Reviewer's report

Title: Cost-minimization analysis of XELOX and FOLFOX4 for treatment of colorectal cancer to assist decision-making on reimbursement

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Reviewer: Shanlian Hu

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Comments on the paper “CMA of XELOX and FOLFOX4 for treatment of colorectal cancer to assist decision-making on reimbursement).

The objective of paper is to compare the cost-consequence analysis of two regimens between capecitabine (Xeloda) +oxaliplatin and 5–fluororuracil/folinic acid +.oxaliplatin. Cost minimization analysis method was adapted by using Garrison’s model. The parameters of effectiveness were collected from literatures and cost data were used from Hong Kong government Hospital Authority and hospital medical records. My fundamental question is that without clinical trial, whether the modelling evaluation results are accepted by Hong Kong Hospital Authority during policy-making?

The paper shows the value of innovative drug – Capecitabine (Xeloda). Although the purchase price of capecitabine is higher, the total cost of XELOX regimen per patient is cheaper than that of FOLFOX4 regimen either total expected cost or unscheduled cost. It has offered the evidence to support the XELOX regimen could be reimbursed by HA formulary in the future.

The paper clearly acknowledge and disclosure the funding of study and possible interest conflict of some authors.

Discretionary revisions:

1. If possible, the authors could briefly describe the payment system in Hong Kong hospital. Because the average cost of bed-day and outpatient visits are valued based on fee schedule (expected), which are not the real cost occurred in the hospital.

2. The time horizon of the study was last for five years (2004-2008). Is discounting cost used in the analysis?

Minor essential revisions:

1. The societal costs are subjectively estimated. Do authors compare the real travel time and travel cost from questionnaire surveyed with the estimated ones.

2. Oxaliplatin as alkylateing agent sometimes causes severe allergic reaction. What kind of side effect has been happened during the treatment in this study?
3. To give the definition of unscheduled cost. Is unscheduled cost really caused by the side effects?

Major compulsory revisions:

1. The comparability analysis of demographical and clinical characteristics between two groups is listed in Table 1. The statistical significance of difference in each item should be calculated, especially, age and some outcome results (e.g., number of metastatic sites, the percentage of patients had liver metastases and the status of survival).

2. Are those differences influenced on the resource use and costs?

3. The disadvantage of the study is using the expected costs or health resource rather than the real cost and resource used paid by patients, or record from patient’s medical history. It is hardly convincing the conclusion that FOLFOX4 is really 37%-49% more expensive than XELOX.

4. Modelling requires details. What kind of effectiveness (or efficiency) was used in US Garisson’s model from the literature? Do those preferred outcome measure also exist in author’s study? If using those data from Hong Kong setting what are the CMA results?

5. Authors choose the full dosage, removal oxaliplatin and different perspective of costs to do an univariate sensitivity analysis, what respective ranges are chosen to check the robustness of results should be mentioned in the paper. Oxaliplatin is a part of two regimens, can we removal it as a factor in sensitivity analysis?

6. As mentioned in the paper, the cost of capecitabine is quite different between US and Hong Kong. the cost of capecitabine, perhaps, could be also changed in one way analysis

7. The limitation of the study should be described at the end of paper.

The paper will be a reference for those countries where only a few capacity building of pharmacoconomic study. The modelling method now become an alternative one for some innovative drugs, that is outcomes data adopted from international multi-center clinical trial, and cost data from local setting. However, policy makers are usually reluctant to accept it at least in China.

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Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have not competing interests