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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastrointestinal Surgery

**ESPS Manuscript NO:** 4770

**Title:** Timing of Chemotherapy and Survival in Patients with Resectable Gastric Adenocarcinoma

**Reviewer code:** 02439559

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:19

**Date reviewed:** 2013-08-26 12:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

the following problems should be answered: 1, whether the patients with preoperative chemotherapy also receive postoperative chemotherapy? In general, it is better to preoperative chemotherapy combined with postoperative chemotherapy; 2, When does preoperative chemotherapy begin, how many times, chemotherapy dose? 3, Preoperative chemotherapy group were too little, it was not balanced compared with postoperative chemotherapy group, Too few patients will affect the reliability of the results. Please answer the above questions.



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastrointestinal Surgery

**ESPS Manuscript NO:** 4770

**Title:** Timing of Chemotherapy and Survival in Patients with Resectable Gastric Adenocarcinoma

**Reviewer code:** 02453874

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:19

**Date reviewed:** 2013-09-27 00:54

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Thank you for the opportunity to review this interesting manuscript by Dr Arrington et al.

Please find below my comments about the methods and the interpretations of this manuscript.

1. The most important question when reporting a null result, as in this manuscript, is what is the power of the study to identify a true difference. Please provide a power calculation for comparing neo-adjuvant and adjuvant regimens.
2. As you have mentioned you are not comparing preoperative chemotherapy with postoperative. The correct comparison is "at least preoperative chemo" with "postoperative chemo". Please revise your wording throughout and in the abstract so that your manuscript accurately reflects this comparison.
3. Please clearly specify your outcome and time scale in the methods section, as right now it is not stated clearly in the manuscript. For example: time to relapse/all cause death/ death attributable to malignancy since diagnosis/chemo/surgery.
4. Are your Log-rank test adjusted (for example using standardization) ? If not and considering the baseline differences among groups you should exert caution in interpreting the results of the Log-rank tests. Also, please report the results of the Log-rank test among stages II and III combined.
5. Please report the HRs and the P-values for all the comparisons mentioned in the results section. Also, please revise your table 3, as for example right now the HR/Pvalue for age in the multivariate analysis is not reported.
6. Please test the proportional hazards assumption for your Cox models and report it.
7. In the discussion you have mentioned that your results support the findings of the MAGIC trial. But you have not reported a comparison between the no chemo group and the perioperative chemo



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group (combined).

8. The largest part of your discussion is a detailed evaluation of the findings of the other studies, especially MAGIC and CLASSIC trials. Please discuss your own results and their implications more.

9. You have mentioned selection bias as a potential limitation of your study. Please explain more and clarify the exact mechanism and direction of selection bias that you think may have happened here.

10. I would suggest that instead of using an automatic stepwise approach for your multivariate analysis you perform a manual one to include some of the important variables such as tumor size and N-stage/Node-status a priori in your model. Although they may not be important for prediction, but your analysis here is evaluating the role of chemo timing and not predicting survival, and your treatment groups were significantly different according to these factors, so it is better that you include them in your models as adjustment variables.

11. As mentioned earlier, your comparison groups are not well defined which results to a dilution of the effect and bias towards the null. Additionally, you are not able to adjust for specific regimens used or completion of chemotherapy. All of these make your null results less reliable/conclusive, especially in the absence of a power calculation..



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### ESPS Peer-review Report

**Name of Journal:** World Journal of Gastrointestinal Surgery

**ESPS Manuscript NO:** 4770

**Title:** Timing of Chemotherapy and Survival in Patients with Resectable Gastric Adenocarcinoma

**Reviewer code:** 00069855

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:19

**Date reviewed:** 2013-09-30 13:45

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Dear Authors: Thank you for sending your manuscript that titled as "Timing of Chemotherapy and Survival in Patients with Resectable Gastric Adenocarcinoma" to World Journal of Gastrointestinal Surgery. The clinical data you presented is useful, the writing is fluent, and the ethics concern is met with the requirement of current publishing regulations. However, according to the title and statements in your manuscript, it will be better to also provide survival time for patients without chemical treatment, and then compare these data in either Figure 1 or Table 3. If you can provide the data, please also give t value and P value in Abstract and Results. Best Wishes,  
Sincerely Yours, Shuangteng He, M.D., Ph.D



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastrointestinal Surgery

**ESPS Manuscript NO:** 4770

**Title:** Timing of Chemotherapy and Survival in Patients with Resectable Gastric Adenocarcinoma

**Reviewer code:** 02569618

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:19

**Date reviewed:** 2013-10-02 19:35

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The perioperative therapy study in gastric cancer is complex and requires a serious methodology I think the purpose of the review study lacks serious design flaws. I do not think the approach that the authors can make any valid conclusions reached. Limitations: - Retrospective - Shows very heterogeneous. - Poor design of the groups: in the neoadjuvant group of patients may have received adjuvant therapy or not later - No information about the type of chemotherapy received. - No information on any adverse effects or treatment dropout One major flaw is that the authors have not considered the potential benefit of neoadjuvant therapy in reducing tumoral stage. Tumor stage has been established postoperatively, according to the histological study of the surgical specimen, Therefore, the analysis of the results is not valid