Canadian Deprescribing Network (CaDeN) goals are to:

- Reduce harm by raising awareness and cutting risky prescriptions for seniors by 50% by 2020.
- Promote health by ensuring access to safer drug and non-drug therapies.
- PPIs - They are overused, may cause more harm than good and safer alternatives exist.

http://deprescribing.org/caden/

Choosing Wisely Canada is a campaign to help clinicians and patients engage in conversations about unnecessary tests and treatments, and make smart and effective care choices.

https://choosingwiselycanada.org/
Disclosure

• Pam McLean-Veysey, Team Leader Drug Evaluation Unit
  – DEU funded by the Drug Evaluation Alliance of NS. (DEANS).
  – DEU prepares Drug Evaluation Reports for the Atlantic Common Drug Review (ACDR)
  – Has no conflicts of interest

• Dr. David Marsters
  – Has nothing to disclose

Outline

– Deprescribing initiatives for PPIs
– Three cases
– Algorithm
– Evidence
– Discussion on cases
WHAT IS DEPRESCRIBING

• The planned and supervised process of reducing or stopping medications that may no longer be of benefit or may be causing harm.

• Goal: reduce medication burden while improving quality of life.

• Deprescribing: done in partnership with a health care provider.

• May be reasons to continue taking certain medications or reasons why close supervision is needed while stopping.

• Deprescribing involves patients, caregivers, healthcare providers and policy makers.

---

Canadian Deprescribing Network (CaDeN) goals are to:
- Reduce harm by raising awareness and cutting risky prescriptions for seniors by 50% by 2020.
- Promote health by ensuring access to safer drug and non-drug therapies.
- PPIs - They are overused, may cause more harm than good and safer alternatives exist.
- [http://deprescribing.org/caden/](http://deprescribing.org/caden/)
WHY DEPRESCRIBE PPIS?

• There is high prevalence of use, overuse and chronic use of PPIs without a clear indication.
  – Inappropriate use of PPIs in 40% - 65% of patients.

• Reports of potential adverse events

• Pantoprazole - fifth most common drug prescribed in Canada in 2012.
  – 11 million prescriptions
  – PPIS $250 million in Canadian Public Plans (out of $7.8 billion)

• Canadian initiatives selected PPIs as an important class of medications for developing deprescribing guidelines

Canadian Deprescribing Network (CaDeN) goals are to:
- Reduce harm by raising awareness and cutting risky prescriptions for seniors by 50% by 2020.
- Promote health by ensuring access to safer drug and non-drug therapies.
- PPIS - They are overused, may cause more harm than good and safer alternatives exist.
- http://deprescribing.org/caden/
Clinical Practice Guidelines

Deprescribing proton pump inhibitors
Evidence-based clinical practice guideline

Barbara Farrell PharmD ACPR FCSHP  Kevin Pottie MD CCP MCSC FCSP  Wade Thompson ACPR
Lisa Pizzola MSc  Farah Joy Rashid ACPR  Carlos Rojas-Fernandez PharmD  Kate Walsh ACPR
Vivian Welch PhD  Paul Moayyedi MBChB PhD MPH

Canadian Family Physician • Le Médecin de famille canadien | VOL 63: MAY • MAI 2017

CASE 1: MEDICATION REVIEW FOR ESTHER S

- 80 yo female; hypertension, hyperlipidemia, no previous CV event;
- Lost 30 pounds since moving into Seniors apartments 2 years ago (diet improved, exercise program).
- Feels great!
- Medications:
  - HCTZ 25 mg daily
  - Enalapril 5 mg daily
    - current BP 130/79 – last year 140/90
  - Atorvastatin 20 mg daily
    - Current LDL 2.0 mmol/L – previous level unknown
  - Vitamin B₁₂ 1000 mcg p.o. daily x 15 years
  - Pantoprazole 40 mg daily x 30 years
  - Zolpidem 5 mg hs
DAUGHTER WANTS TO KNOW
“DOES SHE NEED ALL HER MEDICATIONS?”

- You heard something about PPI overuse.

