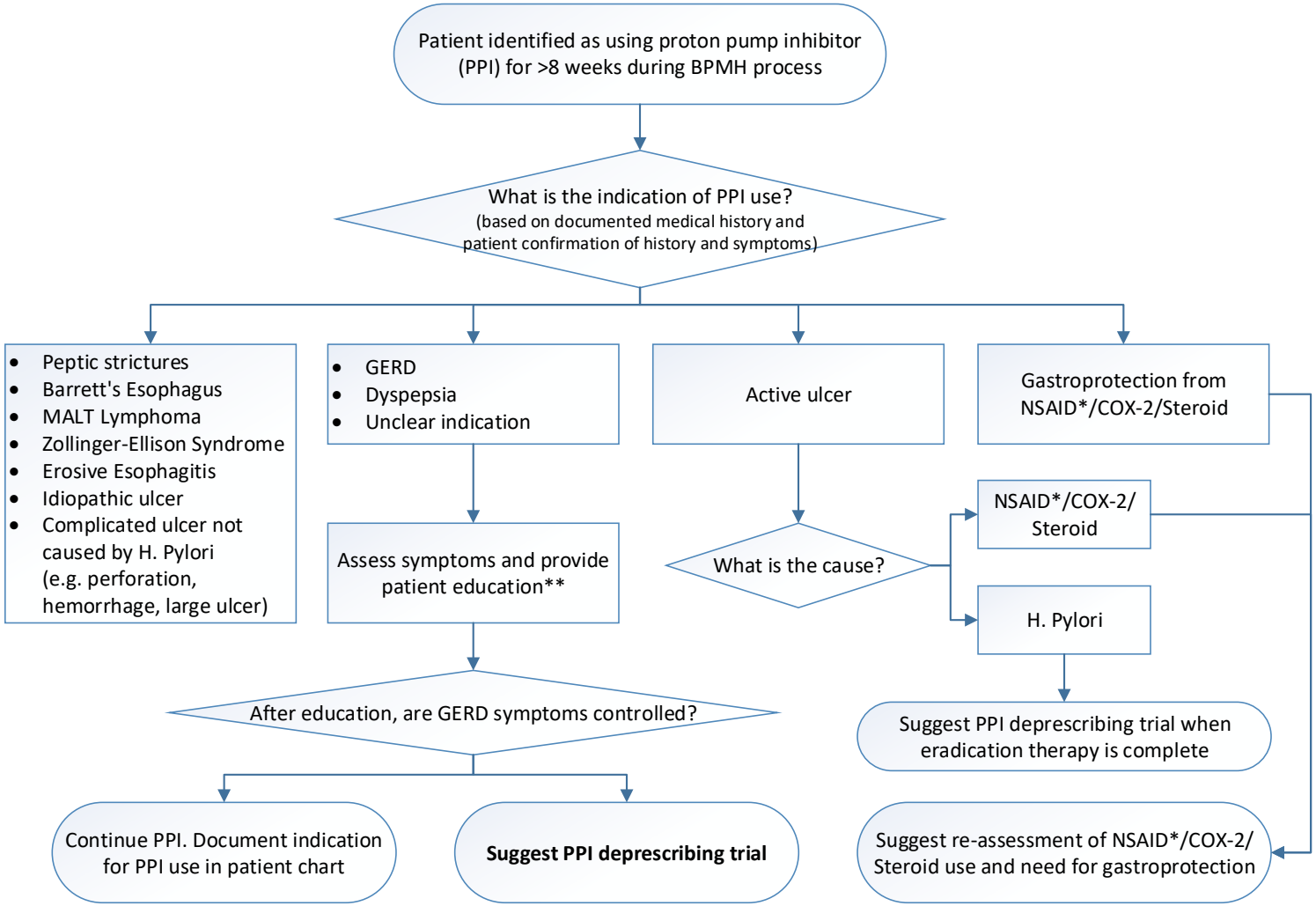
AJKD 2017; 70(5):611-618

Baseline Demographics

Characteristic	Total (n=35)
Age (y) Mean ± SD (Range)	65 ± 16.5 (33-92)
Gender	21 males, 14 females
Dialysis Vintage (months) Median	40 (23.2, 57.2)
Total Number of Medications Mean ± SD (Range)	13.4 ± 4.3
Comorbidities	
Hypertension	31
Diabetes Mellitus	21
Cardio Vascular Disease	21

AJKD 2017; 70(5):611-618

Deprescribing Algorithm for Proton Pump Use in Hemodialysis Patients



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PPI deprescribing trial:

1.Record frequency of GERD symptoms over 2 weeks after identification during BPMH process (if applicable)

2.Taper PPI

    1.If above standard dose, decrease to standard dose x 1 week.

        a.Standard doses are:

            1.Pantoprazole: 40mg

            2.Lansoprazole and dexlansoprazole: 30mg

            3.Esomeprazole, omeprazole and rabeprazole: 20mg

        b.Reduce to 50% of standard dose x 2 weeks then discontinue

3.Counsel patient on PRN antacid options for quick relief or rebound symptoms a appropriate for the patient.

4.Record frequency of GERD symptoms and PRN antacid use in 2 weeks post-intervention and compare to pre-intervention.

    1.If frequency of symptoms reduced, discontinue PPI permanently

    2.If frequency of symptoms increased:

        a.Consider H2RA:

•Ranitidine 150mg po qhs

•Famotidine 10mg po qhs (maximum 20mg po qhs in dialysis)

        a.Consider re-initiating PPI at standard dose

1.Document result of PPI discontinuation trial in patient chart

Re-assessment of NSAID/COX-2/steroid and gastroprotection: Clinical judgment of whether NSAID*/COX-2/steroid can be discontinued:

    1. If NSAID*/COX-2/steroid discontinued, **suggest discontinue PPI as per "PPI deprescribing trial" above**

    2.If NSAID/COX-2/steroid to be continued, clinical judgment of whether gastroprotection is required

        a.Gastroprotection required: continue PPI.

