Supplemental materials for:

Clyne B, Smith SM, Hughes CM, Boland F, Bradley MC, Cooper JA, Fahey T. Effectiveness of a multifaceted intervention for potentially inappropriate prescribing in older patients in primary care: a cluster-randomized controlled trial (OPTI-SCRIPT Study). *Ann Fam Med*. 2015;13(6):545-553.

Supplemental Appendix 1: Selected Prescribing Criteria/Prescribing Indicator

Criteria	Concern	Prevalence in Ireland*
PPI for peptic ulcer disease at full therapeutic dosage for >8 weeks	Earlier discontinuation or dose reduction for maintenance/ prophylactic treatment of peptic ulcer disease, oesophagitis or GORD is indicated	16.69%
NSAID (>3 months) for relief of mild joint pain in osteoarthritis	Simple analgesics are preferable and usually as effective for pain relief	8.76%
Long-term (i.e. >1 month), long-acting benzodiazepines, e.g. chlordiazepoxide, flurazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam	Risk of prolonged sedation, confusion, impaired balance, falls	5.22%
Any regular duplicate drug class prescription, e.g. 2 concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors. Excludes duplicate prescribing of drugs that may be required on a PRN basis, e.g. inhaled beta 2 agonists (long and short acting) for asthma or COPD, and opiates for management of breakthrough pain	Optimization of monotherapy within a single drug class should be observed prior to considering a new class of drug	4.78%
TCAs with an opiate or calcium channel blocker	Risk of severe constipation	2.05%
Aspirin at dosage >150 mg/day	Increased bleeding risk, no evidence for increased efficacy	1.69%
Theophylline as monotherapy for COPD/Asthma	Risk of adverse effects due to narrow therapeutic index	1.18%
Use of aspirin and warfarin in combination without histamine H_2 receptor antagonist (except cimetidine because of interaction with warfarin) or PPI	High risk of GI bleeding	1.09%
Doses of short-acting benzodiazepines, doses greater than: lorazepam (Ativan®), 3 mg; oxazepam (Serax®), 60 mg; alprazolam (Xanax®), 2 mg; temazepam (Restoril®), 15 mg; and triazolam (Halcion®), 0.25 mg	Total daily doses should rarely exceed the suggested maximums	1.54%
Prolonged use (>1 week) of first generation antihistamines, i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine	Risk of sedation and anticholinergic side-effects	0.96%

Warfarin and NSAID together	Risk of GI bleeding	0.75%
Calcium channel blockers with chronic constipation	May exacerbate constipation	0.68%
NSAID with history of peptic ulcer disease or GI bleeding, unless with concurrent histamine H_2 receptor antagonist, PPI or misoprostol	Risk of peptic ulcer relapse	0.67%
Bladder antimuscarinic drugs with dementia	Risk of increased confusion, agitation	0.46%
TCAs with constipation	May worsen constipation	0.45%
Digoxin at a long-term dosage >125 µg/day (with impaired renal function)	Increased risk of toxicity	0.36%
Thiazide diuretic with a history of gout	May exacerbate gout	0.36%
Glibenclamide (with type 2 diabetes mellitus)	Risk of prolonged hypoglycaemia	0.29%
Aspirin with a past history of peptic ulcer disease, without histamine H2 receptor antagonist or PPI	Risk of bleeding	0.22%
Prochlorperazine (Stemetil®) or metoclopramide with Parkinsonism	Risk of exacerbating Parkinsonism	0.21%
TCAs with dementia	Risk of worsening cognitive impairment	0.18%
TCAs with glaucoma	Likely to exacerbate glaucoma	0.14%
TCAs with cardiac conductive abnormalities	Pro-arrhythmic effects	0.14%
Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis	Risk of major systemic corticosteroid side-effects	0.14%
Bladder antimuscarinic drugs with chronic prostatism	Risk of urinary retention	0.14%
NSAID with heart failure	Risk of exacerbation of heart failure	0.07%
TCAs with prostatism or prior history of urinary retention	Risk of urinary retention	0.07%
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in COPD/Asthma	Unnecessary exposure to long-term side-effects of systemic steroids	0.07%
Bladder antimuscarinic drugs with chronic	Risk of acute exacerbation of	<0.01%

glaucoma	glaucoma	
NSAID with SSRI	Increased risk of GI bleeding	N/A
Bladder antimuscarinic drugs with chronic constipation	Risk of exacerbation of constipation	N/A
Prednisolone (or equivalent) > 3 months or longer without bisphosphonate	Increased risk of fracture	N/A
NSAID with ACE-inhibitor	Risk of kidney failure, particularly with the presence of general arteriosclerosis, dehydration or concurrent use of diuretics	N/A
NSAID with diuretic	May reduce the effect of diuretics and worsen existing heart failure	N/A

Abbreviations – ACEI (angiotensin-converting-enzyme inhibitor); COPD (chronic obstructive pulmonary disease); GI (gastro-intestinal); NA (not available); GORD (gastro-oesophageal reflux disease); NSAID (Nonsteroidal anti-inflammatory drug); PPI (Proton Pump Inhibitor); PRN (Pro re nata, as needed); SSRI (Selective serotonin reuptake inhibitor); TCA (Tricyclic Anti-depressant)

