

Strategies to foster appropriate proton pump inhibitor use

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Preface

Contributions of student

Wade Thompson (WT) is the principal author of all thesis content.

For the study described in Chapter 1, WT conceived and designed the study, collected and analyzed data and drafted the manuscript. Cody Black (CB) served as a second reviewer for the scoping review. All authors provided critical feedback and approved the manuscript.

The concept for the study outlined in Chapter 2.2 was conceived by WT, Barbara Farrell (BF), Lisa McCarthy (LM), Lisa Dolovich (LD), Kednapa Thavorn (KT), Yan Li (YL) and Denis O'Donnell (DO). The study was designed by WT, Matt Hogel (MH), YL, DO, KT and CB. Data was collected by WT, MH and DO. Wade Thompson analyzed data with assistance from KT and MH. The manuscript was written by WT. All authors provided critical feedback on the manuscript and approved it.

WT conceived and designed the study outlined in Chapter 3 with feedback from thesis advisory committee members. He collected and analyzed all data and wrote both manuscripts in Chapter 3. All authors provided critical revisions and approval for manuscripts.

Approvals

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The study conducted in Chapter 3.2 and 3.3 was approved by both the Ottawa Health Science Network (OHSN) and Bruyère Research Ethics Board (see Appendix 5). The project in Chapter 2.2 was reviewed and approved by the long-term care home as an evaluation of a quality improvement initiative.

Abbreviations

ASD: acid-suppressing drug

CAD: Canadian dollars

CPS: control preferences scale

GERD: gastroesophageal reflux disease

GI: gastrointestinal

GP: general practitioner

GRADE: grading of recommendations, assessment, development and evaluation

H2RA: histamine-2 receptor antagonist

ICMJE: International Committee of Medical Journal Editors

IPDAS: International Patient Decision Aid Standards

ITS: interrupted time series

LA: Los Angeles

NSAID: non-steroidal anti-inflammatory drug

OPEN: Ontario Pharmacy Research Collaboration

OTC: over-the-counter

PPI: proton pump inhibitor

PRISMA: preferred reporting in systematic reviews and meta-analyses

PtDA: patient decision aid

PUD: peptic ulcer disease

QoL: quality of life

RCT: randomized controlled trial

Abstract

This thesis examines strategies to address the inappropriate proton pump inhibitor (PPI) use. A scoping review was conducted to examine patient preferences and values towards PPI initiation and continued treatment, as well as their attitudes towards reducing PPI use (deprescribing). Symptom control (reflux, heartburn) was a driver for patients to seek treatment. Patients were concerned about symptoms returning if they reduced their PPI use but were interested in using less medication if possible. Patients were open to discussing PPI reduction and valued clear communication about rationale and potential benefits/harms. As such, shared and informed decision-making (including eliciting patient values) is important in the choice to continue a PPI or try deprescribing.

A decision-support tool for clinicians, aimed at the decision to continue a PPI versus try deprescribing, was implemented over 12 months in one long-term care home in Ottawa. The tool led to a non-statistically significant decrease in PPI use after it was implemented, but PPI usage began to gradually increase after six months. Strategies to sustain use of deprescribing initiatives are needed.

Finally, a consult patient decision aid (PtDA) was developed and piloted in three Ottawa area clinics, and aimed to facilitate shared decision-making surrounding the decision to continue or try to reduce a PPI during a healthcare visit. Based on a sample of 12 patients, the consult PtDA increased knowledge about the decision and increased decisional confidence. After receiving the consult PtDA, 8/12 (75%) patients chose to reduce their PPI use and 4/12 (25%) chose to continue their PPI.

Chapter 1: Introduction

1.1 Proton pump inhibitor use

Proton pump inhibitors (PPIs) are used to treat upper gastrointestinal (GI) conditions such as gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD). PPIs heal esophagitis and resolve symptoms in around 60-80% of patients with GERD after four to eight weeks of treatment, while the recommended duration of treatment with patients with PUD is 2-12 weeks in those at low risk of a GI bleed [1,2]. Though the majority of patients with severe GERD or grade C-D esophagitis [1] relapse if therapy is discontinued, patients with mild or moderate symptoms may not need continuous PPI therapy long-term. This is reflected in guidelines which suggest only a limited duration of PPI use in most patients [1,2] with mild or moderate symptoms. However, many continue to use these drugs without ongoing need (a potentially inappropriate prescription), and no reassessment of whether the drug is still indicated. Conversely, an appropriate PPI would be one where the patient still has an ongoing need for therapy, and the drug is effective and well tolerated.

Observational studies suggest rates of inappropriate PPI use between 44 and 79% [3–5]. This is of both clinical and economic concern. Meta-analyses of cohort and case-control studies suggest PPIs are associated with harms including *C. difficile* infection, pneumonia and fractures [6–8], though some of these associations have been questioned [9]. Unnecessary use contributes to polypharmacy (defined as use of more medications than is clinically indicated, or as use of >5 or >10 medications[10]) and

healthcare costs. Public drug programs in Canada (excluding Quebec) spent \$247 million dollars on PPIs in 2012 [11].

Polypharmacy is a growing concern in Canadian seniors. For example, in 2012 66% of persons 65+ in Canada were taking 5 or more drugs, while over 25% were taking 10 or more [12]. In long-term care (LTC) facilities, 61% of residents were taking 10 or more medications. Polypharmacy has important clinical consequences, including an increased risk for adverse drug events, hospitalizations and falls [10]. Unfortunately, some of this medication use is unnecessary or potentially inappropriate. A cross-sectional study using 2013 data from six Canadian provinces found 37% of older persons (65+) were taking at least one potentially inappropriate medication [13]. Medication use can climb in older adults due to multiple co-morbidities, multiple prescribers and hospitalizations [14,15]. However, ongoing use of medications is not always revisited. As a patient ages, a drug that was once indicated and helpful may no longer be so, and may be causing more harm than good. Therefore, it is important to reassess use of medications particularly in older persons.

Given the rate and impact of potentially inappropriate medication use, strategies are required to manage this problem. "Deprescribing" is one such strategy, which is defined as the planned and supervised process of dose reduction or stopping a medication that may be causing harm or no longer be providing benefit [16,17]. National networks of deprescribing researchers, advocates, educators and policy makers have formed in Australia and Canada in recent years [18,19]. The Choosing Wisely movement in

Canada and the USA has also focused on unnecessary medication use, including PPIs [20].

Until recently, there had been a relative lack of guidance on how clinicians can approach deprescribing. While general guidance is available [19], systematic reviews have found that barriers exist both at the prescriber and patient level. Patients may fear deprescribing due to lack of understanding as to why it may be considered, while prescribers see it is a time and resource-intensive process [21,22]. However, clear communication from prescribers and developing a plan in collaboration with a patient have been suggested as potential facilitators [23]. Unfortunately, there are a lack of tools available to facilitate these discussions in practice [23].

Given rates of inappropriate medication use (and specifically PPIs), patients' PPI use may be reassessed in various healthcare settings, including long-term care (LTC) and primary care. This can be due to concerns surrounding safety and drug costs [24].

Some patients may wish to try having their PPI "deprescribed" due to concerns surrounding adverse effects or to reduce their pill burden, though some patients may be concerned about symptoms returning [25–27]. As such, a patient's decision surrounding PPI deprescribing is a preference sensitive decision, where the best option depends on the preference for a specific outcome (e.g. using less pills or avoiding symptom relapse) [28].

Clinicians need tools to assist them in re-evaluating a patient's need for continued PPI use, or whether attempting deprescribing is possible. Such tools should incorporate

patient preferences into decision-making given the preference sensitive nature of PPI use. Clinicians can therefore be helped by tools that facilitate discussions with patients across practice settings. Our research group previously conducted a systematic review (and updated an existing systematic review) [29,30] to develop a PPI deprescribing guideline that assists clinicians in evaluating and discussing continuation versus deprescribing PPIs where appropriate [31]. We have been exploring ways to enhance uptake of implementation of strategies to optimize PPI use in clinical practice.

This thesis describes strategies to foster appropriate PPI use in both long-term care and primary care.

1.2 Patient values and preferences surrounding proton pump inhibitor use: a scoping review

The following manuscript is formatted for Patient (not submitted).

Wade Thompson, Cody Black, Lise M Bjerre, Barbara Farrell, Vivian Welch, Peter Tugwell

1.2.1 Abstract

Background: Proton pump inhibitors (PPIs) are used to treat patients with various upper gastrointestinal (GI) diseases. Some patients require only a limited duration of treatment yet remain on PPIs long-term. Patients should be offered the choice of continuing their PPI long-term or trying to reduce the dose or to stop, a choice dependent on values and preferences surrounding PPI treatment.

Objectives: Systematically scope the available evidence on patient values and preferences surrounding continued PPI treatment and/or the decision to try a reduction in their PPI. Identify studies which have examined this topic, summarize the literature and identify gaps in knowledge.

Data sources: MEDLINE, EMBASE, Cochrane Library, grey literature as of August 9, 2016

Eligibility criteria: Study of any design examining patient values and preferences toward PPI treatment and/or deprescribing.

Participants: Patients \geq 18 years taking PPIs for upper GI diseases

Results: Twelve eligible studies (7 surveys, 4 qualitative interview studies, 1 randomized controlled trial) were located. One study only examined values and preferences towards reducing PPI use, five studies looked only at PPI treatment (initiation and/or continuation), four studies assessed attitudes to both PPI treatment and reduction and two studies evaluated attitudes towards PPI treatment and switching (to alternative PPIs). Ten out of 12 studies involved patients with esophagitis, gastroesophageal reflux disease, or upper GI symptoms. Patients value symptom control highly and worry about symptoms returning if the PPI is reduced. They are encouraged if their physician provides advice and education. Between 40 and 90% of patients are willing to at least discuss options with their physician (continue vs. reducing their PPI use). Approximately 40% of patients are willing to try to reduce or stop their PPI with physician advice. All 5 studies that examined reducing PPI use suggest patients should understand the rationale for considering continuation versus deprescribing of PPIs and should know what to expect from deprescribing (possible rebound symptoms). Patients appear to be more comfortable with reducing the PPI versus outright stopping and are encouraged by the knowledge they can return to their previous dose if symptoms return and are bothersome.

Discussion: The findings from these studies echo previous literature on patient preferences for deprescribing – patients are generally open to discussing reducing PPI use. Patients value education on the rationale for deprescribing, knowledge of what to expect and being involved in planning. Future studies should evaluate structured decision-making tools, and should incorporate more discussion of potential long-term adverse effects of continued PPI use.

Conclusions: Patients are willing to discuss the option of continuing PPI use or trying to reduce their PPI; however, a range of attitudes exist. The results suggest that reducing a PPI is a preference-sensitive decision. Therefore, patient attitudes should be elicited and incorporated into shared decision making surrounding the decision to continue or try deprescribing a PPI and structured tools will be helpful to encourage this.

Limitations: Small studies with heterogeneous populations.

1.2.2 Introduction

Proton pump inhibitors (PPIs) are used to treat upper gastrointestinal (GI) symptoms, such as heartburn and disorders including peptic ulcer disease and gastroesophageal reflux disease (GERD) [32]. Patients with GERD experience frequent bothersome upper GI symptoms such as heartburn, acid reflux and pain in the esophagus, and may have esophagitis [1,2]. This can impair function, disrupt sleep and reduce quality of life [33,34]. Proton pump inhibitors are effective in managing the upper GI symptoms associated with GERD – around 60-80% of patients have their symptoms resolved after one to two months [1]. Peptic ulcer disease requires PPI treatment, though the recommended duration of PPI use is short-term (2 to 12 weeks) in patients at low risk of GI bleeding [2].

There is robust evidence that a minority of patients require long-term PPI therapy (e.g. those with chronic non-steroidal anti-inflammatory use, Barrett's esophagus, moderate-high risk of GI bleed, severe symptoms) [1,35]. However, in recent years attention has been paid to the majority who using PPIs "inappropriately" (i.e. without an ongoing indication). Cross-sectional studies suggest rates of inappropriate use around 50-80% depending on the practice setting [4,5,36]. Patients with mild/moderate GERD or upper GI symptoms, whose symptoms are resolved after one to two months of PPI treatment may not require long-term therapy [1]. Further, patients who are treated for peptic ulcer disease whose symptoms are resolved after treatment, and have no ongoing risk

factors, may not need PPIs long-term [1]. Yet, many continue on these drugs indefinitely. Unnecessary PPI use is a clinical and economic concern. In 2012, Canadian public drug programs spent \$247 million dollars on PPIs [11]. Meta-analyses of observational studies suggest PPIs are associated with a small increased risk of *C. difficile*, fractures and pneumonia [6–8], though the risk of fractures has been questioned [9].

Systematic reviews have been conducted assessing satisfaction with PPI treatment in GERD patients. One systematic review (n=11 studies) found that between 59 and 84% of patients with GERD are satisfied with treatment [33]. Patients with more severe or frequent symptoms at baseline, or those with residual symptoms despite PPI treatment tended to be less satisfied with treatment. In these studies, satisfaction was generally measured via response to a single question using a 7-point Likert scale (from completely dissatisfied to completely satisfied). Another systematic review found that PPIs also appear to improve quality-of-life in patients whose symptoms respond to treatment (n=9 studies, e.g. improved mean physical health score on short-form health survey-36 by 12% in one study) [37]. However, patients whose symptoms persist despite PPI therapy have less improvement in quality-of-life (8-16% lower physical health-related quality of life scores). While such studies provide insight into patient satisfaction and quality-of-life with PPI therapy, they do not closely examine what is important to patients regarding PPI treatment, and the range of attitudes and values towards PPIs.

Deprescribing is the planned process of reducing or stopping medications with the goal of reducing burden of care and improving quality of life. The decision to try deprescribing should be shared between a patient and clinician, and should incorporate patient values and preferences surrounding PPI treatment [23]. Preferences and values surrounding deprescribing vary. Some patients value using fewer medications while others may be concerned about symptoms coming back or an underlying disease worsening and prefer to continue a medication [22]. As such, a patients' decision about deprescribing is influenced by preferences and values (a preference-sensitive decision) [28]. Therefore, it is critical to understand the range of patient attitudes, values and preferences that exist towards both treatment with PPIs and the shared decision to try deprescribing. Clinical evidence suggests that PPIs can be deprescribed in around 15-65% of eligible patients depending on the patient population and indication for use, though these studies only assessed clinical outcomes [38,39].

No studies providing an overview of patient values and preferences related specifically to PPI treatment could be located. Therefore, the purpose of this scoping review was to identify and synthesize literature that examines the range of patient values, preferences and attitudes towards PPI treatment and the decision to deprescribe a PPI, as well as identify gaps in knowledge in this area. The subset of patients using PPIs for GERD, uninvestigated upper GI symptoms (e.g. heartburn, acid regurgitation) or would be eligible to discontinue their PPI (no indication for continued therapy) were of specific interest.

1.2.3 Methods

Methodology was guided by Arskey & O'Malley's framework and Joanna Briggs Institute methodology for scoping reviews [40,41]. An *a priori* protocol was developed and followed.

Review questions

- 1) What are patients' values and preferences surrounding use of proton pump inhibitors?
- 2) What are patients' values and preferences surrounding deprescribing of proton pump inhibitors?

Searches

The following databases were searched using medical subject headings and keywords on August 9, 2016: MEDLINE (via OVID, 1946 onward), Cochrane Library (via OVID), and EMBASE (via OVID, 1974 onward). The search was supplemented by scanning reference lists of included studies, and searching for additional studies on Google Scholar. UpToDate, Scopus and the TRIP database were also searched. There was no restriction based on language for the literature search. The search strategy is outlined in Appendix 1. It was adapted from an existing patient values filter [42], developed in MEDLINE and adapted for the other databases.

Types of studies included

Consistent with established scoping review methodology, specific exclusion criteria based on study design was not applied *a priori* [40,41]. Studies which evaluated patient

values, preferences or attitudes related to PPI treatment (either continuation or deprescribing) were included. These could have included, for example, focus groups, interviews, surveys or clinical studies (e.g. randomized controlled trials [RCTs]) if patient values were assessed.

Participants/population

The population of interest was adults using PPIs for upper GI disorders. Studies involving adults 18 years of age or older in any setting were included. There was no limitation on duration of proton pump inhibitor use or indication. However, patients using PPIs for GERD, esophagitis, uninvestigated upper GI symptoms (e.g. heartburn, acid regurgitation) and patients who would be eligible to discontinue their PPI (no indication for continued therapy) were of specific interest.

Preferences and values

Studies that evaluated values and preferences regarding one or more of: receiving a PPI, continuing a PPI long-term and/or having the PPI deprescribed were included.

Outcomes

The outcome of interest was any method of assessment /evaluation of patient values and preferences related to PPI use. Outcomes could have been reported as qualitative syntheses of interviews or focus group data or through quantitative measures. Studies that only reported quality-of-life (QoL) or patient satisfaction via a scale as part of a

clinical trial were not included as there are existing systematic reviews on these topics [34,37].

Data extraction

Two independent reviewers (WT, CB) first screened titles and abstracts with respect to the eligibility criteria outlined above. Full text articles were obtained for any titles/abstracts that appeared to meet eligibility criteria or where eligibility could not be adequately judged based on title or abstract. Two reviewers (WT, CB) then independently assessed full text articles for eligibility.

One reviewer (WT) extracted study data from eligible articles using a structured and piloted data extraction form. The following information was collected: patient information (age, proportion of males/females, indication for PPI use, duration of PPI use), study design, methodology, intervention/comparison characteristics, duration of study, methods of enrollment, and outcome data. A second reviewer (CB) checked the extraction for accuracy.

Strategy for data synthesis

Characteristics of eligible studies were extracted and results were analyzed narratively. Consistent with scoping review methodology, no formal quality assessment of included studies was conducted [40,41] though we did comment on limitations of studies. The characteristics and findings of each eligible study were summarized in tabular form. The findings were categorized based on treatment with PPIs and deprescribing of PPIs, and summarized these findings in a table.

1.2.4 Results

Search results

The search produced 851 results (see Figure 1 for PRISMA flow diagram). Thirty-six full-text articles were screened against eligibility criteria and 12 articles were eligible for inclusion. Reasons for exclusion included: explored clinical outcomes only (n=6), did not examine values and preferences (n=12), not on PPIs (n=1), review or commentary not examining values and preferences (n=5).

Characteristics of included studies

Eligible studies are summarized in Table 1. Seven studies involved survey or questionnaire results [43–46,26,47,48], four studies summarized qualitative interview data [24,49,27,25] and one RCT [50] reported patient preferences toward PPI treatment. One study only examined values and preferences towards reducing PPI use, five studies looked only at PPI treatment (initiation and/or continuation), four studies assessed attitudes to both PPI treatment and reduction and two studies evaluated attitudes towards PPI treatment and switching to alternative PPIs. Table 2 provides a summary of patient values, preferences and attitudes towards treatment with PPIs and potential deprescribing of PPIs identified from eligible studies.

Summary of findings

Several themes were identified related to PPI initiation and continued use, which are described in Table 2.

1. Patients try over-the-counter (OTC) medications and lifestyle measures before seeking medical attention. Between 60 and 81% of patients use OTC products prior to seeing their physician, and 66 to 76% of patients use lifestyle measures prior to seeking drug treatment [26,27].

2. Symptom control is highly valued by patients. Initial GI symptoms hinder daily life in 48-60% of patients, and 96% of patients remember initial symptoms (acid reflux, pain in esophagus, heartburn) as “debilitating” [45,26]. The most important characteristics of a medication to treat upper GI symptoms have been reported by two studies to be: rapid onset, long-lasting pain control, and safety [45,50]. Hungin et al reported that 74% of patients’ decision to take a PPI was driven by how severe symptoms are, and that compliance was driven primarily by symptom control (80% of patients stated they would only take their PPI as long as symptoms were a problem). Proton pump inhibitors are viewed as an effective therapy by patients. Boath et al [25] found that 100% of patients stated PPIs were the most effective therapy they had tried, while Spijker-Huiges found 96% of patients viewed PPI therapy as effective or very effective [26]. Chey et al reported 65% of GERD patients were completely or very satisfied with PPI treatment and Goh et al found that around 75% of GERD patients stated PPIs managed their symptoms “to some degree”.

3. The duration of intended PPI use is not always explained to patients. A cross-sectional study by Pasina et al reported that only 38% of patients received any information on the intended duration of PPI treatment when it was prescribed. Between 80 and 90% of patients (with upper GI symptoms and/or GERD) using PPIs long-term believed they required chronic PPI therapy [44,27].

4. Patients are concerned about adverse effects. Between 29 and 60% of patients worry about adverse effects of PPIs; however, Chey et al found that patients who were highly satisfied with PPI treatment were less concerned about long-term adverse effects (OR 0.83, 95% CI 0.76 to 0.92) [44,25].

5. Patients want to minimize their exposure to PPIs if possible. Between 68 and 100% of patients report that they would like to take the lowest effective dose of a PPI or take only when needed [44,49].

