Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

# 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)

Cardiovascular risk factors and cognitive performance among people living with HIV: cross-sectional study in the country of Georgia

### **Authors**

Baliashvili, Davit; Imerlishvili, Esma; Karaulashvili, Ana; DeHovitz, Jack; Gustafson, Deborah R.; Djibuti, Mamuka

#### **VERSION 1 - REVIEW**

Reviewer 1

Name Brew, Bruce

Affiliation University of New South Wales, Department of Neurology

Date 15-Sep-2024

COI none

This is an interesting small study that has importance for Georgia. The findings are not new on the international stage though. A cautionary note should be considered by the authors in relation to stating that the cognitive impairment is vascular. The cognitive profile of HIV and vascular cognitive impairment are almost indistinguishable. Therefore the findings could relate to HIV per se, vascular disease or more likely both

Reviewer 2

Name D'Ascenzo, Fabrizio

Affiliation San Giovanni Battista, Molinette

Date 06-Jan-2025

COI None

Interesting paper

Some issues should be added

Abtract: p value should be added

Methods: do authjors think that sefl reported methods may be worth of? did thy check them?

Graphical expression of multivariable analysis should be added

Methods: did authors have data about cd4 cell count and/or hiv rna which have been linked to atherosclerotis events?

discussion: HIV patients have different kind of plaques compared to non hiv. (quote onPMID: 29803160). Do authors think this is a potential mechanism?

# **VERSION 1 - AUTHOR RESPONSE**

Reviewer: 1

Prof. Bruce Brew, University of New South Wales

Comments to the Author:

**Comment 2**: This is an interesting small study that has importance for Georgia. The findings are not new on the international stage though. A cautionary note should be considered by the authors in relation to stating that the cognitive impairment is vascular. The cognitive profile of HIV and vascular cognitive impairment are almost indistinguishable. Therefore the findings could relate to HIV per se, vascular disease or more likely both

**Response 2**: We agree with the reviewer that there are multiple neuropathological, including vascular, mechanisms related to cognitive impairment or poorer cognition. We added a note in the discussion stating that our findings, in this older sample of PLWH >=40y, may not be related to HIV alone, but to comorbid vascular, inflammatory, and other aging-related brain and peripheral events. (lines 279-280).

Reviewer: 2

Dr. Fabrizio D'Ascenzo, San Giovanni Battista

Comments to the Author:

Interesting paper

Some issues should be added

Comment 3: Abtract: p value should be added

**Response 3**: We thank the reviewer for noticing the missing p-values in the abstract. We added the p-values after confidence intervals in places where we report association between FRS and cognitive assessment results. (lines 46 and 47)

**Comment 4**: Methods: do authjors think that sefl reported methods may be worth of? did thy check them?

**Response 4**: We thank the reviewer for raising an important question. We agree that some of the information collected through self-report might be less reliable, but most of the main findings in our study are based on either lab tests or validated assessment tools. All the laboratory assessments were conducted in highly skilled laboratory. Diabetes was partially self-reported, which we acknowledge in the discussion (lines 296-298). We also collected CD4 and viral load information based on self-reports, but due to a large proportion of missingness, we did not include these variables in the analysis.

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Comment 5: Graphical expression of multivariable analysis should be added

**Response 5**: We thank the reviewer for the suggestion. We added figure 2 which represents the associations between FRS and each of the cognitive assessments based on multiple linear regression analyses.

**Comment 6**: Methods: did authors have data about cd4 cell count and/or hiv rna which have been linked to atherosclerotis events?

**Response 6**: We agree with the reviewer about importance of CD4 cell count and HIV RNA. Unfortunately we did not conduct lab tests for these. As mentioned in the response to comment #4, we collected self-reported information on the most recent results of CD4 and viral load, but due to large proportion of missingness and unreliability of self-reported results, we did not use those variables in the analysis.

**Comment 7**: discussion: HIV patients have different kind of plaques compared to non hiv. (quote on PMID: 29803160). Do authors think this is a potential mechanism?

**Response 7**: We thank the reviewer for providing this additional reference and potential mechanism. We added the difference in plaque morphology as one of the potential mechanisms of association in the discussion section (lines 286-287)