**Prevalence – the proportion of the study population with 1 or more potentially inappropriate medications*

Appendix 2 OPTI-SCRIPT Website materials

Table A2.1 OPTI-SCRIPT treatment algorithm example

Proton Pump Inhibitors (PPIs)

Section A Potentially Inappropriate Prescription:

Full therapeutic dose >8/52 → Not indicated

Long term PPI use is associated with an increased risk of fractures and may be associated with an increased risk of Community Acquired Pneumonia and C. difficile diarrhoea

Section B Alternatives:

Consider the following alternatives:

1. Discontinuation or dose reduction for maintenance therapy and gastroprotection
2. Pharmacological Alternatives

1. Discontinuation or dose reduction for maintenance therapy and gastroprotection

PPI	*Full therapeutic dose Inappropriate for >8/52*	*Maintenance Dose / Gastroprotection*
Omeprazole	≥ 40mg / day	20mg / day
Esomeprazole	≥40 mg / day	20 mg / day
Lansoprazole	≥ 30 mg / day	15 mg / day
Pantoprazole	≥ 40 mg / day	20 mg / day
Rabeprazole	> 20 mg / day	10 - 20 mg / day

2. Pharmacological Alternatives

Pharmacological Alternative	Dose Recommendations	Co-Admin with Alternative Not Recommended	Co-Admin Caution	Non-pharmacological Alternative
H2 antagonist	1. Ranitidine: 150mg BD, maintenance dose 150-300mg daily			
Occasional reflux can be treated with OTC preparations	1. Gaviscon Advance: 1-2 tabs or 5-10ml after meals and bedtime			

Patient Information Leaflets:

PPIs for people with peptic ulcer disease, please click
http://hrbcentreprimarycare.ie/OPTISCRIPT/Files/1_PPI_PUD.pdf

PPIs for people with gastro-oesophageal reflux disease (GORD), please click
http://hrbcentreprimarycare.ie/OPTISCRIPT/Files/2_PPI_GORD.pdf

Section C: Background Information

Managing gastro-oesophageal reflux disease (GORD)

- Offer a full-dose PPI (omeprazole 40mg/day) for 1 month to all people with endoscopically determined oesophagitis or endoscopy-negative reflux disease.
- Advise that symptoms may recur after stopping treatment, and to return for treatment if they experience persistent or recurrent symptoms.
- For those whose symptoms persist, offer a further month of full-dose PPI.
- For people with persistent, severe symptoms, consider a double-dose PPI (omeprazole 40mg bd) for a further month.
- For people with a particular problem with nocturnal symptoms that do not respond to PPI therapy, consider adding an H_2-receptor antagonist at bedtime in the short term (e.g. intermittent 2-week courses of Ranitidine 150mg nocte).
- For people who do not respond to a second month of full-dose PPI or a month of double-dose PPI, consider a trial of treatment with an H_2-receptor antagonist (ranitidine 150mg bd) or a prokinetic (domperidone 10mg tds) or referral for further management of refractory GORD.

Managing peptic ulcer disease (PUD)