Esther says she:

- recalls having heartburn
- did not see a GI specialist and was not admitted to hospital for GI bleed etc.
- currently has no GI issues but
  - “does not want to upset the apple cart”
CASE 2: WAYNE M

- 85 y.o male, STEMI, drug eluting stent 5 years ago. Just moved into a NH.
- Pharmacist says a medication review is in order.
- Medications
  - Esomeprazole 40 mg twice daily
  - Rosuvastatin 40 mg daily
  - Metoprolol 25 mg daily
  - ASA 82 mg daily
  - Clopidogrel 75 daily
  - Nitroglycerin spray prn
  - Vitamin D 800 units daily
  - Calcium 500 mg daily
  - Colace prn
  - Naproxen 500 mg BID for osteoarthritis
WAYNE M

• Diagnosis of erosive esophagitis with Barrett’s Esophagitis upon scope 10 years ago
  – Initiation of esomeprazole 40 mg bid.

• Currently states his osteoarthritis and muscle soreness bothers him more than anything
CASE 3
KRISTI S

• 35 year old female
• Uncomplicated GI bleed at age 28
  – High doses of NSAIDs for frequent migraines
  – Stopped NSAIDs at time of bleed
• Omeprazole 20 mg bid since GI bleed
• Recently using OTC PPIs
• Asks pharmacist about stopping the PPI since reading articles on internet

https://www.npr.org/sections/health-shots/2016/02/15/465279217/popular-heartburn-pills-can-be-hard-to-stop-and-may-be-risky
IN THESE CASES DO YOU...

A. Continue PPI
B. Stop PPI immediately
C. Decrease the dose and continue daily for 4 weeks and reassess
D. Decrease to “on demand” and reassess
E. Stop PPI and prescribe ranitidine 150 mg daily
HITTING THE HEADLINES

Proton pump inhibitor-associated pneumonia: Not a breath of fresh air after all?

Alexander L Fohl, Randolph E Regal

Research

Original Investigation

Association of Proton Pump Inhibitors With Risk of Dementia: A Pharmacoepidemiological Claims Data Analysis

Willy Geer, PhD, Klaus von Holz MD, PhD, Friedelie Thoret MD, MSc, Karl Broch MD, Wolfgang Maier MD, Anni Fink MS, Gabriela Oehmmer MD, PhD, Britta Knorr MD, PhD

Original Investigation

Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease

Betegnana Line, MD, Xiao Chen, MD, Frances P Million MD, PhD, Yongqiang Song, MD, Alex K Chang, MD, MD, Josef Corneli MD, PhD, Monique L Guert MD, PhD

NIH Public Access

Author Manuscript

Published as final edited item on:


Association of Long-term Proton Pump Inhibitor Therapy with Bone Fractures and Effects on Absorption of Calcium, Vitamin B12, Iron, and Magnesium

Tetsuhiko Ita, MD, PhD1 and Robert T. Jensen, MD2

1 Department of Medicine and Bioregulatory Science, Graduate School of Medical Science, Kyushu University, Fukuoka, Japan

2 Digestive Diseases Branch, National Institutes of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892

Potential harms of proton pump inhibitor therapy: rare adverse effects of commonly used drugs

Amine Benmassaoud MD, Emily G. McDonald MD, Todd C. Lee MD MPH

CADTH Evidence Driven.

Proton Pump Inhibitors (PPIs) and Clostridium difficile Infection (CDI)

What does the evidence say?

There is an association between PPI use and CDI. CADTH reviewed all the available evidence: 7 systematic reviews and 22 observational studies. The review was limited by some lower-quality studies.1
PPIS SAFE …
BUT NOT WITHOUT POTENTIAL RISKS

• Chronic use of PPIs is associated with risks. RxFiles, Farrell
  – Increased risk of enteric infections
    • (e.g., Clostridium difficile, Campylobacter, Salmonella, spontaneous bacterial peritonitis)
  – Pneumonia
  – Vitamin and mineral deficiency (Hypomagnesemia, Vitamin B12 deficiency)
  – Fractures
  – Acute interstitial nephritis and chronic kidney disease
  – Gastric atrophy
  – Intestinal metaplasia
  – Diarrhea
  – Headache
  – Mortality?
Potential PPI Adverse Effects

Gastroenterology 2017;153:35–48
HOW MUCH RISK?

