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

We read with great interest the Review article by Khoo et al. (Epidemiology of the idiopathic inflammatory myopathies, *Nat. Rev. Rheumatol.* **19**, 695–712 (2023))[1] and would like to point out findings not included in the Review that shed new light on the epidemiology of idiopathic inflammatory myopathies (IIMs) and future research agendas.

The authors reported that the incidence of IIMs ranges from 2 to 20 cases per million person-years[1] and suggested that these variations might reflect the need for better methodological homogeneity rather than true epidemiological differences. Indeed, complete case ascertainment is difficult to achieve in IIM epidemiology. There are no International Classification of Diseases (ICD) codes that cover the entire IIM spectrum, and patient care involves many different specialists owing to the systemic nature of IIM. Although use of the capture–recapture method might overcome this limitation, none of the studies referenced by Khoo et al.[1] used this tool to estimate the entire IIM epidemiology. Bohan and Peter's criteria were most frequently used, although they lack specificity; the 2017 EULAR–ACR criteria for classification of IIM have better sensitivity and specificity, but were used by only two referenced studies[1].

Shortly before the publication by Khoo et al.[1], we reported IIM incidence in eastern France as determined by use of four-source capture–recapture analysis combined with the 2017 EULAR–ACR criteria[2]. The reported incidence of 8.22 cases per million person-years was close to that found in a previous meta-analysis (7.98 cases per million person-years)[3], further validating the results yielded by use of this methodology.

As highlighted by Khoo et al.[1], there remain some shortcomings of the 2017 EULAR–ACR criteria in identifying the whole spectrum of IIM. In particular, several extramuscular signs are not taken into account despite being common initial manifestations that can remain isolated throughout follow-up[4], and over ten IIM-specific autoantibodies are not considered in the criteria. How this issue affects current knowledge of IIM epidemiology deserves further discussion.

In a John Hopkins cohort, 9% of patients positive for myositis-specific autoantibodies did not fulfil the 2017 EULAR–ACR criteria. This misclassification affected up to one-quarter of those with non-anti-Jo1 antisynthetase antibodies[5].

As noted in the supplementary information of our population-based survey, 43 patients tested positive for IIM-associated autoantibodies and showed signs of connective tissue disease incident during the study period, but did not fulfil the 2017 EULAR–ACR criteria and were thus excluded from the estimation of incidence rate[2]. Of these 43 patients, 15 (34.9%) had antisynthetase autoantibodies (namely anti-Jo1 ($n = 7$), anti-PL12 ($n = 6$) or anti-PL7 ($n = 2$) antibodies), thus fulfilling proposed (but not validated) criteria that enable the diagnosis of antisythetase syndrome (ASyS) even with slight or no muscle involvement or dermatomyositis rash[6]. Twenty-four other patients had autoantibodies associated with scleromyositis (anti-Ku ($n = 14$) or anti-PM/Scl ($n = 10$) antibodies), an overlap syndrome of inflammatory myopathy and systemic sclerosis (SSc) for which there are currently no criteria[7]. Importantly, although patients with these autoantibodies frequently show clinical features of SSc, in more than two-thirds of the cases they do not fulfil the 2013 EULAR–ACR criteria for SSc[8,9] and thus they are not recorded in the epidemiology of SSc.

Together, these additional data show that the current EULAR–ACR IIM criteria miss patients with ASyS and scleromyositis, leading to an underestimation of IIM incidence by more than one-quarter. The EULAR–ACR classification of antisynthetase syndrome project and the 273rd ENMC workshop (https://go.nature.com/3TapafP) will help to increase awareness and recognition of ASyS[6]. We propose that further research should also focus on classification criteria for scleromyositis.

There is a reply to this Correspondence by Khoo et al. *Nat. Rev. Rheumatol.* https://doi.org/10.1038/s41584-024-01106-8 (2024).

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Competing interests

The authors declare no competing interests.