

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 52097

**Title:** L-carnitine supplementation in non-alcoholic fatty liver disease: A systematic review and meta-analysis

**Reviewer's code:** 00607640

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's country:** Taiwan

**Author's country:** United Kingdom

**Manuscript submission date:** 2019-10-22

**Reviewer chosen by:** Jie Wang

**Reviewer accepted review:** 2019-11-04 17:44

**Reviewer performed review:** 2019-11-07 12:52

**Review time:** 2 Days and 19 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 checked="" 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

The authors reviewed randomised trials reporting effects of dietary L-carnitine supplementation in non-alcoholic fatty liver disease. The literatures cited in the manuscript are convincing and valuable. The conclusion is insightful, and could be helpful in clinic study. In overall, this review manuscript is well organized and is highly recommend.

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

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

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 52097

**Title:** L-carnitine supplementation in non-alcoholic fatty liver disease: A systematic review and meta-analysis

**Reviewer's code:** 00227368

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Professor

**Reviewer's country:** Turkey

**Author's country:** United Kingdom

**Manuscript submission date:** 2019-10-22

**Reviewer chosen by:** Jie Wang

**Reviewer accepted review:** 2019-11-24 09:17

**Reviewer performed review:** 2019-11-24 09:19

**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



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## **SPECIFIC COMMENTS TO AUTHORS**

Not goog enough analysis

## **INITIAL REVIEW OF THE MANUSCRIPT**

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

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- ☐ Plagiarism
- ☐ No

### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 52097

**Title:** L-carnitine supplementation in non-alcoholic fatty liver disease: A systematic review and meta-analysis

**Reviewer's code:** 03293832

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Senior Research Fellow

**Reviewer's country:** Japan

**Author's country:** United Kingdom

**Manuscript submission date:** 2019-10-22

**Reviewer chosen by:** Jie Wang

**Reviewer accepted review:** 2019-11-25 07:58

**Reviewer performed review:** 2019-11-28 06:42

**Review time:** 2 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 checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript reviews systemically the randomized trials of investigating the effects of dietary L-carnitine supplementation on liver biochemistry, liver fat and insulin sensitivity in NAFLD and performs meta-analysis. The contents are well-written and meta-analysis is performed properly. I suggest that the manuscript is acceptable in the World Journal of Gastroenterology.

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

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

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [ Y ] No

##### ***BPG Search:***

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- ☐ Plagiarism
- ☐ [ Y ] No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 52097

**Title:** L-carnitine supplementation in non-alcoholic fatty liver disease: A systematic review and meta-analysis

**Reviewer's code:** 00008577

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Associate Professor, Professor

**Reviewer's country:** Italy

**Author's country:** United Kingdom

**Manuscript submission date:** 2019-10-22

**Reviewer chosen by:** Jie Wang

**Reviewer accepted review:** 2019-11-07 05:31

**Reviewer performed review:** 2019-12-01 16:30

**Review time:** 24 Days and 10 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 type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input checked="" 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**

The authors have performed a meta-analysis about the role of L-Carnitine for the treatment of NAFLD. The meta-analysis, from the methodological point of view, is well conducted. The selection criteria of the studies and analyses were rigorously carried out. Furthermore, the authors correctly mention all the limits of the work. However, I have many doubts about the usefulness of a meta-analytical work for the following reasons:

1. includes only 5 studies (for a total of 338 patients) which, as also indicated by the authors, 3 are of poor methodological quality (inadequate randomization or of dubious correctness).
2. The only significant outcome is the reduction of ALT (ASTs are not significant), which however also presents a high heterogeneity between studies. This ALT reduction is, in my opinion, not sufficient to speculate a favorable effect on NAFLD while the authors consider this outcome relevant and build their discussion on this topic.
3. As far as steatosis reduction is concerned, I believe it is difficult to give adequate information because in 2 studies with ultrasound L-Carnitine has no effects, while for the remaining 2 (1 with histology and 1 with CT) the steatosis is reduced but few patients are enrolled and the studies are badly done and very heterogeneous.
4. The studies are also heterogeneous with regard to duration of therapy, formulation of L-Carnitine and dose. Therefore it is difficult to establish which is the correct dosage of supplementation to propose.
5. Finally, Carnitine is mainly contained in red meat, and has been associated in numerous studies published in TOP journals (J Am Heart Assoc. 2019 May 7; 8 (9): e011037; Atherosclerosis. 2016 Apr; 247: 64-9 ; Nature Medicine 2013; 19: 576-585) to increase atherosclerosis and cardio-vascular events, through its metabolism in TMAO mediated by intestinal microbiota. Even postulating that L-Carnitine can reduce steatosis and hepatic inflammation, it is difficult to propose the treatment for patients who have cardiovascular disease as their primary cause of





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morbidity and mortality. The authors have not addressed this problem at all.

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

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##### ***BPG Search:***

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- ☐ No