        b.Gastroprotection not required: **suggest PPI deprescribing trial**

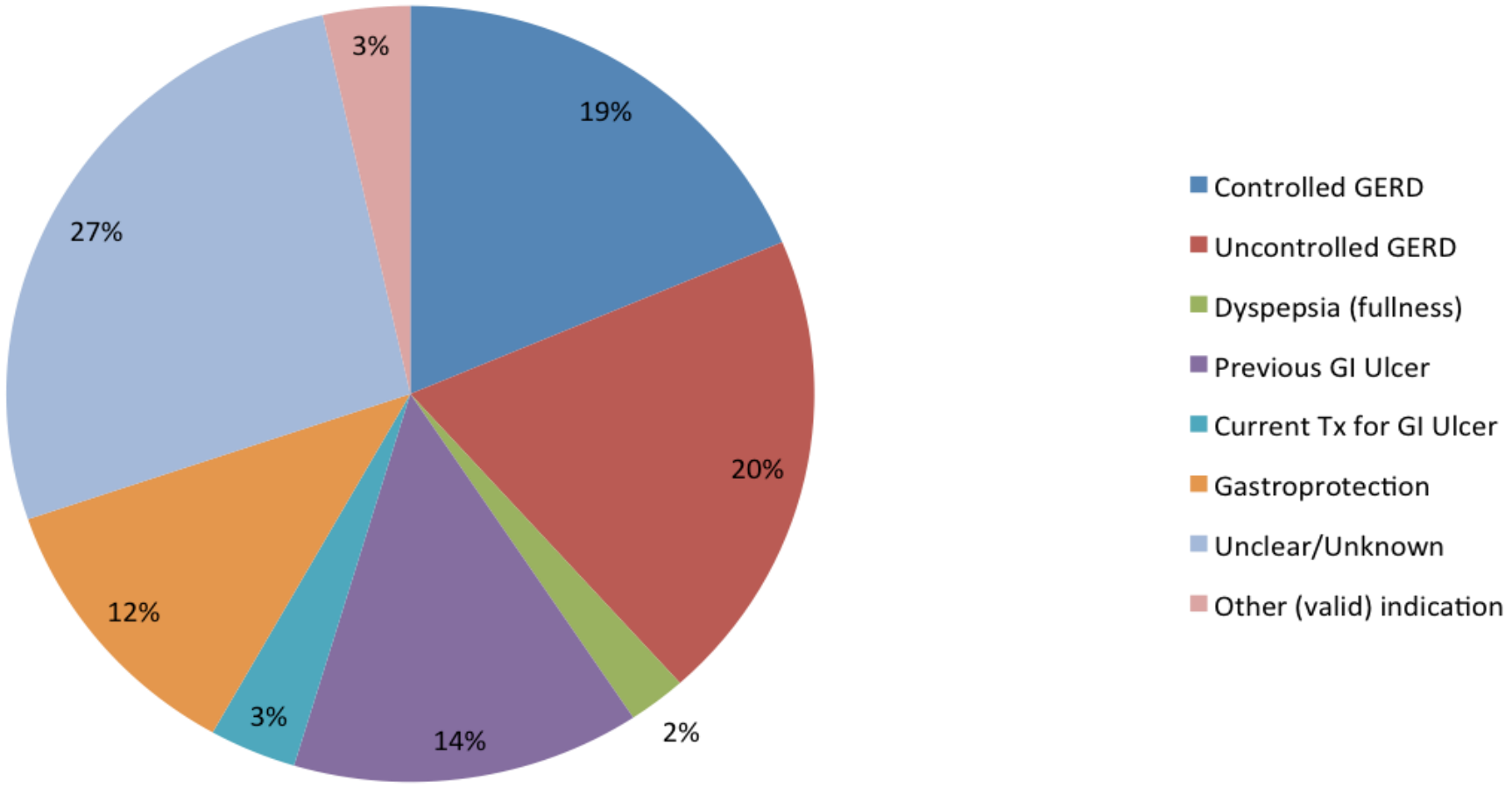
1.Document result of re-assessment in patient chart.

Efficacy and safety parameter for deprescribing PPI:

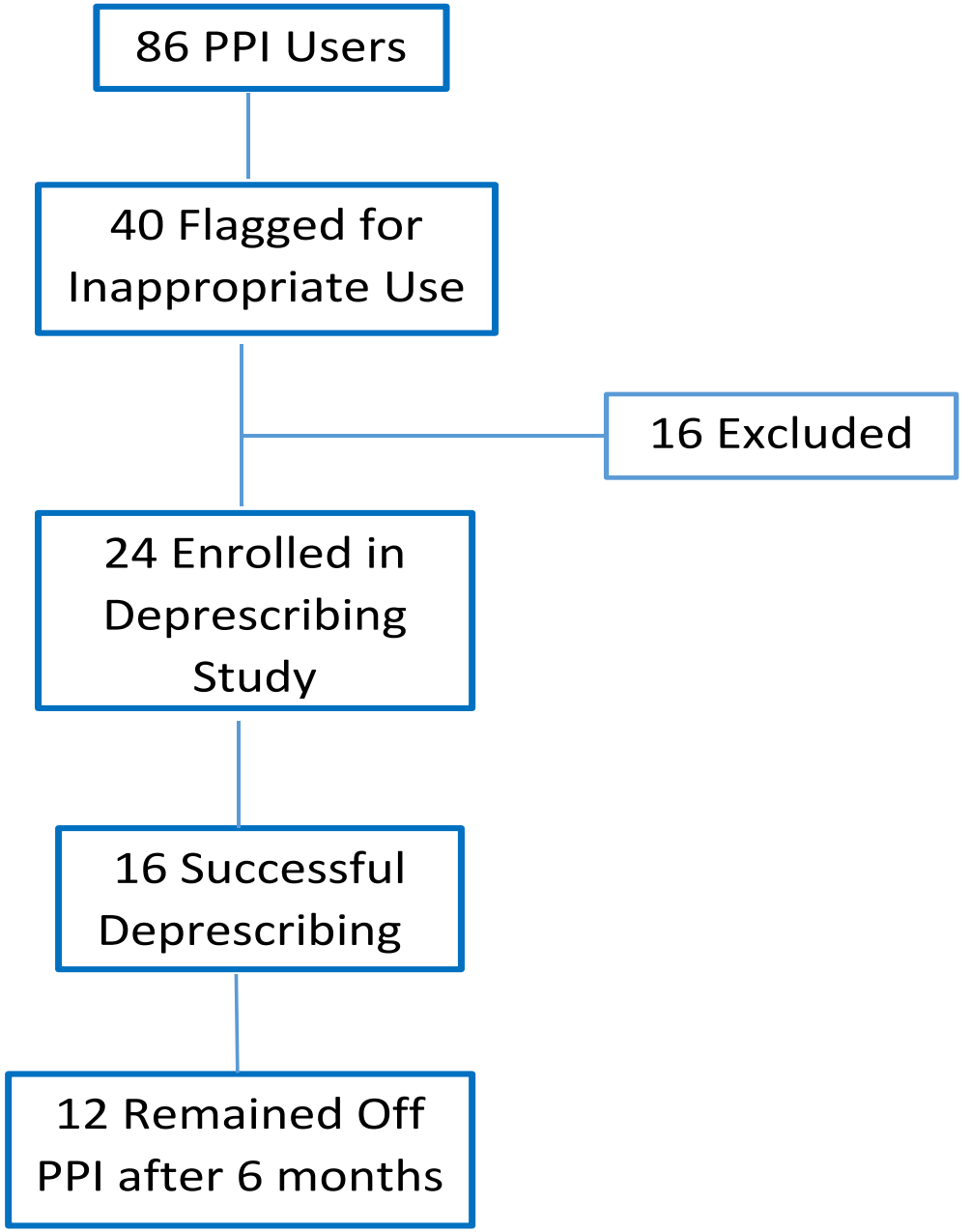
•Monitor frequency of symptoms as per "PPI deprescribing trial" above to ensure efficacy and safety of discontinuation

