

## Increased Incidence of Giant Cell Arteritis in Urban Areas?

To the Editor:

Giant cell arteritis (GCA) is the most common systemic vasculitis in adults. The pathogenesis and the etiology of the disease are not fully understood, and environmental factors, which may influence the incidence and prevalence, are poorly investigated. Only a few small studies have previously addressed the potential influence of rural or urban residence on the occurrence of GCA<sup>1,2,3</sup>. In 2017 we published the results of a 41-year study of 743 patients with GCA from Bergen Health Area (Norway), in which incidence estimates were stratified by sex, age, biopsy result, and erythrocyte sedimentation rate<sup>4</sup>. Bergen Health Area is a mixed urban and rural area. In this report we present incidence estimates stratified by centrality, which may clarify the influence of rural versus urban residence on the incidence of GCA.

This study was approved by REK sør-øst B regional ethics committee (study reference 2012/643/REK sør-øst B), who granted permission to access records without obtaining consent from patients owing to the long duration of the study and late onset of the disease.

We performed a hospital-based retrospective cohort study including patients diagnosed with GCA during 1972–2012. The study setting was Bergen Health Area, consisting of 3 somatic hospitals that provide specialist healthcare services to the inhabitants of 22 municipalities in Hordaland County in western Norway. We collected data on patients registered with the diagnosis of GCA in any of the study hospitals between January 1, 1972, and December 31, 2012. The patients' addresses were obtained from the Norwegian population register, and municipalities were classified as urban (code 1 and 2) or rural (including remote areas, code 3 thru 6) using Statistics Norway 2017 classification of centrality<sup>5</sup>. Further details about the inclusion process and statistical methods have been published previously<sup>4</sup>.

We included 743 patients; 72% women and 66% with a positive

temporal artery biopsy. A total of 484 patients (65%) had a residential address in a municipality classified as urban and 259 (35%) in a rural municipality. The annual cumulative incidence of GCA per 100,000 persons  $\geq$  50 years was 17.1 (95% CI 15.9–18.4) for urban areas and 16.1 (95% CI 14.9–17.3) for rural areas ( $p = 0.46$ ). Corresponding numbers for biopsy-proven GCA was 11.7 (95% CI 10.6–12.7) for urban and 10.4 (95% CI 9.4–11.4) for rural areas ( $p = 0.10$ ). There were large annual fluctuations in both urban and rural incidence (Figure 1 and Figure 2). The annual cumulative incidence for the entire catchment area has been published<sup>4</sup>.

This 41-year study of 743 patients with GCA did not reveal any significant difference in incidence between urban and rural areas. This differs from 3 previously published German reports<sup>1,2</sup>, which found both prevalence and incidence to be higher in urban areas. German point prevalence reports from 1994 and 2006 found prevalence rates almost twice as high in urban compared to rural areas, and a 10-year (1982–1991) incidence study reported urban incidence about double that of rural incidence. However, our study demonstrated large fluctuations in annual incidence in both urban and rural areas. Over the entire 41-year period we found no significant difference between rural and urban populations. Further, the numbers of patients in the German reports were small, 79 in 1994 and 80 in 2006, compared to 743 in our study. Acknowledging the great variance in annual incidence, a study of a rather small patient cohort during a short period of time could represent a random extreme rather than a representative result.

We note that our study is a hospital-based referral study, reporting incidence of GCA, whereas 2 of the German reports were population-based prevalence studies. Differences in demographic factors or medical care infrastructure may have influenced the results. Possible biases, which may overestimate the prevalence in urban areas, include the possibility that persons with severe chronic disease might move to an area with a center for secondary/tertiary healthcare services. It is also possible that the presence of a university medical center may have led to greater awareness and