Themes related to deprescribing were also synthesized (see Table 2).

1. Patients are willing to discuss PPI reduction. Forty to 90% of patients report being open to discussing having their PPI deprescribed [43,47,25].

2. Patients are willing to try deprescribing and try to reduce PPI use on their own. When asked outright about whether they would be enthusiastic about stopping their PPI only 6 to 10% of patients agree [26,25]. When asked if they would consider having their PPI deprescribed under their physician's advice, 42% of patients were amenable in one study [26]. Between 10 and 43% of patients attempt to reduce their PPI use on their own (e.g. taking as needed, every other day, lower dose) [26,47,49,25].

3. Symptom control is also important for deprescribing. Spijker-Huiges et al reported that 68% of patients would not accept even minor symptoms returning after stopping a PPI, while Boath et al found that 90% of patients would be worried about symptoms returning if a PPI was stopped [26,25].

4. Communication is highly valued by patients. Smeets et al evaluated an intervention to reduce PPI therapy in primary care. They found that 76% of patients were dissatisfied because they did not receive information on rebound symptoms and 50% of patients were dissatisfied because the rationale for PPI reduction was not explained to them [43]. In the Smeets study, patients rated communication about reasons for reducing PPI use and the possibility of rebound symptoms as being highly important (mean 3.23 out of 4; 4 = utmost importance). They also valued being involved in the decision to reduce (mean 3.25 out of 4). When considering the decision to try to reduce their PPI use, patients value knowing they can return to their previous dose or restart their medication. In studies that found patients were open to trying to reduce their PPI use, authors

reported that patients would only be willing to try if they knew they could go back to their previous dose or medication [26,49,25,50].

1.2.5 Discussion

This scoping review found that bothersome symptoms are a main reason patients initially seek PPI treatment, and that patients taking PPIs long-term believed they require chronic therapy. Further, fear of symptom return may also be a driver of long-term PPI use. However, the nature and duration of PPI treatment may not be discussed at the outset of therapy in many cases (only 38% of patients reported having duration explained to them in one study). Between 30 and 60% of patients are worried about long-term adverse effects of PPIs, though studies evaluating attitudes toward adverse effects came from the early 2000s when less was known about harms of PPIs.

Patients were generally open to discussing trying to reduce their PPI use, and endorsed wanting to use the lowest effective dose of a PPI if that was possible. Patients felt that communication about the rationale for deprescribing, and the possible outcomes is important, and also value being involved in the decision/planning. These results suggest that patients would like to have clinicians outline why a PPI would be deprescribed, work together with the patient to develop a specific plan for withdrawal and educate the patient on outcomes of deprescribing. This aligns with what is reported in other literature on deprescribing . A 2013 systematic review of patient barriers and enablers of deprescribing reported that a major barrier to deprescribing is when patients have poor understanding of the rationale for deprescribing and are not part of the planning [22]. A

2015 qualitative study of n=27 patients also highlighted the importance of patient-prescriber communication in discussing deprescribing [51].

Patients appear to be more comfortable with using a lower dose or using on-demand (as needed until symptoms resolve) as opposed to stopping completely [49,25] though this was not asked directly in any of the studies. This would be in line with clinical evidence. Tapering, lowering the dose and on-demand use are the strategies often recommended [1,31,52,53] when deprescribing PPIs whereas RCT evidence suggests abrupt discontinuation increases the risk of symptom relapse. A double-blind RCT in 109 patients (mean age 73) with healed mild-moderate esophagitis found abrupt discontinuation of a PPI led to relapse of esophagitis in 70% of patients versus 20% who continued their PPI over 6 months [54]. Thus, abrupt discontinuation is typically not recommended [31,52,53].

In summary, clinicians should be aware that various patient attitudes exist towards continued PPI treatment and the decision to try reducing their PPI use. Most patients are willing to discuss the options, and may be amenable to trying to reduce their PPI use with clear communication and expectations. Some patients will be keen to reduce their medication use, while others will be concerned about symptoms coming back. As such, the decision is heavily dependent on patient preferences, and can be considered a preference-sensitive decision [28].

Implications for practice

It is important to be mindful of patient values and preferences, and incorporate them into shared decision making discussions. This is especially important in discussions surrounding deprescribing, since these decisions may be heavily dependent on patient values [23]. This scoping review identified three implications for clinicians.

1. Communicating expected duration at outset may help patients understand that therapy may not be required long-term. Many patients accept long-term therapy because they do not want to experience symptoms and have their daily function or sleep disrupted. However, we found that prescribers rarely discussed expected treatment duration when initiating a prescription [47].

2. A discussion of continuation versus deprescribing of a PPI can be initiated in eligible patients. Clinicians can explain why PPI deprescribing could be considered and ask patients about which option they may prefer (e.g. use a lower dose or use only as needed when symptoms return [on-demand]). Many patients will be reluctant to attempt PPI deprescribing because they fear symptoms coming back and do not want to tolerate even mild symptoms returning.

3. Expectations and planning should be discussed with patients. Patients appear to be more open to the idea of reducing their PPI if they know they can return to their previous dose. Therefore, patients should be advised that if symptoms return and are severe, bother them or interfere with their lives, they can return to their previous PPI dose or

restart their PPI. Some patients will not want to tolerate even mild symptoms; however, some may be willing to accept mild symptoms if it means reducing their medication burden. Patients appear to be more comfortable with the idea of lowering a dose or self-regulating their PPI use versus outright stopping; therefore, it is important to discuss the options with patients.

Gaps in knowledge

Existing literature provides insight into patient attitudes towards PPI treatment and deprescribing. Future work should analyze these attitudes more in-depth. For example, there is little information on patient preference for one deprescribing regimen over another (e.g. using a lower dose versus on-demand). It would also be helpful to have a better idea of how patients view the trade-off between symptom control and taking fewer pills. While this scoping review found that communication was important, it would be valuable to understand what specific information (e.g. estimation of risk of symptom relapse, long-term adverse effects) would help patients make decisions surrounding continuation versus deprescribing of PPIs. Finally, there is little information on patient preferences for a deprescribing plan (e.g. frequency and type of follow-up).

Much of the data on patients' views towards long-term risks of PPI comes from the early 2000s. Given more recent evidence on long-term adverse effects of PPIs, an up-to-date look at patient attitudes towards long-term PPI use is warranted.

Finally, structured tools which incorporate estimates of benefits/harms will be helpful to facilitate discussions of continuation versus deprescribing of PPIs [23] as deprescribing is a preference-sensitive decision [28].

Limitations

Given this was a scoping review, the results and explore the topic rather than providing definitive evidence. Some of the studies poorly described the included patients (e.g. specific GI disorder, indication, or duration of use) while others involved a very specific group of patients in a small geographical area, which may limit generalizability of findings. Further, many of the studies involved different study designs and small sample sizes, introducing heterogeneity into our results. As this was a scoping review, we did not formally assess quality of studies. Nevertheless, we were able to identify several common themes and patterns among the identified studies.

1.2.6 Conclusion

Long-term PPI use is common though some patients may not have an ongoing indication for use. It is important for prescribers to be aware of the range of patient values and preferences that exist related to PPI treatment and deprescribing. Twelve studies were found which investigated patient attitudes towards PPI treatment and deprescribing. Most patients are willing to engage in discussions surrounding continued PPI use versus deprescribing. This scoping review suggests that patients appear to place a high degree of value on symptom control and are fearful of symptoms returning

should they reduce their PPI use; therefore, many are resigned to long-term use. Many patients report not being willing to try deprescribing, though most patients endorse preferring to take the lowest effective dose of a PPI and some patients attempt to reduce PPI use on their own. Patients value communication. They are more comfortable with PPI deprescribing if they receive education on why it is being considered, know what to expect (e.g. possibility of symptoms returning) and know that they can restart their PPI or return to the previous dose if they cannot tolerate deprescribing. Therefore, while some patients will not want to attempt deprescribing (and not want to accept risk of even mild symptoms returning), some patients are willing to trial deprescribing as long as they understand why it is being done and have a clear idea of what to expect.

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1.2.8 Tables and Figures for Chapter 1.2

Figure 1. PRISMA flow diagram.

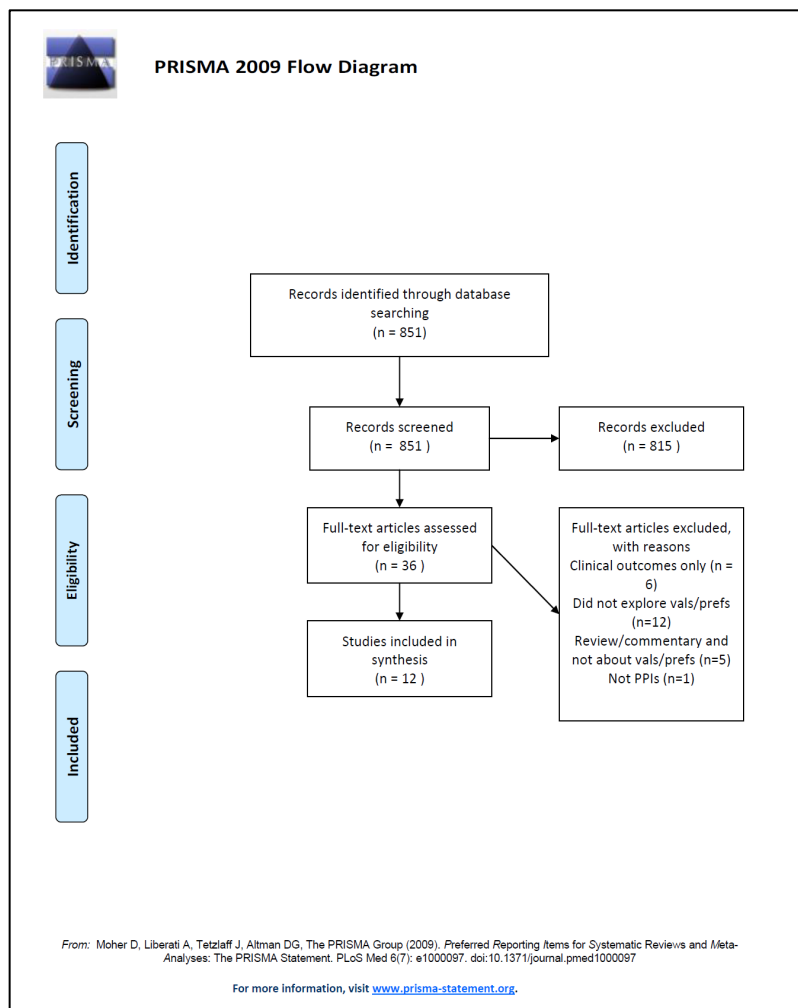


Table 1.1. Characteristics of included studies.

Study	Methodology	Patients	Findings	Comments
Smeets 2009	Validated postal survey questionnaire sent to long-term ASD (PPI or H2RA) users (at least 180 daily doses in last year, not on chronic NSAIDs), 16% of whom had participated in a program to reduce ASD use (protocol for reducing sent to general practitioners) Gathered information on patient preferences and experiences reducing ASDs in group that was part of reduction program	n=977 patients taking ASDs (82% PPIs) not involved in reduction program n=188 patients taking ASDs (79% PPIs) involved in reduction program; mean age 42 years (23% age 75+), 88% of ASDs prescribed by GP, 63% low education level, 45% rated health as good	In patients part of reducing program: 70% report having no problem being approached about reducing 50% report that their GP rarely or never elaborated on why to stop ASD 76% of patients stated GP did not discuss possibility of rebound effects Patients felt that GP support and communication, as well as patient involvement important in decision to reduce PPIs; patients (n=173) rated importance of communication 3.23/4 and patient involvement 3.25/4 when reducing ASDs	16% of patients who participated in reduction program were able to stop ASDs versus 7% in non-participating group Majority of patients were dissatisfied with GPs due to lack of support and communication throughout process, including not having rationale for reducing explained, and not outlining possible rebound symptoms
Pollock 2000	Qualitative study: structured interviews discussing patient ideas regarding PPI treatment efficacy, the role of preventive behaviours, anticipated outcomes and the relationship between patients and physicians Discussed methods of rationing PPI use including: reducing dose, changing to a different PPI, using on-demand ("self-regulation") Identified key themes from patient interviews	n=82 with repeat prescriptions for PPIs (52% female), age 28 to 83, mainly from working class background (not further defined or measured) 19/82 patients had at some point during PPI treatment attempted a dose reduction advised by their physician	~33% of patients had attempted to self-manage upper GI symptoms with PPIs (i.e. take on-demand); other 67% would not deviate from physician's instructions to take daily Patients are encouraged to attempt to reduce PPI use if they know they can go back on their PPI or return to the previous dose (13/19 patients [68%] happy to try lower dose though 6/13 [46%] needed to return to higher dose; only 1/6 [17%] unhappy with experience) Patients should have an idea of what to expect when their PPI is reduced (potential for rebound symptoms or return of disease; occurred in 37% of patients reducing PPI use) Patients worried about long-term adverse effects were more likely to self-regulate PPI treatment (frequency not reported)	Also interviewed GPs, many of whom endorsed a policy of using the lowest effective PPI dose when possible and acknowledged over-prescribing of PPIs as a problem Less than 50% of GPs would actively encourage on-demand PPI use
Johnson 2002	Double-blind, double-dummy randomized	n=240 (233 ITT) taking PPIs for ≥ 56	Patients reported most important characteristics of a	The authors reported no difference in

	<p>crossover trial</p> <p>Five general practice centers in the United Kingdom and Ireland</p> <p>Patients randomly received omeprazole 20mg once daily x 4 weeks or rabeprazole 20mg once daily x 4 weeks then crossed over</p> <p>Measured attitudes to changing medications and ranked most important three characteristics of a medication for GERD</p>	<p>days with symptoms currently managed, mean age 59 years (range 30-79), 45% female, 98% Caucasian, 92% GERD patients</p> <p>n=217 responded to attitudes to changing medication questionnaire (patients could select one or more of five statements to reflect their attitude)</p>	<p>medication for GERD were rapid onset and lasting pain control; ease of swallowing and unpleasant side-effects were second; handling, taste and positive side-effects were third most important (quantitative results not reported)</p> <p>105/217 (41%) of patients reported being open to switching PPIs only if they knew they could switch back to the old PPI if they didn't like the new one</p> <p>Overall, 84.4% of patients would be willing to try an alternate PPI; however, 14.8% would not be willing to change if they were happy with their current PPI</p>	<p>treatment preference score between rabeprazole or omeprazole suggesting these two PPIs have similar clinical efficacy</p>
Hungin 1999	<p>Validated questionnaire sent to 175 patients taking long-term PPIs (>1 year) asking about PPI adverse effects, efficacy and compliance (aim of study was to assess factors influencing compliance)</p> <p>Participants given 17 questions and could agree or disagree with statements</p>	<p>n=158, 44% female, mean age 61 years (range 14 to 91 years), 85% taking omeprazole</p>	<p>Compliance in patients taking PPIs is driven by the presence of symptoms and severity of symptoms</p> <p>n=46 answered every question:</p> <p>80% of patients take PPIs only if they feel symptoms are a problem</p> <p>68% of patients prefer to take PPIs only when they want to</p> <p>90% of long-term PPI users felt they needed PPI therapy for their condition</p> <p>29% of patients had a fear of side-effects from PPIs and 47% worry their body may become "used to the treatment"</p>	<p>Unclear of indication for PPIs in this sample</p> <p>34% of patients reported not understanding how treatment works</p>
Grime 2002	<p>Open two hour interviews of patients patients < 45 years of age taking "long-term" PPIs; researchers identified key themes and conducted content analysis of interview data</p> <p>Researchers specifically interested</p>	<p>n=10, 8 patients <40 years and 2 patients 40-45, 50% female, 80% with various upper GI symptoms</p>	<p>80% patients tried over-the-counter medications first (e.g. H2RA) before starting on PPIs and reported PPIs to be more effective</p> <p>PPIs allowed patients to resume normal day to day life and not worry about symptoms</p> <p>60% of patients viewed PPIs</p>	<p>50% of patients had no clear explanation for symptoms and had difficulty understanding why they were experiencing symptoms</p>

	in views of younger patients on long-term PPI use		as a way to palliate symptoms but not as a cure for underlying problem	
			60% of patients worried about long-term adverse effects of PPIs	
			30% of patients concerned about taking PPIs for "rest of their lives"	
			100% of patients expressed wanting symptom control with the minimum dose of PPI; however, 20% took more than prescribed PPI dose to achieve symptom resolution	
			80% of patients felt they would not be able to stop taking PPIs	
Grime 2001 (same sample as Pollock 2000)	Semi-structured interviews; discussed knowledge of disease, experience with treatment, relationship with physician and control over symptoms Researchers identified key themes through content analysis of interview transcripts (coded by two authors)	n=82, 52% female, age 28 to 83 years, mostly working class background, "most" patients had esophagitis	96% remember initial symptoms as debilitating and unpleasant, 8% took PPIs as first treatment tried "Very few" patients (frequency not reported) had heard about PPIs before they were prescribed, many did not ask questions about PPIs during the medical visit Patients view PPIs as most effective way to manage symptoms (frequency not reported); many believe symptoms will return if they stop taking (frequency not reported) Patients more concerned about long-term adverse effect of PPIs than physicians (frequency not reported) ~66% had an effort to modify lifestyle to manage symptoms	Physicians also interviewed – anticipated difficulty in reducing or stopping PPIs due to perceived effectiveness from patients
Goh 2014	Questionnaire (GERD in Asia Pacific Survey) delivered to in-person to patients with GERD treated with PPIs Investigated well-being of patients, satisfaction with PPI	n=450 patients, 53% female, aged 21-55 years with GERD currently taking PPIs (mean duration of PPI therapy = 3 years)	60% of patients felt GERD seriously disrupted their life; 20% reported that symptoms still impacted daily life despite PPI treatment ~75% reported PPIs managed symptoms to some degree (30% reported incomplete response)	Patients from Thailand (n=80), Philippines (n=80), Indonesia (n=80), Taiwan (n=80), Korea (n=80), Hong Kong (n=50)

	therapy, symptom control, breakthrough symptoms and patient-desired outcomes of PPI therapy		<p>Patients reported that ideal GERD treatment would keep patients free from symptoms (59% reporting particularly at night)</p> <p>Patients also felt a GERD medication should be safe for long-term use (60% of patients), reduce patients worry about symptoms (58%), and act quickly (<30 minutes) (50%)</p> <p>81% of patients attempted self-treatment before seeing a physician</p>	
Condra 1999	<p>Mailed patient satisfaction survey to patients whose PPI was switched from omeprazole to lansoprazole as part of a formulary change</p> <p>Questions on treatment preference and willingness to pay additional cost for a particular PPI</p>	n=158 (53% response rate), mean age 65 years (SD 12), 96% male, diagnosis of GERD treated with PPI > 4 months	<p>64% of patients preferred original PPI (omeprazole) over new PPI (lansoprazole); 36% preferred new PPI</p> <p>Of patients with a preference, 69% reported being willing to pay extra fee for preferred PPI (20% would pay up to \$10 per month)</p>	No difference in clinical symptom score between omeprazole and lansoprazole
Chey 2010	<p>Online survey assessing length of PPI therapy, satisfaction, perceptions about long-term use and adverse effects, use of OTC medications</p> <p>Patients had GERD and were on PPIs > 1 month</p> <p>Primary outcome was to identify predictors of patient satisfaction with PPIs (using multivariable logistic regression)</p>	N=1013 patients, mean age 50.9 years (range 19 to 84), 50% female, 94% had GERD > 12 months, 82% taking PPIs > 1 year, 56% annual income >\$50 000 USD	<p>65% of patients completely or very satisfied with PPI treatment (more likely to be satisfied with PPI if complete symptom relief)</p> <p>Patients with mild symptoms more likely to be satisfied with therapy versus those with moderate symptoms (74% vs 61%, p = 0.001)</p> <p>Patients highly satisfied with PPIs significantly less likely to worry about long-term use (OR 0.83, 95% CI 0.76 to 0.92), less likely to use OTC medications (OR 0.84, 95% CI 0.75 to 0.95), more likely to report complete symptom relief (OR 1.95, 95% CI 1.70 to 2.24)</p>	125/1013 (12%) of patients taking PPIs on-demand
Pasina 2016	Cross-sectional study in nine community pharmacies in Italy; pharmacists interviewed patients using a questionnaire and collected information on history	N=260, mean age 62.1 years (SD 16.6), 49% female, 17.7% with GERD, 31% for gastroprotection, 17% unknown, 31% unspecified gastroprotection (i.e.	<p>~40% of patients were in favour of PPI discontinuation</p> <p>62% of patients did not receive any information about the duration of PPI treatment when prescribed</p>	Authors conclude that results highlight need for education about original indication and expected duration of therapy, as well as specific instructions

