Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

did not stratify patients according to already published clinical subclassification, and incorporated instead some criteria such as involved anatomical areas, and the inflammatory burden reflected by Hurley stage, associated inflammatory diseases, and the C-reactive protein serum level. Although we agree these criteria are likely to lack discriminating power, we were able to show that the most inflammatory forms are preferentially associated with the presence of ASCAs, and at this stage we may claim that HS-related autoinflammatory syndromes are one of the endotypes associated with this biomarker. However, we agree with van Straalen that prospective studies stratifying patients with HS at the clinical level with more granularity is of major interest when considering disease heterogeneity.

Whether such biological heterogeneity is underlined by a specific genetic background is at the center of the other van Straalen's major comment. We are aware that a study in patients with Crohn disease unraveled some correlation between the presence of a specific variant of *NOD2* (3020insC) and the presence of ASCA, with an impact of allelic dosing on ASCA IgA titers.[5] In line with van Straalen, we tend to believe that specific genotypes are likely to influence the likelihood to develop ASCA as a surrogate biomarker of gut dysbiosis. However, although we did not investigate the genetic status of *NOD2* in our patients with HS, we did sequence all exons from this gene by the Sanger method in patients with HS-related autoinflammatory syndromes, and could not detect a mutation in any of the analyzed patients, as reported in Gottlieb et al.[6] This limited set of data is in line with previous publications showing no evidence for mutations of NOD2 in patients with HS.[7] That said, we agree that it remains possible that some genotypes of NOD2 or other innate immune genes predisposing to CD may overlap between inflammatory bowel diseases and HS subpopulations, influencing the diseases patterns through common dysbiotic features.

In conclusion and referring to van Straalen's last remark on the diagnostic value of ASCA across different ethnic backgrounds, we can just agree that this parameter will have to be part of future studies investigating clinical and biological phenotypes/genotypes/microbiome correlations in HS.

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The clinical relevance of the clinical cytological grading in patients with chronic rhinosinusitis with nasal polyps

To the Editor:

Smell dysfunction is a common symptom and has a diagnostic value in the workup of patients with chronic rhinosinusitis with nasal polyps (CRSwNP) as recently outlined by Mullol et al.[1] Notably, loss of smell has been proposed as one of the main criteria for an indication of and response to the new biological treatments.[2] Of note, it has been very recently reported that a significant part (20%-60%) of the patients with coronavirus disease 2019 (COVID-19) experienced the loss of smell; anosmia can be the first presenting symptom and so the European Rhinologic Society advised that patients with sudden-onset loss of smell should be considered to be COVID-19 positive (www.europeanrhinologicsociety.org).

CRSwNP is characterized by a type 2 inflammation and is frequently associated with some comorbidity, including asthma, aspirin sensitivity, and allergy.[3] Type 2 inflammation leads to eosinophils and mast cells recruitment and activation in upper airways. Therefore, to document the presence of inflammatory cells in the nose by nasal cytology is a simple and fruitful way to assess the severity of disease and evaluate the response to treatments.[4] Nasal cytology is a well-standardized method that may be applied to all nasal inflammatory disorders.[5] Therefore, nasal cytology may be performed as a useful step in the workup of patients with CRSwNP. As a consequence, a clinical cytological grading (CCG), including the documentation of possible asthma, allergy, or aspirin sensitivity comorbidity, and the presence of eosinophils and/or mast cells in the nose, has been proposed as a precision medicine–based approach in the management of patients with CRSwNP.[6] In particular, 3 CCG grades were defined on the basis of the score: low (1-3), medium (4-6), and high (≥7). A recent study provided evidence that a CCG value of more than 4 was a reliable (area under the curve, 0.83, and adjusted odds ratio, 7.46) cutoff to identify patients with CRSwNP with olfactory dysfunction.[7]

Smell loss is a clinical marker of CRSwNP severity and is associated with type 2 inflammation: both conditions indicate a biological approach.[1] The CRSwNP overall prevalence has been approximately estimated to be 2% to 4% of the general population