- Absolute risks are low

- Evidence derived primarily from observational studies and ongoing.

BUT

- Risk deserves consideration,
  - Especially in an elderly population
    - multiple comorbidities
    - potential for medication related problems.

- Evidence suggests high utilization with no appropriate indication.
### Appendix 3: Ranges of frequency ratios for harms associated with proton pump inhibitors, and related references

<table>
<thead>
<tr>
<th>Harm</th>
<th>Frequency ratios (and confidence intervals)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk of fractures (overall)</td>
<td>RR - 1.14 (1.06, 1.24) – 1.29 (1.18, 1.41)</td>
<td>[1–4]</td>
</tr>
<tr>
<td>Increased risk of spine fracture</td>
<td>RR - 1.07 (1.01, 1.14) – 1.56 (1.31, 1.85)</td>
<td>[2–4]</td>
</tr>
<tr>
<td>Increased risk of hip fracture</td>
<td>RR - 1.16 (1.07, 1.27) – 1.30 (1.19, 1.43)</td>
<td>[2–6]</td>
</tr>
<tr>
<td>Clostridium difficile infections</td>
<td>RR - 0.9 (0.90, 1.50) – 5.0 (1.3, 19.4)</td>
<td>[7–12]</td>
</tr>
<tr>
<td>Clostridium difficile-related diarrhoea</td>
<td>RR - 2.04 (1.93, 2.17) – 2.74 (1.85, 4.07)</td>
<td>[13,14]</td>
</tr>
<tr>
<td>Campylobacter infections</td>
<td>RR - 3.5 (1.1, 12.0) – 11.7 (2.5, 54.0)</td>
<td>[12]</td>
</tr>
<tr>
<td>Salmonella infections</td>
<td>RR - 4.2 (2.2, 7.9) – 8.3 (4.3, 15.9)</td>
<td>[12]</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>RR - 1.17 (1.11, 1.24) – 1.65 (1.25, 2.19)</td>
<td>[15–17]</td>
</tr>
<tr>
<td>Hospitalisation for community-acquired pneumonia</td>
<td>RR - 1.05 (0.89, 1.25)</td>
<td>[17]</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>OR - 1.39 (1.19, 1.64)</td>
<td>[18]</td>
</tr>
<tr>
<td>Gastric atrophy</td>
<td>OR - 1.50 (0.59, 3.80)</td>
<td>[19]</td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>OR - 1.46 (0.43, 5.03)</td>
<td>[19]</td>
</tr>
<tr>
<td>Simple ECL hyperplasia</td>
<td>OR - 5.01 (1.54, 16.26)</td>
<td>[19]</td>
</tr>
<tr>
<td>Focal ECL hyperplasia</td>
<td>OR - 2.48 (0.44, 14.13) – 3.98 (1.31, 12.16)</td>
<td>[19,20]</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>OR - 1.08 (0.96, 1.20)</td>
<td>[21]</td>
</tr>
<tr>
<td>Corporal chronic inflammation</td>
<td>OR - 1.30 (0.68, 2.48)</td>
<td>[20]</td>
</tr>
<tr>
<td>Increased risk of vascular events among patients taking clopidogrel</td>
<td>RR - 1.10 (0.75, 1.61) – 1.60 (1.07, 2.40)</td>
<td>[22–31]</td>
</tr>
<tr>
<td>Bacterial peritonitis</td>
<td>RR - 2.22 (1.28 – 3.83) – 3.15 (2.09, 4.74)</td>
<td>[32–35]</td>
</tr>
<tr>
<td>Small intestine bacterial overgrowth</td>
<td>RR - 2.82 (1.24, 4.21)</td>
<td>[36]</td>
</tr>
</tbody>
</table>

[http://www.cfp.ca/content/cfp/suppl/2017/05/05/63.5.354.DC1/Harms.pdf](http://www.cfp.ca/content/cfp/suppl/2017/05/05/63.5.354.DC1/Harms.pdf)
Table 3. Absolute and RR for Adverse Effects Associated With Long-Term PPIs

