

PPIs: Navigating The New Heartburn Headache

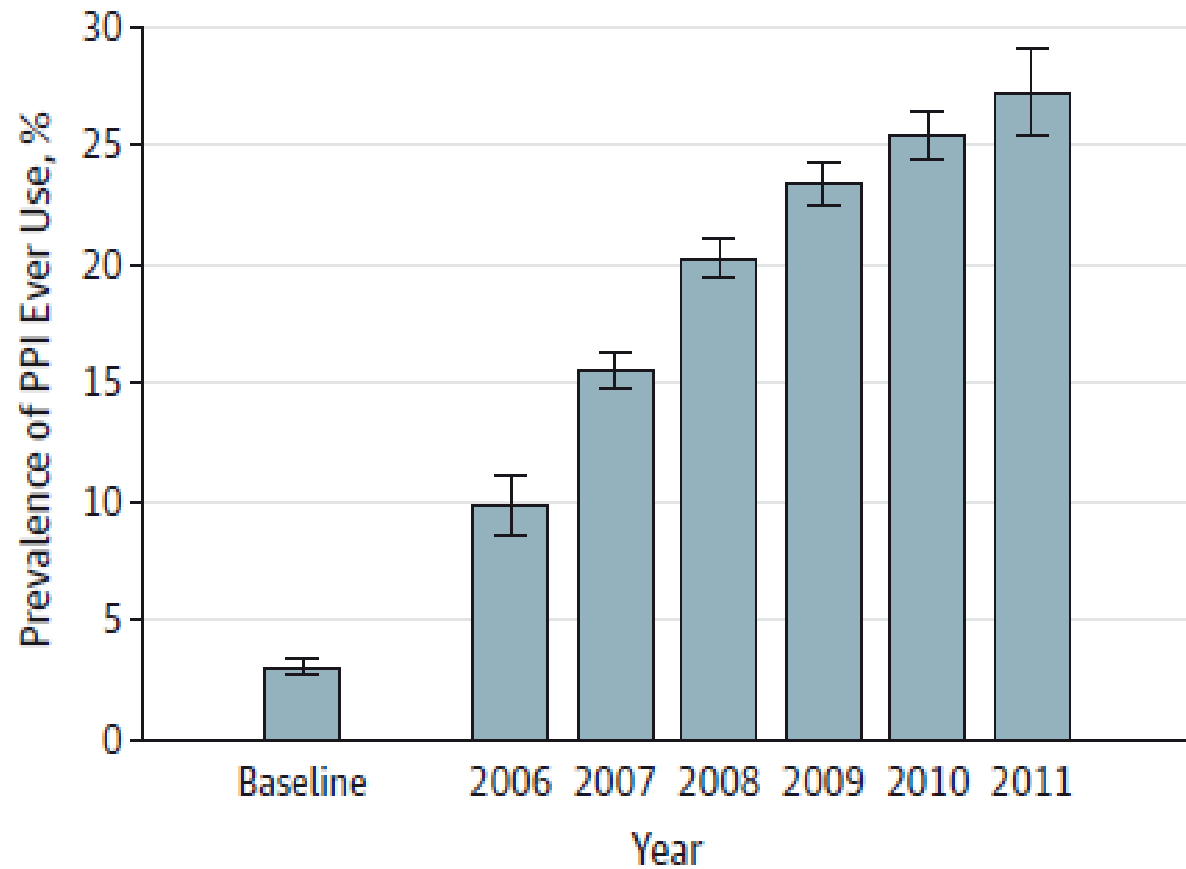
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PPI Problems

- Widespread use, often with no clear indication
- Emerging evidence of harm promoted in general media
 - CKD: evidence warrants consideration
 - Dementia: evidence is questionable
- Rebound secretion makes discontinuing difficult
 - Often requires a taper