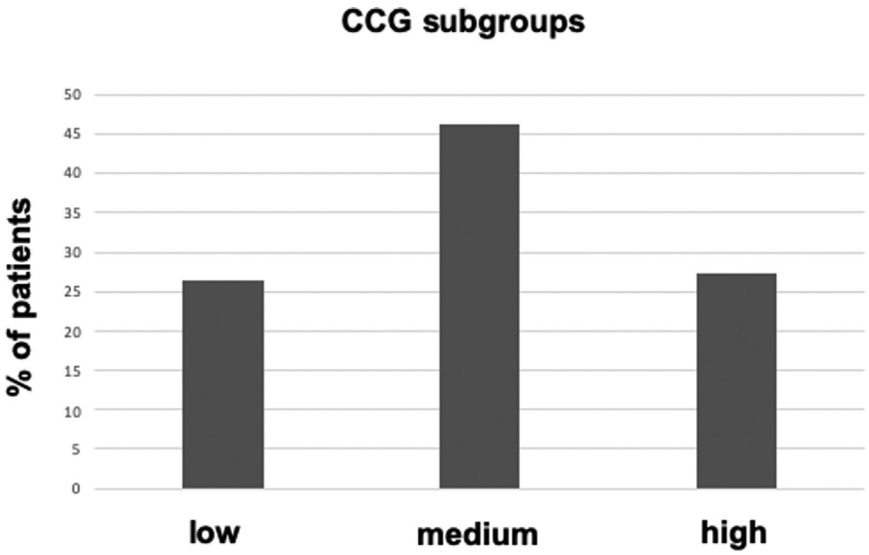

FIG 1. Distribution of the frequency concerning 791 patients with CRSwNP stratified according to CCG.

and approximately 30% of these patients also have asthma.[2] On the basis of these epidemiological considerations, a large group of Italian outpatients with CRSwNP (791; 424 males, mean age, 48.8 years) was recruited in a real-world study to define the distribution of the CCG grades. The preliminary results showed that 210 (26.5%) outpatients had low-grade CCG, 366 (46.3%) medium, and 215 (27.2%) high (Fig 1). High-grade CCG was frequently characterized by mixed cytological phenotype and severe progress. Patients with CRSwNP deserve adequate management and optimal identification of the best-tailored therapy; in this regard, CCG could be a fruitful tool. In particular, considering the estimated prevalence of CRSwNP and the current findings, it could be reasonably expected that at least 5 million Europeans have CRSwNP with high-grade CCG. Therefore, intercepting the most severe patients and launching an early and tailored treatment, including the new biologics, could positively modify the natural history and improve the quality of life.

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Reply

To the Editor:

In response to the correspondence reported by Gelardi et al,[1] we would like to say that the sense of smell has recently become relevant because a number of studies have shown that olfactory dysfunction may be considered a relevant clinical marker of severity not only in chronic rhinosinusitis with nasal polyps (CRSwNP) but also in other type 2 inflammatory diseases such as allergic rhinitis, asthma, and nonsteroidal anti-inflammatory drug–exacerbated respiratory disease.[2] In consequence, the loss of smell and its recovery have been adapted by Education, Innovation and Research in Allergy and Airway Diseases and European Position Paper on Rhinosinusitis and Nasal Polyps international consensus as 1 of the 5 main criteria to define both the indication for and the response to biological treatment in severe CRSwNP.[3] Among these criteria various methods have been accepted for both the diagnosis of loss of smell and the presence of type 2 inflammation.

It is well known that loss of smell is frequently associated with viral (common cold) and postviral acute rhinosinusitis, the postviral origin being one of the main causes for permanent olfactory loss in the adult population.[2] Although the loss of smell and/or taste has been recently linked to coronavirus disease 2019, associated or not with local or systemic symptoms of the disease,[1] more epidemiological and pathophysiological research is still needed to identify the potential role of the loss of smell and/or taste as a clinical marker of coronavirus disease 2019 (COVID-19) and its severity.

The clinical cytological grading score, reported by Gelardi et al,[1] which is based on clinical outcomes and nasal cytology, looks a reliable method to assess nasal inflammation and even