<table>
<thead>
<tr>
<th>Potential Adverse Effect</th>
<th>Relative Risk</th>
<th>Reference for Risk Estimate</th>
<th>Reference for Incidence Estimate</th>
<th>Absolute Excess Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease</td>
<td>10% to 20% increase</td>
<td>Lazarus et al.</td>
<td>Lazarus et al.</td>
<td>0.1% to 0.3% per patient/y</td>
</tr>
<tr>
<td>Dementia</td>
<td>4% to 80% increase</td>
<td>Haenisch et al.</td>
<td>Haenisch et al.</td>
<td>0.07% to 1.5% per patient/y</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>30% to 4-fold increase</td>
<td>Yang et al.</td>
<td>Yang et al.</td>
<td>0.1% to 0.5% per patient/y</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>No association in RCTs</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Small intestinal bacterial overgrowth</td>
<td>2-fold to 8-fold increase</td>
<td>Lo et al.</td>
<td>None available</td>
<td>Unable to calculate</td>
</tr>
<tr>
<td>Campylobacter or Salmonella infection</td>
<td>2-fold to 6-fold increase</td>
<td>Bavishi et al.</td>
<td>Crim et al.</td>
<td>0.03% to 0.2% per patient/y</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>50% to 3-fold increase</td>
<td>Xu et al.</td>
<td>Fernandez et al.</td>
<td>3% to 16% per patient/y</td>
</tr>
<tr>
<td>Clostridium difficile infection</td>
<td>No risk to 3-fold increase</td>
<td>Furuya et al.</td>
<td>Lessa et al.</td>
<td>0% to 0.09% per patient/y</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>No association in RCTs</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Micronutrient deficiencies</td>
<td>60% to 70% increase</td>
<td>Lam et al.</td>
<td>Bailey et al.</td>
<td>0.3% to 0.4% per patient/y</td>
</tr>
<tr>
<td>Gastrointestinal malignancies</td>
<td>No association in RCTs</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

NOTE. This table provides absolute and RR estimates based on RCTs, meta-analyses, or large observational studies. The purpose of this table is to enable easy comparison of absolute and RR estimates. Readers should not assume that we believe there is a causal relationship when risk estimates are given. Table 3 provides our best summary of the evidence for potential PPI-associated adverse effects.

*Estimates are for adults (mean age 50 years) with a baseline estimated glomerular filtration rate >60 mL/min/1.73m².

*Estimates are for noninstitutionalized adults age 75 years or older.

*Estimates are for adults with a mean age of 77 years.

*Estimates are for patients with cirrhosis with ascites and assume use of spontaneous bacterial peritonitis prophylaxis with antibiotics.

*Estimates are for community-acquired CDI.

*Estimates are for noninstitutionalized adults and are based on vitamin B₁₂ deficiency, defined by both a low vitamin B₁₂ level and an elevated methylmalonic acid level.
DO I STILL NEED THIS MEDICATION?

https://www.deprescribingnetwork.ca/
• For adults (>18 y) with upper GI symptoms, who have completed a minimum 4-wk course of PPI treatment, resulting in resolution of upper GI symptoms, we recommend the following:

• Decrease the daily dose or stop and change to on-demand (as needed) use
  (strong recommendation, low-quality evidence)*
  – Alternatively

• Consider an H2RA as an alternative to PPIs
  (weak recommendation, moderate-quality evidence)
**WHAT IS THE EVIDENCE?**

