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Dear World Journal of Gastrointestinal Oncology,

Please find attached the revised manuscript for the Review Article. Of note, this manuscript was designed as a Descriptive Review. While it was not designed as a formal Systematic Review, a thorough literature review was performed by the authors.

The three reviewers comments have been carefully considered and the revised manuscript edited to incorporate their comments (changes visible via Track Changes function).

(i) Comments of Reviewer Code 02445553:

A well written Review. 1. However, it should be updated by mention and discussion of two recent publications: Tarantino et al. Ann Surg 1015;262:112-120 Ishihara et al. Int J Colorect Dis 2015;30:807-812 Both articles deal also with symptomatic patients, but use modern statistical analys. The former is a very large register study. 2. The secondary endpoint "pain" is poorly discussed. It should be emphasized that, unless primary resection of rectal cancer is performed, there is a risk for non treatable pain, secretion and bleeding in late stages of the patient's life.

Authors's Response:

1. The Discussion has been updated to include both the aforementioned papers from 2015, which provide further population registry data to support primary tumour resection, but also identifies the limitations of these methods. 2. The Discussion has been revised to include reference to symptomatic complications, particularly pain, as a significant burden.

No quality of life data exists in the literature for this patient population. In the palliative setting, patient reported outcomes, both global quality of life (including functional outcomes) plus symptomatic scores are essential. Treatment options need to be evaluated with respect to their impact on symptoms which can significantly impair patients' quality of life, such as pain, diarrhoea, tenesmus, faecal incontinence, etc. It is very likely that symptomatic local complications, particularly in rectal cancer patients, were under-reported in the included studies, given their retrospective nature. Pain from locally advanced rectal cancer can be an extremely debilitating complication, and other local complications can significantly impede social, emotional and physical functioning. Future studies should focus on global and symptomatic quality of life outcomes, and indeed most currently recruiting RCTs do have these as a secondary endpoint. (Revised manuscript, Page 16)

(ii) Comments of Reviewer 2455208:

A very interesting article, setting important clinical dilemmas. Due to the nature of the problem and the lack of reliable data, one should not expect a straightforward answer. Languagewise is at the level of a native English speaker. The construction is also according to widely accepted guidelines for systematic reviews (like PRISMA) The results, although based on non-solid data, show that as chemotherapy advances, "heroic" operations of the past, gradually loose ground. However, the most important drawback is that colon and rectal cancers were studied as an entity. This is not only because radiotherapy is a very important adjuvant in rectal tumours, but also because from a technical point of view, a rectal T4 tumour is totally different from a colon T4. There is no doubt that authors acknowledge and describe this issue in the manuscript. Under the light of the above, if the initial dilemma could be extended to "surgical or non-surgical management of stage IV colorectal cancer", a distinction between colonic and rectal could be critical

Author's Response:

The Reviewer's comments are very valid. Unfortunately, the original papers did not, in the most part, differentiate between colonic and rectal tumours, and therefore it is impossible to make this distinction, and tease out the differences, in this Review article. The use of up front radiotherapy as a primary treatment modality in rectal cancers was poorly reported, and we are thus unable to include this treatment modality ("non-surgical management") in the scope of the Review Article. This may largely be due to the fact that, for asymptomatic primary tumours, radiotherapy would not be indicated for "symptomatic" issues, and reserved as a salvage therapy for progressive symptomatic disease, rates of which were reported and included in the article as part of complication rates in the Primary Chemotherapy group. Alternatively, "neoadjuvant" Radiotherapy +/- Chemotherapy followed by surgery would be included in the cohort designated to Primary Tumour Resection. The above omission has been highlighted in the Discussion of the revised manuscript.

(iii) Comments of Reviewer 45997

In this review paper, Wilkinson and colleagues evaluated management of asmptomatic primary tumours in stage IV colorectal cancer, referring previous studies. This is a carefully done study and the findings are of considerable interest. I have no serious criticism regarding methodology, results and interpretation of the results.

Please do not hesitate to contact me with any questions or suggestions.

Dr Kate Wilkinson