Change in Prevalence of PPI Use Over Time

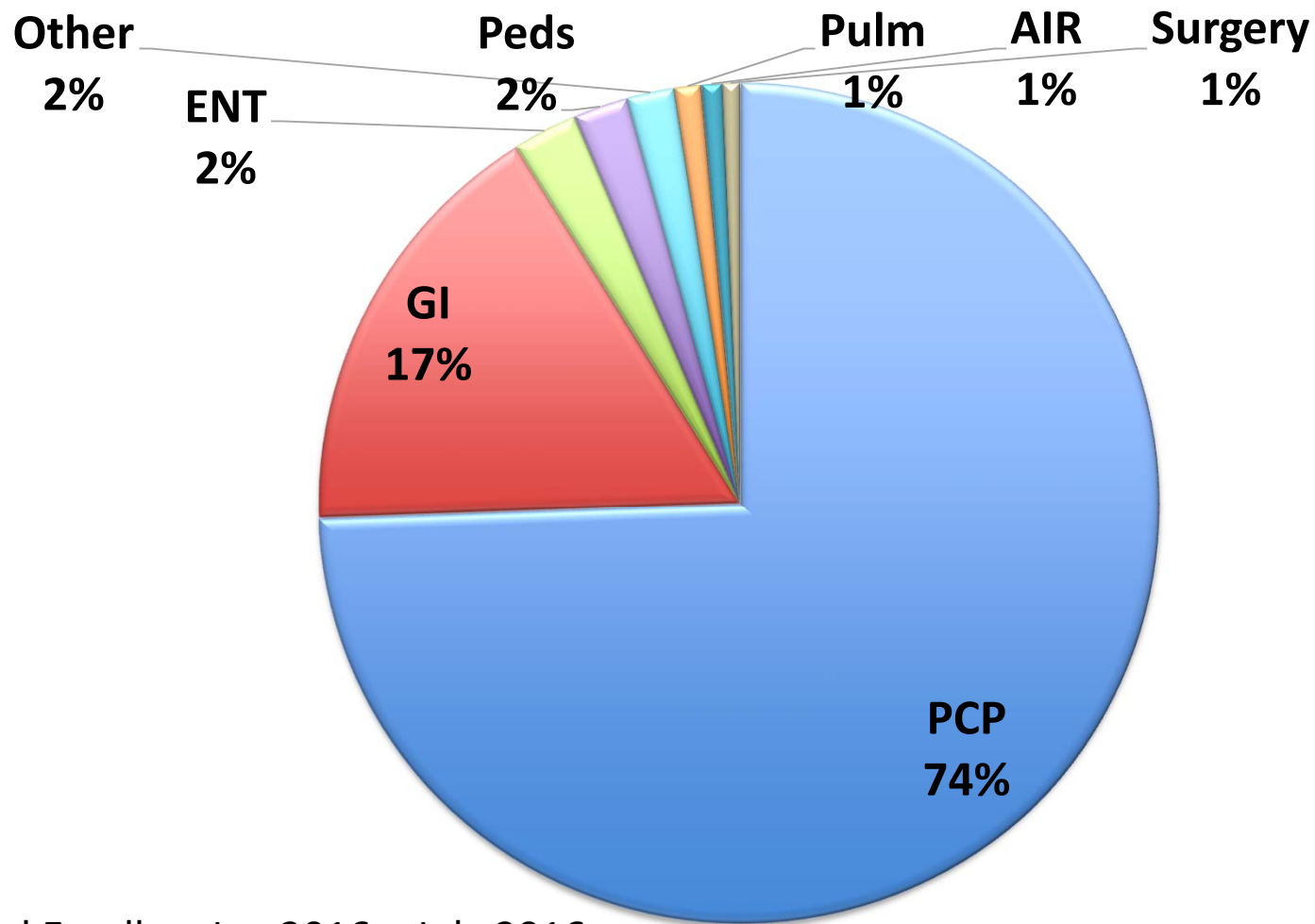


Costs

- United States: \$11 billion annually on PPIs
- AHP[†]: \$3 million in 2015 on PPIs
 - Inhaled corticosteroids: \$1.8 million in 2015
 - Anticholinergic bronchodilators: \$600,000 in 2015

†Commercial Excellus patients

PPI Prescribing Patterns in AHP



Commercial Excellus: Jan 2016 – July 2016



How Many Truly Need Chronic Therapy?

