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Letter to the Editor

Letter to editor–Beetroot juice intake positively influenced gut microbiota and inflammation but failed to improve functional outcomes in adults with Long COVID

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Calvani et al. proposed a model using partial least squares discriminant analysis (PLS–DA) to comprehensively investigate the effects of beetroot juice supplementation on inflammatory markers, fecal metabolites, and metagenomic parameters [1]. In their study, PLS–DA models were constructed separately for each biological domain, specifically for fecal metabolites, metagenomic data, and inflammatory markers. Subsequently, low-level data fusion models were developed to integrate the information from these individual data matrices into a unified model. This integration aimed to enhance the understanding of the interrelationships among the diverse biological domains assessed and potentially improve the accuracy of outcome predictions. The robustness of all PLS–DA models was confirmed through repeated double cross-validation [1].

It is essential to rigorously address the inherent biases associated with feature importances derived from Partial Least Squares Discriminant Analysis (PLS-DA) [2–6]. The conclusions drawn by Calvani et al. may be misleading due to these biases, potentially resulting in erroneous interpretations of the data. While cross-validation is a robust method for evaluating prediction accuracy, it falls short in validating the reliability of feature importance metrics. Researchers should be mindful of fundamental principles in machine learning, specifically that cross-validation effectively assesses predictive accuracy but does not reliably gauge feature importance while machine learning models inherently generate biased feature importances.

It is critical for researchers to distinguish between the two distinct objectives of machine learning: making accurate predictions and assessing feature importances. The primary goal of machine learning is to develop models that accurately predict the target variable, whereas feature importance metrics are intended to illustrate the relationships between the target and predictor variables. Due to the model-specific nature of these importance measures, those derived from PLS-DA and similar techniques are often susceptible to biases, which can obscure the true relationships between the target and the features [2–6].

Thus, comprehensive understanding and careful interpretation of feature importance in the context of PLS-DA are paramount. Failure to recognize these biases may lead to misguided conclusions about the effects of interventions, such as beetroot juice supplementation, and their underlying biological mechanisms. Therefore, researchers must adopt a critical perspective when interpreting feature importance scores, considering complementary methodologies and validation techniques that can provide a more accurate representation of the relationships within their data.

This paper elucidates the reasons why PLS-DA inherently biases feature importances, which can lead to flawed conclusions regarding the influence of beetroot juice supplementation and its biological effects. It emphasizes the need for caution when interpreting feature importances from PLS-DA and advocates for the use of complementary bias-free methods such as Spearman's correlation with p-values to validate findings in future research [7–9].

Over 100 peer-reviewed articles addressed bias issues in feature importances from machine learning models. Partial Least Squares Discriminant Analysis (PLS-DA) is a widely used method for classification and regression tasks, particularly in high-dimensional data scenarios. However, PLS-DA can inherently induce biased feature importances for several reasons, which can be categorized into algorithmic, mechanical, statistical, and other influencing factors.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

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Code availability

Not applicable.

Authors' contributions

Yoshiyasu Takefuji completed this research and wrote this article.

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Conflicts of interest

The author has no conflict of interest.

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