Proton Pump Inhibitors and the Treatment of GERD, Dyspepsia, and NSAID-associated Peptic Ulcer Disease

Presenter

Title

Affiliation

Date
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Outline

- Objectives
- Background
- Approach to diagnosing Dyspepsia vs. other GI Conditions (including GERD and NSAID-associated PUD)
- Managing GERD, NSAID-associated PUD, and Dyspepsia
- PPIs in Practice – Prescribing Points
Objectives

- Review diagnostic criteria for GERD, Dyspepsia, and Peptic Ulcer Disease (including NSAID-related Upper GI Problems and H. Pylori)
- Review the treatment of these conditions, including the role of PPIs
- Review points for prescribing PPIs in practice
  - Efficacy of different PPIs for initial therapy
  - Double dosing in initial therapy
  - Role in asthma, laryngeal symptoms, cough
Background

Canadian Agency for Drugs and Technologies in Health (CADTH)

CADTH is an independent, not-for-profit agency funded by Canadian federal, provincial, and territorial governments to provide credible, impartial advice and evidence-based information about the effectiveness of drugs and other health technologies to Canadian health care decision makers.
Stakeholders:

- Physicians, pharmacists, nurses, other allied health professionals
- F/P/T Governments
- Consumers
- Manufacturers
- Collaborators in Canada and internationally
What is COMPUS?

- Identify evidence-based optimal drug therapy
- Evaluate current use & identify gaps
- Provide strategies & tools
- Support & encourage informed decision making
- Build networks & partnership
Why PPIs?

PPI topic selection criteria included:

- Over- or under-use
- Size of patient population
- Potential impact on health outcomes and cost-effectiveness
- Potential to effect change
- Benefit to multiple jurisdictions
- Measurable outcomes
PPI Project Process

• Identify, summarize and evaluate the clinical evidence in the form of evidence-based statements

• Produce reliable economic evidence

• Understand the current practice in Canada related to PPI prescribing and use

• Identify gaps in practice highlighting areas where current practice differs from the evidence
PPI Project Process

• Develop key messages regarding the evidence-based statements to address the gaps in practice.

• Select interventions to support the key messages and effect change in the prescribing and use of PPIs.

• Develop intervention tools for implementation.

• Develop an evaluation framework to measure the effect of the interventions.
Identifying the Evidence

- Clinical Practice Guidelines (CPGs) & Consensus Documents (CDs)
- Extracted PPI–related recommendations and statements
- Compiled a synopsis of existing statements and recommendations
- Evaluated all relevant cited references (AMSTAR<sup>SR</sup>, adapted SIGN 50 checklist<sup>RCT</sup>, cohort, observational)
- Identified & evaluated relevant new evidence not yet incorporated in the CPGs
Identifying Evidence-based Optimal Drug Therapy

- PPI Expert Review Panel reviewed results, voted on statements
- Stakeholder feedback/input (interim reports containing statements and evidence posted on web)
- Published scientific report March 2007
- Develop strategies to support implementation of Optimal Drug Therapy
- Ongoing process to maintain information on Optimal Drug Therapy
PPI Expert Review Panel (ERP)

BC  Dr. J. Rideout, Family Physician
AB  Dr. S. van Zanten, Gastroenterologist
AB  Dr. A. Thomson, Gastroenterologist
SK  Dr. M. Caughlin, Family Physician
SK  Dr. B. Schuster, Pharmacist
MB  Dr. L. Targownik, Gastroenterologist
ON  Dr. A. Holbrook, Pharmacologist
ON  Dr. M. Brouwers, Methodologist
ON  Ron Goeree, Health Economist
ON  Dr. M. Man-Son-Hing, Geriatrician
ON  Dr. J. Marshall, Gastroenterologist
NS  Pam McLean-Veysey, Pharmacist
Conditions related to PPI Project

- Dyspepsia
- GERD
- Peptic Ulcer Disease (PUD)
- *H. Pylori* Infection
- NSAID Associated Ulcer
Dyspepsia
Canadian Dyspepsia Working Group Definition

“Dyspepsia is a symptom complex of epigastric pain or discomfort thought to originate in the upper gastrointestinal tract, and it may include any of the following symptoms:

- heartburn, acid regurgitation,
- excessive burping/belching,
- increased abdominal bloating,
- nausea,
- feeling of abnormal or slow digestion or early satiety.”

