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315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Clinical Infectious Diseases

**ESPS Manuscript NO:** 5443

**Title:** Is there an unrecognised role for Campylobacter infections in the development of chronic diseases?

**Reviewer code:** 00029421

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-09-09 16:53

**Date reviewed:** 2013-09-20 02:00

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 checked="" 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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

This is a timely and interesting review of the known and potential systemic effects of campylobacter infection. I have a few comments for consideration by the authors: 1. suggest reorganise the sections so that the most important/convincing association are placed first with less convincing ones later in ms. 2. have a look again at the introduction/abstract and title section - there is a little confusion in how the authors dichotomise known non-gi manifestations such as polyneuropathies from those that are more speculative - e.g. see title and last paragraph of intro. 3. in places it is difficult to be sure what the overall thrust or point of the deliberation is - there is a tendency to present facts in single sentences without establishing a flow of logic to the over all point being made - eg last paragraph of page 9, last sentence of sle section. 4. more critical analysis and interpretation would be useful in places - e.g. do the authors really feel that the existing data support a role for campy in celiac disease? 5. the section on ibd and ibs are important (and should be upfront after gbs in my view). However they need some tweaking : authors need to ref jess et al (gut 2010;60;318) on ibd association and consider the subsequent critique of riddle et al in gut in terms of the potential for spurious association - this is complex area that deserves a nuanced analysis. Line5-7 page 13 are a misrepresentation of the situation - we dont usually find translocated organisms in patients . Similarly the statement about cdt in ibs (lines 17-18, p 14) presents an extremely speculative concept as a fact. The "i" in ibs stands for "irritable" - specifically it is not "inflammatory" 6. the introductions to the sections give very basic descriptions of the conditions and i think these are too simplistic for clinicians/clinical journal. Furthermore the intro statement on ibd suggests a lack of understanding of the conditions - e.g. most of my patients with crohns have colonic involvement



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with cramps and bloody diarrhoea. 7. i suggest the psoriatic arthritis section is too weak to stand alone. 8. all the muscles are not necessarily involved in gbs (line 16, p5) 9. line 29/30 page 4 appears to contradict the previous statements re asymptomatic carriage. 10. there is a tendency to overuse adverbs at the start of sentences - see lines 18-23, p 4. 11. abstract : - there are more than 15 campylobacter species - at least 17 named and prob 23 according to ncbi. 11. there are a number of misspellings, grammar and syntax issues thru the ms that need ed review.

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**Name of Journal:** World Journal of Clinical Infectious Diseases

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**Title:** Is there an unrecognised role for Campylobacter infections in the development of chronic diseases?

**Reviewer code:** 00506600

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-09-09 16:53

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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 checked="" 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"/> Rejection
<input type="checkbox"/> Grade E (Poor)		<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 paper is well-researched and well-written. The paper is also quite intriguing. However, the authors should not claim (as in the abstract) that it is a “systematic” review. It does not describe a systematic process by which the literature was searched, relevant studies identified, and findings extracted. There is no systematic review of the available evidence and no summary tables of evidence from the literature. In most of the disease-related sections the authors list the studies (mainly case reports) that suggest a link between Campylobacter spp. and the disease, without describing or critically evaluating the evidence, or quality of the studies cited. The primary contribution of this paper to clinical epidemiology and medicine is the description of studies (rather than a critical evaluation of the evidence) pertaining to a potential role of Campylobacter spp. to chronic autoimmune disease etiology. Its contribution will be to facilitate clinicians and researchers to become more aware of “connecting the dots” in the potential role of Campylobacter for chronic diseases. However, a more critical reading and interpretation of the available evidence is warranted. There are several descriptions and interpretations in the manuscript that require revision in this regard. The interpretation of the Becker et al study on page 7 (lines 22-24), that the study established a 10-fold increase in myocarditis after Campylobacter infection is not a valid interpretation based on the statistical data. In the original study, the investigators found only a single case of myocarditis in each of the two groups (Campylobacter and control). The point estimates for incidence of myocarditis in the two groups appear different because of the different sample sizes, but the 95%CI indicate that no empirical evidence of a difference is provided. The interpretation of the original authors is correct, the results are inconclusive: they were not able to confirm an association between Campylobacter and



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myocarditis, nor could they definitively rule out an association. Perhaps more telling is that only 1 of 6,204 cases of Campylobacter patients in the study experienced myocarditis in the following year. Thus, the primary evidence cited to support a link between Campylobacter and myocarditis is unconvincing. A balanced review will provide this data as well. Further, what is the (quality of) evidence indicating that males may be more susceptible to cardiomyopathy after Campylobacter-related symptoms? Similarly, regarding the Gradel et al study, it should be noted that only 1.2% of those exposed to Salmonella/Campylobacter were diagnosed with IBD after an average of 7.5 years of follow-up. Thus, while the study identified bacterial exposure as a statistically significant risk factor for IBD, the effect size was relatively small and the relative importance of Campylobacter as an agent of disease should be acknowledged (consistent with the description of negative studies later in the section). Another example: what is the nature and quality of the evidence provided in the Lapadula et al study supporting a link between Campylobacter and psoriatic arthritis?