

February 7, 2014

Dear Editor World Journal of Gastrointestinal Oncology

Please find enclosed the edited manuscript in Word format (file name: Harms and side effects of colon cancer surveillance 5.0.doc).

Title: Invited review: Do the benefits outweigh the side effects of colorectal cancer follow-up?

Author: Augestad KM, Rose J, Crawshaw B, Cooper G, Delaney CP

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 7602

The format has been updated and revision has been made according to the suggestions of the reviewer:

Reviewer 1

Thank you for the opportunity to review this manuscript. In general it is a nice invited review. There are several small suggestions you may consider:

1. Please re-review to correct the grammatical and spelling errors in the manuscript [(i.e., "intensive follow-up is 5-10 % by, ") --what is the "by" for?; diagnosls vs diagnosis] These are easy to fix, though distracting for the reader. Re-run your spell checker too.

Reply: Thank you for informing us. We have, to the best of our knowledge, corrected the spelling mistakes.

We have corrected the abstract text to:

.....meta-analyses have suggested an overall survival improvement of 5-10% by intensive follow-up."

2. Introduction of acronyms should first be spelled out (QoL in Core tips)).

Reply: We have corrected this and acronyms are spelled out.

Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

3. When you introduce the concept that preventative programs can harm patients, it would be nice to place a few reasons how (unneeded surgery/procedures, costs, etc).

Reply: We absolutely agree with this point of view, and have already written something about this in the introduction part, i.e.

“Secondly, the side effects of CRC follow-up must be compared to the survival benefits. Well-known side effects of preventive programs are a) over-diagnosis, b) somatic complications caused by testing, c) negative psychological consequences of follow-up, and d) impact of a false positive (leading the patient to believe that he or she has recurrent disease) or false negative (leading to a potentially diagnostic delay) tests. “

4. What about the negative side effects (on the other side of the argument) of no surveillance or prolonged intervals and the patients that stress out without knowledge? You mention the negative psychological impact with over testing and waiting for the results, but it is clear it works both ways--do we have an obligation to address those people too?

Reply: Absolutely. We have added a separate section in the paper addressing these issues, i.e.

“ There is no existing evidence that participation in a follow-up program leads to increased personal well-being. Some researchers have investigated the psychological effects of colorectal cancer follow-up [19-22]. None of the resulting studies have found improvement in the patient QoL with follow-up.”

5. Of note, there has been a systematic review of this topic in the Journal of Ca by Patrick Young and colleagues.

Reply: Thank you for telling us about this interesting paper. We have included the paper in our review and cited it in the reference list.

6. In this paper, remember not everyone is aware of what constitutes intensive vs. standard and this should be in the introduction.

Reply: We agree, after having reviewed the international literature, there exist controversies on how to define an intensive follow-up program. We have added the following paragraph in the introduction:

Most national follow-up programs recommend intensive follow-up. However, there exist controversies on how to define an “intensive” follow-up program. This is mirrored in the fact that there does not exist one similar national follow-up program. In general, a intensive follow-up program consists of regular testing (usually every 3 months the first two years) and consultation, whereas a low intensive is defined as no testing and regular consultations.

7. Dividing up into colon and rectal is also important as there are things described in rectal that may not be applicable to colon (ERUS/MRI) etc.

Reply: We agree and have added a paragraph regarding this, i.e.

“Most national follow-up programs make a distinction between rectal cancer and colon cancer surveillance. This is reflected in the difference of recommended radiological test modalities.”

8. I believe reassurment in figure 2 is spelled wrong.

Reply: This is corrected

Reviewer 2

The authors should present an unbiased summary of the current understanding of this topic. Are the benefits worth the harms and costs?

Reply: Thank you for your point of view. We believe this is a balanced and unbiased summary of the current understanding of CRC follow-up.

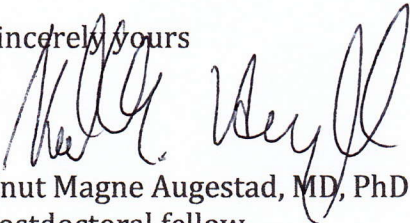
Will all clinically important outcomes considered? This issue should be discussed.

Reply: This is absolutely right; we have included all clinically important outcomes in our manuscript.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Gastrointestinal Oncology.

Sincerely yours



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