AJKD 2017; 70(5):611-618

Indication for PPI



PPI – Deprescribing



Monitoring for PPI

- **Two Weeks - Monitored for GERD symptoms**
  - 7 patients represcribed after 2 weeks (GERD symptoms)
  - 1 patient deceased dose

- **After 6 months**
  - 3 patients restarted because of GERD symptoms
  - 1 patient passed away

Reasons for disagreement with deprescribing algorithm (n=36)

Description of explanation	Number of drugs not included in study
Patient is still producing urine and nephrologist believes diuretic will make a difference in inter-dialytic weight gain (diuretic only)	16
Patient admitted to in-patient unit during deprescribing rounds	5
Patient transferred to another facility during deprescribing rounds	4
Patient on vacation during deprescribing rounds, or will be away during algorithm monitoring period.	3
Patient anxious about stopping a medication	3
Patient non-adherent to dialysis so would be difficult to monitor any changes after intervention	3
Patient had cognitive impairment so unable to safely monitor GERD symptoms (PPI only)	2
Patient was prescribed medication by another MD and nephrologist does not feel comfortable D/C the drug	2
Patient is to receive transplant from living-donor next week and nephrologist does not want to make changes to medications	1
Nephrologist believes quinine works for leg cramp indication (quinine only)	1
TOTAL	40

Note: patients may be taking more than one target medication (e.g. statin with a PPI)

AJKD 2017; 70(5):611-618

Table 2: Summary of screened target medications

Target Medication	Number of target meds (n=171)	Number of medications flagged by algorithm to deprescribe (n=71)	Number of medications enrolled in deprescribing trial (n=35)	Number medications successfully deprescribed (n=35)	Number of medications successfully deprescribed at 6 month (n=19)
Quinine	5	5	2	2	0[1]
Diuretics	31	31	10	9	8[2]
Alpha-1 blockers	14	3	3	3	3
Statins	95	1	1	1	1
PPI	86	40	24	16	12[3]
Total (drugs)	231	80	40	31	25

[1]One patient passed away after 5 months. The other patient was re-prescribed after 5 months.
[2]One patient restarted taking diuretic because of miscommunication with family member.
[3]One patient passed away after 5 months. This is the same patient who was deprescribed quinine.
Note: patients may be taking more than one target medication (e.g. statin with a PPI)

AJKD 2017; 70(5):611-618

Results - Endpoints

- **Primary endpoint:**
  - 31/40 (77%) medications were successfully deprescribed.
- **Secondary endpoints:**
  - The average number of medications per day decreased from 13.4 ± 4.3 to 12.7 ± 4.4 (n=35) after the deprescribing trial.
  - Patient safety and satisfaction

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Limitations

- Small sample size, single center
- PPI indication often unclear– based on patient information and chart
- Patient may continue to use medication at home
- A new medication may be prescribed during deprescribing trial

AJKD 2017; 70(5):611-618

Conclusion

- Validate and implement a safe and practical tool to deprescribe 5 specific drugs for HD patients
- Helped guide clinical practice- especially for trainees
- Increased awareness of inappropriate medication use

AJKD 2017; 70(5):611-618

Future Studies

Deprescribing

Can-SOLVE CKD Network

The Canadians Seeking Solutions and Innovations to Overcome Chronic Kidney Disease

Strategy for Patient-Oriented Research
SPOR
Putting Patients First

Development and Validation of A Deprescribing Toolkit

- ✓ Deprescribing Algorithm (for clinicians)
- ✓ Evidence Table (for clinicians)
- ✓ Monitoring Tool (for clinicians)
- ✓ Patient Information Toolkit (for patients):
  - ✓ video + bulletin

Medications for Deprescribing

- Statins
- PPIs
- Quinine
- Alpha Blockers
- Diuretics
- Prokinetic Agents
- Gabapentinoids
- Allopurinol
- Benzodiazepines/Z-drugs

Development of Each Algorithm

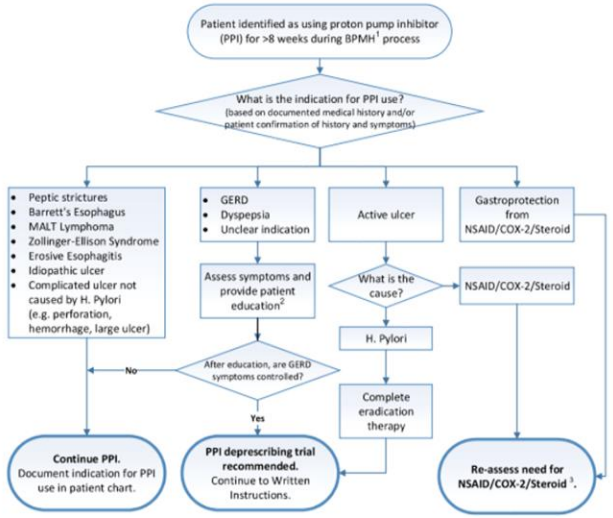
- Formal Literature Search completed for each medication
  - Safety
  - Efficacy
  - Monitoring
  - Deprescribing