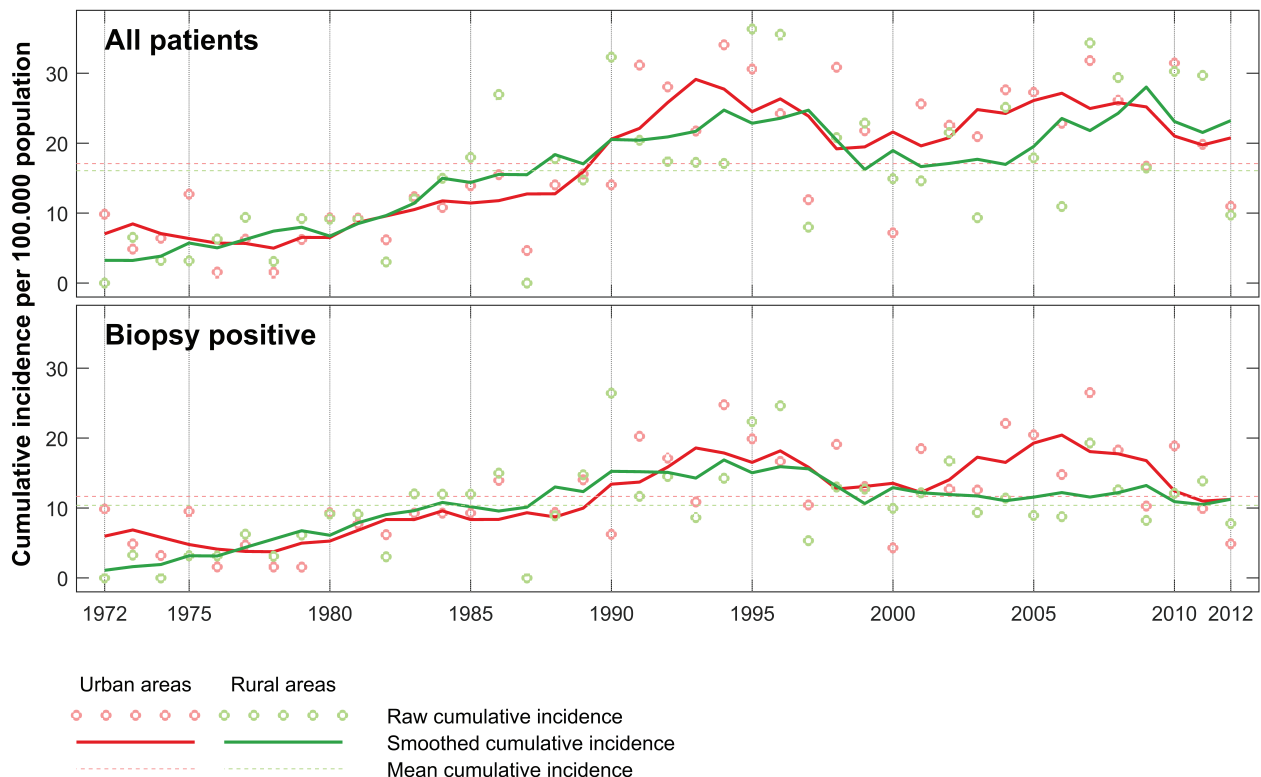


Figure 1. Annual incidence of giant cell arteritis in Bergen Health Area, 1972–2012.

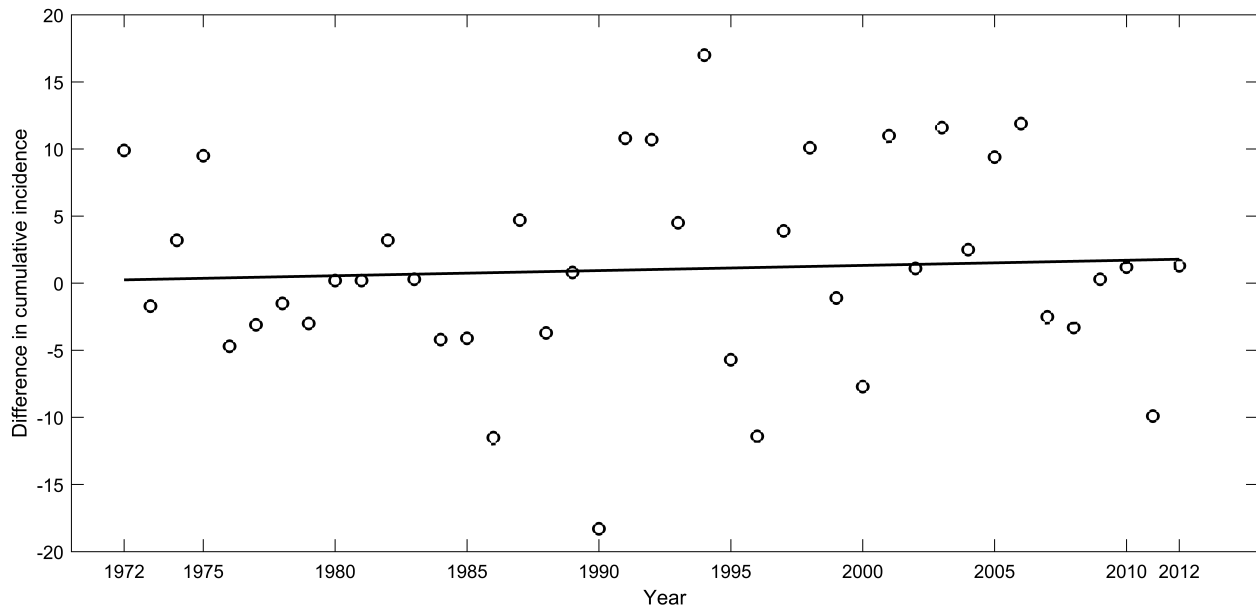


Figure 2. Numeric difference in annual incidence of giant cell arteritis (GCA) in urban versus rural areas. Points plotted represent the absolute numeric difference between annual cumulative incidence of GCA in urban and rural areas of western Norway for each of the 41 years of the study period. The solid black line represents a linear trend line.

improved diagnostic yield in urban areas. This may be more common in Germany than in Norway. We note that in our study the urban area (city of Bergen) is in immediate proximity to the rural areas studied. This may be a limitation if rural/urban differences in incidence were associated with airborne exposures or infectious epidemics. In contrast, the German prevalence reports compared GCA cases in cities located 30–70 km from the corresponding rural areas. However, our cohort is large and well-characterized following a meticulous chart review, which provided generally complete baseline data. Our results therefore indicate that differences in the occurrence of GCA between urban and rural areas might not be present or at least not as substantial as previously reported. Further studies are required to determine whether there is a true difference.

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