A new tool for stratifying children with suspected Sjögren's disease

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Little is known about the natural course and long-term outcomes of childhood-onset Sjögren's disease due to its low prevalence, difference in clinical presentation between children and adults, and lack of good quality research in paediatric populations. Delays in recognition of childhood-onset Sjögren's disease are potentially explained by the heterogeneity of clinical manifestations at disease onset (1-3) and the poor performance of adult classification criteria in children (4, 5). Increased awareness of health professionals and involvement of multi-specialties are needed to improve disease recognition. Furthermore, research into this rare disease is limited by challenges in recruiting large cohorts for patient stratification, and the lack of age-specific classification criteria to enable selection of homogeneous clinical phenotypes for personalised management or inclusion in clinical trials to support evidence-based recommendations (6).

Zeng and colleagues (ref) proposed a novel scoring system to stratify children with suspected Sjögren's disease. This data-driven approach was applied to a large cohort of 217 children with childhood-onset Sjögren's disease using 33 indicator variables including: disease outcome measures validated in adult Sjögren's disease, clinical features more commonly reported in children (e.g. recurrent parotitis/glandular swelling and candidiasis), autoantibodies and other serological markers, salivary gland (SG) biopsy focus score, and subjective and objective measures of dryness, as well as SG ultrasound, which is not included in the adult classification criteria. Using these data, in an effort to align with the different patient categories described in adults (7, 8), three distinct groups were defined using latent class analysis; Class-I (dryness-dominant), Class-II (high symptoms) and Class-III (low symptoms). The weighted Florida Scoring System (FSS) was then derived employing the 33 clinical variables and used to stratify children into the three defined classes.

A similar diagnostic score based on weighted serological and SG features was proposed previously, based on expert consensus rather than data-driven methodology and requiring invasive labial minor SG biopsy, SG scintigraphy or parotid sialography (9). The FSS relies on subjective assessment of dryness and fatigue, the ESSDAI-articular domain, blood test parameters and SG ultrasonography, aspects which highlight the obvious advantage of the FSS in terms of feasibility for routine care implementation.

Zeng and colleagues (REF) recommended follow-up strategies for children based on FSS scores, although future research into cluster stability over time is needed to validate their proposed management approach. Notably, the recent prospective evaluation of two large adult Sjögren's disease cohorts identified that the three distinct patient classes changed over 5-year follow-up (8), suggesting that cross-sectional cluster or score-based stratification is

unlikely to provide the best strategy for long-term follow-up management decisions. Interestingly, children in this study had a low prevalence of anti-SSA/SSB antibodies, particularly for children stratified in Classes-II and -III, which is different from other paediatric cohorts diagnosed based on expert opinion (2, 5), therefore it is not unexpected that only few children fulfilled the adult classification criteria. Anti-SSA/SSB positivity and SG ultrasound were included in the FSS score despite a higher proportion of children having a positive SG biopsy rather than these features. This indirectly suggests that a positive SG biopsy is less specific, as one in two children stratified in Classes-II or -III had a positive biopsy, despite being recommended for less frequent follow-up or deemed less likely to have Sjögren's disease based on FSS stratification. The selection of children to this study was based on expert opinion, and dependent on local referral pathways and access to Oral Medicine specialists, suggesting a possible inclusion bias which may have influenced the cohort characteristics and led towards over-representation of some groups., Children included in Class-II had joint hypermobility, temporomandibular dysfunction, migraines and joint pains in a significant proportion, which could explain their high symptom burden, independent of Sjögren's disease. Furthermore, significant ethnic differences were identified between the three classes. Thus, the FSS requires further validation to establish its wider clinical utility.

However, this robust study significantly progresses our understanding of the heterogeneity of childhood-onset Sjögren's disease and raises awareness about the difficulty in diagnosing children in the absence of the objective features of dryness or immune abnormalities which are the hallmarks of this condition in adults. The inclusion of self-reported outcomes in children as young as 6-years is particularly relevant considering the impact of disease on quality of life. This work increases the confidence of the paediatric rheumatology community to take the next steps towards proposing and validating much-needed classification criteria for timely diagnosis and optimal management of children with this condition and provides future opportunities for research into long-term outcomes of children with suspected Sjögren's disease.

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(REF) The paper reference should be included here but not available as yet.