Background:

The lack of pediatric classification criteria for axial disease is a major impediment to the conduct of clinical trials for juvenile spondyloarthritis (JSpA).

Objectives:

We aimed to develop classification criteria for axial JSpA that will enable identification of a more homogeneous group representative of children with SpA and axial disease for entry into observational or clinical trials. These criteria are not intended to capture all possible subjects, but instead most patients with shared key features of axial disease. Treatment and diagnostic decisions should adhere to evidence-based recommendations.

Methods:

304 cases with JSpA and suspected axial disease from 6 international centers were collected on a standardized case report form; all had an MRI that was reviewed by an independent team of experts in musculoskeletal imaging. Candidate criteria were developed in an earlier phase of the project through an iterative process that included an international Delphi exercise for item generation, systematic literature review, and an item reduction exercise. Using the preliminary candidate criteria, 14 international clinical SpA experts scored and rank-ordered 20 representative SpA cases. During four, 3-hour virtual meetings, the clinical expert panel reviewed the interrater reliability of case ranking, refined the criteria definitions and domain levels, and participated in a multi-criterion decision consensus methodology exercise to generate relative weights of the criteria. The expert panel assessed whether the criteria weighting was in accordance with their consensus clinical judgment as a test of face validation of the weighting/scoring system and revisions were made as necessary. Next, 30 cases from the derivation cohort were scored and ranked using the relative weights for each category and domain. Each expert independently determined the score or “threshold” below which they were no longer confident enough that a patient had axial disease to enroll the child in a Phase 3 randomized clinical trial of a drug with unclear efficacy and safety. Results of this exercise were discussed and a provisional threshold score for classification was achieved by consensus.

Results:

The preliminary axial disease criteria for JSpA included the PRINTO provisional criteria for enthesitis/spondylitis-related JIA or a rheumatologist diagnosis of SpA as obligatory entry criteria as well as additive weighted criteria for 7 domains (SIJ active inflammation on imaging, SIJ structural lesions on imaging, pain chronicity, pain pattern, pain location, morning stiffness, and genetics)(Figure). Interrater reliability of the pre-consensus meeting case rankings was poor (Kendall’s correlation coefficient was 0.20 for clinical data-only and 0.23 for clinical plus imaging data). The multi-criterion decision analysis was repeated for the imaging domains when the initial criteria weighting was not in accordance with the expert panel’s opinion. The multi-criterion decision analysis involved a total of 58 pairwise decisions agreed by expert consensus. After criteria weights and additive scores were re-calculated, experts reached consensus for axial disease in JSpA for all cases scoring 55 and greater.

Conclusion:

Using an iterative process, the JSpA axial disease criteria definitions were refined, preliminary weights were generated, and a provisional threshold score for classification was determined. The most heavily weighted domains were active inflammation and structural lesions on imaging. Imaging typical of sacroiliitis was necessary, but not sufficient without any clinical criterion, to surpass the axial disease classification threshold.

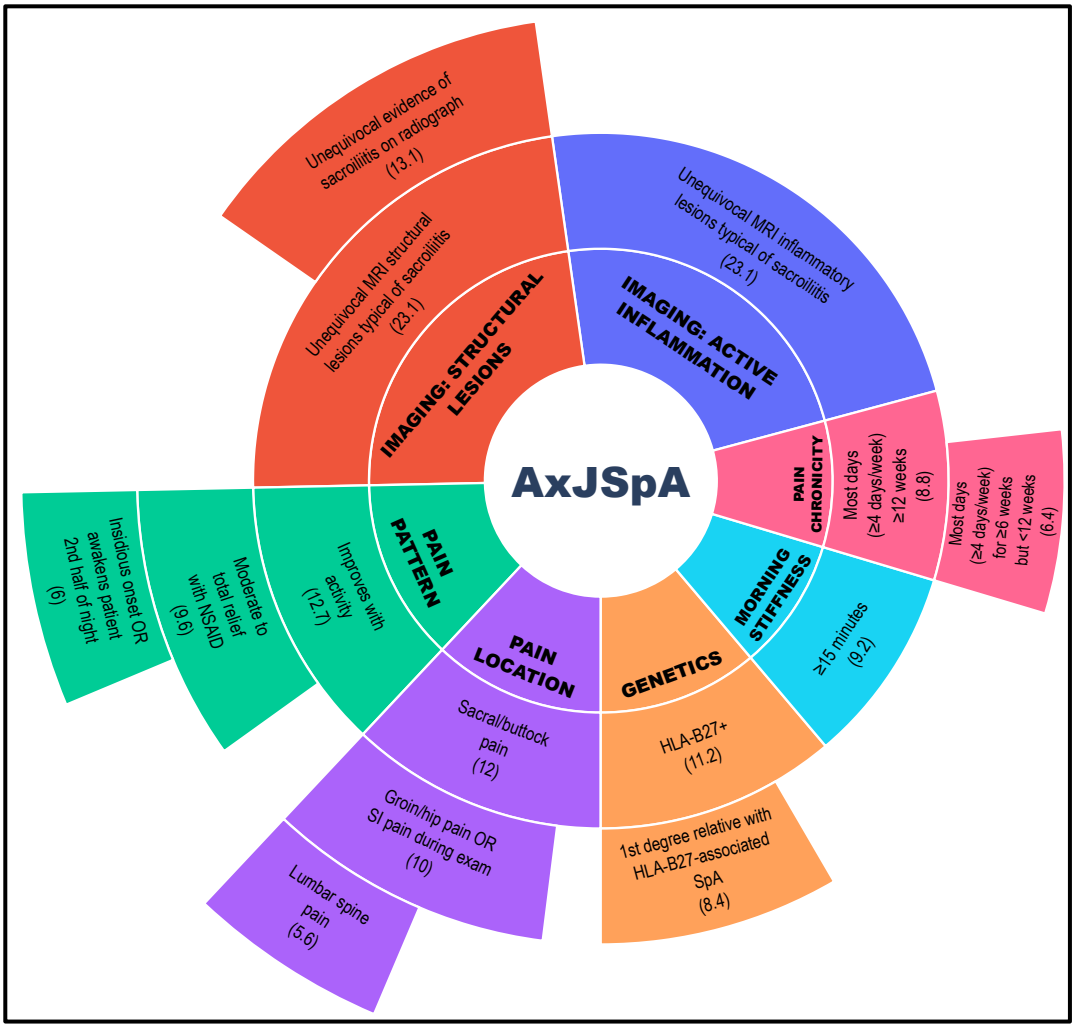

Figure. Axial juvenile spondyloarthritis (AxJSpA) classification criteria domains and levels. The first ring represents the domains and the items branching out are the levels moving from highest level (closest to center) to lowest level (farthest from center) in each domain. Assigned weights are shown below each item description.