- Approximately 35% of patients receiving a PPI do not have an indication
 - Range: 20 – 70%
- 49% of patients initiated on a PPI are not re-evaluated for symptom improvement or need for continued therapy

“A large number of patients are taking PPIs for no clear reason – often remote symptoms of dyspepsia or ‘heartburn’ that have since resolved.”

JAMA Internal Med Feb 2016

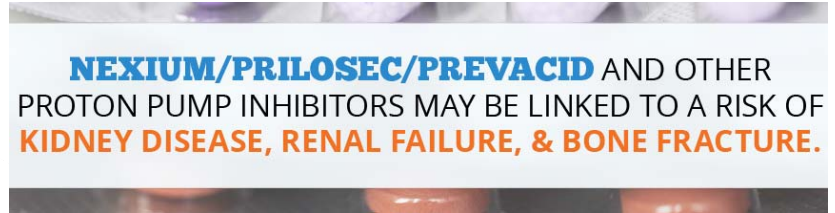
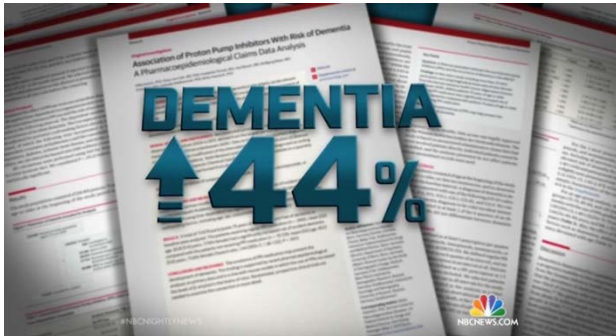
Ann Pharmacother. 2015 Jan;49(1):29-38
Am J Manag Care. 2010 Sep;16(9):e228-34
JAMA Intern Med. 2016 Feb;176(2):172-4

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HEALTHY LIVING

Gastric Reflux Drugs May Be Tied To Dementia Risk

But it's hard to know if participants in a new study were at an increased risk to begin with.



Nexium: Is the Purple Pill Shutting Your Kidneys Down? – Should You Be Taking It?

YOUR HEALTH

Popular Heartburn Pills Can Be Hard To Stop, And May Be Risky



February 15, 2016 · 4:41 AM ET



PPIs & CKD

Research

Original Investigation

Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease

Benjamin Lazarus, MBBS; Yuan Chen, MS; Francis P. Wilson, MD, MS; Yingying Sang, MS; Alex R. Chang, MD, MS; Josef Coresh, MD, PhD; Morgan E. Grams, MD, PhD

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PPIs & CKD

- Evaluate risk of new onset CKD with PPIs relative to H2RAs and no therapy
 - Previous literature has shown increased risk of AKI and acute interstitial nephritis associated with PPIs
- Well-designed, highly valid, NIH-funded observational cohort
 - Conducted in 2 separate US populations