Van Zanten 2000
Uninvestigated Dyspepsia

Investigated (non-ulcer) Dyspepsia

Endoscopy

Canadian Agency for Drugs and Technologies in Health

Agence canadienne des médicaments et des technologies de la santé
Uninvestigated Dyspepsia

What would the endoscopic findings be if every dyspepsia patient underwent urgent endoscopy?
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 50</td>
<td>661 (64%)</td>
</tr>
<tr>
<td>≥ 50</td>
<td>379 (36%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>520 (50%)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>991 (95%)</td>
</tr>
<tr>
<td><strong>Hp positive</strong></td>
<td>301 (30%)</td>
</tr>
</tbody>
</table>
Prevalence of Clinically Significant Findings by Age

Canadian Agency for Drugs and Technologies in Health
Agence canadienne des médicaments et des technologies de la santé

Thomson 2003
Prevalence of Clinically Significant Findings by Age

> 40% erosive esophagitis

<table>
<thead>
<tr>
<th>Area</th>
<th>&lt; 50 (N = 661)</th>
<th>50+ (N = 379)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>45.7%</td>
<td>49.6%</td>
</tr>
<tr>
<td>Stomach</td>
<td>15.7%</td>
<td>22.7%</td>
</tr>
<tr>
<td>Duodenum</td>
<td>9.5%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Any Area</td>
<td>55.7%</td>
<td>62.3%</td>
</tr>
</tbody>
</table>

Thomson 2003
Endoscopic Findings by *Hp* Status

- **N** = 1013
- *Hp* prevalence 30%

<table>
<thead>
<tr>
<th>Condition</th>
<th>H.p. -ve</th>
<th>H.p. +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflux Esoph.</td>
<td>46.2</td>
<td>35.5</td>
</tr>
<tr>
<td>GU</td>
<td>2</td>
<td>5.6</td>
</tr>
<tr>
<td>DU</td>
<td>1.3</td>
<td>6.6</td>
</tr>
</tbody>
</table>

Thomson 2003
What does the CADET-PE study tell us?

Most endoscopic abnormalities are covered by either a course of acid suppressive therapy or anti-Hp treatment.

Thomson 2003
Uninvestigated Dyspepsia

- Prompt endoscopy does not produce better outcomes than empirical PPI therapy
- Endoscopy is not warranted in the majority of cases of dyspepsia
- Treatment as uninvestigated dyspepsia

Van Zanten 2000
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?
2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?
3. Is the patient using NSAIDs (including ASA)?
4. Is the dominant symptom heartburn, acid regurgitation, or both?
5. Is the patient infected with *H. pylori*?
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?
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5. Is the patient infected with *H. pylori*?

Van Zanten 2000
Are there other possible causes for the symptoms?

- Cardiac
- Hepatobiliary
- Medication-induced
- Lifestyle
- Dietary indiscretion

If YES → treat as appropriate
## Medications Associated with Dyspepsia

<table>
<thead>
<tr>
<th>NSAIDS/ASA/COX2 inhibitors</th>
<th>metformin (Glucophage®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>acarbose (Prandase®)</td>
<td>antibiotics (erythromycin)</td>
</tr>
<tr>
<td>alcohol</td>
<td>orlistat (Xenical®)</td>
</tr>
<tr>
<td>alendronate (Fosamax®)</td>
<td>potassium</td>
</tr>
<tr>
<td>corticosteroids</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td>iron</td>
</tr>
</tbody>
</table>

*Thomson 2002
Bazaldua 1999*
## Herbs Noted to Have Side Effects That May be Confused with Dyspepsia

<table>
<thead>
<tr>
<th>HERB</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic</td>
<td>Stomach burning, nausea</td>
</tr>
<tr>
<td>Gingko</td>
<td>Mild GI disturbances</td>
</tr>
<tr>
<td>Saw palmetto</td>
<td>Upset stomach</td>
</tr>
<tr>
<td>Feverfew</td>
<td>GI disturbances</td>
</tr>
<tr>
<td>White willow</td>
<td>Possible ADR similar to salicylates</td>
</tr>
</tbody>
</table>

*Thomson 2002  Bazaldua 1999*
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?

2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?

3. Is the patient using NSAIDs (including ASA)?

4. Is the dominant symptom heartburn, acid regurgitation, or both?

5. Is the patient infected with *H. pylori*?
Does patient have Alarm symptoms or is patient > 50 yrs?

VBAD
- Vomiting
- Bleeding/anemia
- Abdominal mass/unexplained weight loss
- Dysphagia
- Age > 50

If YES \(\rightarrow\) further investigation is warranted

Van Zanten 2000
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?
2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?
3. Is the patient using NSAIDs (including ASA)?
4. Is the dominant symptom heartburn, acid regurgitation, or both?
5. Is the patient infected with *H. pylori*?
Is patient using NSAIDs (including ASA)?