	<p>of PPI use, preference for PPI withdrawal and previous attempts to withdraw</p> <p>Patients could have been using PPIs for GERD, ulcer treatment, gastroprotection, dyspepsia, Zollinger-Ellison syndrome</p>	<p>not due to NSAID use or valid indication)</p> <p>48% of patients with no indication for PPI use; 52% had valid original indication</p>	<p>10% of patients without an indication for PPI therapy had previously tried to withdraw from PPIs versus 24% in those with a valid original indication</p> <p>75% of patients without a valid indication had discussed withdrawal with their physician versus 31% of patients with a valid indication originally</p> <p>Most (frequency not reported) patients had been instructed to abruptly stop their PPI if advised to withdraw (those attempting to withdraw had high rate of failure)</p>	<p>for withdrawal and discussion of patient preferences surrounding withdrawal method</p>
Boath 1997	<p>Semi-structured interviews at home or phone with patients from one group medical practice in the UK who were using PPIs; interviews assessed: how patients were taking PPIs, perceptions of efficacy, satisfaction, feelings about discontinuing treatment</p>	<p>N=20, 55% female, age 28 to 68 years, 50% of patients had reflux esophagitis and hiatus hernia, 25% had esophagitis alone</p>	<p>Only 5% had heard about PPIs before prescribed</p> <p>100% of patients felt PPIs were most effective treatment they had tried (80% reported that PPIs changed their life; however, 25% of patients still used OTC antacids rarely)</p> <p>75% of patients felt PPIs allowed them to drink and eating what they want</p> <p>20% of patients had intentionally missed doses and reported wanting to take less of the medication</p> <p>Patients reported being concerned about long-term effects (frequency not reported)</p> <p>10% of patients said they would like to stop and remaining patients worried about symptoms returning if stopping; 90% of patients were amenable to switching to another drugs, but would like to know that they can restart on their old drug/dose if necessary; patients also open to reducing dosage of PPI</p> <p>10% of patients had an accurate idea of cost of PPIs</p>	

Spijker-Hughes 2006	<p>Questionnaire sent to patients on ASDs with no clear indication for continued therapy</p> <p>Questionnaire assessed opinion on discontinuing ASDs and general questions on ASD treatment</p>	<p>N=318 (64% response rate), mean age 66 years (SD 12), 59% female, 80% using PPIs, heartburn was chief complaint of 75% of patients, 52% had symptoms for > 10 years</p>	<p>Most (frequency not reported) patients waited 1 to 5 years before seeking medical help; 48% reported symptoms impairing daily life</p> <p>96% of patients viewed ASD therapy as effective to very effective; 95% reported ASDs improved their quality of life</p> <p>15% of patients took ASDs on-demand</p> <p>60% of patients used OTC medications prior to ASD therapy</p> <p>76% used lifestyle measures prior to ASD therapy (e.g. lifting head of bed) and 49% continued this while on ASD</p> <p>43% of patients had attempted stopping at some point (96% restarted ASD due to symptom return, 18% using on-demand instead of using previous dose)</p> <p>42% of patients willing to try to stop ASDs under physician advice, only willing if they knew they could restart ASD if symptoms reoccurred</p> <p>6% enthusiastic about stopping</p> <p>68% of patients would not accept even minor symptoms returning after stopping</p>	<p>This sample had lower rate of smoking, drinking and overweight individuals compared to general population</p>
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Abbreviations: ASD = acid suppressing drug, PPI = proton pump inhibitor, H2RA = histamine-2 receptor antagonist, OTC = over-the-counter medication, SD = standard deviation, NSAID = non-steroidal anti-inflammatory drug, GP = general practitioner, GERD = gastroesophageal reflux disease, OR = odds ratio, CI = confidence interval, on-demand = taking a PPI as needed daily until symptoms go away, then stopping

Table 1.2. Summary of patient values, preferences and attitudes towards PPIs.

ATTITUDES TOWARDS PPI TREATMENT	OTC treatment use	60-81% of patients use OTC treatment (e.g. antacids, H2RAs) for upper gastrointestinal symptoms before seeking medical attention and starting a PPI
	Lifestyle measures	66-76% of patients attempt to use lifestyle interventions to manage symptoms prior to seeking treatment
	Symptom control	<p>PPIs are viewed as the most effective drug to control symptoms by patients and allow them to resume normal activity</p> <p>Seeking and continuing drug therapy (PPIs) is driven by the need to control symptoms and reduce interference with normal activities (e.g. sleep) – patients value symptom control highly</p> <p>Patients believe medications used to treat upper GI symptoms should have rapid onset and long-lasting symptom relief; patients also report that medications (PPIs) should reduce worry about symptoms</p> <p>80-90% of long-term PPI users believe will need their PPI long-term</p>
	Lack of information on PPI duration	62% of patients do not receive any information on the expected duration of PPI therapy when the drug is prescribed
	Dose concerns	80% of patients report that they would take PPIs as long as symptoms are a problem; though 68-100% of patients agree that they would like to take the lowest dose that is effective
	Adverse effects	29-60% of patients worry about long-term adverse effects
	ATTITUDES TOWARDS DEPRESCRI BING	Open to discussion
Willingness to try reducing PPI use	<p>Few patients (6-10%) report being enthusiastic about stopping PPIs when initially asked; though a substantial portion of patients (20-50%) report attempting to reduce their PPI use on their own</p> <p>Around 40% of patients (from studies identified) would be willing to try to reduce PPI use (lower dose or stop) if their physician thought it was a good idea, but only if they could restart if symptoms recurred</p>	

Symptom control	Patients' biggest concern in deprescribing PPIs is the possibility of symptoms returning (90% of patients; 68% of patients will not tolerate even minor symptoms returning)
Communication	<p>Guidance and clear communication are important – patients appreciate understanding the rationale for deprescribing and receiving specific advice on a deprescribing plan</p> <p>Patients like to know the possible outcomes of deprescribing PPIs (e.g. rebound symptoms)</p> <p>Patients are encouraged if they know they can restart their PPI or return to the previous dose if necessary</p>

Appendix 1. Search strategy.

MEDLINE

1. *patient acceptance of health care/
2. *Patients/ed, px
3. *family/ed, px
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Cochrane

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9. exp *Antacids/
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12. 8 or 9 or 10 or 11
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14. limit 13 to exclude medline journals

Chapter 2: Strategies to foster appropriate proton pump inhibitor use in long-term care

2.1 Background and rationale

Proton pump inhibitor use is common among older persons in long-term care (LTC). Cross-sectional studies conducted in the United States suggest approximately 40-60% of LTC residents take PPIs [1,2]. The Canadian Institute of Health Information estimate that 37% of LTC residents take PPIs [3]. Some patients require long-term therapy (e.g. at moderate or high risk of gastrointestinal [GI] bleeding due to chronic NSAID use or previous GI bleed, Barrett's esophagus, severe symptoms at baseline), though many continue on PPIs without an ongoing indication. Inappropriate PPI use (i.e. use without an ongoing indication) occurs frequently in older persons, both in the community and in long-term care [4,5]. A cross-sectional study of 98 newly admitted LTC residents at a home in the United States found 50% of PPI prescriptions were inappropriate [1], while another study in 440 newly admitted LTC patients found 61% of PPI prescriptions were inappropriate [4].

Proton pump inhibitors have been associated with a small increased risk of *C. difficile*, pneumonia and fractures [6–8], though some of these associations have been called into question [9]. These risks are increased in older persons, and thus inappropriate PPI use is particularly concerning in this population (specifically in LTC where transfers to

hospital [e.g. due to falls, altered mental status][10] and infectious diseases are common) [5].

Given the potential impact of inappropriate PPI use, our research group developed a PPI deprescribing guideline to address this growing problem. We used evidence from this PPI deprescribing guideline to develop a decision support tool [11] that could be used by physicians and pharmacists to guide a decision regarding continuation versus deprescribing of a PPI (after appropriate discussion with the patient or the individual with power of attorney). In LTC, physicians and pharmacists complete a mandatory medication review every three months for each patient; therefore, the decision support tool could be used with each review to reassess PPI use.

This decision support tool was piloted in a LTC facility in Ottawa, Ontario over 15 months as part of a study examining development and implementation of deprescribing guidelines in primary care and LTC [12]. This chapter describes the effect of this decision support tool on PPI use and costs over that period within one LTC facility.

2.2 Effect of a proton pump inhibitor deprescribing guideline on drug usage and costs in long-term care

The following is a manuscript published in Journal of Post-Acute and Long-Term Care Medicine (JAMDA) in July 2016.

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2.2.1 Abstract

Objectives: To assess the effect of a proton pump inhibitor (PPI) deprescribing guideline on PPI usage and PPI drug costs in one long-term care home in Ontario, Canada.

Design: Interrupted time series analysis to compare monthly PPI usage and average monthly PPI cost per resident 9 months before guideline implementation to 12 months after.

Setting: One long-term care home in Ottawa, Ontario, Canada.

Participants: Long-term care residents prescribed a PPI over a 21 month period (n=335).

Intervention: PPI deprescribing guideline and decision support tool used during quarterly medication reviews.

Measurements: (1) Total number of PPI prescriptions (PPI usage) and (2) average PPI drug cost per resident. We also measured the proportion of residents whose PPI was deprescribed in the pre-guideline period and post-guideline period.

Results: The deprescribing guideline was associated with a decrease in PPI usage but the association was not statistically significant (-8.7 prescriptions, 95% CI -22.0 to 4.6). The PPI guideline led to a significant decrease in average monthly PPI drug cost per resident over time (0.16 CAD reduction per month; 95% CI -0.29 to -0.03). In the 9 months pre-intervention, 57/205 (27.8%) of eligible residents had their PPI deprescribed, and in the 12 months post-intervention 134/268 (50.0%) of eligible residents had their PPI deprescribed (difference in proportions of 22.2%; 95% CI: 13.4 to 30.4).

Discussion/Conclusion: The deprescribing guideline was associated with a decline PPI usage; however, this negative association was not statistically significant. PPI usage declined in the initial six months after guideline implementation but began to climb back to baseline after this, which may explain the lack of a significant reduction in PPI usage. This suggests that it was difficult to maintain PPI deprescribing efforts long-term. While implementation of a PPI deprescribing guideline may lead to an initial reduction in PPI usage, and a significant reduction in the average cost of PPI prescriptions over time, it is imperative to explore ways to sustain deprescribing guideline use.

Keywords: deprescribing, inappropriate prescribing, proton pump inhibitors, long-term care, homes for the aged

2.2.2 Introduction

Proton pump inhibitors (PPIs) effectively treat several upper gastrointestinal disorders. In many patients (such as those with mild to moderate gastroesophageal reflux), the duration of therapy should be short-term (e.g. four to eight weeks)[13]. Some patients continue PPIs beyond the recommended duration [5,14–16]. In long-term care (LTC), 50% of residents may be receiving an inappropriate PPI[1], while older patients may be at higher risk of continuing PPIs unnecessarily after hospital discharge[16]. PPI use has been associated with harms such as *C. difficile* infection and fractures, the risks of which are already increased in older persons [6–8,17]. Around \$250 million was spent on PPIs by public drug programs in Canada in 2012, much of which may be excessive [18]. There is a need to reduce unnecessary PPI use through deprescribing (the planned, supervised tapering and/or stopping of drugs), which may reduce PPI spending and risk of adverse effects. We developed a PPI deprescribing guideline and decision support tool[11] and implemented it at three LTC homes as part of a larger research study evaluating development and implementation of deprescribing guidelines[12]. In this paper, we describe the effect of implementing the guideline on PPI usage and drug costs in one long-term care home in Ottawa, Ontario.

2.2.3 Methods

We conducted a retrospective, time series analysis from November 2013 to July 2015, using pharmacy drug utilization records in one 450 bed long-term care home in Ottawa, Ontario. While we implemented the guideline in three homes, this home was the only

one interested in conducting a drug utilization review related to the project. The time period was divided into 21 monthly intervals (9 months before guideline implemented and 12 months after). We measured 12 months post-guideline implementation since the implementation process occurred over three months (it may have taken some residents up to three months to have their PPI reviewed since medication reviews occur quarterly). Residents were eligible if they received a PPI prescription at any point during the 21 month period. As such, we allowed for new residents to enter the study (i.e. new admissions or new PPI prescriptions), and existing residents may have dropped out (discharged or died) or stayed in the sample. Therefore, the denominator may change each month (i.e. number of residents whose PPI could be deprescribed that month). We did not collect any demographic or resident-specific information such as number of concomitant medications, age, comorbidities, etc.

The deprescribing guideline was implemented in July 2014. We presented a Powerpoint summary of the PPI deprescribing guideline and our decision support tool

(<http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/ppi-deprescribing-algorithm-cc.pdf>)[11] to physicians, pharmacists and nurses at an in-person meeting at the LTC home. The support tool was used during individualized quarterly medication reviews by the physicians and pharmacists. Our outcomes of interest were: (1) monthly PPI usage and (2) monthly average PPI cost per resident.

PPI usage was defined as the total number of PPI prescriptions each month. PPI deprescribing was classified as: complete cessation, using a lower dose or switching to

as needed or “on-demand” therapy. To capture deprescribing interventions whereby a PPI was not ceased completely, we subtracted prescriptions where the PPI dose had been lowered (e.g. changed from high-dose PPI to low-dose PPI, changed from twice daily dose to once daily dose) or switched to “on-demand” use from the total (the total already took into account cases where the PPI was stopped completely). PPI cost included drug cost only (professional fee and markup not included). Unit drug costs were obtained from Ontario’s drug formulary for publicly funded drugs [19]. For drugs not covered by the public formulary, we used the pharmacy provider’s drug cost (drugs provided by pharmacy wholesaler). Data on the number of residents overall at the LTC home was provided by the pharmacy provider. Drug cost was calculated as the average PPI cost per resident. There were no changes in physician reimbursement, prescribing limitations, drug coverage or legislation that may have affected physician prescribing of PPIs in LTC over the time period of the study.

We used segmented interrupted time series (ITS) regression analysis with adjustment of autocorrelation [20] to assess the impact of PPI guideline implementation on PPI usage and associated cost. The analysis provides an estimation of changes in level and trend in pre- and post-intervention periods. The level is defined as the value at the beginning of a given period (intercept) while the trend represents the rate of change during a study period (slope). We compared the level and trend of the segment after the intervention with those of the segment before the intervention. Our model evaluated the effect of the intervention, the effect of time and the intervention*time interaction (effect of the intervention over time). We assessed for autocorrelation using the Durbin-Watson

statistic. We performed analysis using the PROC AUTOREG command in SAS 9.4® (SAS Institute, Cary, North Carolina, USA).

We also compared the proportion of eligible residents whose PPI was deprescribed in the entire 12 months after the guideline was implemented to the proportion of eligible residents whose PPI was deprescribed in the 9 months leading up to guideline implementation (difference in proportions test assuming independent samples, 95% confidence interval). The project was approved by the LTC home's internal research ethics board as an evaluation of a quality improvement initiative.

2.2.4 Results

Proton pump inhibitor usage from November 2013 to July 2015 is displayed in Figure 1. A total of 335 residents received a PPI prescription over the 21 month period. At baseline, there were 147 residents on PPIs. The sample at guideline implementation was 180 residents, and in the last month of the study the sample was 206 residents. The mean number of new residents entering the sample each month was 8.7 residents (standard deviation 3.1). Following guideline implementation PPI usage dropped by 8.7 prescriptions (95% CI -22.0 to 4.6, $p=0.19$). Guideline implementation did not result in a significant change in slope (reduction in PPI usage) in the 12 months post-implementation (1.42 fewer prescriptions per month, 95% CI -4.40 to 1.56, $p=0.34$). Before implementation of the deprescribing guideline, there was an upward increase in average monthly PPI cost per resident (0.14 CAD; 95% CI 0.03 to 0.25, $p=0.016$). Following guideline implementation, the average monthly PPI cost dropped by 0.56

CAD per resident (95% CI -1.12 to 0.01, $p=0.059$). PPI deprescribing guideline implementation resulted in a significant change in slope, suggesting that average monthly PPI costs per resident decreased over time (0.16 CAD per month reduction; 95% CI -0.29 to -0.03, $p=0.019$). In the entire 9 months pre-intervention, 57/205 (27.8%) of eligible residents had their PPI deprescribed, and in the entire 12 months post-intervention 134/268 (50.0%) of eligible residents had their PPI deprescribed. This represents a difference in proportions of 22.2% (95% CI: 13.4 to 30.4, $p<0.00001$).

2.2.5 Discussion

Our results show that implementation of a deprescribing guideline and support tool at this LTC home was associated with a decrease in PPI prescribing; however, the reduction in use mainly occurred within six months after the start of the intervention and use gradually climbed back up, resulting in no significant difference in use by the end of the study period (see Figure 1). The guideline was associated with a significant decrease in average monthly PPI cost per resident over time, which remained significant across the study period (though began to climb back up towards the end of the study).

There are several possible explanations for these findings. Interest and uptake of the guideline may have waned over time. New residents admitted on PPIs months past the implementation date may not have been targeted initially for deprescribing while staff and clinicians got to know the resident. New residents may have had valid indications for PPIs and have not been eligible for deprescribing. The number of new residents

entering the sample remained relatively constant over time; however, the size of the sample continued to grow throughout the study (from 147 at baseline, to 180 at implementation, to 206 at the end of the study). This could be explained by the fact that many residents were maintained on a lower dose of PPI compared to baseline versus having the PPI stopped completely. These residents would still be eligible to have their PPI further reduced (or stopped completely) and were thus still counted in the overall sample. It is also possible that symptoms recurred, which may have necessitated restarting a PPI. Unfortunately, the nature of this drug utilization review did not allow use to capture symptom relapse rates. Lastly, we implemented an additional guideline pertaining to a distinct drug class seven months after implementation of the PPI guideline. It is possible that the focus was shifted to the new drug class and thus fewer PPIs were being targeted. Guidelines can be challenging to implement and continued use is often difficult to maintain [12,21]. Our PPI usage results speak to the importance of maintaining efforts to deprescribe past initial implementation of an intervention. This may mean exploring effective approaches to sustaining guideline use such as incorporating the decision support tool into electronic health records/routine care processes or offering periodic educational outreach [21].

While there was no significant reduction in PPI usage, we did find a statistically significant increase in the overall number of deprescribing events post-implementation (comparing events in the entire pre-guideline period to the entire post-guideline period). Our results (22% increase in deprescribing rate) are consistent with other interventions to reduce PPI use, which demonstrate rates of deprescribing around 20-50%[22,23].

The pre-guideline deprescribing rate of 25% is consistent with a retrospective cohort study (n=10,731) which found PPIs were discontinued in around 25% of LTC residents within 180 days of being admitted, without any specific deprescribing intervention in place [24].

Time-series analysis demonstrated that implementation of the deprescribing guideline significantly reduced the average cost of PPIs per resident over time. Residents whose PPIs were deprescribed continued to accrue savings in subsequent months; however, average cost per resident began to rise slowly towards the end of the data collection period. While significant costs savings were seen when the guideline was implemented, strategies that result in sustained clinician behavior change would likely be necessary to maintain reductions in PPI spending. Our results provide insight into trends in PPI use following a deprescribing intervention. A clinical pharmacist intervention has been shown to reduce PPI drug utilization and cost in an ambulatory care setting; however, the duration of follow-up in this study was only five months[25]. Thus, it is difficult to evaluate whether such an intervention produces meaningful reductions in PPI use long-term. Our results suggest that despite an initial substantial reduction, PPI usage eventually crept back up after a deprescribing intervention was offered.

Our study had important limitations. We did not collect data on any covariates such as age, gender, duration of PPI use or indication and therefore we could not control for patient-level confounders that may have explained our result. These covariates may have been impactful considering there were new admissions and deaths over our study

period. A control group was not used; however, the ITS design allows us to adjust for history and maturation by using multiple assessments of the outcome measures both before and after the intervention [26].

Use of our guideline and decision support tool in larger randomized trials should provide a picture of whether they are effective in improving appropriate PPI use. More comprehensive pharmacoeconomic analyses (incorporating more detailed information on direct costs, cost of symptom relapse, etc.) will help to evaluate whether PPI deprescribing is cost-effective in LTC.

2.2.6 Conclusions

Implementation of a PPI deprescribing guideline at this LTC site led to an initial reduction in PPI usage that was difficult to maintain more than six months beyond the implementation period. As such, there was no statistically significant reduction found in PPI usage post-implementation. However, there was a statistically significant reduction in average PPI costs per resident over time. Our results suggest that a PPI deprescribing guideline may reduce PPI use and costs in LTC, but opportunities to maintain guideline use should be explored. Further work should focus on developing more comprehensive pharmacoeconomic analysis of PPI deprescribing in LTC to determine cost-effectiveness.

Funding

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<http://www.health.gov.on.ca/en/pro/ministry/research/hsrf.aspx>

Conflicts of interest

The authors declare no conflicts of interest.

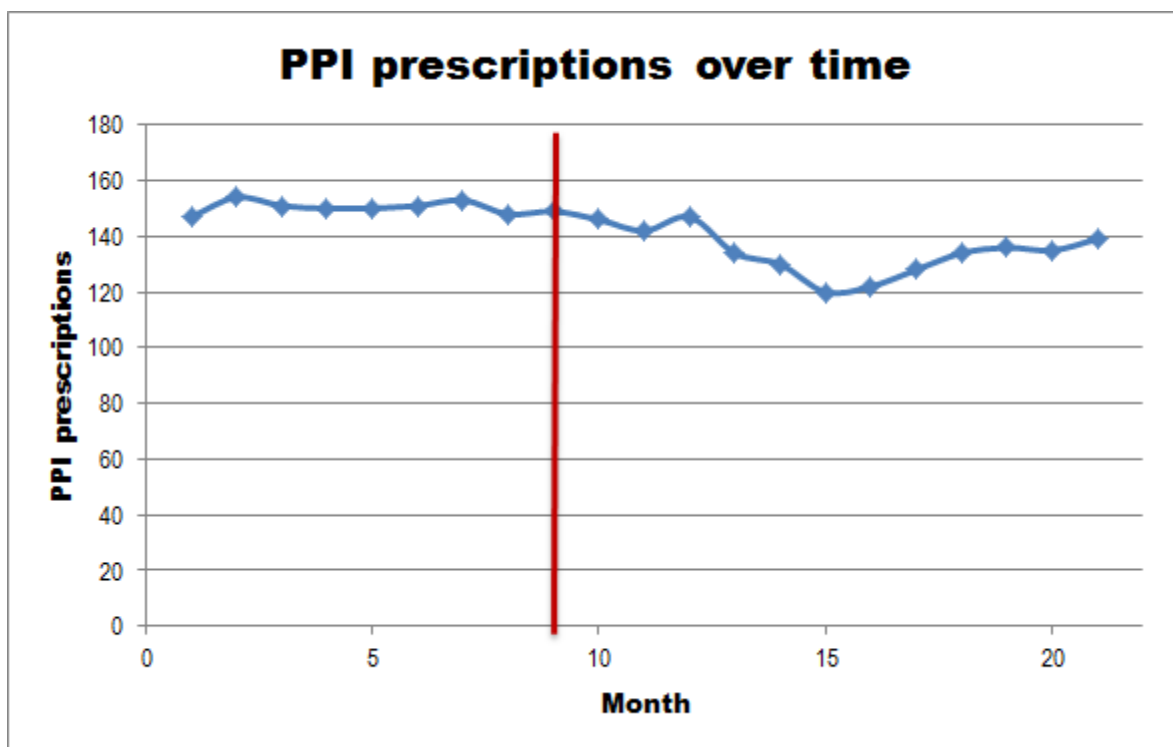
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2.2.8 Figure for Chapter 2

Figure 2.1. PPI usage across 21 months.



Chapter 3: Strategies to foster appropriate PPI use in primary care

3.1 Background

3.1.1 Rationale

Discussing deprescribing can be difficult for clinicians in primary care. A 2014 qualitative systematic review of 21 studies found that lack of time and proper resources/tools were a common barrier to discussing deprescribing [1]. Prescribers cite a perceived difficulty in engaging patients in these discussions, and an inability to accurately convey benefits and harms. They also worry about how patients will perceive deprescribing.

The decision to continue a PPI or try deprescribing should be shared between a patient and clinician (prescriber or pharmacist) [2]. Patients should be informed about the benefits and harms of options, and should feel confident in their decision [3].

Unfortunately, there is currently a lack patient-focused tools that support discussions surrounding continuation versus deprescribing of a medication. A 2016 review of shared decision making for deprescribing highlighted the need for tools to engage in deprescribing discussions, and to elicit patient preferences related to benefits and harms [2]. Such tools should be delivered efficiently, such that they are useful in a primary care environment.

There is a clear need for tools which foster shared decision making surrounding continuing or deprescribing a medication, and which are useful in busy clinical practice.

3.1.2 Previous research

Previous studies of strategies to improve inappropriate PPI use have focused on prescriber education, patient education or incorporated processes into electronic medical records [4–8]. These strategies demonstrate PPI deprescribing success rates ranging from 14-64%[4]. However, none of these studies employed structured approaches to shared decision making and incorporating patient values and preferences into deprescribing discussions. Incorporation of preferences is important given the preference-sensitive nature of deprescribing decisions (see chapter 1).

Further, deprescribing success (i.e. cessation rate) should not be seen as the only outcome of interest. Rather, studies also need to look at how these decisions are made. A successful decision is one that incorporates patient values, preferences and goals and one that the patient is informed about and feels confident in [9]. Therefore, the discussion should be framed around a decision to continue a PPI or to try deprescribing (versus deprescribing only).

3.1.3 Patient decision aids

Patient decision aids (PtDAs) inform patients on benefits and harms of treatment options and aim to increase patient knowledge of their health condition and treatment options while also achieving decisions congruent with patient values [10]. They help patients clarify what is important to them about different options, have realistic expectations of options and feel supported in their decision [3].

Patient decision aids also make patients feel confident in the decisions they make. Decisional conflict is the feeling of not being certain about a course of action, due to uncertainty about outcomes and values or lack of knowledge [11]. A systematic review of 115 studies shows that PtDAs lower decisional conflict, reduce the proportion of patients who are undecided about decisions and improve knowledge of options [10].

PtDAs can be developed using templates available on-line from the Ottawa Hospital Research Institute's PtDA group. Development should be guided by the International PtDA Standards Collaboration (IPDAS) criteria, which outlines items pertaining to the quality and standards of PtDAs [12]. We are aware of only two PtDAs for stopping drugs, one for stopping antidepressants (meets 18 out of 22 of the applicable IPDAS criteria)[13] and one for stopping life-prolonging treatments at end of life (meets 18 out of 22 applicable IPDAS criteria) [14]. The use of PtDAs is compelling for the decision to continue a medication or have it deprescribed since this decision is influenced strongly by patient values and preferences (a preference-sensitive decision [15]), as well as knowledge of benefits and harms.

3.1.4 Consult patient decision aids

PtDAs can be delivered on their own or as part of a consultation with a healthcare professional (called a consult PtDA) [16]. Traditional PtDAs are usually completed by the patients alone and take longer to complete. Therefore, they may not allow engaged and collaborative discussion of a treatment decision. Their impact in influencing actual healthcare decisions can also be difficult to ascertain [16]. Conversely, consult decision aids (consult PtDAs) are delivered in real time and may be more effective in facilitating discussions with patients to foster shared decision making during a healthcare consultation [16]. Consult PtDAs allow for an interactive discussion of the healthcare decision and can tailor the discussion to a patient's individual situation. Further, consult PtDAs facilitate a shared healthcare decision in real time during a healthcare visit, which may be desirable for certain decisions such as the decision to continue a medication [16]. Because consult PtDAs are a time-efficient manner to facilitate shared decision making surrounding continuation versus deprescribing of a medication, we elected to use this format for our PtDA.

3.1.5 User-centered design

A growing area of research in the field of PtDAs is user-centered design of PtDAs. User-centered design seeks to involve patients and clinicians (users) in development of a healthcare tool [17]. The framework is derived from the idea that those who interact/use

a product or service should be involved in its design. User-centered design has not been extensively studied in healthcare [17]; however, IPDAS recommends that patients and clinicians should be involved in development of PtDAs to ensure usability and acceptability [18]. The framework suggests having patients collaboratively develop the tool and an iterative process of refining based on feedback and review of the tool. The PtDA should also be designed based on understanding the needs and goals of patients and clinicians [17]. The user-centered design framework guided development of our consult PtDA.

3.2 Methods

The following manuscript is in press at Canadian Pharmacists Journal

Should I continue taking my acid reflux medication? Design of a pilot before/after study evaluating a patient decision aid

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3.2.1 Abstract

Background: Proton pump inhibitors (PPIs) effectively treat conditions such as gastroesophageal reflux disease. Evidence-informed guidelines support a limited duration of use in patients with mild or moderate reflux symptoms but many continue on these drugs unnecessarily. PPIs are associated with harms including *C. difficile* infection and fractures. Unnecessary use contributes to polypharmacy and healthcare costs. Patients need to decide whether to continue taking their PPI, use a lower dose or stop and use it on-demand. This decision should be made collaboratively between a patient and clinician (e.g. pharmacist) and involves weighing the risk of symptom return against potential benefits such as using less medication. Patient decision aids (PtDAs) inform patients on benefits/harms of options and improve ability to make informed decisions that are consistent with values. We developed a consult PtDA aimed at the choice to continue a PPI, use a lower dose/stop and use on-demand, and will evaluate the effect of the PtDA on decision-making parameters and PPI use.

Methods/Design: Before/after study. The PtDA was developed using a user-centered approach. It will be delivered to patients in consultation with a pharmacist. Patients will be ≥ 18 years old, on PPI $>$ four weeks, asymptomatic for reflux/upper gastrointestinal symptoms, and have no indication for continued PPI use. Primary outcome: difference in proportion of patients preferring to continue their PPI after receiving the PtDA compared to before. Secondary outcomes: change in patient knowledge, expectations and decisional conflict before and after the PtDA; whether patient decisions are congruent with their values; agreement in patient and pharmacist rating of shared decision-making; the proportion of patients whose PPI was changed at eight weeks; symptom relapse at eight weeks.

Discussion: Our PtDA aims to empower patients to make a decision about continuing their PPI that is educated and consistent with values. The PtDA has the potential to reduce inappropriate PPI use and its harms.

Trial Registration: NCT02558049

Keywords

Patient decision aid
Proton pump inhibitors
Gastroesophageal reflux disease

3.2.2 Background

Proton pump inhibitors (PPIs) treat upper gastrointestinal conditions such as gastroesophageal reflux disease (GERD). They resolve symptoms in around 80% of patients with erosions present after four to eight weeks of treatment (and about 60% of patients without erosions) [19]. Though the majority of patients with severe symptoms relapse if therapy is discontinued, patients with mild or moderate symptoms may not need continuous daily PPI therapy long-term [19]. Prospective observational studies and cross-sectional studies suggest rates of inappropriate PPI use between 44 and 79% [5,20–22]. Meta-analyses of cohort and case-control studies suggest PPIs may be associated with harms including *C. difficile* infection, pneumonia and fractures [23–25], though some of these associations have been challenged [26]. Public drug programs in Canada spent \$247 million dollars on PPIs in 2012 [27].

The decision to continue a PPI, use a lower dose or stop and use on-demand (only when symptoms come back) should be informed and made collaboratively between a patient and clinician (prescriber or pharmacist). Supervised dose reduction or stopping a medication that may no longer be needed is termed “deprescribing”[28,29]. Our

research group conducted a systematic review [30] and developed a PPI deprescribing guideline to assist clinicians in deprescribing PPIs where appropriate [30,31], and we have been exploring ways to implement these tools.

Patients may fear deprescribing and not understand when it can be considered [32]. Qualitative evidence suggests that patients accept PPIs are appropriate if their physician is continuing to prescribe them [33]. Even when a clinician feels deprescribing a PPI is appropriate, patients struggle to decide whether they wish to pursue deprescribing [32]. Thus, there is an opportunity to educate patients about this decision. Patients should feel confident in the decision they make, and make a decision that is consistent with their values [9]. They should have sufficient knowledge of their options and of possible outcomes [34,35].

Patient decision aids (PtDAs) outline the probability of benefit and harm associated with different treatment options and allow patients to identify what matters most to them [36]. They increase knowledge, help patients feel supported in their decision and achieve decisions congruent with values [36]. PtDAs can be delivered in consultation with a healthcare professional. Pharmacists are well-positioned to implement consultation PtDAs, which can be delivered in a 10 to 15 minute visit [37]. A 2014 systematic review (n=21 studies) suggests prescribers' lack of access to resources (e.g. a pharmacist) and knowledge is a barrier to deprescribing [1]. Pharmacists can help to overcome these barriers, and are therefore a key resource in engaging patients to discuss deprescribing.

We developed a consult PtDA to support patients in making the decision of whether to continue, stop and use on-demand or use a lower dose of PPI and will evaluate the effect of the PtDA when delivered by a pharmacist. We also aim to show how pharmacists, as drug therapy experts, can act as key facilitators of the discussion surrounding deprescribing, and the deprescribing process.

3.2.3 Methods/Design

Research questions

A. In patients ≥ 18 years of age who have used PPIs for > 4 weeks with upper gastrointestinal (GI) symptom resolution, and have no indication to continue treatment, does a PtDA aimed at helping patients' decide whether to continue a PPI or stop and use on-demand/use a lower dose of their PPI:

- 1) affect patient decision preference?
- 2) improve patient knowledge surrounding the decision?
- 3) affect patient expectations?
- 4) affect decisional conflict?
- 5) produce choices that are congruent with patient values?

B. When the PtDA is provided in consultation with a pharmacist, does shared decision-making (SDM) take place (according to both the patient and clinician)?

C. Eight weeks after patients have received a consultation involving the PtDA, what is the effect on prescribing of PPIs?

D. In patients who have chosen to use a lower PPI dose or stop and use on-demand, is there any difference in symptom control at eight weeks compared to those who have continued taking their PPI?

Design of the study

This study will use a before/after design. This study design is recommended for pilot testing of PtDAs according to the International Patient Decision Aid Standards (IPDAS), and has been widely used to this end [34,38–40].

Patients will have an appointment with a pharmacist to go through a PtDA to discuss the decision (probabilities of benefit and harm, individual values and preferences).

Following the appointment, patients can follow up with their family physician should they wish to pursue deprescribing, or can receive instructions from the pharmacist. While the pharmacist is conducting the study visit, implementing the decision aid is a collaborative effort. For example, prescribers have referred patients to the pharmacist to discuss their PPI, and pharmacists can discuss the eligibility of a particular patient with the prescriber in advance of an appointment.

The PtDA has been developed using a user-centered design approach, which included patient representatives as part of the development committee [18,41]. The PtDA was drafted using an online tool (<https://decisionaid.ohri.ca/eTraining/>) and qualifying, certification and quality criteria set out by IPDAS [12]. It was revised in iterations based on feedback from our team.

Setting and participants

We set out to conduct the study at two Ottawa area primary care clinics, but due to low recruitment have expanded to recruit units at a continuing care hospital. Eligibility criteria are outlined in Table 1. Our study protocol has been approved by the Bruyère Research Institute and Ottawa Health Science Network Research Ethics Boards.

Analysis

We will use the SURE test to measure decisional conflict/confidence [42]. We will also measure patient knowledge and realistic expectations before and after using the PtDA. We will analyze these continuous outcomes with paired t tests (5% significance level). Patients will be asked to indicate which option they prefer (continue PPI, stop and use on-demand/use a lower dose, or unsure) before and after the consultation, and we will analyze this outcome using McNemar's test (5% significance level). The congruence between patients' choice and values will be evaluated using multivariable logistic regression [43]. Both the patient and pharmacist will rate the perception that SDM took place using the control preferences scale [44–46] and the agreement between patient

and pharmacist ratings will be measured. After eight weeks, the proportion of patients continuing on PPIs at their pre-PtDA dose will be measured. Symptoms will also be assessed at eight weeks in all patients [47]. Our sample size is based on the paired difference in the proportion of patients preferring to continue on their PPI before the PtDA consult compared to after [48]. To detect a difference in paired proportions of 15% (80% power, alpha of 5%) we need a sample size of 54.

3.2.4 Discussion

Our research group developed three deprescribing guidelines, the first of which focuses on PPIs. We also implemented our deprescribing guideline into primary care practices [49] in a previous phase of our research. This PtDA is a tool to further facilitate implementation of these guidelines and involve patients in the decision-making process. We recognize the importance of patient values surrounding the decision to continue or stop a medication, thus we want to empower patients to make an informed decision.

A 2014 systematic review (n=21 studies) suggests that barriers to prescribers discussing deprescribing are: lack of prescriber time during appointments, competing priorities, access to key resources (e.g. a pharmacist) and lack of a stimulus to review medications [1]. This project seeks to overcome those barriers by having a pharmacist use their knowledge and expertise to become a champion of appropriate PPI use, and to have dedicated 10 to 15 minute appointments to address this issue.

The 2014 systematic review described above also noted challenges in confirming the indication or rationale for a drug being started, as well as uncertainty about whether a patient was eligible for deprescribing [1]. This problem has also been described by other researchers. For example, an Australian study to reduce inappropriate PPI use could not verify the indication for 15 out of 57 patients [5]. We have encountered similar difficulties in recruiting patients so far, where it has been time-consuming to identify eligible patients, and there is uncertainty about whether a patient is eligible to consider the option of having a PPI deprescribed. Thus, while inappropriate PPI prescribing appears to be common, actually attempting interventions to reduce PPI use in practice is challenging.

Our study is limited by a before/after design and a small sample size. However, it will provide valuable information about whether the PtDA is helpful and impactful in clinical practice. This study will lay the foundation for a larger randomized controlled trial to more thoroughly investigate whether our PtDA influences decisions surrounding PPI treatment and actual PPI prescribing rates. Widespread utilization of our PtDA could reduce rates of inappropriate PPI use and thus incidence of rare harms and unnecessary healthcare expenditures.

3.2.5 Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; WT reports an MSc stipend from the Government of Ontario, LMB reports personal fees and non-financial support from Department of Family Medicine, University of Ottawa, non-financial support from Bruyère Research Institute, grants from Canadian Institutes for Health Research, grants from Ministry of Health and Long-Term Care of Ontario, outside the submitted work; no other relationships or activities that could appear to have influenced the submitted work.

3.2.6 Acknowledgements

The authors would like to acknowledge Dr. Dawn Stacey for her suggestions surrounding study design and analysis.

3.2.7 Supplemental methodological information

The following information was not included in the manuscript but has been added here to provide additional detail and context to the manuscript content.

Decision aid development

We chose to use a consult PtDA to allow clinicians to engage in a patient-centered discussion surrounding continuing a PPI and to facilitate shared decision making. As

patient engagement and shared decision making is particularly important in discussions about whether to continue or have a medication deprescribed [15], we felt that using a consult PtDA would be an appropriate choice compared to using a traditional PtDA.

The consult PtDA was developed using user-centered design [26]. Our development team included a two patients, one family physician, one rheumatologist, two pharmacists and epidemiologist/methodologist. According to the user-centered design framework, our first step was to understand patient goals, views and decision making needs related to PPI use. We used literature on patient values and preferences surrounding PPI use, experience from clinicians who have discussed PPI deprescribing with patients and feedback from patient representatives. We then developed our prototype based on this information. The consult PtDA was refined through iterations of revisions by the development team (patients and clinicians) as well as revisions from practicing pharmacists who would use the consult PtDA.

For estimates of benefits and harms, we used data from a systematic review completed by our research group [13].

Outcome measurement

We chose outcomes recommended for pilot testing of PtDAs by IPDAS and the Ottawa Hospital Research Institute group [17,19]. Perceptions of shared decision making will be

assessed using the Control Preferences Scale (CPS), which has been widely used to this end in PtDA studies [30,31].

3.2.8 Tables and Appendices for Chapter 3.2

Table 3.1. Eligibility criteria.

Inclusion criteria
<ol style="list-style-type: none"> 1. \geq 18 years of age 2. Taking a PPI for mild/moderate upper GI symptoms (mild or moderate gastroesophageal reflux disease [GERD]/esophagitis Los Angeles [LA] Grade A or B) for at least 4 weeks with resolution of symptoms 3. Currently asymptomatic
Exclusion criteria
<ol style="list-style-type: none"> 1. Severe GERD or upper GI symptoms, esophagitis LA Grade C or D at baseline 2. Taking PPI for gastroprotection (at moderate or high risk of GI bleeding) 3. History of Barrett's esophagus 4. History of bleeding peptic ulcer 5. Taking PPI for treatment of current ulcer not healed

Appendix A. Proposed statistical methods for outcome analysis.