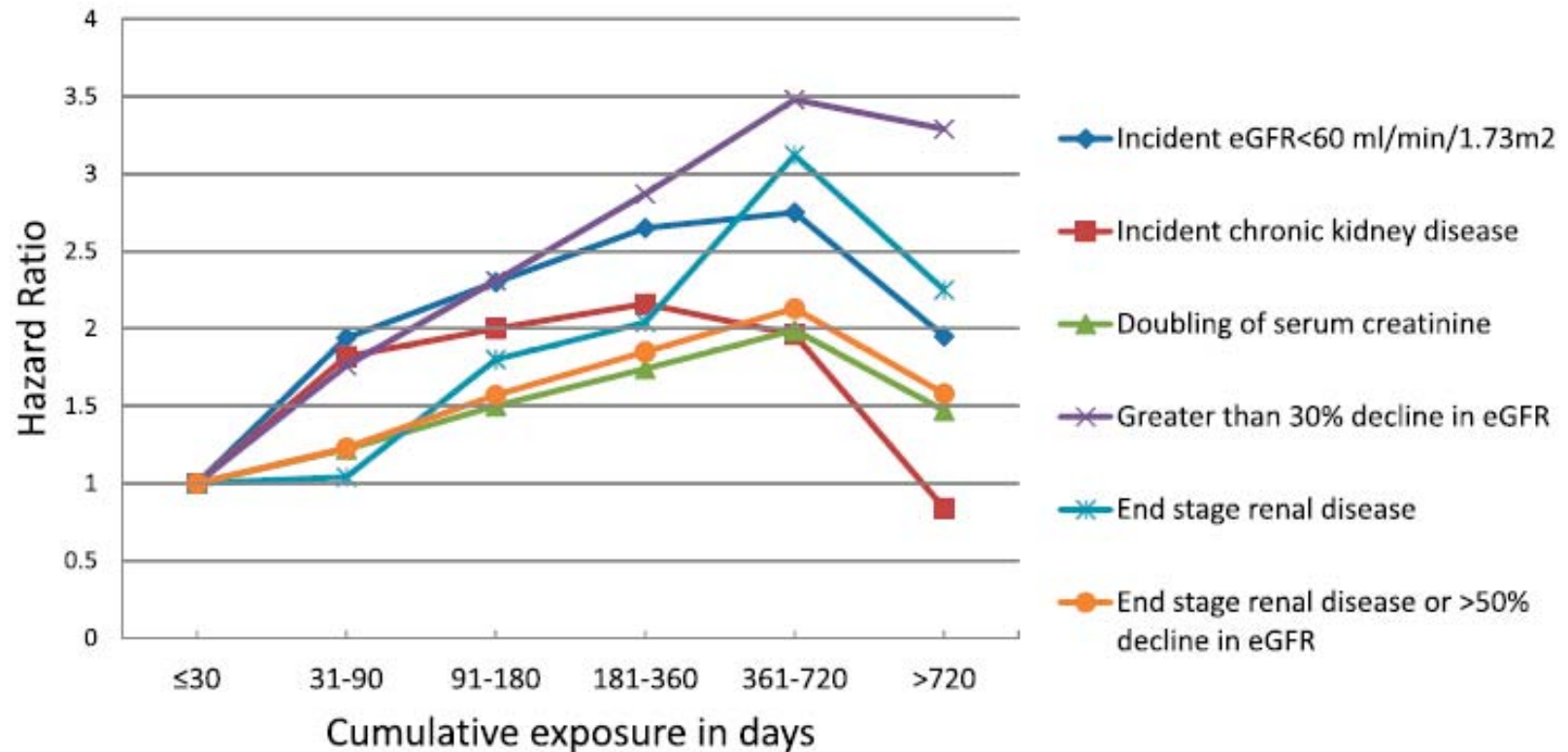
PPIs & CKD

- **PPI vs. no therapy:** 17 – 50% increase risk of new CKD
 - 10 year NNH: 30 – 58
 - Once daily PPI: 15% increase risk
 - Twice daily PPI: 46% increase risk
- **PPI vs. H2RA:** 29 – 50% increase risk
- **H2RA vs. no therapy:** no increase risk of harm
- Similar results observed for incidence of AKI

Relative to no therapy or H2RA, PPI users had an increased risk of CKD and risk was not observed with H2RA

PPIs & CKD

Duration of PPI exposure and risk of renal outcomes



PPIs & Dementia

Research

Original Investigation

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

Willy Gomm, PhD; Klaus von Holt, MD, PhD; Friederike Thomé, MSc; Karl Broich, MD; Wolfgang Maier, MD;
Anne Fink, MSc; Gabriele Doblhammer, PhD; Britta Haenisch, PhD



