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.

This paper was submitted to another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers’ comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>White Rice, Brown Rice and the Risk of Type 2 Diabetes: A Systematic Review and Meta-Analysis</th>
</tr>
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<tbody>
<tr>
<td>AUTHORS</td>
<td>Yu, Jiayue; Balaji, Bhavadharini; Tinajero, Maria; Jarvis, Sarah; Khan, Tauseef; Vasudevan, Sudha; Ranawana, Viren; Poobalan, Amudha; Bhupathiraju, Shilpa; Sun, Qi; Willett, Walter; Hu, F.B; Jenkins, David; Mohan, V; Malik, Vasanti</td>
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VERSION 1 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Wendean Marsh</th>
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</thead>
<tbody>
<tr>
<td>Department of Children and Families, State of Wisconsin</td>
<td>n/a</td>
</tr>
<tr>
<td>GENERAL COMMENTS</td>
<td>I am a layperson. My experience with T2 Diabetes is as a caregiver for an elderly parent, and as someone who has hypoglycemic tendencies myself.</td>
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<table>
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<tr>
<th>REVIEWER</th>
<th>Norhayati Mohd Noor</th>
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<tbody>
<tr>
<td>Universiti Sains Malaysia</td>
<td>n/a</td>
</tr>
<tr>
<td>GENERAL COMMENTS</td>
<td>Introduction The literature review is adequate. Methods Please apply the PRISMA flow chart version 2020. This is an updated version, therefore, please apply the version for a review update. Please provide the search strategy for each database. Higgins 2011 was an old reference. The current version is 2021. Results Acceptable Discussion Page 17. Line 6-26 This is suitable for Introduction. Page 16. Line 36-49. These are known facts that could be in the</td>
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Introduction or removed from the Discussion.

Page 17. Line 29-49. This is describing the findings in Malik (27). At a review level, it should be hypothesis-generating of new information and not based on the result/discussion of an included study.

There are other reviews comparing brown rice and white rice that should be included and compared in the Discussion. Whether there is agreement or disagreement with other reviews. For example, Anis Farhanah et al. The effect of a brown-rice diet on glycemic control and metabolic parameters in prediabetes and type 2 diabetes mellitus: a meta-analysis of randomized controlled trials and controlled clinical trials. PeerJ 2021; 9:e11291 doi:10.7717/peerj.11291

Page 19. Line 43-47. Please replace or rephrase this sentence on the “limited data from the US.” It should conclude the important findings of the review.

REVIEWER
Shoichiro Tsugane
National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health and Nutrition

REVIEW RETURNED
n/a

GENERAL COMMENTS
In this systematic review and meta-analysis registered in the PROSPERO, Yu et al. have investigated an association of white rice and brown rice with type 2 diabetes (T2D). Through comprehensive literature search, they identified 17 original articles from 8 cohort studies providing 18 estimates for meta-analysis (15 for white rice, 3 for brown rice). Consistent with prior reports, they found a positive association between white rice intake and the risk of T2D, while an inverse association between brown rice and T2D risk. In their dose-response analysis, a linear dose-response at intake levels above 300 grams of white rice intake/day was observed. In addition, meta-analysis of RCTs comparing brown rice to white rice on cardiometabolic risk factors was also conducted with inconsistent findings, except an increase in HDL in the brown rice.

Although the findings of this paper are largely consistent with previous meta-analyses on the association between rice and T2D, the manuscript is well-written and provides important updated evidence and new evidence from RCTs. However, there are several points that the authors may consider.

1. Pooling the estimates comparing extreme categories of intakes are widely used; however, I believe such practice is not ideal because ranges of rice intakes substantially differ across studies. Instead, the authors could have performed individual participant data meta-analysis to solve these issues. I understand that it is not easy to do, but I think it is feasible for this group of researchers. It may be helpful at least discuss this point.

2. There are several previous meta-analyses on the association between white rice intake and T2D (BMJ. 2012 Mar 15;344:e1454., Diabetes Res Clin Pract. 2021 Feb;172:108651.) by some authors of this manuscript. The former showed a positive association in Asian (Chinese and Japanese) and null association in Western and the latter showed a positive association in Asian women. It would be helpful for readers if the authors could compare the findings of this paper with previous meta-analyses. Considering these previous
findings and the findings of this manuscript, I think it is not appropriate to stratify by China, South Asia, and the rest of the world including many Asians. Instead, as in Supplemental figure 6, the stratification by non-rice-consuming or rice-consuming, or less than 300 g/day or more, may be more appropriate and the effects of sex, age, follow-up year, and diet quality adjustment should be examined mostly in rice-consuming countries with positive association.