OUTCOME	HOW MEASURED	STATISTICAL TEST
Decision preference/choice	Preference: continue PPI, use lower dose/stop and use on-demand, or unsure before and after receiving PtDA Dichotomous outcome (continue/unsure vs. use lower dose/stop and use on-demand since patients who are unsure would continue on their PPI)	Change in preference before and after; compare proportion wanting to continue PPI using difference in paired proportions (McNemar's test)[48]
Decisional conflict/confidence	SURE test (Yes =1, No =0) measured as a score out of 4 Score of 4 suggests confident in decision and score <4 suggests decisional conflict	Paired t test comparing SURE score before and after patient receives PtDA
Knowledge	Knowledge questionnaire Measured as a score out of 100, will calculate mean test score before and after PtDA	Paired t test comparing mean test score (out of 100) before and after PtDA
Realistic expectations	Measured as a score out of 100 (correct response if within correct quartile of probability ranging from 0-100 for outcome), will calculate mean test score before and after PtDA	Paired t test comparing mean realistic expectations test score before and after PtDA
Values/choice congruence	In patients passing knowledge test (>50%) Patient preference (dichotomized as above) and value rating when	Multiple logistic regression with dichotomous outcome of continue PPI or lower dose/on-demand PPI and the following variables: value rating (continuous measure from 1-5,

	<p>completing decision aid</p> <p>Patient rating of value (1 to 5) placed on potential benefits and harms</p>	<p>1: favours deprescribing – 5: favours continuation), age, gender, level of education, duration of PPI use</p>
<p>Change in PPI prescription eight weeks after consult</p>	<p>Follow up at eight weeks to assess any change in PPI prescription</p>	<p>Proportion of patients whose PPI prescription is changed after eight weeks</p>
<p>Symptom control at eight weeks</p>	<p>Follow up at eight weeks to ask about symptom control</p> <p>Four point scale: no symptoms, mild symptoms, moderate symptoms, severe symptoms [47]</p> <p>Compare symptom control in patients who had PPI deprescribed versus those who continued</p>	<p>Multiple logistic regression (dichotomous outcome of no symptoms or symptoms and the following variables: age, gender, level of education, duration of PPI use, three levels of PPI use: continued use, lower dose, stop and use on-demand)</p>
<p>Patient perception that SDM took place</p>	<p>Modified control preferences scale rated by both patient and pharmacist</p>	<p>Agreement between pharmacist and patient measured using kappa coefficient</p>

3.3 Results

The following manuscript is formatted for Family Practice (not submitted)

Shared decision making surrounding continuation or deprescribing of a proton pump inhibitor: development and evaluation of a consult patient decision aid

Authors

Wade Thompson, Barbara Farrell, Vivian Welch, Peter Tugwell, Cynthia Way, Lisa Richardson, Lise M. Bjerre

3.3.1 Abstract

Background: Approximately 40-80% of patients continue on long-term proton pump inhibitors (PPIs) without ongoing need. This is concerning given potential harms associated with PPI use and increased spending on PPIs. Patients may face the decision to continue their PPI long-term or to try and reduce PPI use (try deprescribing: use as needed [“on-demand”] or use a lower dose). This decision should be informed, shared with a clinician and based on patient values.

Objectives: Develop and pilot test a consult patient decision aid (PtDA) aimed at facilitating discussion of continued PPI use versus trying to reduce PPI use.

Design: Before/after study. The PtDA was delivered during a 15 minute consultation with a clinical pharmacist.

Setting: Clinics in Ottawa, Canada (two primary care clinics and one geriatric outpatient clinic)

Subjects: Adults ≥ 18 years of age, on PPIs > 4 weeks for mild-moderate gastroesophageal reflux disease (GERD) or upper gastrointestinal (GI) symptoms, asymptomatic, no indication for continued PPI use

Outcome measures: Decision preference (continue PPI vs. try to reduce PPI), knowledge test score (%), realistic expectations test score (%), decisional confidence (SURE score; out of 4 with scores ≤ 3 suggest decisional conflict); agreement on whether shared decision-making occurred; values-choice congruence; PPI status at 8 weeks; upper GI symptoms at 8 weeks.

Results: Twelve patients were recruited. There was no significant difference in the proportion of patients changing their preference before and after the consult PtDA ($p=0.32$). After the consult PtDA, 75% (9/12) of patients preferred to reduce their PPI use while 25% (3/12) preferred to continue. The consult PtDA increased patient knowledge scores (median increase 36%, $p = 0.001$) and realistic expectations scores (median increase 37.5%, $p = 0.016$). The median decisional confidence score after the PtDA was 4.0 (median increase 1.0 from baseline, $p = 0.014$). The weighted kappa for agreement on whether shared decision-making occurred was 0.50 (95% CI 0.15 to 0.85). Valuing deprescribing was associated with non-significant increased odds of preferring to try deprescribing (OR 4.1, 95% CI 0.69 to 24). Eleven out of 12 patients enacted their plan following the visit (7 lower dose, 2 on-demand, 2 continue PPI) and 1 patient chose to continue their PPI and speak to their physician. At 8 weeks, one patient who switched to a lower dose had mild symptoms— no other patients reported any symptoms.

Conclusion: The consult PtDA led to improved knowledge and expectations of the decision to continue a PPI, and improved decisional confidence. Patients felt involved and engaged in decision making, and their values tended to align with their preferences. The consult PtDA allowed for decisions to be made in real-time during a 15 minute consult with a clinical pharmacist. The consult PtDA could therefore be useful in fostering shared decisions surrounding continued PPI use in busy primary care environments. Recruitment was low due to barriers in screening for patient eligibility, which may impair uptake and usability of this intervention.

3.3.2 Background

Long-term proton pump inhibitor (PPI) use is appropriate in some patients; however, many patients continue PPIs without an ongoing indication. Inappropriate PPI use is common in primary care, long-term care and hospital settings with rates of inappropriate use between 40 and 80% [5,22,50,51]. This is concerning given the association between PPI use and a small but important increased risk of fractures, pneumonia and *C. difficile* infection [23–25], though the association with fracture risk has been questioned [26]. Further, spending on PPIs is high – Canadian public drug programs spent \$247 million on PPIs in 2012 [27]. In patients without an ongoing indication for PPI use (e.g. Barrett’s esophagus, moderate-high risk of GI bleed, severe esophagitis), evidence-based guidelines GERD guidelines suggest attempts to reduce or stop PPI use in patients whose symptoms are healed after 4 to 8 weeks [19]. These concerns are echoed by Choosing Wisely Canada, who suggest attempts to reduce or stop PPIs yearly in asymptomatic GERD patients with no indication for continued PPI use [52].

Patients may fear symptoms returning when considering deprescribing of a PPI (planned, supervised dose reduction or stopping) though between 40 and 90% of patients are open to discussing the choice of continuation versus trying deprescribing of a PPI [53–55]. Some patients may also be keen to reduce the amount of pills they take and worry about adverse effects of PPIs [55,56]. The decision to continue a PPI or try deprescribing therefore depends largely on patient preferences and values, and can be

considered a preference-sensitive decision [15]. Patients' preferences should therefore be incorporated into decision making with a clinician (e.g. physician or pharmacist), and patients should be informed about the benefits and harms of different options [2].

Previous studies of interventions to address inappropriate PPI use have included patient or prescriber education, or deprescribing tools, though none of these studies incorporated patient values and preferences into decision-making [4,8].

We developed a consult patient decision aid (PtDA) to facilitate discussions surrounding the decision to continue a PPI or have it deprescribed (use a lower dose, or use "on demand" [as needed]). PtDAs educate patients on the benefits and harms of treatment options, and allow patients to clarify what is important to them about the decision [3].

They improve patient knowledge as well as improving confidence in decisions [3].

Because the decision to try deprescribing is particularly preference-sensitive, a PtDA can ensure preferences are incorporated into decision-making [15]. Consult PtDAs can be used during a health care visit and may be preferred over traditional PtDAs because they encourage discussion and decision-making in real time [16]. To our knowledge, this is one of the first studies to evaluate use of a consult PtDA.

3.3.3 Methods

We conducted a before-after study. The trial protocol was registered at clinicaltrials.gov (NCT02558049). The methods are described in detail elsewhere [57]. We developed our consult PtDA according to International Patient Decision Aid Standards criteria using the principles of user-centered design [41]. The consult PtDA was developed using a published template [16] by a team of patients (n=2) and clinicians (n=5), with feedback from practicing pharmacists (n=2). It was delivered by a clinical pharmacist (LR, CW, WT) during a 15 minute consult in two primary care clinics and a geriatric outpatient clinic in Ottawa, Canada. Following the consult, if a decision was reached, the pharmacist could develop a plan in collaboration with the patient (with the physician's previous approval) or the patient could discuss with their physician separately. Patients were: ≥ 18 years of age, taking PPIs for at least 4 weeks, asymptomatic and had no indication for continued use (history of GI bleed, current ulcer, Barrett's esophagus, severe esophagitis, gastroprotection due to moderate-high bleeding risk).

Our primary outcome was change in decision preference (continue/unsure vs. deprescribe) before and after the consult PtDA was delivered, measured using McNemar's test (5% significance level). We measured change in knowledge test score, realistic expectations, and decisional confidence (before and immediately after the PtDA) using the Wilcoxon sign rank test (5% significance level). Decisional confidence was measured using the SURE test (out of 4); a score of 4 indicates a patient is

confidence in their decision whereas a score of <4 indicates decisional conflict [42]. We conducted follow-up at 8 weeks to assess symptom control (using a four point symptom scale: no symptoms, mild symptoms [awareness of symptoms but easily tolerated], moderate symptoms [discomforting and causing interference in normal activities], severe symptoms [incapacitating, inability to perform normal activities]) [47]. In patients passing the knowledge assessment ($>50\%$), we performed simple logistic regression to assess whether patient values were associated with preference (continue vs. try deprescribing). Patients rated the importance of each outcome to them on a scale of 1-5. We calculated the mean for all outcomes to evaluate patient values (mean score from 1-5; score of 1 suggests preference to continue, score of 5 suggests prefer to try deprescribing). Patients and pharmacists separately and blindly rated how decision making occurred during the encounter on a scale of 1 (patient made decision alone) to 5 (pharmacist made decision alone), where 3 reflects a decision shared equally [44,46,58]. The agreement between the pharmacist and patient ratings was measured using a weighted kappa statistic.

3.3.4 Results

Recruitment took place between March and December 2016. Pharmacists screened 338 patients for eligibility and twelve eligible patients provided consent to participate. Common reasons for exclusion included: appropriate use of PPI for gastroprotection, uncertain of original indication and short-term (<4 week) use. Patient characteristics are

in Table 3.2. Decision preference results are summarized in Table 3.3 and decision-making parameters are in Table 3.4. At baseline, 8/12 (67%) patients preferred to try deprescribing, 3/12 (25%) preferred to continue and 1/12 (8%) was unsure. No patients were unsure of their preference after going through the PtDA. One patient changed their preference from “unsure” before the PtDA to “continue” after, and one changed from “continue” before to “lower dose” after. No patients changed from preferring to try deprescribing to preferring to continue. There was no significant difference in the proportion of patients whose preference changed after going through the PtDA ($p = 0.32$). The consult PtDA increased patient knowledge (median increase 36%, interquartile range [IQR] 36%, $p=0.001$) and realistic expectations (median increase 38%, IQR 50, $p=0.016$) and improved decisional confidence (median increase in SURE score 1.0, IQR 1.5, $p=0.014$). The weighted kappa for pharmacist and patient rating of shared decision making was 0.50 (95% CI: 0.15 to 0.85). Pharmacists and patients agreed on the extent of shared decision making in 7/12 interactions (4/12 agreed a shared decision occurred, 3/12 that the patient made the decision). In 3/12 interactions patients felt that they made the decision, while in 2/12 interactions the patient felt a shared decision was made but the pharmacist felt the patient made the decision. Eleven out of 12 patients enacted their plan during the pharmacist visit (one patient chose to continue and speak to their physician). Therefore, after the consult PtDA, 75% of patients had their PPI deprescribed (7 lower dose and 2 on-demand) and 25% of patients continued their PPI. In patients preferring to try deprescribing after the consult PtDA, the mean values rating was 3.24 (SD 0.82), while in patients preferring to

continue the mean values rating was 2.26 (SD 1.0). Valuing deprescribing was associated with increased odds of preferring to try deprescribing (OR 4.1 for each 1 unit increase in values rating, 95% CI 0.69 to 24). Follow-up data was available for 10/12 (83%) patients at 8 weeks. All 10 patients were on the PPI dose they had chosen after the consult PtDA visit. Seven out of 10 patients were on a reduced PPI dose (5 lower dose, 2 on-demand) and 3 continued their pre-PtDA PPI dose. One patient using a lower dose reported mild symptoms at 8 weeks, while no other patients had symptoms at 8 weeks.

3.3.5 Discussion

In this small sample of patients on long-term PPIs, our consult PtDA increased knowledge and realistic expectations, and reduced decisional conflict. There was moderate agreement that the consult PtDA led to shared decisions [59]. After their visit with the clinical pharmacist, 75% of patients were on a lower dose of PPI, or were using them on-demand. The consult PtDA was delivered in 10 to 15 minutes and led to decisions being made in real-time for most patients, which is a noted strength of consult PtDAs [16] and is particularly suited to the primary care environment. Our study differs from previous studies addressing inappropriate PPI use in that we engaged patients in a discussion around continued PPI use versus trying deprescribing and elicited their values, as opposed to encouraging deprescribing outright. Decision preference trended towards aligning with values after use of the consult PtDA, though the relationship was

not statistically significant (likely owing to our small sample size). Patients and pharmacists agreed that a shared decision was reached in 4/12 interactions (in 6/12 interactions patients felt they made the decision and in 2/12 patients felt a shared decision occurred but the pharmacist did not). Agreement was measured using a subjective rating scale completed by patients and pharmacists after each encounter. Because encounters were not recorded or independently assessed, it is difficult to determine how or why agreement was not reached in some cases (i.e. was disagreement true or due to limitations in the scale used). Future studies should employ a more objective evaluation of shared decision making (such as an independent assessment of a recorded discussion using a validated scale [e.g. dyadic OPTION instrument]). Nevertheless, it is encouraging that all 12 patients felt involved and engaged in decision making discussions.

There was no difference in the proportion of patients who changed their preference before and after the PtDA (our primary outcome). This may be a reflection of our sample, which was particularly motivated to try deprescribing at baseline (67% preferring to try deprescribing at baseline) compared to what has previously been reported. This may also explain the high proportion of patients choosing to try deprescribing after going through the PtDA. Patients who wanted to continue taking their PPI may not have wanted to engage in a discussion at all, and would not have participated in the study in the first place. We did not expect such a high proportion of

patients to support deprescribing at baseline. For example, a 2006 survey of 318 long-term acid suppressant users found that around 10% of patients were enthusiastic about trying to reduce acid suppressant use, though substantially more patients (40-90%) were willing to at least discuss reduction with their physician [53–55]. This willingness may be a reflection of increased media attention around deprescribing and inappropriate PPI use [60,61]. Though we approached patients describing the study simply as a discussion of continued PPI use or trying a reduction in PPI, the subset of patients who wanted to continue their PPI at baseline may not have been motivated to discuss their options with the pharmacist. While the PtDA improved knowledge and reduced decisional conflict, because our sample was motivated to try reducing PPI use at baseline our results may not be generalizable to the general primary care population.

We had difficulty recruiting patients for our study due to reasons which have previously been reported in the literature on both inappropriate PPI use and PtDAs. One reason for low recruitment may have been that these clinics had already been participating in initiatives to reduce inappropriate PPI use [49]; therefore, the pool of eligible patients may have decreased substantially. The major barrier we encountered was in identifying eligible patients. Clinical pharmacists found this challenging due to lack of information on indications in the electronic medical record (EMR), and found it time consuming to screen patients against eligibility criteria. A 2015 pilot study of PPI deprescribing noted

similar difficulties – it took the pharmacist on average 35 minutes to screen a patient for eligibility, and 15/57 patients' suitability to try PPI deprescribing could not be assessed due to lack of information [5]. In a 2016 pilot study in primary care, there was no indication for 12/46 patients [8]. This highlights a major barrier to addressing potentially inappropriate PPI use in primary care. Discussing continued PPI use with eligible patients would be more feasible if the indication and expected duration of therapy were documented clearly when the PPI was initiated. Continued use could then be discussed using the consult PtDA once that duration was up. However, these discussions do not appear to take place routinely. For example, a 2014 chart review (n=50) reported that 70% of patients had not been asked about the upper GI symptoms over their previous 3 visits to their primary care clinic [62]. A 2016 survey (n=260) found that 62% of patients did not receive any information about the intended duration of their PPI when initially prescribed [54]. As it stands, identifying patients whose inappropriate PPI use could be addressed in primary care is time-consuming due to lack of documented indication and expected duration of use. This limits the ability to apply ameliorating measures such as using a consult PtDA to discuss options.

Implementing PtDAs in primary care faces similar challenges to addressing inappropriate PPI use. A 2015 narrative review of 23 studies on PtDAs [63] in primary care found common barriers to using PtDAs included: disruption of existing workflows/processes, lack of physician time, patient lack of interest in making choice,

viewed as extra work, adds complexity to decisions, need for “distribution rules” (e.g. who gets decision aid, how it is delivered), and need to flag eligible patients. We aimed to address the barriers of physician time and disruption of workflow by having a pharmacist deliver the PtDA in a one brief visit, with a decision made in real time. Using the consult PtDA during the visit itself added no additional work beyond a regular pharmacist visit. However, the overall process was still time-consuming for the pharmacist given difficulty identifying eligible patients as mentioned above.

There were deviations from our trial protocol. We initially set out to recruit 54 patients; however, we were not able to recruit this number during the study timeframe. Based on existing literature [4,53,55], we expected most patients to prefer to continue their PPI at baseline, and expected some of these patients would change their mind and choose to try deprescribing after the PtDA. However, most patients wanted to try deprescribing at baseline which reduced our ability to detect a difference in preference before and after the PtDA. We did not conduct multiple logistic regression of symptom relapse given our small sample size and instability of the resulting model. We used non-parametric statistical methods to analyze decision-making parameters as we had a small sample size and our data was not distributed normally [64]. Our study was limited by its small sample size, lack of a control group, and short-term follow-up regarding symptom control. Further, the results of our study may only apply to patients who are open to the idea of reducing their PPI use at baseline, thus limiting the generalizability of our results.

The consult PtDA could be tested in a larger, randomized trial with a control group receiving usual care to determine whether it has meaningful impact on decision-making and PPI use on a larger scale. Such a trial would likely need a large number of sites to ensure sufficient numbers of participants. The consult PtDA does have the potential to foster decision making in real time, and can thus have a meaningful impact in primary care if patients could be more easily identified.

3.3.6 Conclusion

In summary, our consult PtDA allowed for real-time decisions surrounding continued PPI use versus trying deprescribing in a group of patients who were open to discussing these options. The consult PtDA improved knowledge, realistic expectations and decisional confidence, and engaged patients in decision making during a 10 to 15 minute consultation with a pharmacist. The consult PtDA led to 75% of patients reducing their PPI use after their visit. A major barrier to implementing the PtDA was identifying eligible patients, which limits the likelihood of widespread adoption of this tool. We propose that documenting an indication and intended duration of therapy when a PPI is originally prescribed will enhance the ability to discuss continued PPI use once the intended duration is over.

3.3.7 Declarations

This trial was approved by the Ottawa Health Science Network and Bruyère Research Ethics Boards. The study was unfunded. The authors have no conflicts of interest to declare.

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3.3.9 References for Chapter 3

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3.3.10 Tables for Chapter 3.3

Table 3.2. Patient (n=12) characteristics.

	MEAN	STANDARD DEVIATION
AGE	70.8	8.6
DURATION OF PPI USE (years)	7.3	4.3
	n	%
GENDER		
Male	3	25
Female	9	75
INDICATION		
History of upper GI symptoms treated > 4 weeks and asymptomatic	10	83
Diagnosed GERD	2	17
EDUCATION		
Elementary school	1	8
Some high school	2	17
High school	1	8
College	3	25
Undergraduate	2	17
Graduate or professional degree	3	25

Table 3.3. Decision preference.

		AFTER		
		Continue PPI or unsure	Have PPI deprescribed (lower dose or on-demand)	Total
BEFORE	Continue PPI or unsure	3	1	4
	Have PPI deprescribed (lower dose or on-demand)	0	8	8
Total		3	9	12

Table 3.4. Decision-making parameters and clinical follow-up.

	<i>Median (IQR)</i>		
	BEFORE	AFTER	DIFFERENCE
Knowledge (%)	50.0 (29.5)	72.7 (20.5)	36.4 (36.4), p=0.0010
Decisional conflict (SURE) (out of 4)	3.0 (1.3)	4.0 (0)	1.0 (1.5), p=0.014
Realistic expectations (%)	12.5 (50)	50 (6.25)	37.5 (50), p=0.016
	Symptoms at 8 weeks?		
PPI status at 8 weeks	YES	NO	TOTAL
Continued PPI	0	3	3
On-demand	0	2	2
Lower dose	1*	4	5

* mild symptoms

Chapter 4: General discussion and conclusions

4.1 Summary of results

Inappropriate use of PPIs is common across care environments [1–3], and thus several strategies are needed to approach this problem. Our scoping review showed that few patients (~10%) are enthusiastic about reducing their PPI use, though many (40-90%) are open to discussing options with a healthcare provider [4–6]. Patients fear symptoms returning and concerned about maintaining symptom control, which is a reason many patients prefer to continue on PPIs. Patients value understanding the rationale behind trying to reduce their PPI, knowing what they can expect on reducing and knowing they can return to their previous dose/restart the PPI if necessary [4]. As such, clear communication is key between clinicians and patients.

Tools to guide discussion between a patient and clinician regarding continued PPI use or reducing PPI use may facilitate decision-making in primary care. We developed a consult PtDA for this decision, which was delivered by a clinical pharmacist in primary care during a 10 to 15 minute visit. This consult PtDA improved patient knowledge, realistic expectations and decisional confidence, while engaging patients in decision making. The consult PtDA allowed for decision-making in real time (if a patient was amenable), and resulted in 75% of patients reducing their PPI use. However, the feasibility of delivering this tool in practice may be limited given pharmacists found it

time consuming to screen eligible patients (due to lack of necessary information such as indication, intended duration of use). A more detailed discussion can be found in Chapter 3.