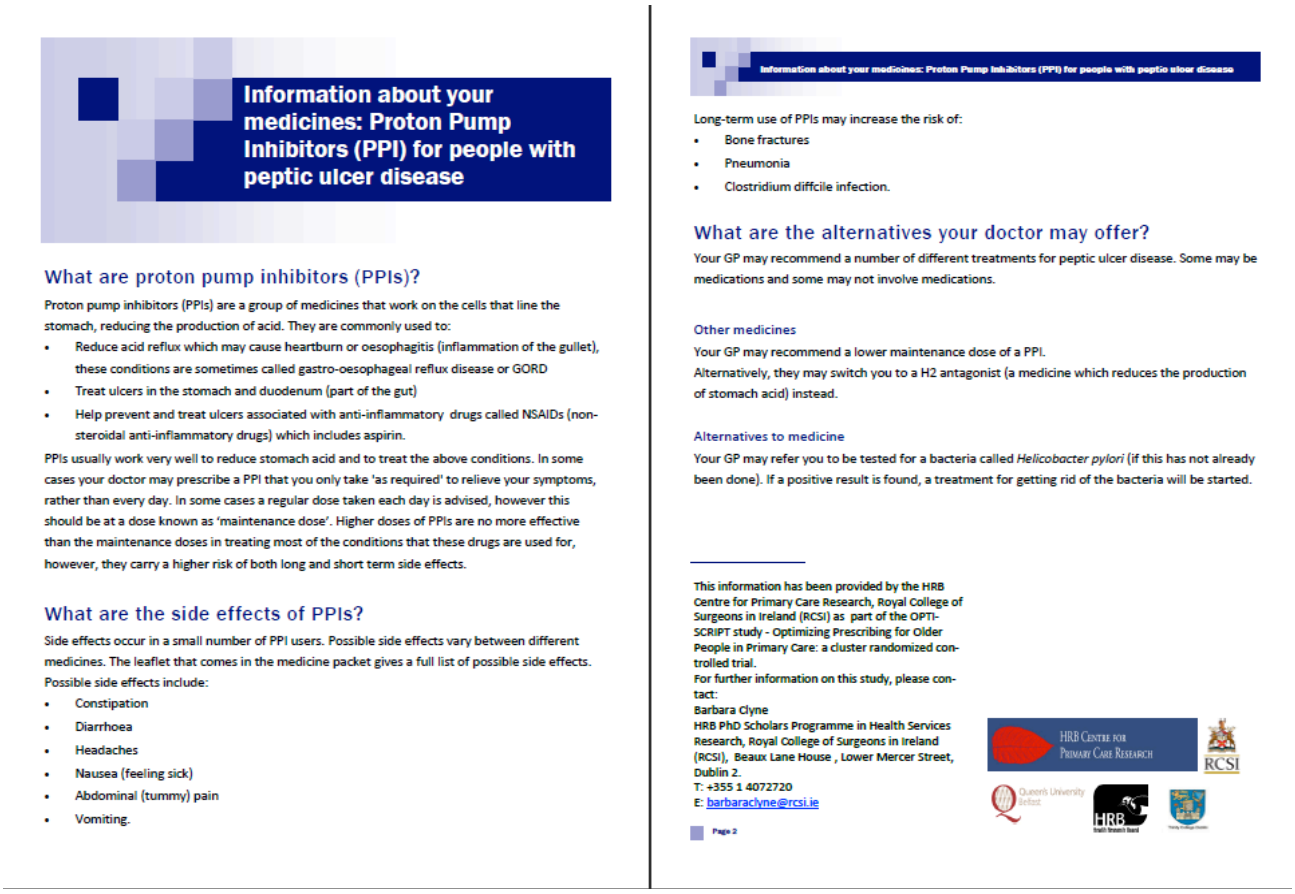
- Test for *Helicobacter pylori* if this has not already been done.
- If the result is negative, treat with full-dose PPI (omeprazole 40mg/day) for 1 or 2 months, depending on the reported severity of ulceration.
- If the result is positive, prescribe eradication therapy (omeprazole 20mg bd + clarithromycin 500mg bd + amoxicillin 1g bd, all for 1 week).
- After at least four weeks of completing eradication therapy, re-test for *H. pylori*. Prescribe an alternative eradication therapy if the repeat test result is positive.
- For gastric ulcers, arrange repeat endoscopy 6–8 weeks after completing treatment.

Reducing risk of NSAID-associated ulceration

If NSAID therapy is absolutely necessary and the individual is aware of the risk of continuing treatment:

- Consider topical agent or prescribe low-dose ibuprofen (400 mg tds) with a PPI (omeprazole 20mg/day). Judgment of risk should include consideration of the individual's age and comorbidity, and the dose and frequency of NSAID used

Table A2.1 OPTI-SCRIPT patient information leaflet



Information about your medicines: Proton Pump Inhibitors (PPI) for people with peptic ulcer disease

What are proton pump inhibitors (PPIs)?

Proton pump inhibitors (PPIs) are a group of medicines that work on the cells that line the stomach, reducing the production of acid. They are commonly used to:

- Reduce acid reflux which may cause heartburn or oesophagitis (inflammation of the gullet), these conditions are sometimes called gastro-oesophageal reflux disease or GORD
- Treat ulcers in the stomach and duodenum (part of the gut)
- Help prevent and treat ulcers associated with anti-inflammatory drugs called NSAIDs (non-steroidal anti-inflammatory drugs) which includes aspirin.

PPIs usually work very well to reduce stomach acid and to treat the above conditions. In some cases your doctor may prescribe a PPI that you only take 'as required' to relieve your symptoms, rather than every day. In some cases a regular dose taken each day is advised, however this should be at a dose known as 'maintenance dose'. Higher doses of PPIs are no more effective than the maintenance doses in treating most of the conditions that these drugs are used for, however, they carry a higher risk of both long and short term side effects.

What are the side effects of PPIs?

Side effects occur in a small number of PPI users. Possible side effects vary between different medicines. The leaflet that comes in the medicine packet gives a full list of possible side effects. Possible side effects include:

- Constipation
- Diarrhoea
- Headaches
- Nausea (feeling sick)
- Abdominal (tummy) pain
- Vomiting.

Long-term use of PPIs may increase the risk of:

- Bone fractures
- Pneumonia
- Clostridium difficile infection.

What are the alternatives your doctor may offer?

Your GP may recommend a number of different treatments for peptic ulcer disease. Some may be medications and some may not involve medications.

Other medicines

Your GP may recommend a lower maintenance dose of a PPI.
Alternatively, they may switch you to a H2 antagonist (a medicine which reduces the production of stomach acid) instead.

Alternatives to medicine

Your GP may refer you to be tested for a bacteria called *Helicobacter pylori* (if this has not already been done). If a positive result is found, a treatment for getting rid of the bacteria will be started.

This information has been provided by the HRB Centre for Primary Care Research, Royal College of Surgeons in Ireland (RCSI) as part of the OPTI-SCRIPT study - Optimizing Prescribing for Older People in Primary Care: a cluster randomized controlled trial.
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