Algorithm (example: PPIs)

Flow Chart for Deprescribing

Proton Pump Inhibitors

in Hemodialysis Patients



[1] BPMH: Best Possible Medication History

[2] Assessment of Symptoms and Patient Education:

Document GI symptoms that patient experiences and provide education as appropriate:

- For GERD symptoms (reflux, heartburn):
  - Educate the patient on non-pharmacological strategies to manage these symptoms (e.g. avoid acidic foods, alcohol & caffeine; quit smoking; avoid laying down after meals)
- For dyspepsia symptoms (feeling of fullness):
  - Educate patient on ways to avoid these symptoms (e.g. eating smaller meals)
  - Advise patient that PPIs are not effective in managing these symptoms and inform them of benefits of deprescribing and/or alternative agents for management of dyspepsia symptoms

[3] If continued NSAID/COX-2/Steroid use is required, continue PPI. If no longer required, suggest PPI deprescribing trial.

Written Instructions for Deprescribing

Proton Pump Inhibitors

in Hemodialysis Patients

1. Educate patient on the rationale for deprescribing: the risks/concerns, benefits, deprescribing plan, symptoms and duration.
   a. See Patient Information Tools (info sheet and video) included.

2. **Baseline Monitoring[1]:** Record frequency of GERD symptoms (if applicable) over 2 weeks prior to beginning deprescribing trial.

3. Taper PPI.
   Note: If symptoms return, use a longer tapering schedule.
   a. If above standard dose, decrease to standard dose over 2-4 weeks.
      i. Standard daily doses are:
         1. Pantoprazole: 40mg
         2. Lansoprazole and dexlansoprazole: 30mg
         3. Esomeprazole, omeprazole and rabeprazole: 20mg
   b. Reduce to 50% of standard dose over 2-4 weeks, then discontinue completely.

4. Provide patient education on non-pharmacologic options for symptom relief (see flow chart footnote #2).
   a. Counsel patient on PRN antacid options for quick relief or rebound symptoms, as appropriate for the patient (e.g. Tums[2], Amphojel[3], Gaviscon[3]).

5. **Safety/Efficacy Monitoring[1]**: Record frequency of GERD symptoms and PRN antacid use in the 2-4 weeks post-intervention and compare to pre-intervention (i.e. baseline).
   a. If frequency of symptoms decreased, discontinue PPI permanently
   b. If frequency of symptoms increased:
      i. Consider H2 Receptor Antagonist (H2RA):
         - Ranitidine 150mg PO QHS or PRN
         - Famotidine 10mg PO QHS[4] or PRN
      ii. If symptoms are not resolved, discontinue H2RA and re-initiate PPI at standard dose

6. Document result of deprescribing trial in patient chart.

[1] Use the **Patient Monitoring Sheet** included with this algorithm for **Baseline Monitoring** and **Safety/Efficacy Monitoring** during the deprescribing trial, as per instructions above.
[2] Avoid in hypercalcemic patients.
[3] Aluminum-free formulations only.
[4] Maximum 20mg PO QHS in dialysis.

Monitoring Tool (example: PPI)

Appendix 4 - Monitoring Sheets Study ID #: _____

Proton Pump Inhibitor Deprescribing Monitoring Form

Algorithm recommended deprescribing? ☐ No ☐ Yes Date: _____
Did the patient consent to the study? ☐ No ☐ Yes Date: _____
Medical team accepted deprescribing? ☐ No ☐ Yes Date: _____
Patient accepted deprescribing? ☐ No ☐ Yes Date: _____

Name of drug: _____ Starting dose: _____

Indication: _____

Baseline Monitoring Start Date: _____

	Frequency of GERD symptoms (Past week)	Comments
Week 1 Date:		
Week 2 Date:		

Continue with deprescribing? ☐ No ☐ Yes

Safety and Efficacy Monitoring* Start Date: _____

	Frequency of GERD symptoms (Past week)	Frequency of PRN antacid use (Past week)	Comments
Week 1 Date:			
Week 2 Date:			
Week 3 Date:			
Week 4 Date:			
Week 5 Date:			
Week 6 Date:			

Success deprescribing? ☐ No ☐ Yes

End Date: _____ Ending Dose: _____

Adverse Events Reported? ☐ No ☐ Yes (see reverse for tracking form)

PG 12

Appendix 4 - Monitoring Sheets Study ID #: _____

Adverse Event Reporting:

Severity	Related to Study?	Action Taken	Outcome of AE	Expected
1 = Mild 2 = Moderate 3 = Severe 4 = Life Threatening	0 = Not related 1 = Unlikely 2 = Possibly 3 = Probably 4 = Definitely	0 = None 1 = Dose change 2 = Medical intervention 3 = Hospital 4 = Resumed initial dose 5 = Other	1 = Resolved 2 = Resolved w/ minor sequelae 3 = Resolved w/ major sequelae 4 = Ongoing treatment 5 = Condition worsening 6 = Death	1 = Yes 2 = No

Description of Adverse Event	Start Date	Stop Date	Severity	Related?	Action	Outcome	Expected?

Additional notes:

_____
_____
_____
_____
_____
_____
_____

PG 13

Evidence Table (example: PPIs)

Evidence Supporting Deprescribing of

Proton Pump Inhibitors

in Hemodialysis Patients

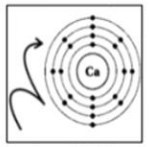
Proton pump inhibitors (PPIs) are usually prescribed for the treatment and prevention of the symptoms of gastroesophageal reflux disease (GERD) and gastrointestinal ulceration (1) (2). When treating these conditions, PPIs are usually indicated for up to 8 weeks and are rarely re-assessed (1) (3). Recent evidence from meta-analyses of observational studies has demonstrated an association with increased risk for developing *C. difficile* infections (4), pneumonia (5), fractures (6) and nutrient malabsorption (7) in the general population. Studies in hemodialysis (HD) patients specifically have associated long-term use of PPIs with lower serum magnesium levels (8-13), reduced bone mineral density (14), reduced calcium transport (15), increased arterial calcification risk (16) and reduced effectiveness of calcium phosphate binders (17) (see **Table 1** for summary of safety data relating to proton pump inhibitor use in hemodialysis patients).

