Response to: 'On using machine learning algorithms to define clinically meaningful patient subgroups' by Knevel and Huizinga

We thank Knevel and Huizinga for their good comments¹ on our work in which we used hierarchical clustering on principal components to define clinically meaningful subgroups of patients with anti-Ku antibodies² and, to a lesser extent, on the work of Mariampillai *et al*³ in which the authors used a similar method to reveal subgroups of myositis and propose a classification of these diseases.

Knevel and Huizinga nicely explain how this statistical tool is a useful alternative to detailed insight in pathogenesis to improve taxonomy and personalise medicine. In this regards, myositis, which is rare and heterogeneous condition, is perfectly fitted for this method.

Knevel and Huizinga also challenge the concern about these techniques raised by Pinal-Fernandez and Mammen through a statistical sophistry.⁴ In this regards, the initiative started by the European League Against Rheumatism (EULAR) to guide the use of big data techniques for rheumatic and musculoskeletal diseases will help to promote the development and the standardisation of these tools.⁵

Finally, Knevel and Huizinga point out the importance of the validation of the findings. Given the extreme rarity of anti-Ku patients, we used k-fold cross-validation method as detailed by the authors.^{1,2} Furthermore, Mariampillai *et al*³ have used the independent cohort of 50 patients to confirm 4 groups of myositis they highlighted through hierarchical clustering on principal components analysis.

As a conclusion, myositis and related conditions are examples of musculoskeletal diseases that are well fitted for big data techniques such as hierarchical clustering on principal components. We welcome the initiative of EULAR to further improve the development and the standardisation of these techniques.⁵

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