



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Experimental Medicine*

**Manuscript NO:** 98543

**Title:** Statins decrease the risk of hepatocellular carcinoma in metabolic dysfunction-associated steatotic liver disease: A systematic review and meta-analysis

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 02861372

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** Egypt

**Author's Country/Territory:** United States

**Manuscript submission date:** 2024-06-29

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2024-08-26 00:42

**Reviewer performed review:** 2024-08-30 11:50

**Review time:** 4 Days and 11 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Thank you for the important research point; You performed a systematic review and meta-analysis to study the effect of statin use on the occurrence of HCC in patients with underlying MASLD and elaborated the role of high dose statins in the prevention of HCC in patients with MASLD. The study concluded that Statin use is associated with a reduced risk of HCC in MASLD patients. A higher cumulative daily dose and lipophilic statin decrease the risk of HCC in MASLD patients. this is the first meta-analysis to assess the variation in HCC risk between statin-using and non-statin-using MASLD patients. Two of the included studies were retrospective; one was a case-control, and one was a prospective cohort The total number of patients in the analysis was 291,685. Of these, 80,247 were statin users, whereas 211,438 were not under therapy with statins. The mean age of the study population was 57.0 ± 12.2 years. please correct the percentage: Further, 49.9% (136,804) were male, and 53.1% (154,880) were female. their sum should be 100% Do all included patients in the study have advanced fibrosis or liver cirrhosis? Please mention the median duration of follow up to calculate the risk of HCC You studied the effect of lipophilic versus hydrophilic statins on the development of HCC :



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please mention the names of the drugs in the included studies Did the included studies mention the side effects of high versus low dose statins particularly in cirrhotic patients? You mentioned in the discussion section that “ a few studies have shown that the use of a higher dose of statin has no significant benefit over a lower dose in the prevention of HCC [80,81].” What was the difference in study design and inclusions between these studies and the others that showed that statins reduced the risk of HCC? you analyzed the data based on the dose of statins and concluded that > 600 cumulative defined daily dose (cDDD) decreases the risk of HCC by 70 % (RR = 0.30, 95%CI: 0.21-0.43), whereas administration of 300-599 cDDD and 30-299 cDDD of statins decreases the risk by 29% (RR = 0.71; 95%CI: 0.55-0.91) and 43% (RR = 0.57; 95%CI: 0.40-0.82), respectively thank you so much