Employers Need to Have a Wider Horizon Than Drug Costs Alone When Considering the Implementation of Health Care Intervention Programs

To the Editor:

The study of Mabasa and Ma in a previous issue of *JMCP* reports on the successful utilization and drug cost savings for proton pump inhibitors (PPIs) in a Canadian employer-sponsored drug plan that implemented a therapeutic maximum allowable cost (MAC) program. Any successful health care intervention program aiming to maximize “value for money” is praiseworthy, especially for diseases that are associated with a high prevalence and/or have high treatment costs. From an employer perspective, however, the current study is associated with a number of fundamental flaws that are essential to point out if similar intervention programs are to be planned and implemented.

Firstly, the study methodology does not allow for a valid comparison of trends between the MAC program and the reference group, since no attempts were made to adjust for the effects of the study groups varying considerably during the study period. For example, the number of patients in the reference group increased by more than 40% during the study period compared with a 21% increase in the MAC group (Table 3 in the authors’ article).

Another important oversight was the failure to assess the effect of drug substitution on the quality of treatment (a fundamental aspect of determining the effects of any medical intervention). Indeed, if quality of treatment is decreased as a result of such substitution, this may have negative effects on nondonor health care utilization such as increased number of physician visits, investigations performed, or even hospitalizations. These generate costs that the Canadian community ultimately has to pay for. In a report issued by a Canadian patient organization, for example, the authors claim that PPI substitution programs are ineffective, have a negative impact on quality of patient care, and ultimately lead to increased overall health care costs.

A third limitation of the study is that it assumed that, at the stated doses, the PPIs provide no therapeutic advantage over one another. According to the Canadian patient organization, this ignores the fact that patients respond differentially to different PPIs for many reasons, including drug interactions, side effects, variations in metabolism, and inappropriate dosage. Indeed, numerous studies have shown differences in effectiveness between alternative PPI treatments, not only between patient management strategies but also in relation to utilization patterns with regard to which patients receive PPI treatment, which type of PPI, and at which doses.

It is notable that patients in the MAC group who did not wish to switch to the cheapest (reference) PPI had to either pay the difference for their PPI or their physician had to apply for special authorization for full reimbursement (i.e., based on clinical judgment, the nonpreferred product would be beneficial to the patient). These are difficult barriers to overcome from a patient perspective, and it is interesting that around two thirds of drug cost savings in the MAC program were due to patients stopping PPI treatment. Moreover, it is notable that, within the wider Canadian Therapeutic Substitution policy and despite prescription barriers, around 25% of patients who did switch to the cheapest PPI were subsequently switched back to their previous PPI treatment following a special authorization. Although this has not been studied, it is very likely that the MAC program led to a varying degree of increased symptom burden for patients who stopped PPI treatment as well as for patients who were switched.

While the authors do not provide such information, it is highly likely that a significant proportion of PPI use was for the treatment of gastroesophageal reflux disease (GERD). In this regard, a large U.S. database study comparing costs for GERD cases (n = 11,653) versus a control group (n = 259,616) found that only 17% of total costs were for prescription drugs; the remainder was accounted for by direct medical costs such as physician visits and investigations, etc. (65%) and indirect employer costs for sick leave, short- and long-term disability, and workers’ compensation (19%). Consequently, focusing on drug costs alone ignores a significant proportion of health care costs relating to GERD and other acid-related diseases. Moreover, the MAC approach does not capture the largest cost of GERD for employers, namely the impact of GERD symptoms or symptoms of other acid-related disorders on reduced productivity while at work. Indeed, GERD symptoms interfere with work not only through disturbed sleep and daytime tiredness but also because they interrupt physical activity.

A recent systematic review of studies using patient-reported data in general working populations indicates that GERD causes a reduction in productivity while at work of around 10% on average. Considerably higher levels of reduced work productivity have been observed in untreated patients with troublesome GERD symptoms, in those with GERD-related sleep disturbance, for example, the mean reduction in productivity was up to 40%. PPI therapy to resolve GERD symptoms helps to address this burden and improves work productivity. Further, a case-control study using objective measurements of hourly and annual at-work productivity confirms that GERD, indeed, has a significant impact on productivity while at work, which supports validity of patient-reported productivity assessments. Assuming an average reduction in at-work productivity of around 10% in the PPI study population (281,951 + 374 = 282,325) and a 40-hour work week, this would correspond to more than 50 million work hours per year in lost at-work productivity due to GERD. Indeed, even small improvements in work productivity are relevant from an employer perspective, with a 2.5% improvement corresponding to 1 hour per patient over a 40-hour work week. These issues are clearly not addressed by a MAC program that focuses on drug costs alone.

In conclusion, PPI and other drug-switching programs need...
to consider the wider horizon of the implications of switching for quality of treatment and effects on costs other than for prescription drugs alone. Consequently, drug costs for PPIs should probably not be the primary target for interventions from an employer perspective.

Peter Wahlqvist, MSc
Senior Health Economics Scientist
Health Economics & Outcomes Research
AstraZeneca R&D Molndal
S-431 83 Molndal
Sweden
Tel: +46 31 776 2345
peter.wahlqvist@astrazeneca.com

DISCLOSURE
The author discloses that he is an employee of AstraZeneca, the manufacturer of the proton pump inhibitor esomeprazole.

REFERENCES
17. Wahlqvist P, Brook RA, Campbell S, et al. Objective measurement of hourly and annual productivity while at work in employees with gastroesophageal reflux disease (GERD) compared with employees without GERD. Gastroenterology. 2006;130(4 suppl 2):AT1005.