*If YES:*

Stop NSAID therapy (if possible)

If symptoms resolve, but analgesic is still required:

- Avoid NSAID if possible (acetaminophen)
- If NSAID must be used:
  - lowest dose
  - shortest duration
  - consider prophylaxis with standard dose PPI, or misoprostol

Van Zanten 2000
**NSAID Prophylaxis Should be Considered for Whom?**

- Prior history of GI event (ulcer, hemorrhage)
- Age >60 years
- High NSAID dosage (>2x normal dose)
- Patients on warfarin and NSAID
- Patients on corticosteroid and NSAID

All patients taking NSAIDS do not require prophylaxis.

*Lanza 1998*
Secondary prevention of gastric and duodenal ulcers:

Standard-dose PPIs are more efficacious than standard-dose H2RA

- NNT $^{GU}=10$
- NNT $^{DU}=27$

Standard-dose PPIs have similar efficacy to misoprostol 400-800mcg/day
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?

2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?

3. Is the patient using NSAIDs (including ASA)?

4. Is the dominant symptom heartburn, acid regurgitation, or both?

5. Is the patient infected with *H. pylori*?
GERD is a condition which develops when the reflux of stomach content causes troublesome symptoms and/or complications.
Is the dominant symptom heartburn, acid regurgitation, or both?

“A burning feeling rising from the stomach or lower chest towards the neck”

Uninvestigated GERD:

- dominant symptoms of heartburn and/or regurgitation
- may be associated with other symptoms such as epigastric pain/discomfort
- not investigated by endoscopy (or upper GI series).

Erosive esophagitis: the presence of reflux symptoms and any length of **mucosal break** in the esophagus as a result of gastroesophageal reflux.

Endoscopy-negative reflux disease (ENRD): individuals with GERD who have normal endoscopy results while off treatment.

Armstrong 2005  
Vakil 2006  
CADTH 2007
Is the dominant symptom heartburn, acid regurgitation, or both?

*If YES:*

- GERD is the likely diagnosis
- Treat as GERD
GERD Treatment

Goals of therapy:

- Resolution of symptoms
- Healing of ulcer or esophagitis, if present
- Prevent long-term sequelae
  - Barrett’s esophagus
  - Bleeding
  - Stricture

Heidelbaugh 2003
GERD Treatment

PPIs or H2RAs?

• Although H2RA therapy is effective in managing many patients, standard-dose PPIs are superior to H2RAs in the initial & maintenance management of uninvestigated GERD and erosive esophagitis.

• PPIs have a similar adverse event rate (generally minor) as H2RAs
GERD Treatment

Initial therapy: 4 – 8 weeks

Following initial therapy:

- Continued PPI therapy is more efficacious than step-down to H2RAs in uninvestigated GERD and erosive esophagitis.

- Alternatives (PPI discontinuation, H2RAs, on demand dosing) to long-term regular use of standard dose PPIs for GERD may be appropriate in select patients.

CADTH 2007
GERD Treatment – Following Initial Therapy

~20% of uninvestigated GERD patients remain asymptomatic off therapy for up to 6 months after a successful initial course (4-8 wks treatment) with a PPI or H2RA

On demand PPI therapy:

- More efficacious than placebo
- More efficacious than continuous standard dose H2RA
- Less efficacious than continuous standard dose PPI
GERD Treatment

If a patient does not respond following 4-8 weeks of PPI treatment:

- Consider:
  - Switching to another standard dose PPI or increasing to double dose PPI (little evidence to support either strategy)
  - investigation (i.e. endoscopy)
  - alternative diagnosis (symptoms may not be acid related)

Armstrong 2005
Heidelbaugh 2003
Van Zanten 2000
Five Key Decision Points
Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?
2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?
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4. Is the dominant symptom heartburn, acid regurgitation, or both?
5. Is the patient infected with *H. pylori*?
Is the patient infected with *H. pylori*?

Non-invasive *H. pylori* test:

If positive → eradication therapy

Can drug therapy impact Hp testing?