<table>
<thead>
<tr>
<th>DECISION DOMAIN</th>
<th>SUMMARY OF REASON FOR DECISION</th>
<th>SUBDOMAINS INFLUENCING DECISION</th>
</tr>
</thead>
<tbody>
<tr>
<td>QoE: Is there high- or moderate-quality evidence</td>
<td>The QoE for symptom relapse with de-prescribing is low</td>
<td>QoE for benefits with on-demand use: moderate</td>
</tr>
<tr>
<td>Yes □ No □</td>
<td>• Low-dose PPIs did not lead to significantly greater relapses than standard-dose PPIs did (RR = 1.16, 95% CI 0.93 to 1.44); on-demand PPI use and step down to an H₂RA increased risk of symptom relapse compared with continuous PPI use (RR = 1.71, 95% CI 1.31 to 2.23, and RR = 1.92, 95% CI 1.44 to 2.58, respectively)</td>
<td>• Lower pill burden: 3.5 fewer pills per week (95% CI -4.89 to -2.18)</td>
</tr>
<tr>
<td>(See references 1-16 in the evidence reviews at CFPlus*)</td>
<td>Our systematic review showed that low-dose PPIs did not lead to a significantly higher GI relapse rate compared with standard doses. On-demand PPI use reduced pill burden. Cost, rare PPI side effects, and drug interactions were noted as potential concerns for continuous PPI use. Low-dose PPIs were thus considered to clearly have greater benefits than harms. On-demand PPI use and a step-down approach to H₂RAs were also noted to have benefits over harms, but this was not as certain as the other de-prescribing approach</td>
<td>Is the baseline risk for benefit similar across subgroups?</td>
</tr>
<tr>
<td>Yes □ No □</td>
<td></td>
<td>Yes □ No □</td>
</tr>
<tr>
<td>(See the description of harms and references 17-20 in the evidence reviews at CFPlus*)</td>
<td></td>
<td>• No evidence that benefits are different in subgroups</td>
</tr>
</tbody>
</table>

*Canadian Family Physician • Le Médecin de famille canadien | VOL 63: MAY • MAI 2017*
THE GUIDELINE DOES NOT APPLY TO PATIENTS ...

• with or who have had Barrett esophagus or severe esophagitis

or

• with a documented history of bleeding gastroenterology ulcers.
  – Consult gastroenterologist if considering deprescribing
Figure 1 Proton Pump Inhibitor (PPI) Deprescribing Algorithm

### Why is patient taking a PPI?
- If unsure, find out if history of endoscopy, if ever hospitalized for bleeding ulcer or if taking because of chronic NSAID use in past, if ever had heartburn or dyspepsia
- Mild to moderate esophagitis or GERD treated x 4-8 weeks (esophagitis healed, symptoms controlled)
- Peptic Ulcer Disease treated x 2-12 weeks from NSAID: H. pylori
- Upper GI symptoms without endoscopy: asymptomatic for 3 consecutive days
- ICU stress ulcer prophylaxis treated beyond ICU admission
- Uncomplicated H. pylori treated x 2 weeks and asymptomatic
- Barrett’s esophagus
- Chronic NSAID users with bleeding risk
- Severe esophagitis
- Documented history of bleeding GI ulcer

### Indication still unknown?

#### Recommend Deprescribing

**Strong Recommendation (from Systematic Review and GRADE approach)**
- Decrease to lower dose (evidence suggests no increased risk in return of symptoms compared to continuing higher dose), or (daily until symptoms stop) (1/10 patients may have return of symptoms)
- Stop PPI
- Continue PPI or consult gastroenterologist if considering deprescribing

#### Monitor at 4 and 12 weeks
- **If verbal:**
  - Heartburn
  - Dyspepsia
  - Regurgitation
  - Epigastric pain
- **If non-verbal:**
  - Loss of appetite
  - Weight loss
  - Agitation

### Use non-drug approaches
- Avoid meals 2-3 hours before bedtime; elevate head of bed;
- address if need for weight loss and avoid dietary triggers

### Manage occasional symptoms
- Over-the-counter antacid, H2RA, PPI, alginates
- Tums®, Rolaids®, Zantac®, Olex®, Gaviscon®
- H2RA daily (weak recommendation – GRADE; 1/5 patients may have symptoms return)

### If symptoms relapse:
- If symptoms persist x 3 – 7 days and interfere with normal activity:
  1. Test and treat for H. pylori
  2. Consider return to previous dose
Proton Pump Inhibitor (PPI) Deprescribing Notes

