

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

#### Title (Provisional)

ASSOCIATION BETWEEN VITAMIN B12 DEFICIENCY AND METFORMIN USE IN TYPE 2 DIABETIC PATIENTS: A CROSS-SECTIONAL STUDY IN A SOUTH VIETNAM TERTIARY HOSPITAL

#### Authors

Phan, Hen Huu; Nguyen, An Thuy Thi; Do, Minh Duc

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### VERSION 1 - REVIEW

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|------------------------|---|
| Reviewer               | 1   |
| Name                   | Dewi, Ayu Putu Madri                              |
| Affiliation<br>Science | Amsterdam UMC Location AMC, Epidemiology and Data |
| Date                   | 10-Mar-2025                                       |
| COI                    | None  |

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*I am an Open Science researcher, who has checked your manuscript for its adherence to a number of Open Science practices.*

*Below you find the checklist that I used to assess your manuscript for adherence to a number of these practices.*

*Based on this assessment, I would suggest the following refinements/additions:*

- 1. Availability of a protocol: Please provide a (link to the) the protocol.*
- 2. Pre-registration: Please provide information on whether and where the study was pre-registered.*
- 3. Open Materials: N/A.*
- 4. Open Data: The manuscript states "The data that support the findings of this study are available within the article text and tables.". This is, however, insufficient to reproduce the complete study. Therefore, please provide a statement about whether and where the **raw data** used for this study can be accessed. Given the potential confidentiality of the data, please specify whether de-identified, metadata, or a subset of the data can still be made publicly available.*
- 5. Open Code: Please provide (a link to) the code used for the analyses in this study.*

6. *Citations: Please provide citations for your materials/data/codes.*
7. *Software and tools used are described: OK.*
8. *Open access publication: OK.*
9. *Reporting checklist provided: OK.*
10. *Preprint: Please state explicitly whether and where the preprint of this study can be found.*

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| <b>Reviewer</b>    | <b>2</b>   |
| <b>Name</b>        | <b>Didangelos, Triantafyllos</b>                               |
| <b>Affiliation</b> | <b>Aristotle University of Thessaloniki, Internal Medicine</b> |
| <b>Date</b>        | <b>25-Mar-2025</b>   |
| <b>COI</b>         | <b>None</b>  |

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The present cross-sectional study examined the prevalence of vitamin B12 deficiency among lean patients with type 2 diabetes. The authors reported that the median duration of metformin use among participants was 10 years, with an average metformin dose of 1700 mg. According to the existing literature, vitamin B12 deficiency can develop after four years of continuous metformin use.

This raises the question: Is there a specific reason that vitamin B12 deficiency did not occur in some patients in Vietnam? Why didn't all participants exhibit vitamin B12 deficiency?

Additionally, the authors did not provide information on other antidiabetic treatments that the participants may have been receiving.

Furthermore, the study lacks novelty, and the patient sample size was relatively small.

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|--------------------|-------------------------------------|
| <b>Reviewer</b>    | <b>3</b>                            |
| <b>Name</b>        | <b>Herbert, Laura L.</b>            |
| <b>Affiliation</b> | <b>University of South Carolina</b> |
| <b>Date</b>        | <b>28-Mar-2025</b>                  |
| <b>COI</b>         | <b>None</b>                         |

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Well written. I have no requested revisions.

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## VERSION 1 - AUTHOR RESPONSE

**Reviewer: 1**

Ms. Ayu Putu Madri Dewi, Amsterdam UMC Location AMC

Comments to the Author:

I have some feedback related to open science practices. Please find attached the feedback details.

*Thank you for your suggestions on open science practices.*

Based on this assessment, I would suggest the following refinements/additions:

1. Availability of a protocol: Please provide a (link to) the protocol.

*The protocol was described in the Material and Method section.*

2. Pre-registration: Please provide information on whether and where the study was preregistered.

*The study was pre-registered and approved by the Ethical Committee of Cho Ray Hospital (approval number 1711/CN-HĐĐĐ)*

3. Open Materials: N/A.

4. Open Data: The manuscript states “The data that support the findings of this study are available within the article text and tables.”. This is, however, insufficient to reproduce the complete study. Therefore, please provide a statement about whether and where the raw data used for this study can be accessed. Given the potential confidentiality of the data, please specify whether de-identified, metadata, or a subset of the data can still be made publicly available.

*Thank you for your suggestions, we made changes to the Data availability statement to ensure open science practice.*

5. Open Code: Please provide (a link to) the code used for the analyses in this study.

*All the analyses performed in this study were accomplished using SPSS Statistics for Windows version 20.0 (IBM Corporation, Armonk, NY, USA). All the analyses can be repeated by appropriate commands in SPSS.*

6. Citations: Please provide citations for your materials/data/codes.

*Thank you for your suggestions, these details were provided in the manuscript.*

7. Software and tools used are described: OK.

8. Open access publication: OK.

9. Reporting checklist provided: OK.

10. Preprint: Please state explicitly whether and where the preprint of this study can be found.

*We did not submit a preprint version of this study.*

## **Reviewer: 2**

Dr. Triantafyllos Didangelos, Aristotle University of Thessaloniki

Comments to the Author:

The present cross-sectional study examined the prevalence of vitamin B12 deficiency among lean patients with type 2 diabetes. The authors reported that the median duration of metformin use among participants was 10 years, with an average metformin dose of 1700 mg. According to the existing literature, vitamin B12 deficiency can develop after four years of continuous metformin use. This raises the question: Is there a specific reason that vitamin B12 deficiency did not occur in some patients in Vietnam? Why didn't all participants exhibit vitamin B12 deficiency?

*Thank you for your questions. There were several reasons why vitamin B12 deficiency did not occur in all the participants:*

*- Not all the participants were treated with metformin for four consecutive years and/or with high metformin dose.*

*- The exact mechanisms of vitamin B12 deficiency in patients treated with metformin remained elusive and who will absolutely develop vitamin B12 deficiency is still an unanswered question. Therefore, current ADA guidelines recommend to screen for high-*

*risk patients and treat if they have vitamin B12 deficiency rather than treating all patients with metformin use for four consecutive years and more.*

Additionally, the authors did not provide information on other antidiabetic treatments that the participants may have been receiving.

*Thank you for the suggestions, the information on other antidiabetic treatments besides metformin was added in the manuscript (line 159-162 and in the Table 1).*

Furthermore, the study lacks novelty, and the patient sample size was relatively small.

*Thank you for your comments, this study was performed without any specific funding, due to the lack of financial support, we could only recruit this number of participants.*