- False negatives are possible
- Discontinue abx/bismuth 4 weeks prior to testing
- Discontinue acid suppression 1 week prior
H. pylori Eradication Therapy

First-Line Triple Therapy

- “1-2-3”
  - 1 week, 2 times a day, 3 drugs
- Currently approved 7-day regimens
  - PPI
  - + clarithromycin (Biaxin®)
  - + amoxicillin or metronidazole

First-Line Quadruple Regimens

- PPI bid + BMT QID (bismuth+metronidazole+tetracycline)
H. pylori eradication – then what?

Is follow-up acid suppression needed?
Not generally indicated for uncomplicated duodenal ulcer

• Exceptions
  • gastric ulcers
  • Patients that remain symptomatic
  • complicated patients with large or refractory ulcers
    • ensure ulcer healing & HP eradicated
  • Maintenance anti-secretory therapy for patients at high risk for recurrence / bleeding
    • e.g. high acid-secretory condition
H. pylori eradication – then what?

Is follow-up testing to confirm eradication required?

- Not generally recommended unless patient remains symptomatic

What if the eradication therapy fails?

- Try a different first-line therapy than the initial therapy tried

Van Zanten 2000
Hunt 1999
Hunt 1998
Five Key Decision Points

Uninvestigated Dyspepsia

1. Are there other possible causes for the symptoms?
2. Does patient have Alarm symptoms (VBAD) or > 50 years of age?
3. Is the patient using NSAIDs (including ASA)?
4. Is the dominant symptom heartburn, acid regurgitation, or both?
5. Is the patient infected with *H. pylori*?

If NO → Dyspepsia is the likely diagnosis

Van Zanten 2000
Dyspepsia Treatment

Non-medical treatment options:

- Avoid foods that worsen symptoms
- Avoid lying down 2-3 hours after eating
- Avoid tight-fitting clothing
- Stop smoking (or reduce smoking)
- Elevate the head of the bed using blocks
- Eat smaller meals and chew food well
- Lose weight, if appropriate
- Review medications used
- Reduce stress

Thomson 2002
Kaltenbach 2006
Heidelbaugh 2003
Dyspepsia Treatment

Over-the-counter (OTC) Medications:

Antacids

- 10-20ml/ 2-4 tabs pc & HS prn (higher doses in GERD)
- Works fast (5-15 minutes)
- Frequent dosing, volume of liquid and taste can be a challenge
  - constipating = calcium, aluminum
  - diarrhea = magnesium
- Consider concurrent clinical conditions & convenience

Thomson 2002
Dypepsia Treatment

Over-the-counter (OTC) Medications (con’t)

H2RAs (Famotidine Pepcid AC, Complete, ranitidine Zantac)

• Symptom relief similar to antacids, but takes 1 hour for effect
• Duration of effect is longer
• Pepcid 10mg-Zantac 75mg 30 tablets ≥$12 (generic <$10)
• Pepcid Complete (Famotidine 10mg/Ca Carb/MgOH) 10 tabs $9
• Famotidine 20mg, ranitidine 150mg – pkg size ≤ 30 tabs

*if on a regular H2RA or PPI, can use an OTC product for occasional symptoms related to dietary indiscretion

Thomson 2002
More than 1/4 of Canadians have symptoms caused by the acid in their stomach. Symptoms can include heartburn, indigestion, bloating and a feeling of fullness.

Whether or not you have been prescribed a medication, there are things you can do that may help reduce your symptoms.

☐ Avoid foods that worsen your symptoms, such as:
  - coffee
  - chocolate
  - acidic foods (e.g., tomatoes, lemons)
  - alcohol
  - overly spicy or high-fat meals
  - carbonated beverages

☐ Do not lie down for 2 to 3 hours after eating
☐ Do not wear tight-fitting clothing
☐ Stop or reduce the amount you smoke
☐ Elevate the head of your bed using blocks or books
☐ Eat smaller meals and chew food well
☐ Lose weight if appropriate

For full project information: www.cadth.ca

If your symptoms are mild or only occur once in a while, you may not need to take regular prescription medication.

You can treat your symptoms whenever they occur using medications available without a prescription at your local pharmacy. There are two types of products you can use:

**Products That Neutralize Acid**
- Liquid or tablets (e.g., Gaviscon®, Maalox®, Tums®)
  - Works fast (5 to 15 minutes), lasts for 1 to 2 hours
  - Pennies per dose, especially using store brand antacids

**Products That Stop Acid Production**
- Zantac®, Pepcid® or generic ranitidine or famotidine
  - Takes ~1 hour for effect, lasts for up to 12 hours
  - Can cost as little as 25 cents per dose

Consult with your **Pharmacist** for the best option for you.