In LTC, use of a PPI deprescribing decision support tool during pharmacist-physician medication reviews resulted in an initial reduction in PPI use after implementation. However, this trend was non-statistically significant over time, which may be explained by a gradual increase in PPI use 6 months after the decision support tool was implemented. There was a small statistically significant reduction in the monthly average cost of PPIs per patient over time. These results speak to the need to find ways to sustain efforts to address inappropriate PPI use. Further discussion on this topic can be found in Chapter 2.

4.2 Significance of findings and future directions

Addressing inappropriate PPI use has been recognized as an important topic to address by groups such as Choosing Wisely Canada, and a panel of 65 Canadian geriatrics experts [7,8]. Our findings suggest that inappropriate PPI use can be addressed in primary care and LTC; however, several challenges exist to implementing these efforts.

Long-term care

A PPI deprescribing decision support tool has the potential to reduce PPI use and costs in LTC. If this decision support tool were implemented on a larger scale (e.g. across Ontario LTC homes), there is the potential to reduce risk of associated harms from PPIs (e.g. *C. difficile* infections) and spending on PPIs. However, our study only investigated drug use and cost. There are other important factors which are necessary to determine overall cost-effectiveness. These include clinician time spent using tools, data on long-term clinical endpoints, cost of symptom relapse and indirect costs, among others. Thus, more sophisticated and comprehensive pharmacoeconomic analysis is required before widespread adoption of the decision support tool could be considered. More research is needed into how use of the decision support tool could be maintained over time. We found an initial reduction in PPI use followed by a gradual climb in PPI use after support tool implementation signaling there were challenges in sustaining use of the tool. This may have been due to implementation of other deprescribing tools for different drug classes 6 months after the PPI decision support tool was introduced. Therefore, reminders may be required to enable continued use. Future research should more closely examine challenges with sustained use of deprescribing initiatives in particular, and address ways to combat these problems. For example, interviews and focus groups with LTC clinicians may help reveal how long-term use can be sustained.

Shared decision-making in primary care

Our PtDA addresses the need for shared decision-making tools surrounding continued medication use versus trying deprescribing [9]. The consult PtDA we developed may be particularly useful in primary care because it can be delivered in a 15 minute consultation and allows for decision-making in real time. Widespread adoption of the PtDA has the potential to improve the quality of shared decision-making in primary care, and to empower patients. We found that most patients using our tool chose to try deprescribing of a PPI (though this may reflect our sample, as outlined in Chapter 3). Thus, our tool may result in reduced rates of inappropriate PPI use, and associated harms as well as drug costs.

Unfortunately, the widespread adoption of our tool may not be feasible currently, as it was time consuming and difficult for pharmacists to identify patients who were eligible to discuss continued PPI use versus trying deprescribing. This is because patients often did not have documented indications in the EMR or any information around ongoing symptoms/expected duration of use, and thus it was unclear whether they were candidates for discussing continued PPI use. This has been documented in previous studies of PPI deprescribing and use of PtDAs in primary care [2,10].

Therefore, future research could focus on two areas. Firstly, exploring ways to better document indications and expected duration of therapy would help in identifying eligible patients. This could include studies incorporating mandatory documentation of indications and expected duration for all new PPI prescriptions. Once the expected

duration of therapy is over, a discussion of continued PPI use versus attempting a trial of deprescribing could take place. This discussion could also take place when a PPI prescription is initiated such that patients have an idea of the expected duration at the outset. Implementing such a system may enhance the use of a consult PtDA in primary care as potential patients would be easily identifiable, and clinicians could be prompted as to when a discussion could take place. Secondly, our consult PtDA could be tested in a larger, randomized trial with a control (usual care) group, which is recommended by IPDAS after piloting of the tool [11]. This would help to evaluate whether use of the consult PtDA has a meaningful/substantive impact on the quality of decision-making, and on rates of inappropriate PPI use on a larger scale and using a more robust design.

4.3 Conclusions

Inappropriate PPI use is common, with rates ranging from 40-80% depending on the care setting and population [2,3,12–14]. This is a recognized problem in Canada, with groups such as Choosing Wisely identifying this as an important issue to address [7]. The strategies evaluated in this thesis have the potential to address this growing problem and its resultant health and cost implications. However, several challenges exist to more widespread adoption of these tools. A consult PtDA improved knowledge, realistic expectations and decision conflict, as well as fostering shared decision-making in a small sample (n=12) of patients in primary care. However, finding patients eligible to discuss continued PPI use proved difficult as screening patients was time consuming

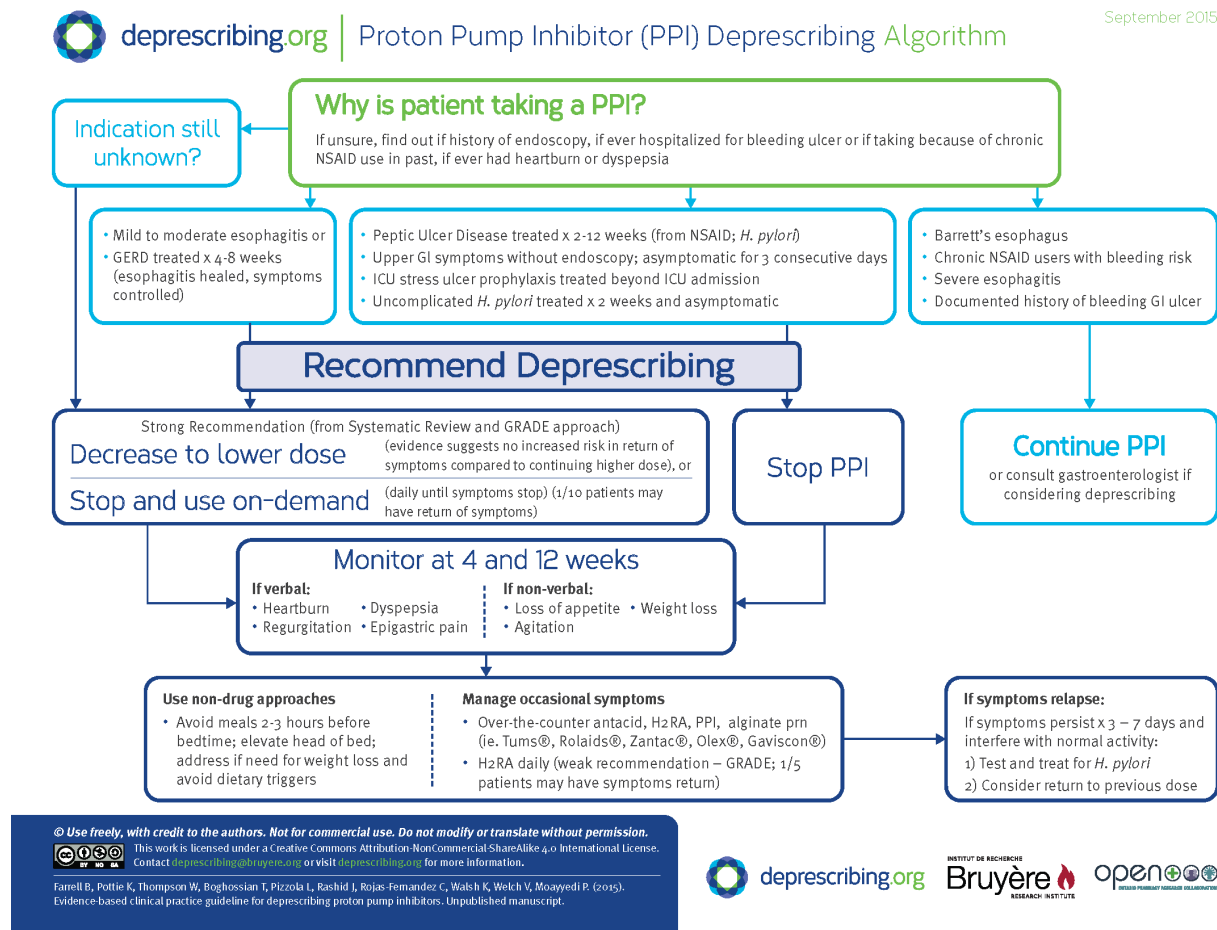
and difficult. A PPI deprescribing decision support tool produced a non-statistically significant reduction in PPI use and small, significant reduction in average monthly PPI cost in LTC. Yet, over time PPI use gradually began to increase suggesting the possibility that implementation efforts were not sustained. Further research is needed to determine how to improve the feasibility of implementing the developed tools in both primary care and LTC settings. Larger studies involving control groups and long-term follow-up are also required to evaluate whether the tools have the ability to significantly affect PPI use and clinical outcomes on a larger scale.

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Appendices

Appendix 1. PPI deprescribing decision support tool.



PPI Availability

PPI	Standard dose (healing) (once daily)*	Low dose (maintenance) (once daily)
Omeprazole (Losec [®]) - Capsule	20 mg ^a	10 mg ^a
Esomeprazole (Nexium [®]) - Tablet	20 ^a or 40 ^b mg	20 mg
Lansoprazole (Prevacid [®]) - Capsule	30 mg ^a	15 mg ^a
Dexlansoprazole (Dexilant [®]) - Tablet	30 ^c or 60 ^d mg	30 mg
Pantoprazole (Tecta [®] , Pantoloc [®]) - Tablet	40 mg	20 mg
Rabeprazole (Pariet [®]) - Tablet	20 mg	10 mg

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)

Key

GERD = gastroesophageal reflux disease	SR = systematic review
NSAID = nonsteroidal anti-inflammatory drugs	GRADE = Grading of Recommendations Assessment, Development and Evaluation
H₂RA = H ₂ receptor antagonist	

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 risk 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

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Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid J, Rojas-Fernandez C, Walsh K, Welch V, Moayyedi P. (2015). Evidence-based clinical practice guideline for deprescribing proton pump inhibitors. Unpublished manuscript.

Appendix 2. Consult patient decision aid.

SHOULD I KEEP TAKING MY ACID REFLUX MEDICATION?

A consult decision aid for you to discuss whether to continue your proton pump

1. Why am I being offered this choice?

<p>YOU HAVE TAKEN A PPI for AT LEAST 4 WEEKS (to treat symptoms such as mild or moderate heartburn or acid reflux or have been diagnosed with mild or moderate gastroesophageal reflux disease - GERD)</p>	<p>Acid reflux happens when acid from your stomach travels into your esophagus (a tube that connects the mouth to the stomach). The acid causes heartburn, pain in the throat or trouble swallowing. PPIs stop release of acid in the stomach.</p>
<p>YOU HAVE NO SYMPTOMS (you no longer have any heartburn, reflux or pain in your throat)</p>	<p>PPIs resolve symptoms and heal about 80 out of 100 (80%) patients after 4-8 weeks. Many people who don't have severe symptoms do not need to keep taking PPIs past 4-8 weeks. Guidelines suggest using the lowest effective dose for the shortest duration.</p>
<p>YOU DO NOT: take regular NSAIDs (e.g. Advil, Aleve), have a history of bleeding in your stomach or intestines, have an ulcer, have Barrett's Esophagus, have a history of severe symptoms or inflammation in your esophagus</p>	<p>Certain people need to take PPIs long-term. It would not be suitable to stop or use a lower dose of PPI in these people.</p>

2. What are your options?

- **Continue taking your PPI as you are now:** continue taking PPI and discuss other options with your health care professional
- ↔ **Use a lower dose of PPI OR stop and use "on-demand"**(take only when you have symptoms, for as long as it takes for symptoms to go away, then stop)

3. Rate the importance of benefits and harms of each option


A. This table shows the best estimate of what happens to 100 people with **mild/moderate acid reflux** who use a **lower dose of PPI** versus those who **continue the same dose for 12 months**.

Use stars ★ to show how much each benefit, risk, or reason matters to you. No stars means not at all. Five stars means a great deal. Circle the number of stars that apply to you.	Continue PPI ●●●	Use a lower dose of PPI ↓	How much does this matter? ⚖️
SYMPTOMS COME BACK 6 more people's ^[++] symptoms will come back	43 out of 100	49 out of 100	★★★★★
Add other reasons to choose continue your PPI at the same dose :			★★★★★

B. This table shows the best estimate of what happens to 100 people with **mild or moderate acid reflux or heartburn** who **stop their PPI and use it only when they need it ("on-demand")** versus those who **continue at the same dose over 3-6 months**.

Use stars ★ to show how much each benefit, risk, or reason matters to you. No stars means not at all. Five stars means a great deal. Circle the number of stars that apply to you.	Continue PPI ●●●	Stop PPI and use "on-demand" ✋	How much does this matter? ⚖️
SYMPTOMS COME BACK 11 more people's ^[++] symptoms will come back	14 out of 100	25 out of 100	★★★★★
LESS PILLS People ^[+++] will take 3.5 less pills per week on average		3.5 less pills per week	★★★★★
Add other reasons to continue taking your PPI at the same dose :			★★★★★

C. There may be a small increased risk of the following side effects associated with **PPI use versus **those not taking PPIs**:**

Use stars ★ to show how much each benefit, risk, or reason matters to you. No stars means not at all. Five stars means a great deal. Circle the number of stars that apply to you.	Continue PPI	No PPI	How much does this matter? 
Community-acquired pneumonia If 10,000 people take PPIs for 1-6 months 18 more people may get community-acquired pneumonia compared to those who do not take PPIs ^[+]	68 out of 10,000 experience this	50 out of 10,000 experience this	★ ★ ★ ★ ★
C. difficile infection If 10,000 people take PPIs 10 more people may get a <i>C. difficile</i> infection compared to those who do not take PPIs over 1 year ^[+]	22 out of 10,000 experience this	12 out of 10,000 experience this	★ ★ ★ ★ ★
Hip Fractures If 100,000 women take PPIs 24 more women may have a hip fracture over 1 year compared to those who do not take PPIs ^[+] If 100,000 men take PPIs 15 more men may have a hip fracture over 1 year compared to those who do not take PPIs ^[+]	<u>Women</u> 105 out of 100,000 <u>Men</u> 66 out of 100,000 experience this	<u>Women</u> 81 out of 100,000 <u>Men</u> 51 out of 100,000 experience this	★ ★ ★ ★ ★

4. What you can do if symptoms come back

If your symptoms come back for more than 3 days and bother you, please contact your doctor or pharmacist. You may have to return to your previous dose.

If symptoms come back but are occasional or mild: consider using an over-the-counter product such as TUMS® or Gaviscon®

Avoiding meals within 2-3 hours of bedtime, raising the head of your bed or weight loss may help control symptoms

5. Which option do you prefer?

- Try to use a lower dose of PPI
- Try to stop PPI and use “on-demand”
- Continue taking my PPI at the current dose

Unsure

6. What are your decision-making needs?

Sure of myself	Do you feel sure about the best choice for you?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Understand information	Do you know the benefits and risks of each option?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Risk-benefit ratio	Are you clear about which benefits and risks matter most to you?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Encouragement	Do you have enough support and advice to make a choice?	<input type="checkbox"/> Yes <input type="checkbox"/> No

The SURE Test ©2008 O'Connor & Légaré.

7. What can you do next?

Discuss the next steps with your pharmacist. You can go to see your doctor about your decision or develop a plan with specific instructions from your pharmacist (your pharmacist will check with your doctor first).

Do not change how you are taking your acid reflux medication without either going to see your doctor or receiving instructions and a plan from your pharmacist.

My plan:





- 1.
- 2.
- 3.



If your symptoms come back for more than 3 days and are interfering with your sleep and/or normal activity, please contact your doctor or pharmacist.

Additional Information

What does the research show?

Blocks of 100 faces show a 'best estimate' of what happens to **100 people** with **heartburn/reflux/GERD** who use a lower PPI dose after **12 months** or use "on-demand" after **3-6 months**. Each face (☺) stands for one person. The shaded areas show the number of people affected. There is no way of knowing in advance if you will be affected. The information shown below comes from clinical trials where patients either used a lower PPI dose, used the PPI "on-demand" or continued taking the PPI as usual.

1) Lowering the dose of your PPI (12 months)			
Symptoms come back [++]	Lower dose of PPI	Continue PPI at same dose	Comments
When the PPI dose is lowered, 49 people's symptoms (heartburn, reflux) come back compared to 43 people who continue at the same dose	49 have symptoms come back, 51 avoid this 	43 have symptoms come back, 57 avoid this 	Out of 100 people, 6 more people's symptoms will come back if they use a lower dose of PPI.
2) Stopping PPI and using "on demand" (only use PPI when needed to manage symptoms) (3-6 months)			
Symptoms come back [++]	On demand PPI	Continue PPI	Comments
When the PPI is stopped and only used "on-demand", 25 people's symptoms (heartburn, reflux) come back compared to 14 people who continue their PPI	25 have symptoms come back, 75 avoid this 	14 have symptoms come back, 86 avoid this 	For every 10 people who use their PPI on-demand, 1 person will have their symptoms come back

			
<p>Pill use (number of PPI pills taken per week) [+++] People who take PPIs “on-demand” take on average 3.5 less pills per week compared to those who continue their PPI</p>			

GRADE system: The quality of the research used to obtain these estimates is rated using the GRADE system: [+++ High quality = further research is very unlikely to change the estimate.](#) [+++ Moderate quality = further research may change the estimate.](#) [++ Low quality = further research is likely to change the estimate.](#) [+ Very low quality = further research is very likely to change the estimate.](#)

The SURE Test: People who answer “No” to one or more of these questions are more likely to delay their decision, change their mind, feel regret about their choice or blame others for bad outcomes. It is important to work through the decision step by step.

Last reviewed: **Jan 2016**. Outcomes from Boghossian T et al. Cochrane Database Syst Rev 2016;in press & adapted from Donnellan C et al. Cochrane Database Syst Rev 2005;18(2):CD003245; Eom et al. CMAJ 2011;183(3):310; Kwok et al. Am J Gastroenterol 2012;107:1011-19; Yu et al. Am J Med 2011;124(6):519-26. Developed by [Thompson W, Farrell B, Welch V, Walsh M, Vanderheyden A, Tugwell P, Bjerre L](#). Based on the Ottawa Consult Decision Aid © 2013 Stacey, Légaré, O'Connor. OHRI & uOttawa, Canada. Icons courtesy of Noun Project: Alex S. Lakas, TukTuk Design, Michael Rowe, Shrihari Sankaran, Sergey Novosyolov.

Appendix 3. Ethics approval.

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uOttawa

October 20, 2015

Mr. Wade Thompson
MSc Student
School of Epidemiology, Public Health and Prevention Medicine,
University of Ottawa
Bruyère Research Institute

**Re: Should I Continue Taking My Acid Reflux Medication?
Development and Pilot Testing of a Patient Decision Aid
(Bruyère REB Protocol # M16-15-046)**

Final Approval

Dear Mr. Thompson,

Thank you for your response to our requested changes. With the revisions, the application has satisfied all ethical requirements

As such, the Bruyère Continuing Care Research Ethics Board (REB) is pleased to give you ethical approval for the period October 20, 2015 to October 20, 2016.

The following documents have been approved:

- Revised Protocol – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix A: Email Recruitment Letter to Participate in Study – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix B: Practice Site Agreement – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix C: Consent to be contacted by research staff – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Recruitment Poster – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix E: Informed Consent for Participants – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix F: Informed Consent for Pharmacists – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix G: Knowledge questionnaire 1 – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix H: Knowledge questionnaire 2 – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix I: Realistic Expectations Questionnaire – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix J: SURE Test – Version 2, Oct 6, 2015 received Oct. 7, 2015
- Appendix K: Control Preferences Scale (patient) – Version 2, Oct 6, 2015 received Oct. 7, 2015

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- Appendix L: Control Preference Scale (pharmacist) – Version 2, Oct 6, 2015 received Oct. 7, 2015

Please provide us with the revised IRIS application once available.

Please provide us with a copy of the final approval letter from OHSN once received.

The Bruyère Continuing Care REB complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement: Ethics Conduct for Research Involving Humans; the International Conference on Harmonization - Good Clinical Practice: Consolidated Guideline; the provisions of the Personal Health Information Protection Act 2004; and the Food and Drug Act of Health Canada and its applicable Regulations.

Please be advised that any complaints made by participants must be reported to the REB.

All changes to the approved protocol must be approved by the REB.

Please complete an Annual Project Update/Notification of Termination form by the approval end date as noted above.

We wish you the best of luck with your research endeavors.



Ottawa Hospital
Research Institute
Institut de recherche
de l'Hôpital d'Ottawa



Ottawa Health Science Network Research Ethics Board/ Conseil d'éthique de la recherche du Réseau de science de la santé d'Ottawa

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<http://www.ohri.ca/ohsn-reb>

November 6, 2015

Dr. Wade Thompson
University of Ottawa School of Epidemiology, Public Health and Preventive Medicine
43 Bruyère St.
Ottawa, Ontario K1N 5C8
K1N 5C8

Dear Dr. Thompson:

Re: Protocol # 20150724-01H Should I Continue Taking My Acid Reflux Medication? Development and Pilot Testing of a Patient Decision Aid

Protocol approval valid until - November 5, 2016

I am pleased to inform you that this protocol underwent delegated review by the Ottawa Health Science Network Research Ethics Board (OHSN-REB) and is approved. No changes, amendments or addenda may be made to the protocol or the consent form without the OHSN-REB's review and approval.

