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Title: Cost-effective Analysis of Proton Pump Inhibitors in Long-term Management of Gastroesophageal Reflux Disease: A Narrative Review

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Abstract: Background: Gastroesophageal reflux disease (GERD) is a common gastrointestinal disorder that results from regurgitation of acid from the stomach into the esophagus. Treatment available for GERD includes lifestyle changes, antacids, histamine-2 receptor antagonists (H2RAs), proton pump inhibitors (PPIs), and anti-reflux surgery. Aim: The aim of this review is to assess the cost-effectiveness of the use of PPIs in the long-term management of patients with GERD. Method: We searched in PubMed to identify related original articles with close consideration based on inclusion and exclusion criteria to choose the best studies for this narrative review. The first section compares the cost-effectiveness of PPIs with H2RAs in long-term heartburn management. The other sections shall only discuss the cost-effectiveness of PPIs in 5 different strategies, namely, continuous (step-up, step-down, and maintenance), ondemand, and intermittent therapies. Results: Of 55 articles published, 10 studies published from 2000 to 2015 were included. Overall, PPIs are more effective in relieving heartburn in comparison with ranitidine. The use of PPIs in managing heartburn in long-term consumption of nonsteroidal anti-inflammatory drug (NSAID) has higher cost compared with H(2)RA. However, if the decision-maker is willing to pay more than US\$174 788.60 per extra quality-adjusted life year (QALY), then the optimal strategy is traditional NSAID (tNSAID) and PPIs. The probability of being cost-effective was also highest for NSAID and PPI cotherapy users. On-demand PPI treatment strategy showed dominant with an incremental cost-effectiveness ratio of US\$2197 per QALY gained and was most effective and cost saving compared with all the other treatments. The average cost-effectiveness ratio was lower for rabeprazole therapy than for ranitidine therapy. Conclusion: Our review revealed that long-term treatment with PPIs is effective but costly. To achieve long-term cost-effective approach, we recommend on-demand approach to treat heartburn symptoms, but if the symptoms persist, treatment with continuous step-down therapy should be applied.

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