

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

**ESPS Manuscript NO:** 7320

**Title:** Smoking increases the risk of Extraintestinal Manifestations in Crohn's Disease but not in Ulcerative Colitis – results from a population based cohort at first diagnosis and during the early course of disease

**Reviewer code:** 00068308

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-11-14 10:44

**Date reviewed:** 2013-12-08 01:31

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

**COMMENTS TO AUTHORS**

Your paper addresses an interesting aspect of IBD in the early stages. Substantial additional information is needed to lend credibility to the authors claim. Please see my comments below

1. The disease phenotype for your patients population is not provided. This is essential for further interpretation. the patient population throughout the results and discussion sections have been grouped loosely and claims of statistical significance made to colonic disease without providing details.
2. What treatment did these patients receive at diagnosis and what was the median duration of such treatment. It is now well accepted that in the well-selected patient earlier introduction of immuno-suppressive therapy alters disease course and outcomes.it is therefore unclear from your data whether this cohort received a step up or step down approach and if this could have affected EIM's.
3. The majority of your EIM's were arthralgias and those which have a strong correlation with disease activity. This makes the above comment even more relevant.
4. Smoking has a strong and well established negative impact on Crohn's disease pathogenesis and outcome. How many of the CD patient sand how many UC patients were smokers at diagnosis? Past history and passive smoking history should be mentioned if available or mentioned as confounders.
5. The statistical analysis with most of the results provided does not reach significance. Yet and in a rather illogical manner the reader is suddenly shown strong correlation with EIM. Is this not a function of smoking affecting CD especially if the disease phenotype was unfavourable in the first instance? The conclusions thus are circumspect and need to be substantiated through disease phenotype and



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markers of disease activity (biochemical, radiological and endoscopic) 6 The relevance of discussion of the HLA associations with EIM's on page 13 is illogical when taken in context. Thus a substantial amount of information is needed with a major revision.

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**Title:** Smoking increases the risk of Extraintestinal Manifestations in Crohn's Disease but not in Ulcerative Colitis - results from a population based cohort at first diagnosis and during the early course of disease

**Reviewer code:** 02439927

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-11-14 10:44

**Date reviewed:** 2013-12-22 21:23

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

**COMMENTS TO AUTHORS**

This manuscript entitled "Smoking increases the risk of Extraintestinal Manifestations in Crohn's Disease but not in Ulcerative Colitis-results from a population based cohort at first diagnosis and during the early course of disease" touched a kind of interesting topic regarding the issue of clinical features of IBD patients. However, there are major problems in the Results and a kind of jump in the interpretation of the results, especially in the Discussion. Major: 1. In the Results, the authors evaluated the EIM such as arthralgia, arthritis, ocular manifestation, sacroiliitis, pyoderma gangrenosum, erythema nodosum and PSC. However, there were no comments about the perianal lesions such as perianal fistula or abscess. Please describe how many patients in the IBD patients were diagnosed perianal lesions. 2. In the Results and Discussion, the EIM was affected by the disease activity of IBD patients. Please described that how many patients were active and inactive disease, and whether there was any difference in the EIM frequency according to the disease activity. 3. In the Results (Table 5), there was no difference of EIM frequency in Ulcerative Colitis. Please comment that whether steroid treatment may be affect the EIM state or not. In addition, in Table 4, please comment about the effect of Steroid and Immunosuppressive treatment on the EIM frequency.

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**Title:** Smoking increases the risk of Extraintestinal Manifestations in Crohn's Disease but not in Ulcerative Colitis - results from a population based cohort at first diagnosis and during the early course of disease

**Reviewer code:** 00032685

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-11-14 10:44

**Date reviewed:** 2013-12-23 19:41

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

**COMMENTS TO AUTHORS**

Interesting paper providing additional information on a not marginal aspect of IBD

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**Title:** Smoking increases the risk of Extraintestinal Manifestations in Crohn's Disease but not in Ulcerative Colitis - results from a population based cohort at first diagnosis and during the early course of disease

**Reviewer code:** 00036624

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-11-14 10:44

**Date reviewed:** 2013-12-24 19:38

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

**COMMENTS TO AUTHORS**

The paper is informative and original in presenting the prevalence of extraintestinal manifestation of disease in a population of patients at first diagnosis of IBD or the early course of the disease. Undoubtedly, the clinical consequences of the findings are substantial. It is quite well written and only some mistyping are scattered in the paper.