

## Supplementary Online Content

McDonald EG, Milligan J, Frenette C, Lee TC. Continuous proton pump inhibitor therapy and the associated risk of recurrent *Clostridium difficile* infection. Published online March 2, 2015. *JAMA Intern Med*. doi:10.1001/jamainternmed.2015.42.

**eAppendix.** Supplemental Appendix.

This supplementary material has been provided by the authors to give readers additional information about their work.

## eAppendix. Supplemental Appendix

### Part A: Comorbidity Assessment:

Comorbidities examined included diabetes (E10.X-E14.X), renal disease (N14.X, N17.X-N19.X, N99.0, P96.0) coronary artery disease (I20.X-I25.X, Z95.5), hypertension (I10.X-I15.X), pulmonary disease (J40.X-J47.X), peptic ulcer disease (K25.X-K29.X), HIV/AIDS (B20.X-B24.X, Z.21), solid and hematological malignancy (C0.X-C96.X), cirrhosis (K74.X), atrial fibrillation (I48.X), congestive heart failure (I11.X, I13.0, I13.2, I50.X, I97.1), stroke (G45.X-G46.X, I63.X-I66.X), and venous thromboembolism (I26.X, I80.X-I83.X, Z8760).

### Part B: Evidence-based indications for PPI use

The assessors were not blinded as to whether the patient was a case or control but the criteria were equally applied.

The following uses were considered appropriate indications based on our internal consensus during other projects involving PPI use and based on studies that have examined evidenced-based indications for PPI therapy<sup>1-8</sup>. All other indications were considered “non-evidence based” unless there seemed to be an equivocal or unusual clinical indication in which case the assessors made a decision based on their explicit clinical judgment as to whether they would have continued the medication in everyday clinical practice.

- 1) Gastric or duodenal ulcer within the past 3 months
- 2) Pathological hypersecretory conditions
- 3) Gastro-esophageal reflux disease with exacerbations within the last 3 months not responsive to H2 blockers and non-pharmacologic techniques
- 4) Erosive esophagitis
- 5) Recurring symptoms recently associated with severe indigestion within the last 3 months not responsive to H2 blocker or non-pharmacologic techniques
- 6) Helicobacter pylori eradication
- 7) Dual antiplatelet therapy
- 8) Antiplatelet therapy with anticoagulants
- 9) Antiplatelet or anticoagulant therapy with history of previous complicated ulcer
- 10) Antiplatelet or NSAID with two of: concomitant systemic corticosteroids, age over 60, previous uncomplicated ulcer, concomitant NSAID or antiplatelet/anticoagulant.

If a patient had a gastrointestinal bleed and was treated at another hospital and this was not included in their medical history admission note, this indication could have been missed. However, this is very unlikely as the health care system almost always routes patients back to the hospital where they have been admitted within the past year.

## References

1. Sung JJ, Chung SC, Ling TK, et al. Antibacterial treatment of gastric ulcers associated with *Helicobacter pylori*. *N Engl J Med*. 01/19 1995;332(3):139-142.
2. Lau JY, Sung JJ, Lee KK, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *N Engl J Med*. 08/03 2000;343(5):310-316.
3. Chey WD, Wong BCY. American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. *Am J Gastroenterol*. 08/ 2007;102(8):1808-1825.
4. Lanza FL, Chan FKL, Quigley EMM. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol*. 03/ 2009;104(3):728-738.
5. Rostom A, Moayyedi P, Hunt R. Canadian consensus guidelines on long-term nonsteroidal anti-inflammatory drug therapy and the need for gastroprotection: benefits versus risks. *Aliment Pharmacol Ther*. 03/01 2009;29(5):481-496.
6. van Vliet EPM, Steyerberg EW, Otten HJAM, et al. The effects of guideline implementation for proton pump inhibitor prescription on two pulmonary medicine wards. *Aliment Pharmacol Ther*. 01/ 2009;29(2):213-221.
7. Lai KC, Lam SK, Chu KM, et al. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. *N Engl J Med*. 06/27 2002;346(26):2033-2038.
8. Pham CQ, Regal RE, Bostwick TR, Knauf KS. Acid suppressive therapy use on an inpatient internal medicine service. *Ann Pharmacother*. Jul-Aug 2006;40(7-8):1261-1266.