3. I was impressed with the authors’ effort to apply the NutriGrade to assess the quality of their findings. Although they have provided the NutriGrade scores, it would be more informative if the authors could give reasons for downgrading each domain of this scoring system. For example, why the Cohort - BR was given a score of 2 for risk of bias domain, while the Cohort-WR was given a score of 1?

4. Uncontrolled confounding and measurement errors in exposure (and outcome) remain to be major limitations in the assessment of the effect of rice on T2D risk. There has been advancement in the methodology over years to quantitively assess the impact of such biases (i.e., quantitative bias analysis). Please clarify this point.

In addition, the uploaded Figure 1 is not complete.

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: 1

Comments:
I am a layperson. My experience with T2 Diabetes is as a caregiver for an elderly parent, and as someone who has hypoglycemic tendencies myself.

We thank the reviewer for their time in reviewing our manuscript.

Reviewer: 2

Comments:
Introduction
The literature review is adequate.

Methods
Please apply the PRISMA flow chart version 2020. This is an updated version, therefore, please apply the version for a review update.

This has been updated.

Please provide the search strategy for each database.

The same search strategy was applied across the databases.

Higgins 2011 was an old reference. The current version is 2021.

We have updated this reference.
Results
Acceptable
Discussion
Page 17. Line 6-26 This is suitable for Introduction.

We have modified the discussion.

Page 16. Line 36-49. These are known facts that could be in the Introduction or removed from the Discussion.

We have modified the discussion.

Page 17. Line 29-49. This is describing the findings in Malik (27). At a review level, it should be hypothesis-generating of new information and not based on the result/discussion of an included study.

We thank the reviewer for this point and have removed this from the discussion as we agree that it does not fit within the scope of the paper.

There are other reviews comparing brown rice and white rice that should be included and compared in the Discussion. Whether there is agreement or disagreement with other reviews. For example, Anis Farhanah et al. The effect of a brown-rice diet on glycemic control and metabolic parameters in prediabetes and type 2 diabetes mellitus: a meta-analysis of randomized controlled trials and controlled clinical trials. PeerJ 2021; 9:e11291 doi:10.7717/peerj.11291

We thank the reviewer for these references and have incorporated them into the discussion.

Page 19. Line 43-47. Please replace or rephrase this sentence on the “limited data from the US.” It should conclude the important findings of the review.

We have modified this sentence but feel that it is important to note in our conclusion that results on brown rice are based on limited data.

Reviewer: 3

Comments:
In this systematic review and meta-analysis registered in the PROSPERO, Yu et al. have investigated an association of white rice and brown rice with type 2 diabetes (T2D). Through comprehensive literature search, they identified 17 original articles from 8 cohort studies providing 18 estimates for meta-analysis (15 for white rice, 3 for brown rice). Consistent with prior reports, they found a positive association between white rice intake and the risk of T2D, while an inverse association between brown rice and T2D risk. In their dose-response analysis, a linear dose-response at intake levels above 300 grams of white rice intake/day was observed. In addition, meta-analysis of RCTs comparing brown rice to white rice on cardiometabolic risk factors was also conducted with inconsistent findings, except an increase in HDL in the brown rice.

Although the findings of this paper are largely consistent with previous meta-analyses on the association between rice and T2D, the manuscript is well-written and provides important updated evidence and new evidence from RCTs. However, there are several points that the authors may consider.

1. Pooling the estimates comparing extreme categories of intakes are widely used; however, I believe such practice is not ideal because ranges of rice intakes substantially differ across studies. Instead,
the authors could have performed individual participant data meta-analysis to solve these issues. I understand that it is not easy to do, but I think it is feasible for this group of researchers. It may be helpful at least discuss this point.

We thank the reviewer for this insightful comment. In addition to the categorical analysis that compared extreme categories of intake we also conducted dose-response meta-analyses.

