Reviewer’s report

Title: Cost-effectiveness of family-history based colorectal cancer screening.

Version: 2
Date: 27 January 2014

Reviewer: Joseph Sung

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COMPULSORY REVISIONS

1) Overall study question and the methodology

- Cost effective analysis in the emerging field of CRC screening is an important question especially in increased risk individuals whereby more intensive screening has been recommended. This paper aims to inform the readers that "family-history based colorectal cancer screening" is cost effective. To make this statement sound, it is more valid to compare "family-history based screening" versus whole population screening instead of various screening methods in patients of moderate risk then make a final comment that the results are similar to other previous cost-effectiveness analyses, if not more cost effective. Currently, what the authors have done is to multiply the incidence of each transition state (e.g. adenoma and cancer rate) by 4 after referring to some published reference, then conclude that colonoscopy every 5 years is the most cost-effective option. Current rationale also needs discussion.

- Most published literature reported a 2-3 fold increased risk of CRC in those with a family history of CRC (John's et al. 2001; Ng et al, 2013; Butterworth et al. 2006), whereas the authors have used a liberal estimate of 3-6-fold increased level of risk compared with the general population

- What is the proportion of patients in the Australian population that have cancer diagnosed before the age 55 as this would be the single most important factor to determine if family-history based screening is cost effective (is it stated in the text?)

- Why did they choose to start screening at the age of 50 in this group? Current guidelines suggest starting screening at 40 or 10 years younger than diagnosis of index case). If the authors target age 55 as the CA colon diagnosis age, the screening should start earlier in this increased risk group

- How did they account for false negative screening results?

2) Details on the methodology
Most studies generally select the discount rate of 3% - what is the rationale of selecting the discount rate per year of 5%?

They include screening until the age of 90 - isn’t this a bit too long?

For the cost of treatment of CA colon of different duke's staging - they really cannot make that an average cost/year, because usually, the cost of surgery or chemotherapy would be included in the first year than in the second year, and there should be a transition state called surveillance after that.

3) Sensitivity analysis

From the manuscript, the authors have included the compliance of screening and levels of CRC risks. Sensitivity analysis is performed to ensure that even if the % of a factor is largely deviated, the hypothesis or the statement still hold true. I believe a lot more factors need to be studied, including:

- Cost of colonoscopy, cost of FOBT
- Proportion of population with a diagnosis of CA colon before the age of 55
- Age of start screening

Only single factor sensitivity analysis has been performed in this study but not multiple factors.

MINOR ESSENTIAL REVISIONS

Page 6: Under screening programmes: Screening according “to” (missing word) the current....

Only direct cost is included in this paper whereas the indirect cost e.g. productivity loss due to hospitalization, clinic visits, transportation have not been included, how about complication of screening and treatment of complication etc...

- Utility is not used i.e. they only count the life year saved, but not QALY, although this is still considered acceptable

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests