



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 47608

**Title:** Quantitative risk of positive family history in developing colorectal cancer: A meta-analysis

**Reviewer’s code:** 02856239

**Reviewer’s country:** United States

**Science editor:** Ruo-Yu Ma

**Reviewer accepted review:** 2019-03-20 11:15

**Reviewer performed review:** 2019-03-20 12:29

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This is an overall interesting meta-analysis and the paper generally well written. I have some requests for improving this. The Figure 1 funnel plot shows clearly unsymmetrical distribution, indicating publication bias. I recommend that the authors



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conduct another analyses focused on well-powered studies excluding those with low-powered studies that were biased. It is evident that there is influence of environment (including the microbiome) on cellular molecules and proteins, affecting cancer risk. The environment broadly include family history (embracing genetics and environment together) and the microbiome; these factors have been shown to affect cancer risk. It should be discussed more in detail. Related to the above point, the authors should discuss the recent trend of molecular pathological epidemiology (MPE). MPE is an emerging field that can link environment including family history, the microbiome, food, and lifestyle to molecular pathologies, often detected in cancers. MPE can contribute to biomarker research and precision medicine. Please discuss MPE. You can find relevant papers easily by net and pubmed search (eg, I see relevant ones such as Gut 2011, Annu Rev Pathol 2019, J Pathol 2019).

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
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- No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 47608

**Title:** Quantitative risk of positive family history in developing colorectal cancer: A meta-analysis

**Reviewer’s code:** 02440973

**Reviewer’s country:** Spain

**Science editor:** Ruo-Yu Ma

**Reviewer accepted review:** 2019-03-20 08:51

**Reviewer performed review:** 2019-04-04 07:40

**Review time:** 14 Days and 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This meta-analysis is of great relevance in the design of the preventive strategies in familial CRC. Although it is well designed according to the guidelines, I find two main drawbacks that limit the study. 1.The authors have included all the available studies.



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This is limiting the applicability of the results. Before 2000, the diagnosis of Lynch syndrome, or other forms of non-polyposis hereditary CRC (MUTYH associated CRC) was not possible. So, all the studies before 2000 could not exclude the hereditary predisposition that now we exclude in routine. In this sense, I recommend the authors to exclude all the studies published before 2000. 2.The conclusions the author produce could be improved. I would recommend them to analyze if the age at diagnosis and the number of FDR influence the RR of CRC detection.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

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