Based on the risks associated with long-term PPI use, deprescribing of these agents should be considered in patients who have been using the agents for over 8 weeks. The algorithm outlines the assessment of patients using PPIs for over 8 weeks. Patients who have an indication for long-term PPI use will be continued on the agent. All other patients will be re-assessed based on their indication for PPI, their reported symptoms and a discontinuation trial would be considered as appropriate. Patients would be monitored for symptoms of GERD before and after discontinuation as per usual practice. Studies showing success rates for PPI deprescribing in the general population are summarized in **Table 2**.

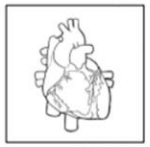
Summary of Safety Risks in Hemodialysis patients (see Table 1):

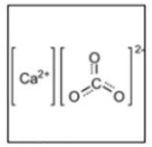
Lower serum Mg


Reduced Bone Mineral Density



Reduced Calcium Transport


Increased Arterial Calcification Risk



↓ effectiveness of $CaCO_3$ $(PO_4)_2$ binders

Table 1. Safety and Efficacy Data Relating to Proton Pump Inhibitor Use in Hemodialysis Patients

Ref.	Type of study + n	Data
Safety Concern: Lower Serum Magnesium		
(8)	• Observational study, incl. cross-sectional & 1-yr retrospective cohort study • n= 399 HD patients	• Serum magnesium levels were lower with PPI use than non-PPI use (2.39+/-0.36 vs. 2.56+/-0.39 mg/dL, P<0.001). In the inflammatory state, a low serum magnesium level is a significant predictor of mortality in HD patients. ○ 29 deaths; High serum hs-CRP levels (>4.04 mg/L) in association with low serum magnesium levels was an independent risk factor for 1-year mortality (hazard ratio: 2.92; 95% CI: 1.53-6.40, P<0.001).
(9)	• Cross sectional study • n= 282 HD patients	• Serum Mg levels were significantly lower among PPI users vs. non-users (0.94+/-0.2 vs. 1.03+/-0.2mmol/L; p<0.0001). The use of PPIs was an independent and strong predictor of low Mg concentrations even in multivariate analysis (OR 3.05; 95% CI 1.2498-7.4594, p=0.01). • Residual renal function didn't show a significant correlation with [Mg] (r=-0.102; p=NS) in both groups.
(10)	• Cross sectional study • n = 1189 HD patients	• Hypomagnesemia was significantly associated with PPI (adjusted OR, OR: 2.05; 95% CI: 1.14-3.69; P = 0.017); Magnesium concentration is a proven predictor of mortality in hemodialysis patients
(11)	• Single-center cross-sectional study • n = 155 HD patients	• Serum Mg levels were significantly lower among PPI users vs. non-users (0.93 vs. 1.02 mmol/L, p < 0.001). This finding persisted after stratifying for dialysate Mg concentration, and after multivariable adjustment (p < 0.001).
(12)	• 3-month chart review • n=62 HD patients	• Use of PPIs was significantly associated with hypomagnesemia (plasma [Mg] 1.48 +/- 0.16 mEq/l in the PPI group vs. 1.65 +/- 0.26 mEq/l in the non-PPI group, p = 0.007). Adjustment for age, diabetes status, duration of dialysis, plasma albumin, Kt/V, nPCR, and diuretic use did not affect the association.
(13)	• Interventional study • n= 115 HD patients	• Mean serum phosphate level increased significantly after administration of either famotidine or lansoprazole (by 6.6 +/- 21.9% or 13.0 +/- 26.3%, p = 0.032 and p = 0.029, respectively). • Mean serum calcium level was unchanged after administration of famotidine, but showed a significant decrease after administration of lansoprazole (by 3.44 +/- 7.73%, p = 0.013). When famotidine was switched to lansoprazole, serum calcium decreased significantly by 3.8 +/- 13.0% (p = 0.0006).
Safety Concern: Lower Bone Mineral Density		
(14)	• Cross sectional study • n= 68 HD patients	• Users of PPIs had lower values of bone mineral density and T-scores at the anatomical regions than non-users
Safety Concern: Reduced Calcium Transport		
(15)	• Cross sectional study • n= 30 HD patients	• Acute gastric acid inhibition by omeprazole reduced the intestinal calcium transport

