Arved Weimann\*

# Influence of nutritional status on postoperative outcome in patients with colorectal cancer – the emerging role of the microbiome

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# **Reviewers' Comments to Original Submission**

## **Reviewer 1: Wolfgang Schwenk**

Oct 19, 2017

Reviewer Recommendation Term:	Accept with Minor Revision	
Overall Reviewer Manuscript Rating:	70	
Custom Review Questions	Response	
Is the subject area appropriate for you?	5 - High/Yes	
Does the title clearly reflect the paper's content?	3	
Does the abstract clearly reflect the paper's content?	3	
Do the keywords clearly reflect the paper's content?	4	
Does the introduction present the problem clearly?	4	
Are the results/conclusions justified?	4	
How comprehensive and up-to-date is the subject matter presented?	4	
How adequate is the data presentation?	N/A	
Are units and terminology used correctly?	5 - High/Yes	
Is the number of cases adequate?	N/A	
Are the experimental methods/clinical studies adequate?	N/A	
Is the length appropriate in relation to the content?	5 - High/Yes	
Does the reader get new insights from the article? 3		
Please rate the practical significance.	5 - High/Yes	
Please rate the accuracy of methods.	N/A	
Please rate the statistical evaluation and quality control.	N/A	
Please rate the appropriateness of the figures and tables.	5 - High/Yes	
Please rate the appropriateness of the references.	5 - High/Yes	
Please evaluate the writing style and use of language.	4	
Please judge the overall scientific quality of the manuscript.	4	
Are you willing to review the revision of this manuscript?	Yes	

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#### **Comments to Authors:**

I would suggest changing the title of the manuscript to "Influence of nutritional Status on POSTOPERATIVE outcome in patients with colorectal cancer – the emerging role of the microbiome". Otherwise I do recommend publishing this overview in INNOVATIVE SURGICAL SCIENCES.

### **Reviewer 2: Dileep N Lobo**

Oct 30, 2017

Reviewer Recommendation Term:	Revise with Major Modifications	
Overall Reviewer Manuscript Rating:	65	
Custom Review Questions	Response	
Is the subject area appropriate for you?	5 - High/Yes	
Does the title clearly reflect the paper's content?	4	
Does the abstract clearly reflect the paper's content?	2	
Do the keywords clearly reflect the paper's content?	4	
Does the introduction present the problem clearly?	3	
Are the results/conclusions justified?	4	
How comprehensive and up-to-date is the subject matter presented?	3	
How adequate is the data presentation?	3	
Are units and terminology used correctly?	4	
Is the number of cases adequate?	N/A	
Are the experimental methods/clinical studies adequate?	2	
Is the length appropriate in relation to the content?	4	
Does the reader get new insights from the article?	4	
Please rate the practical significance.	3	
Please rate the accuracy of methods.	2	
Please rate the statistical evaluation and quality control.	N/A	
Please rate the appropriateness of the figures and tables.	4	
Please rate the appropriateness of the references.	4	
Please evaluate the writing style and use of language.	3	
Please judge the overall scientific quality of the manuscript.	3	
Are you willing to review the revision of this manuscript?	Yes	

#### **Comments to Authors:**

This is a well written review on the impact of nutritional status on outcome in patients with colorectal cancer. The authors have also included a section on the microbiome and discussed this in context with bowel preparation. I have the following comments:

1. The authors should state whether this is a systematic or a narrative review. A search strategy should be mentioned and criteria for inclusion and exclusion of studies should be stated.

2. The aim of the review should also be stated.

3. There seems to be some directly quoted text from the ESPEN Guidelines. If text is being quoted verbatim, perhaps, copyright permission from the publishers should be sought.

4. The names of bacteria should be mentioned in italics.

5. Introduction, para 1, line 2. The word "a" is repeated.

6. Introduction, para 1, line 8. "carcinogenesis" would be preferable to "cancerogenesis".

7. Introduction, para 2, line 4: Please provide a reference for the following statement: "Most patients with colorectal cancer undergoing surgery are overweight or obese.

8. Introduction, para 3: Enhanced Recovery After Surgery, should be explained to the uninitiated reader. Also the preferable references to introduce ERAS in Colorectal surgery are Clin Nutr 2012; 31: 783–800 and Clin Nutr 2012; 31: 801–16

9. Impact of nutritional status, para 1: What do the authors mean by "functional status and dependency"?

10. Serum albumin – the authors should emphasise that serum albumin is more an indicator of inflammatory status and fluid balance rather than nutritional status.

11. Carbohydrate loading – The guidelines quoted "In the ESPEN guidelines carbohydrate loading is recommended in the night before (200 ml) and 2 hrs before surgery (100 ml)" are incorrect. 100 g (800 ml) complex carbohydrate should be given the night before surgery and 50 g (400 ml) 2 hrs before surgery.

12. Some of the references are from the 1970s and are dated. Preferably the authors should limit the references to the last 20 or 25 years to make the review more relevant.

13. The paper could do with some language editing.

## **Authors' Response to Reviewer Comments**

Nov 09, 2017

Point-by-point reply to the reviewers

Thank you very much for your valuable comments.