PPI Availability

<table>
<thead>
<tr>
<th>PPI</th>
<th>Standard dose (healing) (once daily)*</th>
<th>Low dose (maintenance) (once daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (Losec®) - Capsule</td>
<td>20 mg*</td>
<td>10 mg*</td>
</tr>
<tr>
<td>Esomeprazole (Nexium®) - Tablet</td>
<td>20 mg or 40 mg*</td>
<td>20 mg*</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®) - Capsule</td>
<td>30 mg*</td>
<td>15 mg*</td>
</tr>
<tr>
<td>Dexlansoprazole (Dexilant®) - Tablet</td>
<td>30 mg or 60 mg*</td>
<td>30 mg*</td>
</tr>
<tr>
<td>Pantoprazole (Tecta®, Pantoloc®) - Tablet</td>
<td>40 mg*</td>
<td>20 mg*</td>
</tr>
<tr>
<td>Rabeproazole (Patent®) - Tablet</td>
<td>20 mg*</td>
<td>10 mg*</td>
</tr>
</tbody>
</table>

Legend

- a Non-erosive reflux disease
- b Reflux esophagitis
- c Symptomatic non-erosive gastroesophageal reflux disease
- d Healing of erosive esophagitis
- + Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by H. pylori; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing risks of continued PPI use; long-term therapy may not be necessary, and the deprescribing process.

PPI side effects

- When an ongoing indication is unclear, the risk of side effects may outweigh the chance of benefit
- PPIs are associated with higher risk of fractures, C. difficile infections and diarrhea, community-acquired pneumonia, vitamin B12 deficiency and hypomagnesemia
- Common side effects include headache, nausea, diarrhea and rash

Tapering doses

- No evidence that one tapering approach is better than another
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options
- Choose what is most convenient and acceptable to the patient

On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual’s reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual’s symptoms recur, at which point, medication is again taken daily until the symptoms resolve

Farrell et al Can Fam Physician 2017;63:354-64
CASE 1: MEDICATION REVIEW FOR ESTHER S
CAN PPI BE STOPPED?

- **Medications:**
  - HCTZ 25 mg daily
  - Enalapril 5 mg daily
    - current BP 130/79 – last year 140/90
  - Atorvastatin 20 mg daily
    - Current LDL 2.0 mmol/L – previous level unknown
  - Vitamin B₁₂ 1000 mcg p.o. daily x 15 years
  - Pantoprazole 40 mg daily x 30 years
  - Zolpidem 5 mg hs
IN THIS CASE DO YOU...

A. Continue PPI

B. Stop PPI immediately

C. Decrease the dose and continue daily for 4 weeks and reassess

D. Decrease to “on demand” and reassess

E. Stop PPI and prescribe ranitidine 150 mg daily
STRATEGY

Strong Recommendation (from Systematic Review and GRADE approach)
(evidence suggests no increased risk in return of symptoms compared to continuing higher dose), or
(daily until symptoms stop) (1/10 patients may have return of symptoms)

Decrease to lower dose
Stop and use on-demand

Stop PPI

Monitor at 4 and 12 weeks

If verbal:
- Heartburn
- Dyspepsia
- Regurgitation
- Epigastric pain

If non-verbal:
- Loss of appetite
- Weight loss
- Agitation

Use non-drug approaches
- Avoid meals 2-3 hours before bedtime; elevate head of bed; address if need for weight loss and avoid dietary triggers

Manage occasional symptoms
- Over-the-counter antacid, H2RA, PPI, alginate prn (i.e. Tums®, Rolaids®, Zantac®, Olex®, Gaviscon®)
- H2RA daily (weak recommendation – GRADE; 1/5 patients may have symptoms return)

Farrell et al Can Fam Physician 2017;63:354-64
### PPI Availability

<table>
<thead>
<tr>
<th>PPI</th>
<th>Standard dose (healing) (once daily)*</th>
<th>Low dose (maintenance) (once daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (Losec*) - Capsule</td>
<td>20 mg⁺</td>
<td>10 mg⁺</td>
</tr>
<tr>
<td>Esomeprazole (Nexium*) - Tablet</td>
<td>20⁺ or 40⁺ mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid*) - Capsule</td>
<td>30 mg⁺</td>
<td>15 mg⁺</td>
</tr>
<tr>
<td>Dextralansoprazole (Dexilant*) - Tablet</td>
<td>30⁺ or 60⁺ mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Pantoprazole (Tecta*, Pantoloc*) - Tablet</td>
<td>40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Rabeprazole (Pariet*) - Tablet</td>
<td>20 mg</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

