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Reply to: Current classification criteria underestimate the incidence of idiopathic inflammatory myopathies by ignoring subgroups

We thank Giannini et al.[1] for their response (Giannini, M. et al. Current classification criteria underestimate the incidence of idiopathic inflammatory myopathies by ignoring subgroups. *Nat. Rev. Rheumatol.* https://doi.org/10.1038/s41584-024-01105-9 (2024)) to our Review article (Epidemiology of the idiopathic inflammatory myopathies, *Nat. Rev. Rheumatol.* **19**, 695–712 (2023))[2], in which they make several observations of interest. As highlighted in our Review, accurate assessment of the epidemiology of idiopathic inflammatory myopathies (IIMs) is challenging, and is influenced by disease awareness, classification criteria and access to serological and/or histopathological testing[2].

We concur with Giannini et al.[1] that some IIM subgroups lack classification criteria. One such clinical subgroup is overlap myositis, which shares clinical features or autoantibodies with a further autoimmune connective tissue disease (CTD). In established cohorts, up to 27% of patients with IIM have been retrospectively reported to have overlap myositis[3]. The lack of cohorts dedicated to overlap myositis, and its absence from healthcare record diagnostic coding, such as the International Classification of Diseases (ICD), limits the assessment of the true epidemiology of this heterogeneous subgroup.

The issue of including overlap myositis also extends to clinical trials, from which patients with overlapping features are frequently excluded. In a real-world cohort of patients with CTD, 10 out of 22 (45.5%) patients with IIM also fulfilled classification criteria for systemic sclerosis, Sjögren syndrome or systemic lupus erythematosus, which can affect the eligibility for a phase III trial[4].

Although antisynthetase syndrome (ASyS) is not included in the 2017 EULAR–ACR classification criteria for IIM[5], the Classification of Anti-Synthetase Syndrome (CLASS) project is currently underway[6], as Giannini et al.[1] mentioned. Clinical trials in IIM include ASyS[7] but the key inclusion criterion of moderate muscle weakness excludes individuals with ASyS who have predominant extra-muscular disease. With respect to IIM cohorts derived from healthcare databases, the lack of an ICD code affects case ascertainment of ASyS. In addition, skin rashes characteristic of dermatomyositis are frequently found in individuals with ASyS[8] and can lead to misclassification when using the 2017 EULAR–ACR classification criteria alone.

In our Review, we included epidemiological studies published before March 2023. In their paper published in October 2023, Debrut et al.[9] effectively applied capture–recapture methods using four data sources in a region with a population of two million, identifying 106 patients with IIM and estimating 14.9 cases missed by any single source. Capture–recapture methods aim to maximize case ascertainment by using multiple data sources. However, capture–recapture methods have some limitations[10]. First, there is an assumption that the data sources are independent. This is unlikely to be the case for IIM as healthcare record coding depends on a documented diagnosis, which is influenced by serology and histopathology. Statistical modelling can minimize but not eliminate the effect of dependencies. Second, defining the limits of a 'closed' population in IIM can be problematic as clinical review, muscle biopsy and autoantibody testing are performed only at specialized centres. Finally, the resultant population estimates can be biased if one source captures a disproportionately low number of cases.

Ultimately, even with capture–recapture methods, case ascertainment relies primarily on classification and coding. There remains a need for updated, consistent and inclusive criteria. For IIM subgroups such as overlap myositis, the challenge lies in capturing phenotypic and serologic diversity within the confines of healthcare record coding and classification criteria for use in epidemiological research.

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Competing interests

The authors declare no competing interests.