PPIs & Dementia

Original Investigation

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

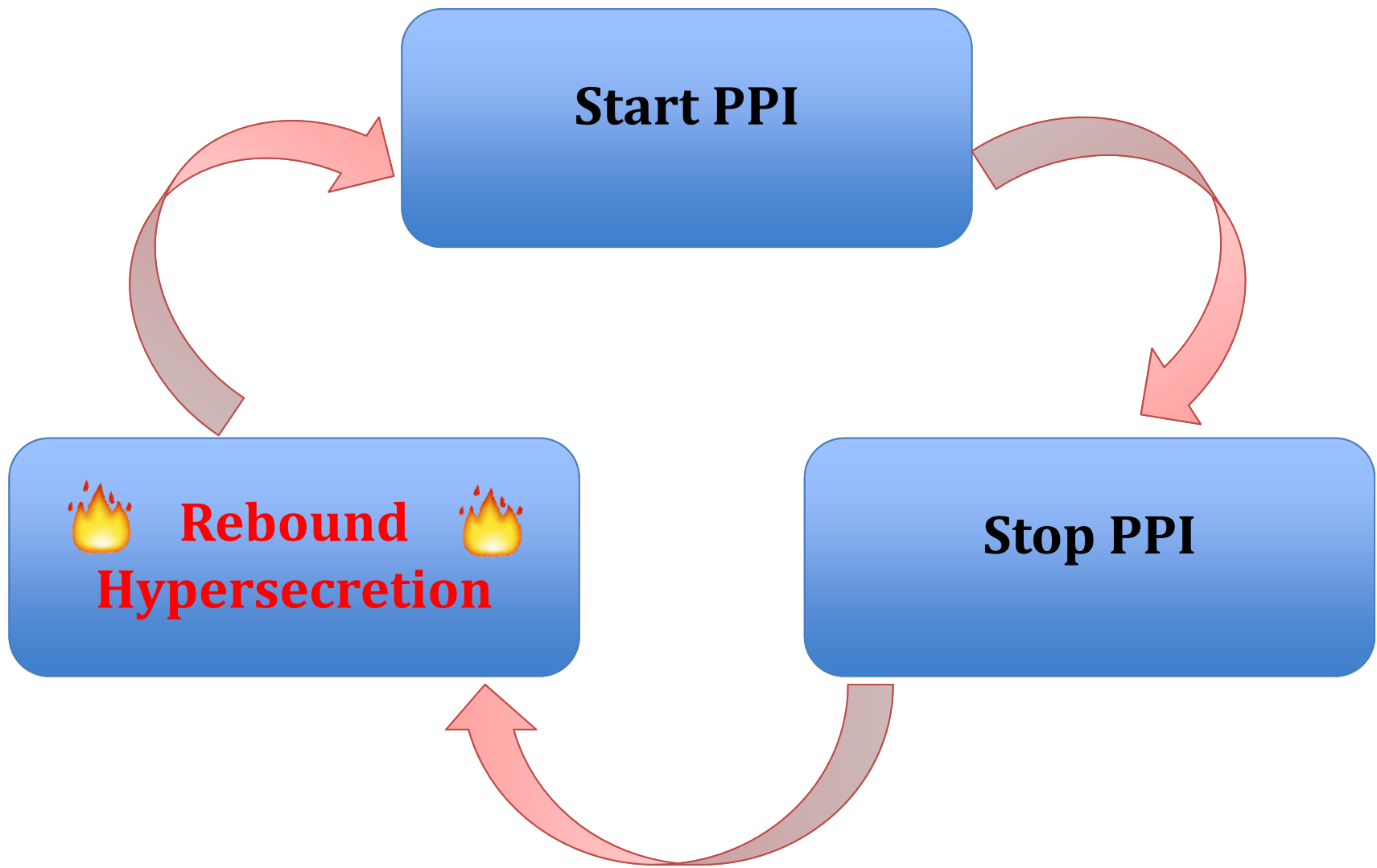
- Review of German prescription and medical claims database
 - Relies on assumption that claims accurately represent patient
- **Regular PPI claims vs. no PPI claims:** 44% more likely to have a new claim for dementia
- Methodology is questionable
 - Failure to properly identify and adjust for competing risk factors
 - Another study using similar German database found slightly protective effect of PPIs for dementia

