

Letter to the Editor (Matters arising from published papers)

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Comment on: Epidemiology of biopsy-confirmed giant cell arteritis in southern Sweden—an update on incidence and first prevalence estimate: reply

DEAR EDITOR, We thank Yang *et al.* [1] for their letter and their interest in our article entitled ‘Epidemiology of biopsy-confirmed GCA in southern Sweden—an update on incidence and first prevalence estimate’ [2].

Yang *et al.* discussed in their letter important aspects regarding the epidemiological studies on GCA. We agree that reasons for discrepancies in the reporting seasonality between studies may be related to methodological issues, such as case definitions, and perhaps the chosen time point of disease onset or performed temporal artery biopsy (TAB). Determining the exact onset of the disease is not always feasible in large scale register-based studies. The ascertainment of the disease onset using case-by-case review of medical records is a clear advantage of the study by Yang *et al.* However, this may not be an achievable task in studies covering longer periods of time and larger populations, as in our population-based study from southern Sweden that included >6500 TABs performed in a 23-year period [2]. In our study, we rely on a previous assessment of diagnostic delay using a sample of 170 cases from our Swedish GCA cohort [3]. The median diagnostic delay in our cohort was previously estimated to be 24 days [interquartile range (IQR) 11–35 days] for patients without visual symptoms and 24 days (IQR 9–45 days) for patients with visual symptoms [3]. Thus, we believe that this delay would not have a major impact on the seasonality of biopsy-confirmed GCA in our study.

In contrast to our findings of decreasing incidence of biopsy-confirmed GCA, Yang *et al.* reported increasing incidence of GCA during 10 years [1]. Given the smaller size of their cohort (64 patients diagnosed with GCA during a 10-year period), the uncertainty around the results is considerable as they could represent differences of a limited absolute number of patients [1]. Furthermore, Yang *et al.* suggest that their observation of an increasing incidence of GCA may be attributed to an ageing population. However, the estimates in our study were age- and sex-standardized and did not support this notion. Another important difference between our study and the commentary of Yang *et al.* is that whereas ours was a population-based study using a

regional database, theirs was conducted at a tertiary centre, which may be prone to referral bias.

In addition to such methodological issues, differences in demography and ethnicity of the populations and in health-care systems in different regions around the world complicate the comparison of studies. We fully agree with Yang *et al.* that increasing access to different imaging modalities may have an important impact. Furthermore, we believe that changes in the background population, with increasing immigration from areas with lower prevalence of GCA, may also have influenced our results.

The burden of GCA includes the whole spectrum of the disease with its different phenotypes. These includes cranial GCA, isolated large vessel vasculitis and PMR overlapping with vasculitis. Large studies covering all these phenotypes are rare and need access to extensive epidemiological resources. Smaller studies may not have the power of representativeness of disease spectrum. Temporal artery biopsy is regarded as the gold standard in diagnosing the cranial arteritis and it is still widely used, especially when facilities of imaging studies are limited. Another important point to consider regarding the epidemiology of GCA is to differentiate between patients with GCA who underwent TAB vs those who did not. The latter group are usually those with large vessel ‘extra-cranial’ vasculitis, usually investigated by imaging studies such as computed tomography angiography (CTA), magnetic resonance angiography (MRA) or PET CT. These patients would not be included in the study by Yang *et al.*, as they only reviewed patients with negative TAB and not those only examined by imaging studies. Accordingly, neither our study nor the study by Yang *et al.* represents the whole spectrum of GCA. We should also add that the use of ultrasound in our area was limited during the study period, although the decrease in the incidence of GCA may be attributed to the use of other imaging modalities.

In agreement with our results, several epidemiological studies including patients with biopsy-confirmed GCA have reported a stable or decreased incidence of the biopsy-confirmed GCA during the past two decades [4, 5]. A similar trend has also been reported in studies including patients fulfilling the ACR 1990 criteria or including patients with positive imaging [6–8].

Interestingly, there were some similarities regarding seasonality between our study and that of Yang *et al.* Although there are obviously major differences in the seasonal changes between Scandinavia and Australia, the top incidence estimate in spring during our study would

correspond to their observation of more frequent disease onset during autumn in the southern hemisphere.

Finally, we totally agree with Yang *et al.* on the unmet need of larger studies that enrol patients from different regions using identical case ascertainment and classification of GCA in order to obtain accurate estimates on the epidemiology of GCA.

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Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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