If your symptoms don’t go away within 2 weeks, or if they get worse: **Contact Your Doctor**

Doctor Signature: __________________________
Pharmacist Signature: ____________________
Dyspepsia Treatment

PPIs or H2RAs?

Initial Standard-dose PPI therapy is more efficacious than standard-dose H2RAs at reducing symptoms in patients with dyspepsia (H. pylori negative, uninvestigated)
PPIs in Practice: Prescribing Points

- Choosing a PPI for initial therapy
- Double-dosing in initial therapy
- Asthma, cough, laryngeal symptoms
Choosing a PPI for Initial Therapy

All PPIs are equally efficacious in the initial treatment of GERD and other common GI conditions.

There are no **clinically** important differences between the PPIs at standard doses for:

- *H. pylori* eradication
- GERD, ENRD, esophagitis
- NSAID-associated ulcer prophylaxis and healing
The Evidence

GERD/ENRD/Esophagitis

- Six good quality systematic reviews showed no clinically important differences in standard-dose PPIs as initial therapy.
- Isolated exceptions, majority showed no differences.
- Comparisons showing some degree of difference involved non-equivalent comparisons (e.g. high dose vs. standard dose).

Edwards 2001
Vakil 2003
Wang 2005
McQuaid 2005
Donnellan 2004
McDonagh 2005
Gisbert 2004
Gisbert 2003
Vergara 2003
The Evidence

*H. pylori* Eradication

Seven systematic reviews (5 of good quality) showed PPIs have similar efficacy when used in triple therapy regimens.

Edwards 2001  
Vakil 2003  
Wang 2005  
McQuaid 2005  
Donnellan 2004  
McDonagh 2005  
Gisbert 2004  
Gisbert 2004  
Gisbert 2003  
Vergara 2003
The Evidence

NSAID Ulcer Prophylaxis
• Good quality systematic review of 7 RCTs (indirect comparison):
  • Different PPIs reduced ulcer risk to a similar degree
  • One RCT directly compared omeprazole vs pantoprazole and found no difference in ulcer risk

NSAID Ulcer Healing
• Good quality systematic review of 3 RCTs (indirect comparison):
  • Similar healing rates for the PPIs that have been studied (omeprazole & lansoprazole)
The Evidence – Limitations

- Isolated studies may show differences in efficacy – must be balanced against the weight of the evidence

- **Caution:** non-equivalent dose comparisons

- No evidence regarding safety and efficacy of switching to a different PPI in patients successfully treated with a given PPI

- Not all comparisons have been made for all indications

- Official indications may be more limited

- Balance evidence with individual patient needs
**Practice Implications**

Prescribing may be optimized by focusing on lower cost PPIs

<table>
<thead>
<tr>
<th>Standard Dose PPIs</th>
<th>Generic Omeprazole 20mg Daily</th>
<th>Pariet® 20mg Daily</th>
<th>Pantoloc® 40mg Daily</th>
<th>Prevacid® 30mg Daily</th>
<th>Nexium® 20mg Daily</th>
<th>Losec® 20mg Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Price†</td>
<td>$1.25</td>
<td>$1.30</td>
<td>$1.90</td>
<td>$2.00</td>
<td>$2.10</td>
<td>$2.20</td>
</tr>
<tr>
<td>Approximate Monthly Price†</td>
<td>$43.00</td>
<td>$44.40</td>
<td>$61.20</td>
<td>$64.00</td>
<td>$66.80</td>
<td>$69.60</td>
</tr>
</tbody>
</table>
Potential Cost-savings to Patients

- Generic omeprazole 20 mg and Pariet (rabeprazole) 20 mg are the least expensive standard-dose PPIs in Canada
- Prescribing a PPI that cost $1.40/day vs. $2.20/day could save almost $300.00 per year in drug costs.
Double vs. Standard Dosing

Doubling the standard daily-doses of PPIs, as initial therapy, is no better than standard daily-dose therapy (in erosive esophagitis)

Double-Dose PPIs – Gaps in Research:

• Uninvestigated GERD with severe symptoms?
• Symptomatic GERD, ENRD, erosive esophagitis despite standard-dose PPI therapy?
The Evidence

High or Double-dose PPIs: initial Rx Erosive Esophagitis

- 6 RCTs\(^{N=1388}\): 2 RCTs very good, 1 good quality, 3 poor quality
- Majority of evidence: no benefit for initial treatment
- Limitation: small number of trials, all of poor quality, specifically addressed Grade 2-4 esophagitis (more severe)
- Esomeprazole 40mg is approved dose for erosive esophagitis:
  - Some but not all trials of 40mg vs standard dose PPIs have shown small but statistically significant benefit: Clinical importance unclear