The Authors Respond:
We appreciate the opportunity for additional dialogue on the effect of a therapeutic maximum allowable cost (MAC) program on the cost and utilization of proton pump inhibitors (PPIs) in an employer-sponsored drug plan in Canada.1 Although the letter by Wahlqvist appears well intentioned, his comments misrepresent some of the main points of the MAC program and can be misleading due to the inadequate presentation and interpretation of the evidence on PPIs.

A fundamental concept in the utilization of a MAC program is that the drugs within a drug class be considered therapeutically interchangeable. The main criticism by Wahlqvist concerns the interchangeability between PPIs, and he argues that there are differences in effectiveness between alternative PPI treatments. It is important to highlight that the data cited by Wahlqvist were mainly comparing esomeprazole to other PPIs. These studies may be considered biased toward esomeprazole and lacking in the strength of evidence because these studies were designed to utilize 2- to 4-fold higher equivalent doses of esomeprazole than the comparator drug.2 Peer-reviewed meta-analysis comparing the efficacy of various PPIs such as by Vergara et al.3 on triple therapy Helicobacter pylori eradication and by Edwards et al.4 for the acute treatment of reflux esophagitis, contradict the argument by Wahlqvist. These meta-analyses are considered a higher level of evidence compared with randomized controlled trials.

Furthermore, the Therapeutic Initiatives group of Canada concluded that no trials have demonstrated an intrinsic therapeutic advantage among PPIs at equivalent doses.5 In addition, the U.S. Food and Drug Administration (FDA), upon review of the evidence on esomeprazole, concluded that
esomeprazole affords rates of healing that are comparable to other PPIs, including omeprazole, and share the same overall acceptable safety profile.\textsuperscript{9}

Other employee benefits providers such as CIGNA HealthCare provide similar coverage of PPIs and consider PPIs to be similar in efficacy and safety.\textsuperscript{6} In their coverage position statement, they mentioned that there are only minor pharmacokinetic differences between PPIs, and these differences are not clinically meaningful. They also mentioned that the only clinically significant interaction among all PPIs is with omeprazole and warfarin. These can be easily managed by adjusting the dose of warfarin and monitoring the international normalized ratio (INR).\textsuperscript{6} Therefore, based on the best available evidence to date, PPIs can be considered interchangeable, and the evidence supports the use of a therapeutic MAC program.

Wahlqvist suggested that we committed an important oversight by failing to assess the effect of drug substitution on the quality of treatment. However, there is evidence suggesting that this type of program does not have a significant impact on clinical outcomes and provides economical advantages. A recent study of the British Columbia therapeutic substitution policy on PPIs showed that there was no increase in monthly hospitalization rates of gastrointestinal hemorrhage or major peptic ulcer disease (PUD) after patients switched to the reference drug, rabeprazole.\textsuperscript{7} Also, the monthly rates of office visits for gastroesophageal reflux disease (GERD), PUD, or gastritis did not significantly change, and total spending on these office visits were similar. This program led to a savings of Can $2.9 million after 6 months from policy change.\textsuperscript{7}

One comment by Wahlqvist was on the larger proportionate increase in the number of PPI patients in the non-MAC reference group in year 3 compared with the MAC group. This was caused by larger growth in non-MAC versus MAC employer groups over the 2-year period from the year ending May 31, 2003, compared with the year ending May 31, 2005, and would not affect the primary utilization measures of the number of claims, days of therapy, and allowed drug cost per patient per year.

We agree with Wahlqvist that GERD can significantly impact a person’s quality of life. This was not disputed in our study. We also agree that patient-specific factors need to be considered when selecting an appropriate PPI. In general, when selecting a medication to use for a patient, the clinician needs to consider, in specific order, the medication’s efficacy, safety profile, the ease of use to facilitate compliance, and, finally, the cost of the medication. For PPIs, the efficacy and safety profile of the available products is considered to be similar and all are taken once daily. Therefore, the cost would be considered the deciding factor when choosing a PPI. Since rabeprazole has the lowest drug cost, it would be appropriate to select this alternative first.

In conclusion, according to evidence-based practice, PPIs are an ideal drug class to utilize in a therapeutic MAC program and their use can lead to substantial drug cost savings without evidence of adverse health outcomes. We recommend that other types of drug classes that fit a similar profile be incorporated in a therapeutic MAC program.

Vincent H. Mabasa BScPharm, ACPR, PharmD
Clinical Pharmacy Practice Leader
Pharmacotherapeutic Specialist—Critical Care
Fraser Health Authority, Royal Columbian Hospital
330 E. Columbia St., New Westminster, British Columbia,
Canada V3KL 3W7
mabasa@interchange.ubc.ca

Johnny Ma, BScPharm
Manager, Health Plan Management
ESI Canada
Mississauga, Ontario, Canada

DISCLOSURES
No outside funding supported the study in the referenced article. Johnny Ma is an employee of the pharmacy benefits manager that administered the maximum allowable cost program described in the article. The authors disclose no potential bias or conflict of interest relating to the article.

REFERENCES

Letters to the Editor
JMCP welcomes letters that serve to clarify subjects published in previous issues of the Journal or regarding subject matter of interest to managed care pharmacists. Letters in JMCP are not peer reviewed but are subjected to editorial review. Letters should be prepared in a word processing program, preferably Microsoft Word, and submitted electronically at jmcp.msubmit.net. See www.amcp.org for details.