



PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 112369

Title: Obesity and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05384903

Position: Peer Reviewer

Academic degree and professional title: Associate Professor, MD

Reviewer's Country/Territory: China

Author's Country/Territory: Australia

Manuscript submission date: 2025-07-24

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-07-29 05:51

Reviewer performed review: 2025-07-30 05:03

Review time: 23 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes Is the content of the Introduction adequate? Yes
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	<p>Is the content of the Materials and Methods complete? Yes</p> <p>Is the description of the experiments clear and complete? Yes</p> <p>Are the experimental data presented in the manuscript's biostatistics content reliable? Yes</p> <p>Are the experimental data of the Results true and reliable? Yes</p> <p>Are the quality and resolution of the images up to standard? Yes</p> <p>Do the selection and design of the figures and tables follow the principles of necessity and clarity? Yes</p> <p>Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? No</p> <p>Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? Yes</p> <p>Is the content of the Discussion reasonable? Yes</p> <p>Is the Conclusion reasonable? Yes</p> <p>Are all references necessary and reasonable? Yes</p> <p>Do authors omit important references? Yes</p> <p>Are all references related to the topic of the manuscript? Yes</p> <p>Does the research scope comply with ethics? Yes</p> <p>Are additional experiments needed for the study? No</p> <p>Will the manuscript's content be of interest to readers? Yes</p> <p>Is the manuscript's text correct, concise, and clear? Yes</p> <p>Do authors only cite their own earlier publications? No</p>
<p>Scientific quality</p>	<p>Grade B (Very good)</p>



Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Review Comments

Title: Obesity and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis

Summary:

This manuscript presents a comprehensive systematic review and meta-analysis examining the association between obesity and colorectal cancer (CRC). The authors synthesize recent observational studies and explore the underlying biological mechanisms linking obesity to CRC. The study follows a rigorous data extraction process, quality assessment, and statistical analysis according to PRISMA guidelines.



The findings demonstrate a significant association between obesity and an increased risk of CRC, with notable differences observed between males and females.

Strengths:

1. The topic is highly relevant and timely, addressing the global obesity epidemic and its potential public health consequences, particularly in relation to CRC.
2. The study design is robust, with a well-conducted meta-analysis using large sample sizes, which enhances the reliability and generalizability of the findings.
3. The manuscript is well-structured, clearly outlining the methodology, inclusion criteria, and statistical techniques used.
4. The inclusion of a qualitative analysis for studies not part of the meta-analysis provides a well-rounded perspective.

Areas for Improvement:

1. Clarification of Methodology:

While the manuscript mentions the use of "random-effects models," it does not fully explain how confounding factors such as age, sex, and physical activity were handled. It would be beneficial to elaborate on the specific confounding variables considered and how they were controlled during the analysis.

2. Discussion of Heterogeneity:

Although the male meta-analysis shows low heterogeneity, the female meta-analysis exhibits moderate heterogeneity. The authors should delve deeper into the potential sources of variability (e.g., lifestyle factors, dietary differences, or regional characteristics) and consider conducting additional subgroup analyses to explore these differences further.

3. Inclusion of More Recent Studies:

The manuscript includes studies published until 2024, but given the rapid pace of research, it may be worthwhile to extend the search period or incorporate more recent



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studies from 2024 onwards to ensure the findings are as current as possible.

4. Enhancing the Biological Mechanisms Section:

The manuscript provides a solid overview of the biological mechanisms linking obesity to CRC. However, a deeper discussion on the role of gut microbiota and its interaction with obesity-induced inflammation would strengthen this section. Additionally, exploring genetic predispositions or biomarkers linked to CRC could offer valuable insights for future research directions.

5. Expanded Limitations Section:

While the authors acknowledge certain limitations, such as the potential for publication bias and the use of BMI as a measure of obesity, a more detailed discussion on how these limitations might impact the conclusions would be helpful. The authors could also outline any steps taken to minimize these biases during the analysis.

Conclusion:

This manuscript provides important insights into the relationship between obesity and colorectal cancer risk. The findings are well-supported by rigorous methodology and contribute to the existing body of literature. Addressing the points raised in the review will further enhance the clarity and impact of the study.



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08703470

Position: Peer Reviewer

Academic degree and professional title: PhD, Research Fellow, Researcher

Reviewer's Country/Territory: India

Author's Country/Territory: Australia

Manuscript submission date: 2025-07-24

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-07-25 03:37

Reviewer performed review: 2025-07-30 05:53

Review time: 5 Days and 2 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? No Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes Is the content of the Introduction adequate? No
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<p>Scientific quality</p>	<p>Grade B (Very good)</p>



Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Originality and Importance: The study addresses a relevant public health concern with increasing global obesity rates and its implications on CRC incidence. Although prior reviews exist, more emphasis could be placed in the Introduction on how recent changes in obesity trends, diagnostic practices, or molecular understanding justify this updated analysis.

2. The search strategy, although mentioned, lacks detailed explanation in the main text. It is unclear how comprehensively the grey literature or unpublished data were searched. PRISMA guidelines were followed, and data sources were clearly reported. Briefly



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summarize key search terms and strategy in the main text, not just in supplementary materials. Mention if PROSPERO registration was considered.