Please find the changes highlighted in the manuscript according to your suggestions.

#### Reviewer #1:

The title was changed.

#### Reviewer #2:

1. It is a narrative review.

2. This narrative review focuses on nutritional status and microbiome and their impact on postoperative outcome in patients with colorectal cancer. A search strategy for literature in PubMed included recent trials, meta-analysis and reviews using the key words colorectal cancer and Enhanced Recovery after Surgery (ERAS), nutrition therapy, conditioning, microbiome, bowel preparation, prehabilitation, immunonutrition.

3. The review is also a contribution for ESPEN guideline implementation. The copyright is held by ESPEN. There is consent of the ESPEN guideline office – Prof. Bischoff, Stuttgart, and the Clinical Nutrition Editor Prof. N. Deutz. It was added ....Recent guidelines for clinical nutrition. The recent evidence has been updated in 2017 in the guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN) for Surgery, available under www.espen.org and published in Clin Nutr 2017; 36: 623–650 (16), copyright held by ESPEN . ... with kind permission from ESPEN.

4. The names of the bacteria were typed in italics.

5. "a" was omitted.

6. Cancerogenesis was changed in carcinogenesis.

7. The text was revised – references were added. More patients with colorectal cancer undergoing surgery are overweight or obese than undernourished (1, 5). Higher body mass index is associated with worse postoperative outcome in laparoscopic colorectal surgery (6).
8. In order to achieve Enhanced Recovery after Surgery (ERAS) multimodality programs including perioperative care pathways have proven clinical effectiveness (7, 8). Early oral food intake is favored, and perioperative nutrition therapy seems to be very "traditional" or even redundant. 7 – Gustaffson et al, 8 – Nygren et al.

9. Functional status was changed in functional capacity and functional dependency in care dependency.

10. While in first line reflecting inflammation and fluid balance, serum albumin level is also associated with impaired nutritional status.
11. Thank you – In the ESPEN guidelines carbohydrate loading is recommended in the night before and 2 hrs before surgery (16).

12. The only reference from the seventies is from G. Hill in the Lancet – it is an important and "classical" paper for perioperative nutrition. ... for 40 years, the high risk to neglect the nutritional status has not changed (13). One reference from the nineties regarding the prognostic value of phase angle was replaced by a brand new one (5).

13. Language editing by a native speaker was performed.

# **Reviewers' Comments to Revision**

## **Reviewer 1: Wolfgang Schwenk**

Nov 20, 2017

Reviewer Recommendation Term:	Accept	
Overall Reviewer Manuscript Rating:	N/A	
Custom Review Questions	Response	
Is the subject area appropriate for you?	4	
Does the title clearly reflect the paper's content?	4	
Does the abstract clearly reflect the paper's content?	4	
Do the keywords clearly reflect the paper's content?	4	
Does the introduction present the problem clearly?	4	
Are the results/conclusions justified?	4	
How comprehensive and up-to-date is the subject matter presented?	4	
How adequate is the data presentation?	N/A	
Are units and terminology used correctly?	4	
Is the number of cases adequate?	N/A	
Are the experimental methods/clinical studies adequate?	N/A	
Is the length appropriate in relation to the content?	4	
Does the reader get new insights from the article?	4	
Please rate the practical significance.	4	
Please rate the accuracy of methods.	N/A	
Please rate the statistical evaluation and quality control.	4	
Please rate the appropriateness of the figures and tables.	4	
Please rate the appropriateness of the references.	4	
Please evaluate the writing style and use of language.	4	
Please judge the overall scientific quality of the manuscript.	4	
Are you willing to review the revision of this manuscript?	Yes	

**Comments to Authors:** 

No further comments

## **Reviewer 2: Dileep N Lobo**

Nov 11, 2017

Reviewer Recommendation Term:	Accept	
Overall Reviewer Manuscript Rating:	75	
Custom Review Questions	Response	
Is the subject area appropriate for you?	5 - High/Yes	
Does the title clearly reflect the paper's content?	4	
Does the abstract clearly reflect the paper's content?	4	
Do the keywords clearly reflect the paper's content?	5 - High/Yes	
Does the introduction present the problem clearly?	4	
Are the results/conclusions justified?	4	
How comprehensive and up-to-date is the subject matter presented?	4	
How adequate is the data presentation?	4	
Are units and terminology used correctly?	5 - High/Yes	
Is the number of cases adequate?	N/A	

Are the experimental methods/clinical studies adequate?	N/A
Is the length appropriate in relation to the content?	4
Does the reader get new insights from the article?	4
Please rate the practical significance.	4
Please rate the accuracy of methods.	N/A
Please rate the statistical evaluation and quality control.	N/A
Please rate the appropriateness of the figures and tables.	4
Please rate the appropriateness of the references.	4
Please evaluate the writing style and use of language.	4
Please judge the overall scientific quality of the manuscript.	4
Are you willing to review the revision of this manuscript?	No: No revision necessary

#### **Comments to Authors:**

I think the authors have address all the points well and the revision is satisfactory.