

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	LAMC2 as a prognostic biomarker in human cancer: a systematic review and meta-analysis
AUTHORS	Fu, Tao; Liu, Jun-Xia; Xie, Juan; Gao, Zhen; Yang, Zhenshan

VERSION 1 – REVIEW

REVIEWER	Gabriel Escarela Universidad Autonoma Metropolitana, Departamento de Matemáticas
REVIEW RETURNED	10-Jun-2022

GENERAL COMMENTS	Steyerberg et al. (2010) provides a taxonomy of different prognostic model evaluation tools. I believe it is possible to deal with discrimination and predictiveness measures. Small sample size is an issue.
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REVIEWER	Manoj Garg Amity University
REVIEW RETURNED	20-Aug-2022

GENERAL COMMENTS	<ol style="list-style-type: none">1. Why Authors have collected data from 25 November 2021. Why not from 2010 to include a greater number of studies to have fair understanding on the expression of LAMC2 and its correlation with clinical and pathological features.2. Why only seven studies, what is unique about these seven studies.3. Author should provide the significance or rationale of this study4. Conclusion: Our results suggested that higher LAMC2 expression was correlated with worse survival. This is nothing new. More than 20 independent studies have already shown in different tumor types.5. Author must include all the major results in the conclusion6. Author should make it clear what tumor types were used for in silico analysis in the abstract part7. LAMC2 has been reported in pancreatic ductal adenocarcinoma,7-10. Author forgot to include and cite very recent and import study on LAMC2 in Pancreatic cancer. Must include PMID: 356997948. Most of the data is from GEPIA or other places on TCGA Data which is not part of seven studies. Why author use TCGA data9. What is the novelty and new information of this study should be highlighted
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REVIEWER	Mingning Qiu Affiliated Hospital of Guangdong Medical University
REVIEW RETURNED	29-Aug-2022

GENERAL COMMENTS	<p>Comments to the Authors: The manuscript submitted for review covers topics related to the potential role of LAMC2 in human cancer. The research was conducted both in meta-analysis and public data analysis. In my opinion, the following points have to be corrected or added prior to the final acceptance of the manuscript for publication as has been detailed below: 1)L 26 missing comma after (OS). 2)L 64 missing and before esophageal squamous cell carcinoma. 3)L 203 Add references to support “Several kinds of research have shown that LAMC2 promotes cancer cells proliferation, motility, and invasion.” I would recommend the author adjust this paragraph the order to make it easier for the reader. 4)Please check the manuscript thoroughly for English grammar.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Gabriel Escarela, Universidad Autonoma Metropolitana

Comments to the Author:

Steyerberg et al. (2010) provides a taxonomy of different prognostic model evaluation tools. I believe it is possible to deal with discrimination and predictiveness measures. Small sample size is an issue.

Answer: Thanks a lot for your professional comments. Steyerberg et al. (2010) provide the prognostic model that can effectively solve discrimination and predictiveness measures. We intend to work on it in the future, and it is also mentioned in the discussion.

In our meta-analysis that starting in November 2021, we through the inclusion criteria and the exclusion criteria to select the studies. We finally included 7 articles, and we also got some conclusions. In the future, we plan to update this meta-analysis. By that time, more studies will be included.

Reviewer: 2

Dr. Manoj Garg, Amity University

Comments to the Author:

1. Why Authors have collected data from 25 November 2021. Why not from 2010 to include a greater number of studies to have fair understanding on the expression of LAMC2 and its correlation with clinical and pathological features.

Answer: Thank you very much for your suggestions. Our sentence is ambiguous; what we want to say is that our search was done on 25 November 2021. The search date is from inception to 25 November 2021. It has been revised.

2. Why only seven studies, what is unique about these seven studies.

Answer: After search according to the search strategy, We through the inclusion criteria and the exclusion criteria to select the studies for meta-analysis. Finally, only seven studies satisfied the inclusion criteria.

3. Author should provide the significance or rationale of this study.

Answer: At the introduction, we mentioned overexpression of LAMC2 has been reported in different tumor types, leading to poor clinicopathological features and short survival time. But individual studies may be inaccurate and inadequate due to their small design and small sample. In contrast, one study demonstrated that downregulated LAMC2 expression leads to poor LNM and TNM stage. And there

was no meta-analysis has been performed to investigate the relationship between LAMC2 and the prognostic value. So we performed the meta-analysis.

4. Conclusion: Our results suggested that higher LAMC2 expression was correlated with worse survival. This is nothing new. More than 20 independent studies have already shown in different tumor types.

Answer: Although many independent studies have already shown these results, there was no meta-analysis for LAMC2 and the prognostic value. We have made a meta-analysis of these literatures, and our meta-analysis suggested this result.

5. Author must include all the major results in the conclusion.

Answer: We thank the Reviewer for pointing out the problem. We have revised the manuscript.

6. Author should make it clear what tumor types were used for in silico analysis in the abstract part.

Answer: We are extremely grateful to the Reviewer for pointing out this problem. We have revised the manuscript.

7. LAMC2 has been reported in pancreatic ductal adenocarcinoma, 7-10. Author forgot to include and cite very recent and important study on LAMC2 in Pancreatic cancer. Must include PMID: 35699794.

Answer: Thank you very much for your professional comments. We have added this reference in our revised manuscript. And it is also mentioned in the discussion.

8. Most of the data is from GEPIA or other places on TCGA Data which is not part of seven studies. Why author use TCGA data.

Answer: We used the TCGA database as another piece of evidence to validate the results of our meta-analysis.

9. What is the novelty and new information of this study should be highlighted.

Answer: To the best of our knowledge, the method of meta-analysis that we adopted is the first time to report that LAMC2 is associated with a poor prognosis and clinicopathologic features in cancer patients.

Reviewer: 3

Dr. Mingning Qiu, Affiliated Hospital of Guangdong Medical University

Comments to the Author:

The manuscript submitted for review covers topics related to the potential role of LAMC2 in human cancer. The research was conducted both in meta-analysis and public data analysis.

In my opinion, the following points have to be corrected or added prior to the final acceptance of the manuscript for publication as has been detailed below:

1) L 26 missing comma after (OS).

Answer: We thank the Reviewer for pointing out the problem. We have finished the modification.

2) L 64 missing and before esophageal squamous cell carcinoma.

Answer: Thank you for pointing this out. The sentence has been modified

3) L 203 Add references to support "Several kinds of research have shown that LAMC2 promotes cancer cells proliferation, motility, and invasion." I would recommend the author adjust this paragraph the order to make it easier for the reader.

Answer: Thank you very much for your suggestions. We have adjusted the order of the sentences to make them easier for the reader.

4) Please check the manuscript thoroughly for English grammar.

Answers: We have carefully checked the grammar and English writing of the manuscript and revised it accordingly.

VERSION 2 – REVIEW

REVIEWER	Manoj Garg Amity University
REVIEW RETURNED	30-Sep-2022
GENERAL COMMENTS	Accepted