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To the Editor of Respiratory Medicine:

It is with great interest that we read the article titled "Clinical epidemiology of familial sarcoidosis: A systematic literature review" by Drs. Terwiel and van Moorsel published recently in *Respiratory Medicine* [1]. Their systematic review on familial sarcoidosis highlights the great heterogeneity in familial disease prevalence and in familial relative risks among published studies. They also emphasize the high heritability (> 60%) of sarcoidosis.

We noticed that our recently published study [2] was not included in this literature summary, likely due to the fact that the submission of this review article in March 2018 occurred before our study was published (August 2018). Our study is the largest investigation of familial aggregation and heritability of sarcoidosis. Because we utilized Swedish population-based register data, biases stemming from selective ascertainment of disease in relatives are minimal and our findings are likely more generalizable. That is because Swedish registers provide data on the entire population's tax-funded and universally accessible inpatient and outpatient care and allows for relatives of registered residents to be unbiasedly identified. With this correspondence, we would like to bring attention to findings in our study that deviate from the conclusions of this literature review so that readers can have a more enriched view.

Prevalence of familial disease. In our population-based sample of more than 20332 proband cases identified between 1964 and 2013 and born in Sweden, we found that approximately 4.1% of these had a first degree relative diagnosed with the disease [2]. This prevalence of familial disease is almost half the pooled prevalence of 9.5% that the authors of the review reported based on hospital-derived patient cohorts. Acknowledging the fact that we may have slightly underestimated the prevalence as our ability to identify sarcoidosis improved with the availability of outpatient data starting 2001, we believe that hospital cohorts are more likely to overestimate familial disease prevalence either due to the clustering of severe cases or the higher probability to enroll when disease is familial.

Familial aggregation estimates. In our study, the relative risk of sarcoidosis associated with having at least one first degree relative with sarcoidosis was 3.7 (95% CI 3.4, 4.1) [2]. This is similar to the overall ACCESS estimate (relative risk 3.8) [3], but lower than the relative risk reported for white Americans (16.6). The relative risk associated with having a half sibling with the disease in our study was lower than the estimate for full siblings (relative risk 1.5), as expected due to half siblings having only 25% genetic similarity [2]. Similar to ACCESS, we did not observe much variation of the relative risks by kinship or sex of the proband and relative, but in contrast to ACCESS, our familial relative risks were slightly higher for probands who were diagnosed before the age of 50 years compared to probands aged 50 or older at diagnosis [2].

Heritability. We estimated the heritability of the disease to be 39% [2], much lower than previously reported [4,5]. The best biometric model that fit our data was one with a shared genetic and non-shared environmental component, and when tested, shared environmental factors did not explain any of the variation in our population [2]. The ceiling heritability calculated using tetrachoric correlations and sarcoidosis prevalence estimates confirmed the validity of our model [2]. A heritability of about 40% highlights the importance of investigating environmental triggers of sarcoidosis occurrence (together with genetic factors) and that sarcoidosis could hopefully be prevented in the near future.

We appreciate the authors' efforts to summarize this cluttered but clinically and etiologically important area of the sarcoidosis literature. To gain a more accurate view of the state of the literature on this topic, we believe that readers should also consider our study findings.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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