

**Research Assessment Exercise 2020**  
**Impact Case Study**

**University:** The Chinese University of Hong Kong

**Unit of Assessment (UoA):** 3 (Clinical Medicine)

**Title of case study:** Acid suppression in the treatment and prevention of peptic ulcer bleeding

**(1) Summary of the impact** (indicative maximum 100 words)

Peptic ulcer bleeding (PUB) is one of the most common medical emergencies. Mortality from PUB varies between 4 to 10%. This occurs mostly in patients with further bleeding. Endoscopic treatment followed by acid suppression has reduced recurrent bleeding, need for surgery and death. In patients who continue to require antiplatelet drugs and non-steroidal anti-inflammatory drugs, we have shown that in addition to *Helicobacter pylori* eradication, maintenance acid suppression reduced risk of further bleeding. In the past two decades, we have seen major reduction in rates of PUB, surgery and mortality from this complication.

**(2) Underpinning research** (indicative maximum 500 words)

In the management of bleeding peptic ulcers, endoscopic therapy in combination with intravenous injection of a high dose proton pump inhibitor (PPI) to render intragastric pH neutral, reduced the rate of recurrent bleeding by 4 fold when compared to only using endoscopic therapy (Lau NEJM 2000). In a subsequent randomized trial, the same regime of PPI, when administered to patients awaiting endoscopy, down-staged endoscopic bleeding stigmata in bleeding ulcers and reduced the need for endoscopic therapy (Lau NEJM 2007).

Among patients infected with *Helicobacter pylori* and with a history of upper gastrointestinal bleeding who were taking either low dose aspirin or non-steroidal anti-inflammatory drugs (NSAID), the eradication of *H. pylori* was found to be equivalent to treatment with a PPI in those on aspirin, but inferior to PPI treatment in those on NSAIDs (Chan NEJM 2001).

In patients who required long-term use of non-steroidal anti-inflammatory drugs, the addition of PPI compared favorably to selective COXIB-inhibitors in the prevention of ulcer bleeding (Chan NEJM 2002).

In arthritis patients starting on long-term NSAID treatment who had a history of peptic ulcer or dyspepsia, screening and treatment for *Helicobacter pylori* infection significantly reduced the risk of peptic ulcer disease (Chan Lancet 2002).

Among patients with a history of aspirin-induced ulcer bleeding who continued to require aspirin for cardiovascular protection, the combination of aspirin and PPI was superior to using clopidogrel in the prevention of recurrent ulcer bleeding. (Chan NEJM 2005).

**(3) References to the research** (indicative maximum of six references)

- i. Lau JYW, Sung JJY, Lee KKC, Yung M, Wong SKH, Wu JCY et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med 2000; 343(5): 310-316.
- ii. Chan FKL, Chung SCS, Suen BY, Lee YT, Leung WK, Leung VKS et al. Preventing recurrent upper gastrointestinal bleeding in patients with *Helicobacter pylori* infection who are taking low-dose aspirin or naproxen. N Engl J Med 2001; 344(13): 967-973.

- iii. Chan FKL, Hung LCT, Suen BY, Wu JCY, Lee KC, Leung VKS et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. *N Engl J Med* 2002; 347(26):2104-2110.
- iv. Chan FKL, To KF, Wu JCY, Yung MY, Leung WK, Kwok T et al. Eradication of *Helicobacter pylori* and risk of peptic ulcers in patients starting long-term treatment with non-steroidal anti-inflammatory drugs: a randomised trial. *The Lancet* 2002; 359(9300): 9-13.
- v. Chan FKL, Ching JYL, Hung LCT, Wong VWS, Leung VKS, Kung NNS et al. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. *N Engl J Med* 2005; 352(3): 238-244.
- vi. Lau JY, Leung WK, Wu JCY, Chan FKL, Wong VWS, Chiu PWY et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. *N Engl J Med* 2007; 356(16): 1631-1640.

**(4) Details of the impact** (indicative maximum 750 words)

The following policies for managing PUB were informed by our research findings.

The use of a high dose PPI after and before endoscopic therapy is recommended in management guidelines of several countries, including the USA, Canada, UK and other European nations. In two published International Consensus Guidelines, the use of a high dose PPI continues to be recommended.

The Maastricht-2 Consensus, for the past two decades, has continued to recommend the eradication of *Helicobacter pylori* before starting patients on long-term NSAID.

The American College of Rheumatology has recommended co-therapy with PPI in high risk patients on NSAIDs or the use of COX-2 inhibitors.

The Joint expert consensus (ACCF/ACG and American Heart Association) revised its former recommendation (i.e., replacing clopidogrel with aspirin in patients with aspirin related peptic ulcer bleeding) to using PPI in conjunction with aspirin.

Having influenced clinical practice by the results of our randomised clinical trials, clinical outcomes have also changed across the world. There has been a significant reduction in rate of further bleeding both in the acute treatment and in long-term prophylaxis against ulcer occurrence and bleeding complications. Over past two decades, emergency ulcer surgery has declined to less than 1% of those admitted with bleeding. Mortality from PUB has declined. We have also seen safer prescription practices in high-risk patients who continue to require aspirin and NSAIDs. Hospitalisation for PUB has declined by at least 2 fold worldwide.

**(5) Sources to corroborate the impact** (indicative maximum of 10 references)

- i. Peter Malfertheiner, Francis Megraud, Colm A O'morain, John Atherton, Anthony TR Axon, Franco Bazzoli, Gian Franco Gensini, Javier P Gisbert, David Y Graham, Theodore Rokkas, Emad M El-Omar, Ernst J Kuipers, European Helicobacter Study Group. [Management of Helicobacter pylori infection—the Maastricht IV/Florence consensus report](#). *Gut* 2012; 61(5): 646-664.
- ii. Deepak L Bhatt, James Scheiman, Neena S Abraham, Elliott M Antman, Francis KL Chan, Curt D Furberg, David A Johnson, Kenneth W Mahaffey, Eamonn M Quigley, Robert A Harrington, Eric R Bates, Charles R Bridges, Mark J Eisenberg, Victor A Ferrari, Mark A Hlatky, Sanjay Kaul, Jonathan R Lindner, David J Moliterno, Debabrata Mukherjee, Richard S Schofield, Robert S Rosenson, James H Stein, Howard H Weitz, Deborah J Wesley.

- [ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents](#). Journal of the American College of Cardiology 2008; 52(18): 1502-1517.
- iii. Peter Malfertheiner, Francis KL Chan, Kenneth EL McColl. [Peptic ulcer disease](#). The Lancet 2009; 374(9699): 1449-1461.
  - iv. Joseph JY Sung, James YW Lau, Graeme Paul Young, Y Sano, HM Chiu, JS Byeon, Khay-Guan Yeoh, KL Goh, J Sollano, R Rerknimitr, Takahisa Matsuda, KC Wu, Simon Ng, Suet Yee Leung, Govind Makharia, Vui Heng Chong, KY Ho, Durado Brooks, DA Lieberman, Francis KL Chan. [Asia Pacific consensus recommendations for colorectal cancer screening](#) Gut 2008; 57(8): 1166-1176.
  - v. Alan N. Barkun, Marc Bardou, Ernst J. Kuipers, Joseph Sung, Richard H. Hunt, Myriam Martel, Paul Sinclair, for the International Consensus Upper Gastrointestinal Bleeding Conference Group. [International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding](#). Annals of Internal Medicine 2010; 152(2): 101-113.
  - vi. [Acute upper gastrointestinal bleeding in adults](#)
  - vii. James Y W Lau, Alan Barkun, Dai-ming Fan, Ernst J Kuipers, Yun-sheng Yang, Francis K L Chan. [Challenges in the management of acute peptic ulcer bleeding](#). The Lancet 2013 Jun 8; 381(9882): 2033-2043.
  - viii. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. [Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update](#). Arthritis & Rheumatism 2000; 43(9):1905-1915.
  - ix. Thomas J. Schnitzer. [Update on guidelines for the treatment of chronic musculoskeletal pain](#). Clinical Rheumatology 2006; 25(Suppl 1): 22-29.