CADTH 2007
McDonagh 2005
The Evidence

Double-dose initial Rx NSAID-induced ulcer

- 2 RCT $n=1476$: double dose omeprazole was not superior to single dose
- both standard and double doses more effective than H2RA (NNT=4-9) and misoprostol (NNT=6-8)
PPIs and Asthma, Chronic Cough, and Laryngeal Symptoms

PPIs are **not efficacious** in treating cough, asthma or laryngeal symptoms that may be associated with GERD.
The Evidence

Asthma with concomitant GERD

One good quality systematic review (12 RCTs, n=432)

• PPI (omeprazole 20-80mg) or H2RA did not improve FEV1, PEF, airway responsiveness or use of inhalers

• 1 RCT (omeprazole 40mg vs placebo) reported improvement in nocturnal symptom score

CADTH 2007
The Evidence

Laryngeal symptoms with Reflux

One good quality systematic review (5 RCTs, n=247)

• **No significant effect** on laryngopharyngeal symptoms (e.g., cough, throat clearing, globus, hoarseness, sore throat)

CADTH 2007
The Evidence

Chronic cough with or without GERD

One good quality systematic review

Chronic cough $\geq 3$ weeks without respiratory symptoms/signs or systemic illness

Cough score at various times

- No benefit of PPI vs. placebo

Limitations:

- Small pooled sample size: analysis likely underpowered
- Heterogeneity in study population
PPIs in Practice: Prescribing Points

- There are no clinically important differences among equivalently dosed PPIs in the initial treatment of most acid-related GI conditions.

- Studies comparing standard doses of PPI to high doses have not shown superiority of starting with the higher dose. Standard-dose therapy should be the initial therapy for most patients.

- Current evidence would suggest PPIs are not efficacious in improving asthma, laryngeal symptoms or chronic cough that may be associated with GERD.
Quick Reference Prescribing Aid

Three Questions to Ask When Considering a PPI

1. **Which PPI should I choose?**
   - On initial therapy, there are no clinically important differences among equivalently-dosed PPIs in the treatment of most acid-related GI conditions.

2. **At what dose should I start?**
   - Studies comparing standard doses of PPI to high doses have **not** shown superiority of starting with the higher dose. Standard-dose therapy should be the initial therapy for all patients.

3. **What won’t a PPI treat?**
   - Current evidence suggests PPIs are not efficacious in improving asthma, laryngeal symptoms, or chronic cough that may be associated with GERD.

For full project information, visit the CADTH web site:

www.cadth.ca

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**Approximate Monthly Cost**

For PPIs and H2RAs

<table>
<thead>
<tr>
<th>PPI</th>
<th>Standard-Dose</th>
<th>Low-Dose PPI</th>
<th>Standard-Dose PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole 40 mg once daily</td>
<td>$43.00</td>
<td>$4.40</td>
<td>$66.80</td>
</tr>
<tr>
<td>Pantoprazole 40 mg once daily</td>
<td>$44.00</td>
<td>$4.40</td>
<td>$66.80</td>
</tr>
<tr>
<td>Omeprazole 40 mg once daily</td>
<td>$46.00</td>
<td>$4.60</td>
<td>$78.60</td>
</tr>
<tr>
<td>Lansoprazole 30 mg once daily</td>
<td>$48.00</td>
<td>$4.80</td>
<td>$88.40</td>
</tr>
<tr>
<td>Nexium 30 mg once daily</td>
<td>$52.00</td>
<td>$5.20</td>
<td>$92.40</td>
</tr>
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</table>

**Canadian Agency for Drugs and Technologies in Health**

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**Canadian Agency for Drugs and Technologies in Health**

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**Agence canadienne des médicaments et des technologies de la santé**
PPI Intervention Tools

Physician Educational Materials:
- Alternate Prescription Pad
- Newsletter “3 Questions to Ask When Starting a PPI”
- Self Audit Form
- Academic Detailing
- Interactive and Didactic Presentation
- Prescribing Aid

Pharmacist Materials:
- Interactive and Didactic Presentation

Patient Education Materials:
- Information Brochure / Alternate Prescription Pad
Questions?
References


References


References


References

15 McDonagh MS, Carson S. Drug class review on proton pump inhibitors: final report update 3. Portland (OR): Oregon Health & Science University; 2005.


References