### Legend

- a Non-erosive reflux disease
- b Reflux esophagitis
- c Symptomatic non-erosive gastroesophageal reflux disease
- d Healing of erosive esophagitis
- + Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

Farrell et al Can Fam Physician 2017;63:354-64
EXTRA CONSIDERATIONS

• Is Esther taking OTC ASA or NSAIDS not on chart?
• Reason for taking Zolpidem?
  – Any relation to GERD?

• What else?

• Lost weight – may reduce GERD symptoms

• D/C PPI - may improve B12 absorption

• Choose strategy to reduce rebound
CASE 2: WAYNE M

- 85 y.o male, STEMI, drug eluting stent 5 years ago. Just moved into a NH.
- Pharmacist says a medication review is in order.
- Medications
  - D/C Esomeprazole 40 mg twice daily
  - Rosuvastatin 40 mg daily
  - Metoprolol 25 mg daily
  - ASA 82 mg daily
  - Clopidogrel 75 daily
  - Nitroglycerin spray prn
  - Vitamin D 800 units daily
  - Calcium 500 mg daily
  - Colace prn
  - Naproxen 500 mg BID for osteoarthritis
IN THIS CASE DO YOU...

A. Continue PPI

B. Stop PPI immediately

C. Decrease the dose and continue daily for 4 weeks and reassess

D. Decrease to “on demand” and reassess

E. Stop PPI and prescribe ranitidine 150 mg daily
- Barrett’s esophagus
- Chronic NSAID users with bleeding risk
- Severe esophagitis
- Documented history of bleeding GI ulcer

Continue PPI
or consult gastroenterologist if considering deprescribing

Farrell et al Can Fam Physician 2017;63:354-64
CAN WAYNE D/C PPI?

• Do not D/C
• Indications for long term PPI
  – EE, Barrett’s
• High risk for a GI Bleed
  – ASA, clopidogrel, naproxen

• But can the dose be reduced?
• Advice for best time of day to take?
### PPI Availability

<table>
<thead>
<tr>
<th>PPI Name</th>
<th>Standard dose (healing) (once daily)*</th>
<th>Low dose (maintenance) (once daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (Losec®) - Capsule</td>
<td>20 mg+</td>
<td>10 mg+</td>
</tr>
<tr>
<td>Esomeprazole (Nexium®) - Tablet</td>
<td>20(^a) or 40(^b) mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®) - Capsule</td>
<td>30 mg+</td>
<td>15 mg+</td>
</tr>
<tr>
<td>Dextansoprazole (Dexilant®) - Tablet</td>
<td>30(^c) or 60(^d) mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Pantoprazole (Tecta®, Pantoloc®) - Tablet</td>
<td>40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Rabeprazole (Pariet®) - Tablet</td>
<td>20 mg</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

### Legend

- \(^a\) Non-erotic reflux disease
- \(^b\) Reflux esophagitis
- \(^c\) Symptomatic non-erotic gastroesophageal reflux disease
- \(^d\) Healing of erosive esophagitis
- + Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)
CASE 3
KRISTI S

• 35 year old female
• Patient had GI bleed at age 28
  – High doses of NSAIDs for frequent migraines
  – Stopped NSAIDs and rarely gets migraine now.
• Omeprazole 20 mg bid since GI bleed
• Wants to stop the PPI since reading articles on internet

IN THIS CASE
• STOP PPI – Follow algorithm for tapering
Figure 1 | Proton Pump Inhibitor (PPI) Deprescribing Algorithm

**Why is patient taking a PPI?**
- If unsure, find out if history of endoscopy, if ever hospitalized for bleeding ulcer or if taking because of chronic NSAID use in past, if ever had heartburn or dyspepsia