Approval is for the following:

- Protocol (version 1) dated November 2, 2015
- English Recruitment Poster (version 1) dated August 24, 2015
- English Email Recruitment Letter (version 1) dated November 2, 2015
- English Telephone Recruitment Script (version 1) dated November 2, 2015
- English Knowledge Questionnaire 1- What I know about Acid Reflux and Heartburn (GERD), and Proton Pump Inhibitors (version 1) dated September 2, 2015
- English Knowledge Questionnaire 2- What I know about Acid Reflux and Heartburn (GERD), and Proton Pump Inhibitors (version 1) dated September 2, 2015
- English Realistic Expectations Questionnaire (version 1) dated September 2, 2015
- English SURE Test (version 1) dated September 2, 2015
- English Patient Control Preferences Scale (version 1) dated September 2, 2015
- English Pharmacist Control Preferences Scale (version 1) dated September 2, 2015
- English Patient 8 Week Symptom Scale (version 1) dated November 2, 2015
- English Participant Information Form (version 1) dated November 2, 2015
- English Consent to be Contacted (version 1) dated November 2, 2015
- English Practice Site Agreement (version 1) dated November 2, 2015
- English Informed Consent for Pharmacists (version 1) dated November 2, 2015
- English Informed Consent for Patients (version 1) dated November 2, 2015

The REB no longer requires a 'valid until' date at the bottom of all approved informed consent forms. The consent forms currently approved for use by the REB are listed above.

If the study is to continue beyond the expiry date noted above, a Renewal Form should be submitted to the REB approximately six weeks prior to the current expiry date. If the study has been completed by this date, a Termination Report should be submitted.

The Ottawa Health Science Network Research Ethics Board (OHSN-REB) was created by the merger of both the Ottawa Hospital Research Ethics Board (OHREB) and the Human Research Ethics Board (HREB) for meetings held at the University of Ottawa Heart Institute.

OHSN-REB complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; the International Conference on Harmonization - Good Clinical Practice: Consolidated Guideline, and the provisions of the Personal Health Information Protection Act 2004.

Appendix 4. Consent forms.

Informed Consent for Patients

Study Title: Should I continue taking my acid reflux medication? Development and pilot testing of a patient decision aid

Principal Investigator: Wade Thompson, RPh, MSc student

Participation in this study is voluntary. Please read this Informed Consent Form carefully before you decide if you would like to participate. Ask the study team as many questions as you like.

Why am I being given this form?

You are being asked to participate in this study because you are a patient at a practice that is participating in study, and you are currently taking an acid reflux medication (proton pump inhibitor or “PPI”) and have no ongoing symptoms such as heartburn or reflux.

Why is this study being done?

The purpose of the study is to provide patients with an information tool (called a “patient decision aid”) about the decision to continue taking their acid reflux medication or to stop/use a lower dose. The aim is to empower patients to make an informed decision that is consistent with what they value about acid reflux treatment. We want to see if our decision aid helps patients make a decision about whether to continue or stop/use a lower dose of their reflux medication.

We estimate that 54 patient participants will be enrolled in the study and 2 pharmacists.

What is expected of me?

If you choose to participate in this study you will be asked to complete some brief questions about your medical history, and fill out three short questionnaires (knowledge questionnaire, decisional confidence questionnaire and questionnaire about your expectations of your decision). This will take about 15 minutes.

You will then have a visit with a pharmacist, who will go through the patient decision aid (information tool) with you. The decision aid contains information about the benefits and harms of continuing your acid reflux medication, using a lower dose or stopping it and

using it only when you need to. The decision aid also helps you clarify which benefits and harms are most important to you. Going through the decision aid will take about 15 minutes.

After you visit with the pharmacist, you will then complete four more short questionnaires (same as above plus one about how you came to a decision), which will again take about 15 minutes. In total, your participation will last around 45 minutes.

You will be provided with information the benefits and harms of continuing your acid reflux medication versus using a lower dose or stopping it and using it only when you need it (on-demand). This study will evaluate the effect of the education tool. After you have received the tool, you may come to an informed decision about which option you prefer to take. After you have made your decision, you are encouraged to (1) discuss it with your doctor or (2) pursue the decision under the guidance and instruction of your pharmacist (your pharmacist will check with your doctor to make sure he/she is okay with this). Do not change how you take your acid reflux medication or stop taking it without either consulting your doctor or receiving instructions from the pharmacist. You must either see your doctor about your decision or receive instructions and monitoring from your pharmacist.

Eight weeks after your visit, the research staff will phone you to determine if any change has been made to your reflux medication prescription and ask you about your symptoms.

How long will I be involved in the study?

The entire study will last approximately 9 months. Your participation in the study will only involve the one 45 minute visit and a phone call eight weeks after your visit. There will be no additional follow-up visits.

Are there any risks?

Patient decision aids have been tested in 115 studies, and there is no evidence that they are harmful in any way. There may be some inconvenience in taking 45 minutes to participate in the study visit, or in completing the questionnaires; however, you do not have to answer any questions that you do not want to. There may be some stress from being faced with the decision at hand. The pharmacist will be present to answer any questions or concerns you may have.

Are there any benefits?

Patient decision aids (the education tool used in this study) have been shown to improve knowledge of health decisions and help patients clarify what is important to them about medication treatments. You may not benefit directly from your participation. However, as a result of participating in the survey, you may gain better insight and understanding into your acid reflux medication.

Am I obligated to participate?

You are under no obligation to participate in this study; participation is completely voluntary. No third party will be notified of your decision to participate. You can withdraw from the study at any time during your visit. If you would like to withdraw, notify the pharmacist or Master's student. If you wish to withdraw your information after you have completed your visit and left the clinic you can email the Master's student Wade Thompson. If you withdraw your consent, the study team will no longer collect any information from you. Information collected up until your withdrawal will continue to be used, unless you request otherwise.

Will I be paid for my participation or will there be any additional cost to me?

You will receive a \$5 Starbucks gift card for participating.

How is my personal information being protected?

Your privacy will be protected throughout the study and in all publications and presentations of the data. You will be assigned a code for all of your questionnaires and forms and your name will not appear in any publications. Research staff will use your name only to review your health record eight weeks after your visit to evaluate any change to your reflux medication prescription. Only the research staff will have access to your health record. Any printed or digital copies of data will only appear with your de-identified information. Printed copies will be stored in the project coordinator's office in a locked cabinet. The master code list will be stored in a separate, password protected file on a secure hospital server. All digital files will be stored in password protected files on secure hospital servers located on password protected computers. Documents and files will be kept for 10 years and then destroyed securely. Bruyère Research Ethics Board, Bruyère Research Institute, Ottawa Hospital Research Institute and Ottawa Health Science Network Research Ethics Board may have access to study documents, under the supervision of the investigator (Wade Thompson), for audit purposes.

Who do I contact if I have any further questions?

If you have any questions about this study, please contact the Master's student Wade Thompson.

This study protocol has been reviewed and approved by the following Research Ethics Boards. Should you have questions about your rights as a study participant you may contact any of the following Individuals or Research Ethics Boards:

1. Ottawa Health Science Network Research Ethics Board.
2. Bruyère Research Ethics Board.

Consent to Participate in Research

Should I continue taking my acid reflux medication? Development and pilot testing of a patient decision aid

- I understand I am being asked to participate in a research study about the choice to continue my acid reflux medication, use a lower dose of it, or use it only when I need it (on-demand)
- I understand that all data will be de-identified and will only be reported in aggregate form.
- I understand research staff will call me to follow-up after eight weeks.
- I understand that my visit will take about 45 minutes to complete.
- I understand this study is being conducted only to evaluate the effect of the patient decision aid on my decision preference, knowledge and expectations.
- I understand I must either (1) see my doctor before I make any change to my acid reflux medication (proton pump inhibitor) prescription or (2) receive instructions and supervision from the pharmacist to change my prescription (who has checked with my doctor first).
- I have read and understand this informed consent form.
- All of my questions have been answered to my satisfaction.
- I understand that I am able to withdraw from the study at any time, without consequences.
- I voluntarily agree to participate in this study
- I will be given a copy of the signed Participant Informed Consent Form

Investigator or Delegate Statement

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

Practice Site Agreement to Participate

Title of study:

Should I continue taking my acid reflux medication? Development and pilot testing of a patient decision aid.

Principal Investigator: Wade Thompson

Your clinic/unit is being asked to participate in a pilot study for the project: Should I continue taking my acid reflux medication? Development and pilot testing of a patient decision aid. This project will empower patients to make an educated, informed decision about whether to continue their proton pump inhibitor (PPI) or stop/use a lower dose. Your Practice's participation in this study is completely voluntary, and you can withdraw your consent to participate at any time.

Participating in this study involves:

- o Having your pharmacist or an MSc student (who is a clinical pharmacist) provide a 15 minute consultation with 10-15 willing patients with the possibility that some patients will contact their physician to pursue their decision
- o Having research staff administer an intake form and measurement tools to patients before and after the consultation
- o Willingness to allow research staff (1 MSc student) to be present
- o Recruitment from April 2016 to May 2016 (approximately)
- o Having recruitment materials posted in your clinic/unit
- o Having team members (nurses and pharmacists) screen patients for eligibility and ask patients if they are willing to be contacted about participating, and having the MSc student approach the consenting patients by phone
- o Having the MSc student phone patients eight weeks after the decision aid consultation to determine if there is any change in PPI prescribing and to assess symptoms

Consent forms will be provided to and signed by the pharmacist and participants. Team member and patient participants will not be identifiable in any presentations or publications resulting from this study.

The MSc student is responsible for obtaining consent of participants, administering intake form and study instruments and ensuring confidentiality is maintained. All participants will be assigned a code in place of their name and will remain de-identified in all reporting. All data and documents will be kept confidential and will be stored in password protected computer files on a secure

hospital server or in a locked filing cabinet in a locked office at Bruyère Research Institute. All paper and electronic copies will be kept for 10 years then securely destroyed.

This study protocol has been reviewed and approved by the following Research Ethics Boards:

1. Ottawa Health Science Network Research Ethics Board.
2. Bruyère Research Ethics Board.

If you have any questions about your Practice's involvement in the study, please contact Wade Thompson.

Consent for your Practice's Participation

Study title: Should I continue taking my acid reflux medication? Development **and** pilot testing of a patient decision aid.

- I understand that I am being asked for my Practice to participate in a research study about a shared decision making tool (patient decision aid) to support the decision to continue a PPI or use a lower dose/use on-demand
- This study was explained to me by the principal investigator Wade Thompson
- I have read, or have had it read to me, each page of this Practice Site Agreement.
- All of my questions have been answered to my satisfaction.
- If I decide later that I would like to withdraw my Practice's participation and/or consent from the study, I can do so at any time.
- I voluntarily agree to have my Practice participate in this study.

- I will be given a copy of this signed Practice Site Agreement.

Team leader

Name(Printed)

Signature

Date

Investigator or Delegate Statement

I have carefully explained the study to the Team Leader. To the best of my knowledge, the Team Leader understands the nature, demands, risks and benefits involved in taking part in this study.

Principal investigator

Wade Thompson

Date

Wade Thompson, RPh, MSc student
University of Ottawa School of Epidemiology, Public Health and Preventive Medicine
Bruyère Research Institute

Appendix 5. Before/after questionnaires.

Participant information form

For the purpose of our research, we would like to collect some basic information about you, and your history of proton pump inhibitor (PPI) use.

You will remain de-identified throughout the study and in all publications and presentations of the data. You will be assigned a code for all of your questionnaires and forms. Research staff will use your name only to review your health record eight weeks after your visit to evaluate any change to your reflux medication prescription. Only the research staff will have access to your health record. Any printed or digital copies of data will only appear with your de-identified information. Printed copies will be stored in the project coordinator's office in a locked cabinet. The master code list will be stored in a separate, password protected file on the Master's student's computer on a secure hospital server. All digital files will be stored in password protected files on secure hospital servers located on password protected computers. All data will be stored at Bruyère Research Institute. Documents and files will be kept for 10 years and then destroyed securely. Bruyère Research Ethics Board and Ottawa Health Science Network Research Ethics Board may have access to study documents, under the supervision of the investigator (Wade Thompson), for audit purposes. Any documents or samples leaving Bruyère Research Institute will contain only your unique study number. This includes publications or presentations resulting from this study.

Please provide the following information:

Age	
Biological sex	
Level of education	<input type="checkbox"/> Elementary school <input type="checkbox"/> Some high school <input type="checkbox"/> High school <input type="checkbox"/> Undergraduate degree <input type="checkbox"/> Graduate degree
Current proton pump inhibitor (PPI) and dose	

Why are you taking a PPI?	<input type="checkbox"/> Mild or moderate <u>diagnosed</u> gastroesophageal reflux disease (GERD) or esophagitis <input type="checkbox"/> Heartburn, reflux, pain in my throat or trouble swallowing but I have <u>never been diagnosed with GERD or esophagitis</u> to my knowledge <input type="checkbox"/> To treat a current ulcer <input type="checkbox"/> To prevent an ulcer (taking an NSAID such as ibuprofen [Advil] or naproxen [Aleve]) <input type="checkbox"/> I have had a gastrointestinal bleed, bleeding ulcer, or ulcer in the past <input type="checkbox"/> Other: _____ <input type="checkbox"/>
How long have you been taking a PPI?	
Do you currently have any symptoms at all (such as reflux or heartburn)?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Do you currently take NSAIDs daily or almost daily (e.g. ibuprofen [Advil], naproxen [Aleve], diclofenac [Voltaren])?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Do you have a history of Barrett's esophagus?	<input type="checkbox"/> Yes <input type="checkbox"/> No

SURE questionnaire

When presented with the decision to continue taking your acid reflux medication (proton pump inhibitor or PPI), or trying to use a lower dose or stopping and using it only when you need it:

Which option do you prefer?

- Continue my acid reflux medication
- Try to use a lower dose of my acid reflux medication or stop and use only when needed
- Unsure

5. What are your decision making needs?

Sure of myself Do you feel sure about the best choice for you? Yes No

Understand information Do you know the benefits and risks of each option? Yes No

Risk-benefit ratio Are you clear about which benefits and risks matter most to you? Yes No

Encouragement Do you have enough support and advice to make a choice? Yes No

WHAT I KNOW ABOUT ACID REFLUX AND HEARTBURN (GERD), AND PROTON PUMP INHIBITORS

Here are some questions about heartburn and acid reflux (also known as gastroesophageal reflux disease or “GERD”), and treatment of these symptoms with acid reflux medications known as proton pump inhibitors (**PPIs**). We would like to know how familiar you are with PPIs before you use our educational tool.

Please show whether you think each statement is true or false, or if you are unsure (circle one answer for each statement):

1. Acid reflux occurs when acid travels from your esophagus into your stomach	True	False	Unsure
2. One of the main symptoms of “GERD” is a headache	True	False	Unsure
3. Once you start taking a PPI, you have to take it for the rest of your life	True	False	Unsure
4. PPIs heal about 90% of patients after 4-8 weeks	True	False	Unsure
5. When people start to take a PPI only when they need them (“on demand” or “as needed”), most people’s symptoms will come back	True	False	Unsure
6. When people start to take a lower dose of their PPI, there is no difference in the number of people whose symptoms come back compared to those who continue at the same dose	True	False	Unsure
7. When people are told to only take PPIs when they need them (“on demand” or “as needed”), they tend to take more pills	True	False	Unsure
PPIs have been associated with the following adverse effects:			
1. Motor vehicle accidents	True	False	Unsure
2. Pneumonia	True	False	Unsure
3. Dizziness	True	False	Unsure
4. Broken bones	True	False	Unsure

REALISTIC EXPECTATIONS QUESTIONNAIRE

1. We are interested in your opinion about the chance of any of your gastrointestinal symptoms (reflux, heartburn) coming back in the next 12 months if you use a lower dose of your acid reflux medication compared to if you keep taking the same dose you are now.

A. If you keep taking the same acid reflux medication dose:

Out of 100 people, how many people will have any of their symptoms come back?

<input type="checkbox"/>	100 out of 100 people will have symptoms come back
<input type="checkbox"/>	75-99 out of 100 people will have symptoms come back
<input type="checkbox"/>	50-74 out of 100 people will have symptoms come back
<input type="checkbox"/>	24-49 out of 100 people will have symptoms come back
<input type="checkbox"/>	0-25 out of 100 people will have symptoms come back
<input type="checkbox"/>	Don't know

B. If you take a lower dose of your acid reflux medication:

Out of 100 people, how many people will have any of their symptoms come back?

<input type="checkbox"/>	100 out of 100 people will have symptoms come back
<input type="checkbox"/>	75-99 out of 100 people will have symptoms come back
<input type="checkbox"/>	50-74 out of 100 people will have symptoms come back
<input type="checkbox"/>	24-49 out of 100 people will have symptoms come back
<input type="checkbox"/>	0-25 out of 100 people will have symptoms come back
<input type="checkbox"/>	Don't know

2. We are interested in your opinion about the chance of your gastrointestinal symptoms (reflux, heartburn) bothering you in the next 3-6 months if you stop your acid reflux medication and use it only when you need it, compared to if you keep taking the same dose you are now.

A. If you keep taking the same acid reflux medication dose:

Out of 100 people, how many people will have bothersome symptoms?

<input type="checkbox"/>	100 out of 100 people will have symptoms come back
<input type="checkbox"/>	75-99 out of 100 people will have symptoms come back
<input type="checkbox"/>	50-74 out of 100 people will have symptoms come back
<input type="checkbox"/>	24-49 out of 100 people will have symptoms come back
<input type="checkbox"/>	0-25 out of 100 people will have symptoms come back
<input type="checkbox"/>	Don't know

B. If you stop taking your acid reflux medication and use it only when you need it ("on demand"):

Out of 100 people, how many people will have bothersome symptoms?

<input type="checkbox"/>	100 out of 100 people will have symptoms come back
<input type="checkbox"/>	75-99 out of 100 people will have symptoms come back
<input type="checkbox"/>	50-74 out of 100 people will have symptoms come back
<input type="checkbox"/>	24-49 out of 100 people will have symptoms come back
<input type="checkbox"/>	0-25 out of 100 people will have symptoms come back
<input type="checkbox"/>	Don't know

HOW WAS YOUR DECISION MADE? (PATIENT)

Please tick the box beside the option which you feel best represents how your decision was made.

<input type="checkbox"/>	I made the decision about which option I chose
<input type="checkbox"/>	I made the final selection after seriously considering my pharmacist's opinion
<input type="checkbox"/>	My pharmacist and I shared responsibility for deciding which option was best for me
<input type="checkbox"/>	My pharmacist made the final decision about which option would be used but seriously considered my opinion
<input type="checkbox"/>	My pharmacist made all the decisions regarding which option I chose

HOW WAS YOUR DECISION MADE? (PHARMACIST)

Please tick the box beside the option which you feel best represents how the decision was made.

<input type="checkbox"/>	The patient made the decision about which option they chose
<input type="checkbox"/>	The patient made the final selection after seriously considering my opinion
<input type="checkbox"/>	The patient and I shared responsibility for deciding which option was best for the patient
<input type="checkbox"/>	I made the final decision about which option would be used but seriously considered my patient's opinion
<input type="checkbox"/>	I made all the decisions regarding which option the patient should take

Symptom scale at 8 weeks

Over the past 7 days, please rate the severity of your symptoms:

- None: no heartburn
- Mild: awareness of heartburn, but easily tolerated
- Moderate: discomforting heartburn sufficient to cause interference with normal activities, including sleep
- Severe: incapacitating heartburn, with inability to perform normal activities, including sleep

Appendix 6. Copies of published articles.



JAMDA

journal homepage: www.jamda.com

Brief Report

Effect of a Proton Pump Inhibitor Deprescribing Guideline on Drug Usage and Costs in Long-Term Care



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A B S T R A C T

Keywords:
Deprescribing
inappropriate prescribing
proton pump inhibitors
long-term care
homes for the aged

Objectives: To assess the effect of a proton pump inhibitor (PPI) deprescribing guideline on PPI usage and PPI drug costs in one long-term care home in Ontario, Canada.

Design: Interrupted time-series analysis to compare monthly PPI usage and average monthly PPI cost per resident 9 months before guideline implementation to 12 months after.

Setting: One long-term care home in Ottawa, Ontario, Canada.

Participants: Long-term care residents prescribed a PPI over a 21-month period ($n = 335$).

Intervention: PPI deprescribing guideline and decision support tool used during quarterly medication reviews.