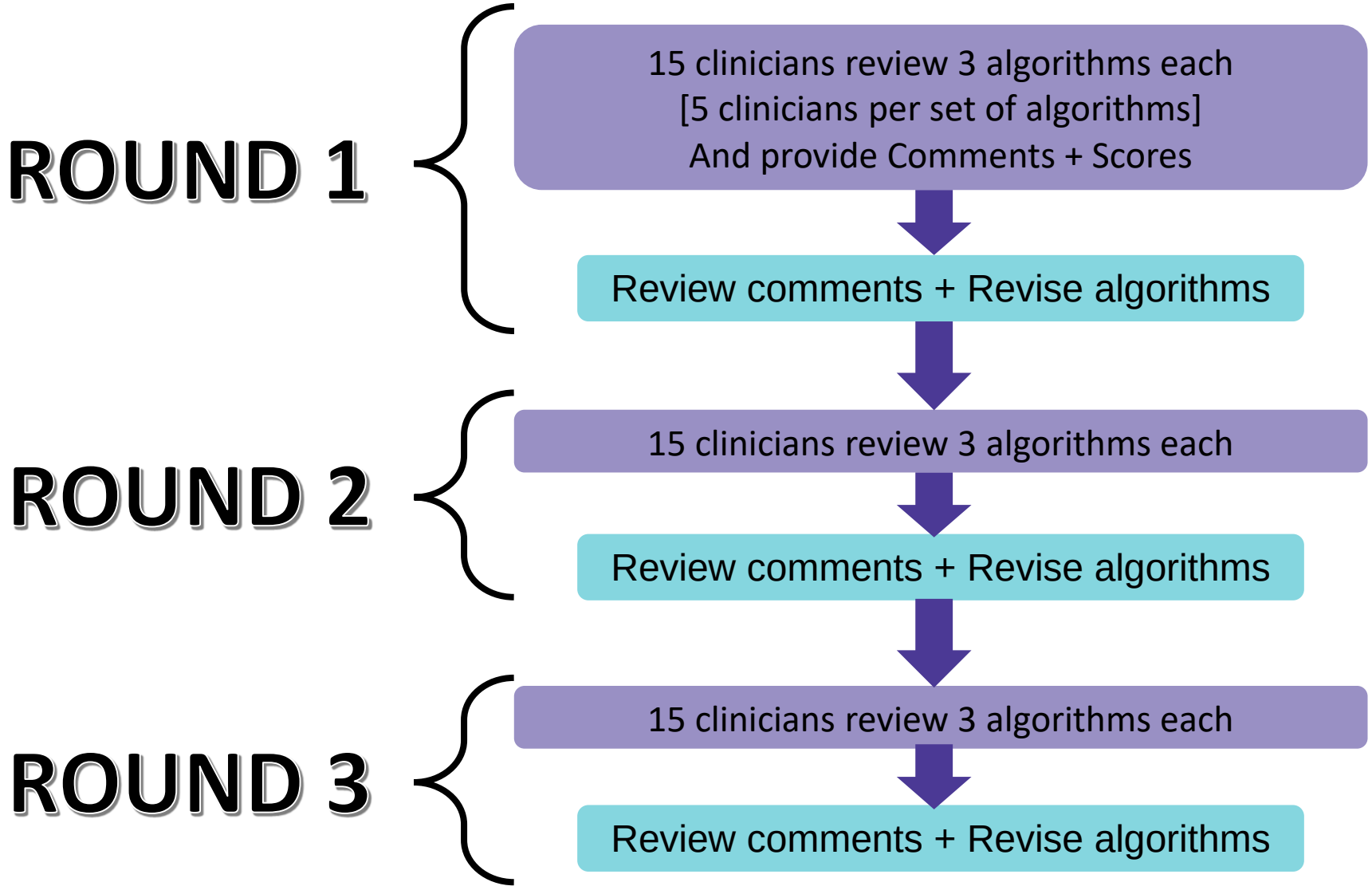
Methods

Validation of Deprescribing Algorithms

-used Lynn Method

Research Nursing 1986

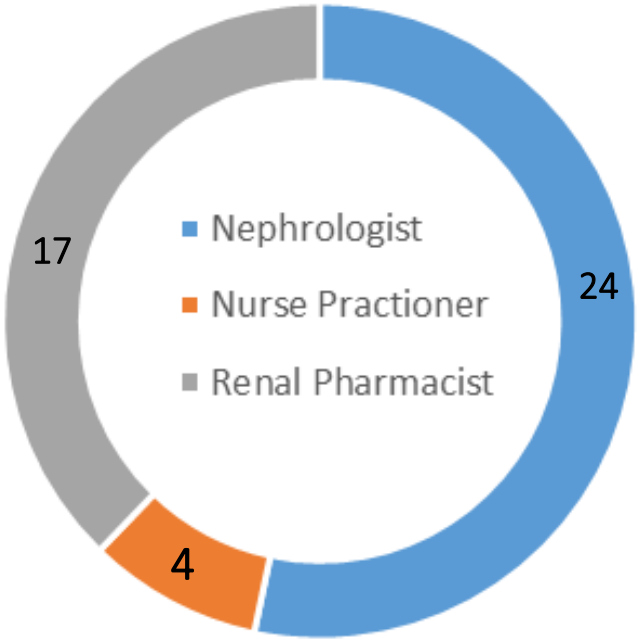
Validation Methodology



Results

Validation of Deprescribing Algorithms

Demographics for Validation Study Participants Count by Profession



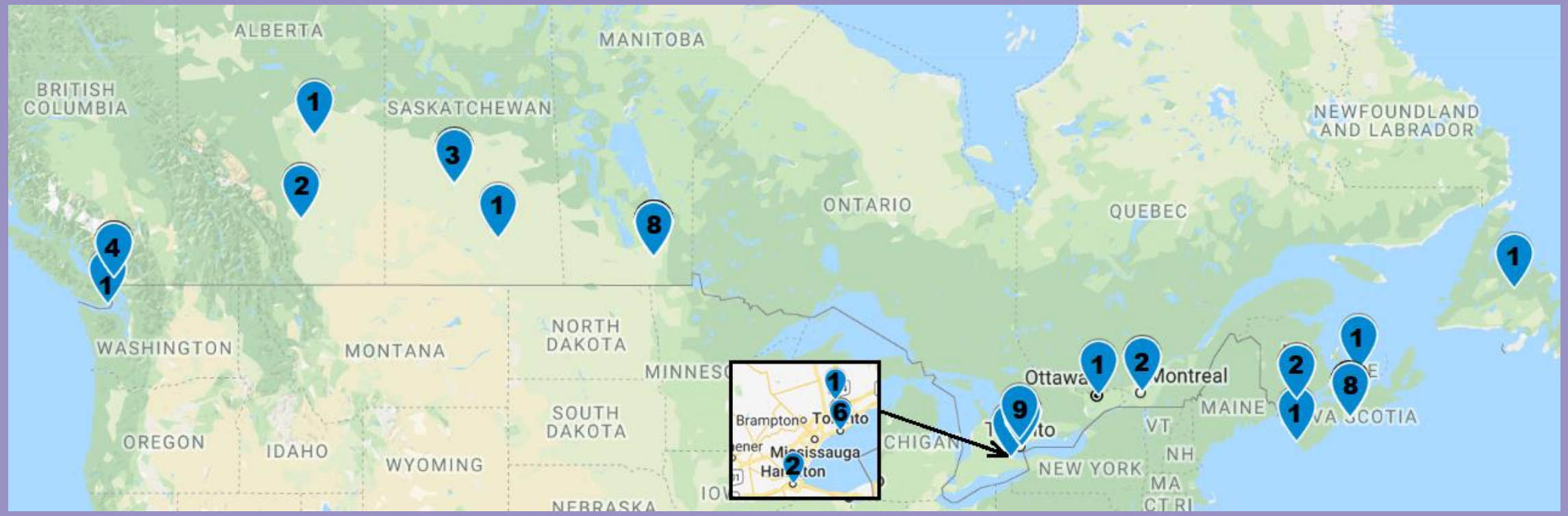
Years practicing:

