PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a multicenter, dual prospective and retrospective cohort study investigating timing of ileostomy closure after anterior resection for rectal cancer: The CLOSurE of Ileostomy Timing (CLOSE-IT) study
AUTHORS	Vaughan-Shaw, Peter G; Gash, Katherine; dams, Katie; Vallance, Abi; Pilkington, Sophie A; Torkington, Jared; Cornish, Julie

VERSION 1 – REVIEW

REVIEWER	Yves Panis Department of Colorectal Surgery Beaujon Hospital Clichy FRANCE
REVIEW RETURNED	28-Apr-2018

GENERAL COMMENTS	The study proposed is about the reason for delay stoma closure after sphincter-saving surgery for rectal cancer in UK. No major critic. Only one comment and one suggestion: I am not sure that the main reason for delay stoma closure is due to medical problem. Delay stoma closure is probably more a logistic problem of UK hospitals. In other words, I am not sure that after this study, it will be possible to improve this delay. Furthermore, as stated in the discussion section, authors recognize that there is a risk of some bias if some surgeons omit to give patients with very long delay of stoma closure In conclusion, and to be honest, I am not sure that this study will help a lot in the near future. Finally, it will be interesting to add a LARS score in the evaluation of the patient, because it will be interesting to see if it confirms or not the recent paper suggesting that function is worse if stoma closure is delayed.

REVIEWER	GH van Ramshorst VU Medical Center Netherlands
REVIEW RETURNED	28-Apr-2018

GENERAL COMMENTS	Introduction: -It would be my suggestion to change chemoradiotherapy into adjuvant chemotherapy, as it is uncommon for patients to undergo chemoradiotherapy after surgery. Methods: -Might I suggest to add that patients will be asked to give informed consent. Have you considered measuring health related quality of life and LARS questionnaires before and after closure in your design?

REVIEWER	Chris Oppong University Hospital Plymouth NHS Trust Plymouth. UK I am a member of the Association of Coloproctology of Great Britain and Ireland
REVIEW RETURNED	11-May-2018

GENERAL COMMENTS	1. This is a much-needed study in the UK. The objectives are convincing and achievable. 2. There is no doubt that cancer patients in the UK wait for an inordinate length of time for closure of their ileostomies. The enormous impact on their quality of life is well documented. 3. The study will provide vital information which will drive a change in surgical practice in the UK which will impact the lives of cancer survivors - a "game changer" 4. It may also provide a template for root cause analysis of other clinical practices in the UK which have not served patients well and inform the development of new relevant guidelines.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Comment 1: I am not sure that the main reason for delay stoma closure is due to medical problem. Delay stoma closure is probably more a logistic problem of UK hospitals. In other words, I am not sure that after this study, it will be possible to improve this delay.

Response: We agree that the majority of delays to ileostomy closure are related to logistics, including waiting lists for appropriate investigations, clinic and theatre time. However, we strongly believe that these issues are not insurmountable and are therefore worthy of attention. There is a recent emphasis within the NHS on improving not only cancer treatment, but the lives of those surviving cancer. There is a realisation that focusing not only on the treatment of cancer, but also on the after-effects of cancer survivorship is critical in improving outcomes for these patients, as detailed in the NHS Department of Health document '*Quality of life of cancer survivors in England: Report on a pilot survey using Patient Reported Outcome Measures*'[1]. Given the link between delay to closure and poorer quality of life, we believe that there will be both the necessary enthusiasm and resource allocation to embrace improved pathways which we aim to develop as part of this research. Indeed, a single study from the UK has shown that timely closure is possible despite the constraints of the NHS; Chand *et al.*, provided patients with an agreed date for closure on discharge from hospital after their index operation, with 67% of suitable patients undergoing closure by 12 weeks and 100% by 1 year [2]. We strongly believe that timely closure can be achieved given the evidence above and have now highlighted these two studies in the ***'Significance and outlook'*** section of our manuscript.

Comment 2: there is a risk of some bias if some surgeons omit to give patients with very long delay of stoma closure

Response: We have asked individual centres to provide data from consecutive patients. Furthermore the data collection will be performed by trainees, with less incentive to exclude certain patients. We believe these steps will minimise inappropriate exclusion of patients and the risk of bias although we acknowledge this cannot be completely prevented. However, data collected from the current study will

be cross-referenced against data from the national bowel cancer audit project in order to identify gross inconsistencies which could reflect bias. This approach has been added to the '***limitations'*** section of the manuscript.

Comment 3: it will be interesting to add a LARS score in the evaluation of the patient, because it will be interesting to see if it confirms or not the recent paper suggesting that function is worse if stoma closure is delayed.
Response: The current study focuses on the processes involved in timely closure to ileostomy and does not seek to repeat the recent work investigating quality of life after stoma delay. We believe that the most pressing need is to determine what factors influence time to closure and using a trainee-led multicentre study is the best way to achieve this. To this end a process where consent is not required will allow the greatest number of patients to be included. However we expect to obtain future ethical approval for a questionnaire to investigate patient reported outcomes. This would be of particular interest after interventions to reduce time to closure are actioned.

Reviewer 2
Comment 1: It would be my suggestion to change chemoradiotherapy into adjuvant chemotherapy, as it is uncommon for patients to undergo chemoradiotherapy after surgery.
Response: We have amended this in the introduction.

Comment 2: Might I suggest to add that patients will be asked to give informed consent. Have you considered measuring health related quality of life and LARS questionnaires before and after closure in your design?
Response: Please see response to **Reviewer 1, Comment 3**

Reviewer 3
Response: We are grateful for the supportive comments.

VERSION 2 – REVIEW

REVIEWER	Yves Panis Beaujon Hospital Clichy FRANCE
REVIEW RETURNED	24-Jun-2018

GENERAL COMMENTS	Paper can now be published in the revised form. Authors answered all the queries.