

**ESPS Peer-review Report**
**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 9429

**Title:** Impact of Clostridium difficile infection on inflammatory bowel disease outcome: a review

**Reviewer code:** 00036648

**Science editor:** Na Ma

**Date sent for review:** 2014-02-13 08:56

**Date reviewed:** 2014-03-02 08:54

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 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)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

**COMMENTS TO AUTHORS**

This review explores the literature pertaining to the outcomes of Clostridium difficile infection (CDI) in patients with IBD. This is a worthwhile topic for review given its clinical relevance and increasing incidence. However I have the following minor concerns for the authors to please address: 1. The authors should clarify and make mention of what was strictly defined to be 'Clostridium difficile in IBD,' as this could lead to quite different outcomes depending on the definition, including how the studies reviewed in this paper diagnosed an episode of C difficile infection (or whether there was significant variation between studies?) and especially relating to outcomes, were the negative outcomes associated with a persistence of CDI/ CDI colonization or perhaps failure of first-line antibiotic therapy such as metronidazole or the type/degree of immunosuppression in the IBD cohorts? Furthermore, an interesting question is how long is the duration of effect of one episode of CDI in IBD on the risk of outcomes such as colectomy or death? In the studies reviewed, does the risk of colectomy for instance pertain to that particular admission or within 30 days, or is there evidence that an episode of CDI has a longer term impact with a more adverse course of disease even distantly 1 or 2 years down the track? Another question is if a patient with IBD has an episode of CDI which is properly treated, is their risk of subsequent CDI episodes greater than an IBD patient with otherwise similar disease characteristics who has never been diagnosed with CDI? Finally another question in terms of outcomes in IBD is does the type of treatment of an episode affect future subsequent outcomes – ie does treatment with metronidazole or vancomycin have a different bearing on outcomes compared with other newer therapies such as newer anti-CDI pharmacotherapy or faecal transplantation? 2. I don't understand why the final section entitled "CDI in IBD patients following



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surgical intervention” is placed after the Discussion just before the Conclusions. This is odd. It would make much more sense to move this perhaps to after the section on “Colectomy rates” which currently ends on page 7, and just prior the section on “Mortality rates”. The Discussion and Conclusions should then close out the review as per normal. 3. The Discussion section contains too much repetition of the results of the review, rather than true Discussion. It should instead focus on the main messages of the review and discuss these, drawing these together in order to provide more clinical relevance/ applicability to the readership (who are primarily clinicians). As an example, instead of repeating the conflicting results in various studies about length of stay, the authors should provide more interpretation of the literature as it stands – in my opinion, based on the literature presented it is fairly clear on balance that CDI has adverse consequences in terms of length of stay overall in IBD (albeit UC>CD).



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### ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

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**Title:** Impact of Clostridium difficile infection on inflammatory bowel disease outcome: a review

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**Date reviewed:** 2014-03-29 07:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Y] 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
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

Clostridium difficile infection (CDI) is well known to be associated with significant morbidity, mortality and costs in the general population, and has long been implicated in worsened outcomes in patients with IBD. The authors of this manuscript do an excellent job of performing an exhaustive literature search of the major databases for all relevant articles of CDI and IBD. The authors carefully reviewed the included studies and showed increased length of stay, Colectomies, Mortality, and Healthcare costs in IBD patients with CDI. The authors then proceed to include a section on CDI of the pouch in patients who are post-surgical resection, which is an ever increasing area of study given recent focus on pouchitis. This is an excellent review, and draws appropriate conclusions while carefully highlighting the limitations of the included studies as retrospective or observational. 1. After the exhaustive search was performed, were all articles included? If not, what percentage were excluded and by what criteria? 2. Were major international GI and infectious disease meeting proceedings surveyed given potential publication bias of negative results? 3. The authors may wish to comment on the role of fecal transplant in CDI management in IBD patients.



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### ESPS Peer-review Report

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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
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### COMMENTS TO AUTHORS

Although the relationship between Clostridium difficile infection (CDI) and inflammatory bowel disease (IBD) was documented more than 20 years ago, there are limited data on the impact of CDI on IBD. The presented article reviews the impact of CDI on IBD outcome with regard to some clinical parameters. A well written review.