Measurements: (1) Total number of PPI prescriptions (PPI usage) and (2) average PPI drug cost per resident. We also measured the proportion of residents whose PPI was deprescribed in the preguideline period and postguideline period.

Results: The deprescribing guideline was associated with a decrease in PPI usage but the association was not statistically significant (-8.7 prescriptions, 95% confidence interval [CI] -22.0 to 4.6). The PPI guideline led to a significant decrease in average monthly PPI drug cost per resident over time (0.16 CAD reduction per month; 95% CI -0.29 to -0.03). In the 9 months before intervention, 57 (27.8%) of 205 eligible residents had their PPI deprescribed, and in the 12 months after intervention 134 (50.0%) of 268 eligible residents had their PPI deprescribed (difference in proportions of 22.2%; 95% CI 13.4–30.4).

Discussion/conclusion: The deprescribing guideline was associated with a decline PPI usage; however, this negative association was not statistically significant. PPI usage declined in the initial 6 months after guideline implementation but began to climb back to baseline after this, which may explain the lack of a significant reduction in PPI usage. This suggests that it was difficult to maintain PPI deprescribing efforts long-term. Although implementation of a PPI deprescribing guideline may lead to an initial reduction in PPI usage, and a significant reduction in the average cost of PPI prescriptions over time, it is imperative to explore ways to sustain deprescribing guideline use.

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Proton pump inhibitors (PPIs) effectively treat several upper gastrointestinal disorders. In many patients (such as those with mild to moderate gastroesophageal reflux) the duration of therapy should

be short-term (eg, 4 to 8 weeks).¹ Some patients continue PPIs beyond the recommended duration.^{2–5} In long-term care (LTC), 50% of residents may be receiving an inappropriate PPI,⁶ whereas older patients

The authors declare no conflicts of interest.

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publish, or preparation of the manuscript. Grant #06674 <http://www.health.gov.on.ca/en/proj/ministry/research/hsr/asp>.

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may be at higher risk of continuing PPIs unnecessarily after hospital discharge.³ PPI use has been associated with harms such as *Clostridium difficile* infection and fractures, the risks of which are already increased in older persons.^{7–10} Approximately \$250 million was spent on PPIs by public drug programs in Canada in 2012, much of which may be excessive.¹¹ There is a need to reduce unnecessary PPI use through deprescribing (the planned, supervised tapering and/or stopping of drugs), which may reduce PPI spending and risk of adverse effects. We developed a PPI deprescribing guideline and decision support tool¹² and implemented it at 3 LTC homes as part of a larger research study evaluating development and implementation of deprescribing guidelines.¹³ In this article, we describe the effect of implementing the guideline on PPI usage and drug costs in one LTC home in Ottawa, Ontario.

Methods

We conducted a retrospective, time-series analysis from November 2013 to July 2015, using pharmacy drug utilization records in one 450-bed LTC home in Ottawa, Ontario. Although we implemented the guideline in 3 homes, this home was the only one interested in conducting a drug utilization review related to the project. The time period was divided into 21 monthly intervals (9 months before guideline implementation and 12 months after). We measured 12 months of postguideline implementation since the implementation process occurred over 3 months (it may have taken some residents up to 3 months to have their PPI reviewed because medication reviews occur quarterly). Residents were eligible if they received a PPI prescription at any point during the 21-month period. As such, we allowed for new residents to enter the study (ie, new admissions or new PPI prescriptions) and existing residents may have dropped out (discharged or died) or stayed in the sample. Therefore, the denominator may change each month (ie, number of residents whose PPI could be deprescribed that month). We did not collect any demographic or resident-specific information, such as number of concomitant medications, age, comorbidities, and so forth.

The deprescribing guideline was implemented in July 2014. We presented a PowerPoint summary of the PPI deprescribing guideline and our decision support tool (<http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/ppi-deprescribing-algorithm-α.pdf>)¹² to physicians, pharmacists, and nurses at an in-person meeting at the LTC home. The support tool was used during individualized quarterly medication reviews by the physicians and pharmacists. Our outcomes of interest were: (1) monthly PPI usage and (2) monthly average PPI cost per resident.

PPI usage was defined as the total number of PPI prescriptions each month. PPI deprescribing was classified as complete cessation, using a lower dose, or switching to as-needed or “on-demand” therapy. To capture deprescribing interventions whereby a PPI was not ceased completely, we subtracted prescriptions where the PPI dose had been lowered (eg, changed from high-dose PPI to low-dose PPI, changed from twice-daily dose to once-daily dose) or switched to “on-demand” use from the total (the total already took into account cases in which the PPI was stopped completely). PPI cost included drug cost only (professional fee and markup not included). Unit drug costs were obtained from Ontario’s drug formulary for publicly funded drugs.¹⁴ For drugs not covered by the public formulary, we used the pharmacy provider’s drug cost (drugs provided by pharmacy wholesaler). Data on the number of residents overall at the LTC home was provided by the pharmacy provider. Drug cost was calculated as the average PPI cost per resident. There were no changes in physician reimbursement, prescribing limitations, drug coverage, or legislation that may have affected physician prescribing of PPIs in LTC over the time period of the study.

We used segmented interrupted time-series (ITS) regression analysis with adjustment of autocorrelation¹⁵ to assess the impact of

PPI guideline implementation on PPI usage and associated cost. The analysis provides an estimation of changes in level and trend in pre- and postintervention periods. The level is defined as the value at the beginning of a given period (intercept), whereas the trend represents the rate of change during a study period (slope). We compared the level and trend of the segment after the intervention with those of the segment before the intervention. Our model evaluated the effect of the intervention, the effect of time, and the intervention*time interaction (effect of the intervention over time). We assessed for autocorrelation using the Durbin-Watson statistic. We performed analysis using the PROC AUTOREG command in SAS 9.4 (SAS Institute, Cary, NC).

We also compared the proportion of eligible residents whose PPI was deprescribed in the entire 12 months after the guideline was implemented to the proportion of eligible residents whose PPI was deprescribed in the 9 months leading up to guideline implementation (difference in proportions test assuming independent samples, 95% confidence interval [CI]). The project was approved by the LTC home’s internal research ethics board as an evaluation of a quality improvement initiative.

Results

PPI usage from November 2013 to July 2015 is displayed in Figure 1. A total of 335 residents received a PPI prescription over the 21-month period. At baseline, there were 147 residents on PPIs. The sample at guideline implementation was 180 residents, and in the last month of the study the sample was 206 residents. The mean number of new residents entering the sample each month was 8.7 residents (SD 3.1). Following guideline implementation, PPI usage dropped by 8.7 prescriptions (95% CI –22.0 to 4.6, $P = .19$). Guideline implementation did not result in a significant change in slope (reduction in PPI usage) in the 12 months after implementation (142 fewer prescriptions per month, 95% CI –4.40 to 1.56, $P = .34$). Before implementation of the deprescribing guideline, there was an upward increase in average monthly PPI cost per resident (0.14 CAD [Canadian dollars]; 95% CI 0.03–0.25, $P = .016$). Following guideline implementation, the average monthly PPI cost dropped by 0.56 CAD per resident (95% CI –1.12 to 0.01, $P = .059$). PPI deprescribing guideline implementation resulted in a significant change in slope, suggesting that average monthly PPI costs per resident decreased over time (0.16 CAD per month reduction; 95% CI –0.29 to –0.03, $P = .019$). In the entire 9 months before intervention, 57 (27.8%) of 205 eligible residents had their PPI deprescribed, and in the entire 12 months after intervention, 134 (50.0%) of 268 eligible residents had their PPI deprescribed. This represents a difference in proportions of 22.2% (95% CI 13.4–30.4, $P < .00001$).

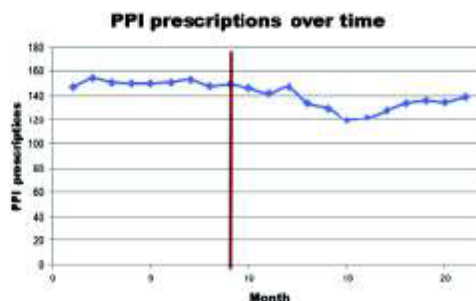


Fig. 1. PPI usage across 21 months.

Discussion

Our results show that implementation of a deprescribing guideline and support tool at this LTC home was associated with a decrease in PPI prescribing; however, the reduction in use mainly occurred within 6 months after the start of the intervention and use gradually climbed back up, resulting in no significant difference in use by the end of the study period (see Figure 1). The guideline was associated with a significant decrease in average monthly PPI cost per resident over time, which remained significant across the study period (although began to climb back up toward the end of the study).

There are several possible explanations for these findings. Interest and uptake of the guideline may have waned over time. New residents admitted on PPIs months past the implementation date may not have been targeted initially for deprescribing while staff and clinicians got to know the resident. New residents may have had valid indications for PPIs and have not been eligible for deprescribing. The number of new residents entering the sample remained relatively constant over time; however, the size of the sample continued to grow throughout the study (from 147 at baseline, to 180 at implementation, to 206 at the end of the study). This could be explained by the fact that many residents were maintained on a lower dose of PPI compared with baseline versus having the PPI stopped completely. These residents would still be eligible to have their PPI further reduced (or stopped completely) and were thus still counted in the overall sample. It is also possible that symptoms recurred, which may have necessitated restarting a PPI. Unfortunately, the nature of this drug utilization review did not allow us to capture symptom relapse rates. Last, we implemented an additional guideline pertaining to a distinct drug class 7 months after implementation of the PPI guideline. It is possible that the focus was shifted to the new drug class and thus fewer PPIs were being targeted. Guidelines can be challenging to implement and continued use is often difficult to maintain.^{13,16} Our PPI usage results speak to the importance of maintaining efforts to deprescribe past initial implementation of an intervention. This may mean exploring effective approaches to sustaining guideline use, such as incorporating the decision support tool into electronic health records/routine care processes or offering periodic educational outreach.¹⁶

Although there was no significant reduction in PPI usage, we did find a statistically significant increase in the overall number of deprescribing events after implementation (comparing events in the entire pre-guideline period to the entire post-guideline period). Our results (22% increase in deprescribing rate) are consistent with other interventions to reduce PPI use, which demonstrate rates of deprescribing of approximately 20% to 50%.^{17,18} The pre-guideline deprescribing rate of 25% is consistent with a retrospective cohort study (n = 10,731) that found PPIs were discontinued in approximately 25% of LTC residents within 180 days of being admitted, without any specific deprescribing intervention in place.²⁰

Time-series analysis demonstrated that implementation of the deprescribing guideline significantly reduced the average cost of PPIs per resident over time. Residents whose PPIs were deprescribed continued to accrue savings in subsequent months; however, average cost per resident began to rise slowly toward the end of the data collection period. Although significant cost savings were seen when the guideline was implemented, strategies that result in sustained clinician behavior change would likely be necessary to maintain reductions in PPI spending. Our results provide insight into trends in PPI use following a deprescribing intervention. A clinical pharmacist intervention has been shown to reduce PPI drug utilization and cost in an ambulatory care setting; however, the duration of follow-up in this study was only 5 months.²⁰ Thus, it is difficult to evaluate whether such an intervention produces meaningful reductions in PPI use long-

term. Our results suggest that despite an initial substantial reduction, PPI usage eventually crept back up after a deprescribing intervention was offered.

Our study had important limitations. We did not collect data on any covariates, such as age, gender, duration of PPI use, or indication, and, therefore, we could not control for patient-level confounders that may have explained our result. These covariates may have been impactful considering there were new admissions and deaths over our study period. A control group was not used; however, the ITS design allows us to adjust for history and maturation by using multiple assessments of the outcome measures both before and after the intervention.²¹

Use of our guideline and decision support tool in larger randomized trials should provide a picture of whether they are effective in improving appropriate PPI use. More comprehensive pharmacoeconomic analyses (eg, incorporating more detailed information on direct costs, cost of symptom relapse) will help to evaluate whether PPI deprescribing is cost-effective in LTC.

Conclusions

Implementation of a PPI deprescribing guideline at this LTC site led to an initial reduction in PPI usage that was difficult to maintain more than 6 months beyond the implementation period. As such, there was no statistically significant reduction found in PPI usage after implementation. However, there was a statistically significant reduction in average PPI costs per resident over time. Our results suggest that a PPI deprescribing guideline may reduce PPI use and costs in LTC, but opportunities to maintain guideline use should be explored. Further work should focus on developing more comprehensive pharmacoeconomic analysis of PPI deprescribing in LTC to determine cost-effectiveness.

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Should I continue taking my acid reflux medication? Design of a pilot before/after study evaluating a patient decision aid

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Background

Proton pump inhibitors (PPIs) treat upper gastrointestinal conditions such as gastroesophageal reflux disease. They resolve symptoms in about 80% of patients, with erosions present after 4 to 8 weeks of treatment (and about 60% of patients without erosions).¹ Although the majority of patients with severe symptoms relapse if therapy is discontinued, patients with mild or moderate symptoms may not need continuous daily PPI therapy long term.¹ Prospective observational studies and cross-sectional studies suggest rates of inappropriate PPI use between 44% and 79%.²⁻⁵ Meta-analyses of cohort and case-control studies suggest PPIs may be associated with harms including *Clostridium difficile* infection, pneumonia and fractures,⁶⁻⁸ although some of these associations have been challenged.⁹ Public drug programs in Canada spent \$247 million on PPIs in 2012.¹⁰

The decision to continue a PPI, use a lower dose, or stop and use on demand (only when symptoms come back) should be informed and made collaboratively between a patient and clinician (prescriber or pharmacist). Supervised dose reduction or stopping a medication that may no longer be needed is termed *deprescribing*.^{11,12} Our research group conducted a systematic review¹³ and developed a PPI deprescribing guideline to assist clinicians in deprescribing PPIs where appropriate,^{13,14} and we have been exploring ways to implement these tools.

Patients may fear deprescribing and not understand when it can be considered.¹⁵ Qualitative evidence suggests that patients accept PPIs as appropriate if their physician continues to prescribe them.¹⁶ Even when a clinician feels deprescribing a PPI is appropriate, patients struggle to decide whether they wish to pursue deprescribing.¹⁵ Thus, there is an opportunity to educate patients about this decision. Patients should feel confident in the decision they make and make a decision that is consistent with their values.¹⁷ They should have sufficient knowledge of their options and of possible outcomes.^{17,18}

Patient decision aids (PtDAs) outline the probability of benefit and harm associated with different treatment options and allow patients to identify what matters most to them.¹⁹ They increase knowledge, help patients feel supported in their decision and achieve decisions congruent with values.¹⁹ PtDAs can be delivered in consultation with a health care professional. Pharmacists are well positioned to implement consultation PtDAs, which can be delivered in a 10- to 15-minute visit.²⁰ A 2014 systematic review ($n = 21$ studies) suggests prescribers' lack of access to resources (e.g., a pharmacist) and knowledge is a barrier to deprescribing.²¹ Pharmacists can help to overcome these barriers and are therefore a key resource in engaging patients to discuss deprescribing.

We developed a consult PtDA to support patients in making the decision of whether to

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continue, stop and use on demand, or use a lower dose of PPI and will evaluate the effect of the PtDA when delivered by a pharmacist (<http://deprescribing.org/resources/deprescribing-patient-decision-aids/>). We also aim to show how pharmacists, as drug therapy experts, can act as key facilitators of the discussion surrounding deprescribing and the deprescribing process.

Methods/Design

Research questions

- In patients ≥ 18 years of age who have used PPIs for >4 weeks with upper gastrointestinal symptom resolution and who have no indication to continue treatment, does a PtDA aimed at helping patients decide whether to continue a PPI or stop and use on demand/use a lower dose of their PPI:
 - affect patient decision preference?
 - improve patient knowledge surrounding the decision?
 - affect patient expectations?
 - affect decisional conflict?
 - produce choices that are congruent with patient values?
- When the PtDA is provided in consultation with a pharmacist, does shared decision-making take place (according to both the patient and clinician)?
- Eight weeks after patients have received a consultation involving the PtDA, what is the effect on prescribing of PPIs?
- In patients who have chosen to use a lower PPI dose or stop and use on demand, is there any difference in symptom control at 8 weeks compared with those who have continued taking their PPI?

Design of the study

This study will use a before/after design. This study design is recommended for pilot testing of PtDAs according to the International Patient Decision Aid Standards (IPDAS) and has been widely used to this end.^{18,22–24}

Patients will have an appointment with a pharmacist to go through a PtDA to discuss the decision (probabilities of benefit and harm, individual values and preferences). Following the appointment, patients can follow up with their family physician should they wish to pursue deprescribing or can receive instructions from the pharmacist. While the pharmacist is

conducting the study visit, implementing the decision aid is a collaborative effort. For example, prescribers have referred patients to the pharmacist to discuss their PPI, and pharmacists can discuss the eligibility of a particular patient with the prescriber in advance of an appointment.

The PtDA has been developed using a user-centred design approach, which included patient representatives as part of the development committee.^{25,26} The PtDA was drafted using an online tool (<https://decisionaid.ohri.ca/eTraining/>) and qualifying, certification and quality criteria set out by IPDAS.²⁷ It was revised in iterations based on feedback from our team.

Setting and participants

We set out to conduct the study at 2 Ottawa area primary care clinics, but because of low recruitment, we have expanded to recruit units at a continuing care hospital. Eligibility criteria are outlined in Table 1. Our study protocol has been approved by the Bruyère Research Institute and Ottawa Health Science Network Research Ethics Boards.

Analysis

We will use the SURE test to measure decisional conflict/confidence.²⁸ We will also measure patient knowledge and realistic expectations before and after using the PtDA (Appendix 1 available at cph.sagepub.com/supplemental). We will analyze these continuous outcomes with paired *t* tests (5% significance level). Patients will be asked to indicate which option they prefer (continue PPI, stop and use on demand/use a lower dose, or unsure) before and after the consultation, and we will analyze this outcome using McNemar's test (5% significance level). The congruence between patients' choice and values will be evaluated using multivariable logistic regression.²⁹ Both the patient and pharmacist will rate the perception that shared decision-making took place using the control preferences scale,^{30–32} and the agreement between patient and pharmacist ratings will be measured. After 8 weeks, the proportion of patients continuing on PPIs at their pre-PtDA dose will be measured. Symptoms will also be assessed at 8 weeks in all patients.³³ Our sample size is based on the paired difference in the proportion of patients preferring to continue on their PPI before the PtDA consult compared with after.³⁴ To detect a difference in paired proportions of 15% (80% power, alpha of 5%), we need a sample size of 54.

TABLE 1 Eligibility criteria

Inclusion criteria
<ol style="list-style-type: none"> 1. ≥ 18 years of age 2. Taking a PPI for mild/moderate upper GI symptoms (mild or moderate GERD/esophagitis Los Angeles Grade A or B) for at least 4 weeks with resolution of symptoms 3. Currently asymptomatic
Exclusion criteria
<ol style="list-style-type: none"> 1. Severe GERD or upper GI symptoms, esophagitis Los Angeles Grade C or D at baseline 2. Taking PPI for gastroprotection (at moderate or high risk of GI bleeding) 3. History of Barrett's esophagus 4. History of bleeding peptic ulcer 5. Taking PPI for treatment of current ulcer not healed

PPI, proton pump inhibitor; GI, gastrointestinal; GERD, gastroesophageal reflux disease.

Discussion

Our research group developed 3 deprescribing guidelines, the first of which focuses on PPIs. We also implemented our deprescribing guideline into primary care practices³⁵ in a previous phase of our research. This PtDA is a tool to further facilitate implementation of these guidelines and involve patients in the decision-making process. We recognize the importance of patient values surrounding the decision to continue or stop a medication; thus, we want to empower patients to make an informed decision.

A 2014 systematic review ($n = 21$ studies) suggests that barriers to prescribers discussing deprescribing include lack of prescriber time during appointments, competing priorities, access to key resources (e.g., a pharmacist) and lack of a stimulus to review medications.²¹ This project seeks to overcome those barriers by having a pharmacist use his or her knowledge and expertise to become a champion of appropriate PPI use and to have dedicated 10- to 15-minute appointments to address this issue.

The 2014 systematic review described above also noted challenges in confirming the indication or rationale for a drug being started, as well

as uncertainty about whether a patient was eligible for deprescribing.²¹ This problem has also been described by other researchers. For example, an Australian study to reduce inappropriate PPI use could not verify the indication for 15 out of 57 patients.³ We have encountered similar difficulties in recruiting patients so far, where it has been time-consuming to identify eligible patients and there is uncertainty about whether a patient is eligible to consider the option of having a PPI deprescribed. Thus, while inappropriate PPI prescribing appears to be common, actually attempting interventions to reduce PPI use in practice is challenging.

Our study is limited by a before/after design and a small sample size. However, it will provide valuable information about whether the PtDA is helpful and impactful in clinical practice. This study will lay the foundation for a larger randomized controlled trial to more thoroughly investigate whether our PtDA influences decisions surrounding PPI treatment and actual PPI prescribing rates. Widespread utilization of our PtDA could reduce rates of inappropriate PPI use and thus the incidence of rare harms and unnecessary health care expenditures. ■

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