JAMA Neurol. 2016;73(4):410-416
JAMA Neurol. 2016 Aug 1;73(8):1025-1026
Int Psychogeriatr. 2016 Jul;28(7):1059-65

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Where Do We Go From Here?





Tapering PPIs

- Reduce dose by 50% x 2 weeks then every other day x 2 weeks
 - Extend interval if needed, avoid returning to previous dose
- H2RA or antacids for breakthrough symptoms
- Advise patients to expect initial worsening of symptoms



How to Safely Stop Taking Proton Pump Inhibitors

What you need to know

What are PPIs?

Proton pump inhibitors (PPIs) are medications used to reduce the amount of acid in your stomach. They are most commonly used to treat heartburn. Examples of PPIs include:

- Prilosec, Zegerid (omeprazole)
- Nexium (esomeprazole)
- Protonix (pantoprazole)
- Prevacid (lansoprazole)
- Dexilant (dexlansoprazole)
- Aciphex (rabeprazole)

Why should I stop my PPI?

Many patients who are taking PPIs for heartburn can control symptoms with small changes to their diet or by using other medications called antacids (i.e. Tums) or H2-receptor blockers (i.e. ranitidine or Zantac) as needed. This may allow you to take fewer pills each day.

Some long-term risks of ongoing use of PPIs are increased risk of infection, and reduced kidney function. Before stopping your PPI, you should talk to your doctor.

I tried to stop my PPI before but my symptoms came back.

If you have been on a PPI for a long time, your body is used to working with one. If you stop a PPI without weaning down, your body may over-react and produce more acid which causes increased symptoms. See the next section, "How to Stop Your PPI".

How to Stop Your PPI

After discussing with your medical team and deciding to wean off the medication you can do the following:

- If you are taking a PPI once daily: start taking one pill every other day, continue for 2 weeks and then stop. If you are on a higher dose, your doctor may start by prescribing a lower one. In this case, take the lower dose once daily for 2 weeks, then every other day for 2 weeks, then stop.
- If you are taking a PPI twice daily: start taking one pill daily 2 weeks, then take one pill every other day for 2 weeks then stop.

Tips for Success

- Symptoms may come back while your body gets used to working without a PPI. These should get better within a few days to weeks. If they develop, wait until they get better before reducing your dose further.
- Use antacids like Tums (or generic) for fast relief. These will work in about 10 minutes.
- Try an H2 blocker like Zantac (ranitidine). These will work in about 1 hour and can be used with antacids.
- Avoid foods that make your symptoms worse (i.e. spicy, fatty, or acidic foods).

When to call my doctor?

- If symptoms appear to be getting worse at any point while you are stopping the medication.
- If after stopping your PPI for 4 weeks you are having symptoms 2 or more times per week.

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Available at <http://ahpnetwork.com/ppi-patient-info/>

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Strategies for Managing Recurrent GERD

- Initial: 4 – 8 weeks, stop when symptoms resolved >2 weeks
- Maintenance: lifestyle modification, H2RA, antacids
- *Symptoms ≥ 2 times per week:*
 - Short 2 – 4 week PPI course
 - On-demand therapy?
 - Long-term therapy at lowest effective dose

Take Away Points

- Many patients are taking PPIs without a clear indication
- Evidence supporting risks of PPIs and CKD is strong enough to warrant consideration
- Evidence around PPIs and dementia is much less compelling
- PPIs need to be tapered to minimize rebound acid secretion