3. Clarify why more of the 16 included studies were not eligible for meta-analysis. Was this due to lack of compatible effect size metrics?
4. Consider subgroup analyses (e.g., geographic region, menopausal status, ethnicity) to identify heterogeneity sources.
5. Some subsections (e.g., adiponectin, leptin) include highly specific signaling pathways, which, while accurate, may overwhelm readers not specialized in molecular oncology. Consider condensing or moving some of this content to supplementary materials or summarizing with more emphasis on how these mechanisms reinforce the epidemiological findings.
6. Figures 1–6 are well-constructed, but they are not embedded in the document text. It's unclear where they are located. Ensure figures are placed immediately after their first mention in the main text and are of publication-quality resolution and are self-explanatory each figure should be understandable on its own with a descriptive title and legend, without requiring the reader to refer back to the main text for interpretation.
7. Language and Style: A thorough language edit is required to improve flow, consistency, clarity and also font size/style.
8. Future research directions could also explore genetic predisposition and interaction with obesity, or more concrete policy/screening implications.
9. Use consistent units and notations (e.g., "BMI \geq 30 kg/m²")
10. Ensure all abbreviations (e.g., AMPK, IGF-1, OB-Rb) are defined at first use.
11. While the manuscript presents a valuable and methodologically strong contribution to the field, it requires revisions to clarify methodological decisions, refine the writing, address heterogeneity, and better integrate biological mechanisms into the overall interpretation of the data.



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Reviewer's code: 05613237

Position: Peer Reviewer

Academic degree and professional title: Associate Research Scientist, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Australia

Manuscript submission date: 2025-07-24

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Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes Is the content of the Introduction adequate? Yes
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Is the content of the Materials and Methods complete?

Yes

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Will the manuscript's content be of interest to readers? **Yes**

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Not Applicable**

Is the manuscript's text correct, concise, and clear? **Yes**



Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This study presents interesting findings with relatively comprehensive analytical results; however, there remain several aspects that require careful refinement to enhance clarity, rigor, and adherence to reporting standards. Below are specific comments for the authors' consideration:

1. Clarification on Study Inclusion in Figure S1: In Figure S1 of the Results section, the final number of included studies is reported as 16. Given that the text mentions 18 studies were initially considered and 3 were excluded, readers may question why the



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total does not align with the expected calculation ($18 - 3 = 15$). A brief explanation of the exclusion process—such as whether one additional study was inadvertently excluded or if there is a discrepancy in the initial count—would resolve this confusion.

2. Choice of Effect Model in Forest Plot (Figure 1): The forest plot in Figure 1 indicates very low between-study heterogeneity ($I^2 = 0$), which suggests no meaningful variability in effect sizes across included studies. In such cases, the fixed-effects model is statistically more appropriate for estimating the overall effect size, as it avoids unnecessary conservatism that may arise from the random-effects model. While technical guidelines permit the use of a random-effects model even when $I^2 = 0$, the fixed-effects model is preferable here to provide a more precise and unbiased summary of the pooled effect.

3. Justification for Excluded Studies in Qualitative Analysis: In the “Qualitative Analysis” subsection of the Results, Figure 3 is referenced to illustrate the exclusion process, but it lacks clear annotations or a supplementary table explaining why 7 specific studies were excluded from the meta-analysis. To improve transparency, the authors should elaborate on the exclusion criteria (e.g., methodological limitations, incomplete data, or relevance to the research question) applied during this phase, either in the text or via a footnote to the figure.

4. Structural Consistency of Paragraphs: The article’s organizational structure could be strengthened. Several sections feature paragraphs with only 1-2 sentences, which are insufficient to function as independent units of discussion. For example, the “Findings from male meta-analysis” and “Findings from female meta-analysis” subsections under Results each contain overly brief content. Merging these into a single, more substantive section that synthesizes sex-specific results would improve readability and logical flow.

5. Placement of Figures in the Discussion Section: Three visually detailed figures are currently presented in the Discussion section. By convention, figures that directly



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present primary or secondary results (e.g., effect estimates, subgroup analyses) should be included in the Results section to immediately support the narrative of key findings. The Discussion should focus on interpreting these results rather than introducing new visual data.

6. Minor Editorial and Formatting Issues: Several details require attention to ensure consistency and adherence to formatting standards:

- In the “Severity of obesity on colon and rectal cancer development” subsection, some sentences lack terminal punctuation (e.g., periods), which disrupts readability.
- The second and third paragraphs of the “Limitations” section similarly omit closing punctuation, which should be corrected.
- Additionally, the first line of the “Altered gut microbiome” subsection in the Discussion is indented inconsistently with other paragraphs (e.g., it may use a half-inch indent versus full alignment with the margin). Standardizing paragraph indentation across the manuscript will enhance visual coherence.

Overall, this study makes a valuable contribution to the field, and addressing these points will further strengthen its clarity, rigor, and impact.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Oncology*

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Title: Obesity and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis

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Peer-review model: Single blind

Reviewer's code: 05613237

Position: Peer Reviewer

Academic degree and professional title: Associate Research Scientist, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Australia

Manuscript submission date: 2025-07-24

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Reviewer accepted review: 2025-10-17 01:56

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Review time: 22 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes Is the content of the Introduction adequate? Yes
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Is the content of the Materials and Methods complete?

Yes

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

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Will the manuscript's content be of interest to readers?
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Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Not Applicable**



Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade C (Good)
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Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

After confirmation, the author has fully addressed all inquiries, and the relevant revisions have also been implemented in accordance with the suggestions. At present, there are no additional recommendations to provide.



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Conclusion	Accept
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	Conflicts-of-Interest: No
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SPECIFIC COMMENTS TO AUTHORS

The authors have fully addressed the raised concerns, and I find that their responses adequately clarify all the points raised. The corrections are reflected in the updated manuscript, including changes in the figure explanations, methodological clarifications, and enhanced consistency in the manuscript. Given these improvements, I believe the manuscript is now ready for acceptance without further revisions. Recommendation: Accept for publication.