2. There are several previous meta-analyses on the association between white rice intake and T2D (BMJ. 2012 Mar 15;344:e1454., Diabetes Res Clin Pract. 2021 Feb;172:108651.) by some authors of this manuscript. The former showed a positive association in Asian (Chinese and Japanese) and null association in Western and the latter showed a positive association in Asian women. It would be helpful for readers if the authors could compare the findings of this paper with previous meta-analyses. Considering these previous findings and the findings of this manuscript, I think it is not appropriate to stratify by China, South Asia, and the rest of the world including many Asians. Instead, as in Supplemental figure 6, the stratification by non-rice-consuming or rice-consuming, or less than 300 g/day or more, may be more appropriate and the effects of sex, age, follow-up year, and diet quality adjustment should be examined mostly in rice-consuming countries with positive association.

We agree with the reviewer and have discussed these other meta-analyses in relation to our findings. We acknowledge the limitation of our subgroup-analysis by geographic region in the discussion but would like to keep it in the manuscript as it is still of interest. To complement this, we also conducted sub-group analysis by whether rice is consumed as a staple food. While it would be of interest to examine sub-groups within this categorization the statistical power may be limited.

3. I was impressed with the authors’ effort to apply the Nutrigrade to assess the quality of their findings. Although they have provided the NutriGrade scores, it would be more informative if the authors could give reasons for downgrading each domain of this scoring system. For example, why the Cohort BR was given a score of 2 for risk of bias domain, while the Cohort-WR was given a score of 1?

The reviewers’ point is well taken and we have added this information.

4. Uncontrolled confounding and measurement errors in exposure (and outcome) remain to be major limitations in the assessment of the effect of rice on T2D risk. There has been advancement in the methodology over years to quantitively assess the impact of such biases (i.e., quantitative bias analysis). Please clarify this point.

We have acknowledged this limitation of the individual studies included in the meta-analysis.

In addition, the uploaded Figure 1 is not complete.

We have fixed figure 1

<table>
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<tr>
<th>REVIEWER</th>
<th>Tsugane, Shoichiro</th>
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<tbody>
<tr>
<td></td>
<td>Research Center for Cancer Prevention and Screening National Cancer Center, Epidemiology and Prevention Division</td>
</tr>
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<td>REVIEW RETURNED</td>
<td>14-Jun-2022</td>
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<td>GENERAL COMMENTS</td>
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according to the reviewers’ comments. However, for my comment regarding the assessment of the quality of evidence, reasons for downgrading each domain seem missing in the revised manuscript, although the author have replied that the information was provided in response to my comment. Please response to my comment and describe clearly how and where they modified the manuscript.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Dr. Shoichiro Tsugane, Research Center for Cancer Prevention and Screening National Cancer Center

Comments to the Author:
Overall, the authors have appropriately revised the manuscript according to the reviewers’ comments. However, for my comment regarding the assessment of the quality of evidence, reasons for downgrading each domain seem missing in the revised manuscript, although the author have replied that the information was provided in response to my comment. Please response to my comment and describe clearly how and where they modified the manuscript.

We apologize that the information about our assessment of the quality of the meta-evidence was lacking detail in our original revised manuscript. We have now provided more detail in the results section:

“Across the individual domains of NutriGrade, the following downgrades were applied: risk of bias for studies of white rice based on mean NOS score; heterogeneity for studies of white rice based on I2 ≥40%; publication bias for studies of brown rice since there were <5 studies; and effect size for studies of white rice and brown rice since pooled RRs were 0.80–1.20 comparing extreme categories. NutriGrade scores for RCTs ranged from 5.9 to 6.9 for outcomes that were assessed in all 11 studies, suggesting that the strength of the evidence from these meta-analyses was considered moderate and low. Across individual domains of NutriGrade, the following downgrades were applied: risk of bias for all outcomes based on Cochrane RoB-2; precision for LDL cholesterol, TG’s, and FBG since 95% CI of pooled mean difference included the null value; heterogeneity for HDL and LDL cholesterol and FBG based on I2 ≥40%; publication bias for HDL cholesterol and FBG; and funding bias for all outcomes since affiliation with private institutions and foundations were noted for some studies (Supplemental Table 4).”

VERSION 3 – REVIEW

<table>
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<tr>
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<td></td>
<td>Research Center for Cancer Prevention and Screening National Cancer Center, Epidemiology and Prevention Division</td>
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<tr>
<td>REVIEW RETURNED</td>
<td>02-Aug-2022</td>
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<tr>
<td>GENERAL COMMENTS</td>
<td>Thank you for your response. I have no further comment.</td>
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