- Mild to moderate esophagitis or GERD treated x 4-8 weeks (esophagitis healed, symptoms controlled)
- Peptic Ulcer Disease treated x 2-12 weeks (from NSAID; H. pylori)
- Upper GI symptoms without endoscopy; asymptomatic for 3 consecutive days
- ICU stress ulcer prophylaxis treated beyond ICU admission
- Uncomplicated H. pylori treated x 2 weeks and asymptomatic
- Barrett’s esophagus
- Chronic NSAID users with bleeding risk
- Severe esophagitis
- Documented history of bleeding GI ulcer

**Recommend Deprescribing**

- **Strong Recommendation (from Systematic Review and GRADE approach)**
  - Decrease to lower dose (evidence suggests no increased risk in return of symptoms compared to continuing higher dose, or
  - Stop PPI or consult gastroenterologist if considering deprescribing

**Monitor at 4 and 12 weeks**
- If verbal:
  - Heartburn
  - Dyspepsia
  - Regurgitation
  - Epigastric pain
- If non-verbal:
  - Loss of appetite
  - Weight loss
  - Agitation

**Tapering doses**
- No evidence that one tapering approach is better than another
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options
- Choose what is most convenient and acceptable to the patient
## COMPARATIVE COSTS

<table>
<thead>
<tr>
<th>PPI cost per tablet or capsule</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Omeprazole</strong></td>
<td></td>
</tr>
<tr>
<td>10 mg $0.21</td>
<td>20 mg $0.41</td>
</tr>
<tr>
<td><strong>Pantoprazole sodium</strong></td>
<td></td>
</tr>
<tr>
<td>20 mg $0.27</td>
<td>40 mg $0.30</td>
</tr>
<tr>
<td><strong>Pantoprazole magnesium</strong></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>40mg $0.19</td>
</tr>
<tr>
<td><strong>Lansoprazole (exception)</strong></td>
<td></td>
</tr>
<tr>
<td>15 mg $0.25</td>
<td>30 mg $0.25</td>
</tr>
<tr>
<td><strong>Rabeprazole</strong></td>
<td></td>
</tr>
<tr>
<td>10 mg $0.12</td>
<td>20 mg $ 0.24</td>
</tr>
</tbody>
</table>

PROTON PUMP INHIBITORS
THE GOOD AND BAD

- PPIs are relatively safe but not without concern
- Short-term PPI use appropriate for many acid–peptic disorders
- Long term use appropriate for severe conditions
- Refer complex GERD for endoscopy and specialist review
- Step down PPI therapy
  - Many options
  - Consider rebound acid hypersecretion before stopping PPI abruptly
- Upfront discussions help manage patient expectations
- Use lifestyle interventions as adjunct therapy
# REFERENCES AND RESOURCES FOR PPI DEPRESCRIBING

<table>
<thead>
<tr>
<th>Resource</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>Clinical Practice Guideline</strong> for deprescribing PPIs. <a href="http://www.cfp.ca/content/cfp/63/5/354.full.pdf">http://www.cfp.ca/content/cfp/63/5/354.full.pdf</a></td>
<td>The guideline is a tool to be used together with consideration of a patient’s personal and medical context. Includes the deprescribing algorithm <em>Canadian Family Physician</em> May 2017 Farrell B et al May 2017</td>
</tr>
<tr>
<td>4. <strong>Choosing Wisely Canada</strong> <a href="https://choosingwiselycanada.org/">https://choosingwiselycanada.org/</a></td>
<td>Start a Local Campaign or Implementation Project!</td>
</tr>
<tr>
<td>5. <strong>Canadian Deprescribing Network (CaDeN)</strong> <a href="http://deprescribing.org/caden/">http://deprescribing.org/caden/</a></td>
<td>CaDeN is a group of individuals who are committed to improving the health of Canadians by reducing the use of potentially inappropriate medicines and enhancing access to non-drug alternatives</td>
</tr>
<tr>
<td>7. <strong>CADTH - COMPUS PPI Project</strong> <a href="https://www.cadth.ca/proton-pump-inhibitor-therapy">https://www.cadth.ca/proton-pump-inhibitor-therapy</a></td>
<td>56 evidence-based statements relating to Gastroesophageal reflux disease, dyspepsia and peptic ulcer disease.</td>
</tr>
</tbody>
</table>