Median: 15

Range: 1-34

Demographics for Validation Study Participants Count by province

National validation of the deprescribing algorithms
15 clinicians per round x 3 rounds = 45 clinicians surveyed



Validation of Patient Information Toolkit

- Using Lynn method (3 rounds of 6 patients)
- Research coordinators and PATIENTS at each site

Validation of Patient Information Tools

Site	Tools Reviewed	Validation		
		Round 1	Round 2	Round 3
Winnipeg, Manitoba	Urate Lowering Agents + A1B	2 patients	2 patients	2 patients
	Gabapentinoids + Benzos	2 patients	2 patients	2 patients
	Loop Diuretics + PPIs	2 patients	2 patients	2 patients
	Quinine + Statins	2 patients	2 patients	2 patients
Vancouver, BC	Urate Lowering Agents + A1B	2 patients	2 patients	2 patients
	Gabapentinoids + Benzos	2 patients	2 patients	2 patients
	Loop Diuretics + PPIs	2 patients	2 patients	2 patients
	Quinine + Statins	2 patients	2 patients	2 patients
Toronto, Ontario	Urate Lowering Agents + A1B	2 patients	2 patients	2 patients
	Gabapentinoids + Benzos	2 patients	2 patients	2 patients
	Loop Diuretics + PPIs	2 patients	2 patients	2 patients
	Quinine + Statins	2 patients	2 patients	2 patients
	Prokinetic Agents	*Completed*		

For each set of “2 patients”:

- 1 patient interviewed by a research assistant
- 1 patient interviewed by a patient partner

Patient Information Tool (example: PPIs)

Deprescribing Proton Pump Inhibitors (PPI)

What is Deprescribing?

- Deprescribing means lowering the dose or stopping a medication that may no longer be helping or may be causing harm

Why Deprescribe in Hemodialysis Patients?

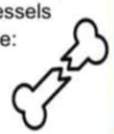
- Hemodialysis patients take up to 12 medications each day
- Since many medications are not studied in hemodialysis patients, the benefits and harms are unknown
- Hemodialysis patients have a harder time getting rid of medications from the body, so patients may have more side effects

What are Proton Pump Inhibitors (PPI)?

- PPIs are used to prevent and treat heartburn and stomach ulcers
- Examples of common PPIs are:
  - **Dexlansoprazole (Dexilant®)**
  - **Lansoprazole (Prevacid®)**
  - **Omeprazole (Losec®)**
  - **Pantoprazole (Tecta®, Pantoloc®)**
  - **Rabeprazole (Pariet®)**
  - **Esomeprazole (Nexium®)**

Why Stop or Reduce Your PPI Dose?

- Usually, only short-term PPI use is required. Taking PPIs long-term in chronic kidney disease can cause:
  - Decreased effectiveness of other medications such as calcium carbonate (TUMS®)
  - Hardening of blood vessels
  - Infections (for example: pneumonia, stomach infections)
  - Bone fractures
  - Fatigue and heart problems



Patients With the Following Should Remain on PPIs:

- Severe esophagus inflammation
- Barrett's Esophagus
- Ulcers from an unknown cause
- Uncontrolled heartburn
- Long-term use of nonsteroidal anti-inflammatory medication (for example: ibuprofen [Advil®] or naproxen)

How to Reduce or Stop PPIs Safely?

- Patients who have been taking a PPI for more than 8 weeks may be considered for the PPI deprescribing trial
- Pharmacists, doctors, and nurse practitioners will help decide the best way to stop PPIs
- This may include lowering the amount or frequency you take for a few weeks prior to discontinuation

What Will Your Healthcare Team be Monitoring?

- Heartburn symptoms
- Antacid use (for example: TUMS®)

What to if Heartburn Symptoms Continue?

If your heartburn symptoms and frequent antacid use continues, your health care team may recommend:

- Returning to previous PPI dose
- Starting a different medication (for example: ranitidine)

Other Ways You Can Manage Heartburn:

- Avoid alcohol, coffee, chocolate, spicy food
- Quit smoking
- Elevate your head in bed
- Weight loss

Your Proton Pump Inhibitor (PPI) Dose Reduction Plan:

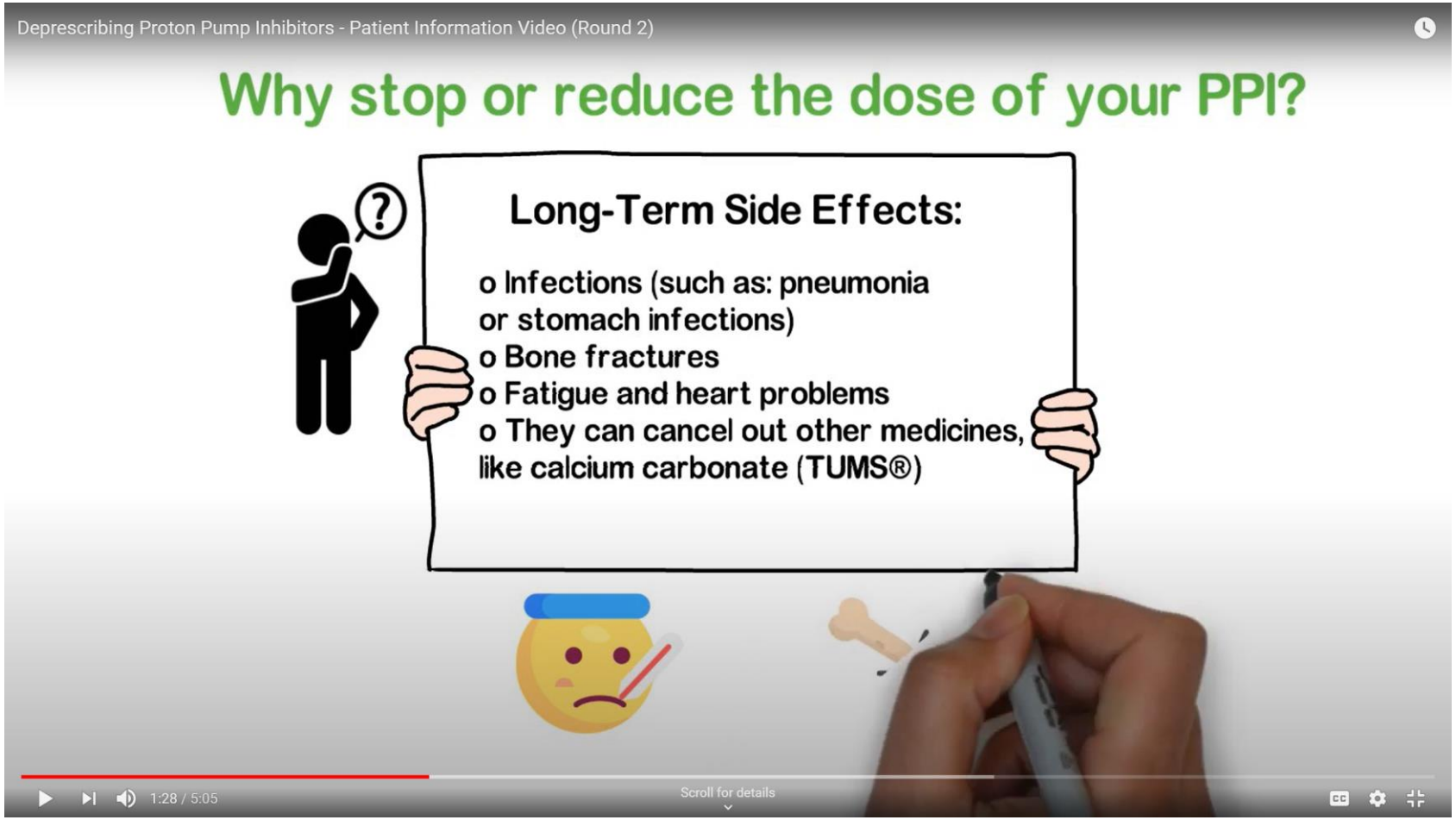
_____

_____

Please contact your doctor or pharmacist before stopping any medications

https://www.youtube.com/watch?v=nFXZijFgnx8

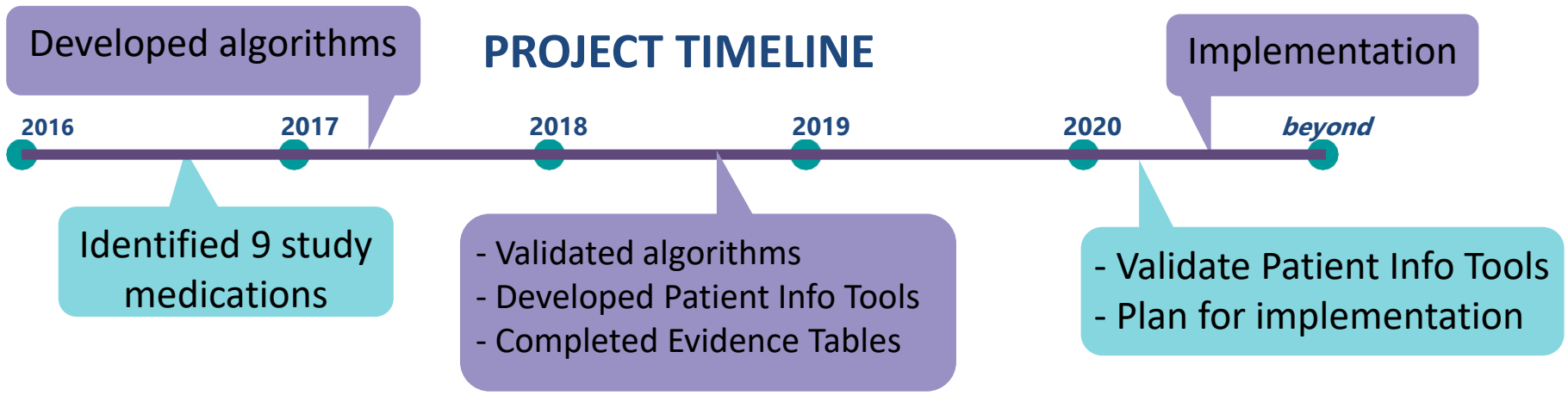
Patient Information Tool (example: PPIs)



https://www.youtube.com/watch?v=nFXZijFgnx8

Deprescribing Implementation

- ✓ Deprescribing Algorithm (for clinicians)
- ✓ Evidence Table (for clinicians)
- ✓ Monitoring Tool (for clinicians)
- ✓ Patient Information Toolkit (for patients): video + bulletin



STrategic Optimization of Prescription Medication Use in Patients on HemoDialysis (STOP Med-HD)

Our **specific objectives** are to:

(1) Assess **safety and effectiveness** of the **deprescribing intervention** in the 6-month study period

- Proportion of successfully deprescribed medications (discontinued or reduced dose)
- Frequency of *clinically significant* adverse events related to deprescribing

(2) Determine the **facilitators and barriers** to implementing this deprescribing intervention at our participating sites

Discussion/ Conclusion

Take Home Messages

- Decreasing medication use in CKD patients can:
  - Reduce adverse events (e.g. falls, hospitalizations)
  - Reduce pill burden and costs
  - Increase adherence with remaining medications
  - Improve quality of life
- All team members have a role to play in the success in optimizing medication use in CKD
- Taking the first step and developing a plan for medication review and strategic prescribing are key to optimization of medications in the CKD population

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Monica Beaulieu
Marello Tonelli
Clara Bohm
Stephanie Dixon
Judith Marin
Cali Orsulak
Jo-anne Wilson

Past RAs: Melissa Lefebvre & Patrick Ng

Conclusion

Can-SOLVE CKD Network

kidney FOUNDATION

Strategy for Patient-Oriented Research SPOR Putting Patients First


QUESTIONS