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Goodbye to the term 'ankylosing spondylitis', hello 'axial spondyloarthritis': time to embrace the ASAS-defined nomenclature

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ABSTRACT

Ankylosing spondylitis (AS) is the historic term used for decades for the HLA-B27-associated inflammatory disease affecting mainly the sacroiliac joints (SIJ) and spine. Classification criteria for AS have radiographic sacroiliitis as a dominant characteristic. However, with the availability of MRI of SIJ, it could be demonstrated that the disease starts long before definite SIJ changes become visible on radiographs. The Assessment of SpondyloArthritis international Society, representing a worldwide group of experts reached consensus on changes in the nomenclature pertaining to axial spondyloarthritis (axSpA), such as the terminology of diagnosis and of assessment of disease activity tools. These are important changes in the field, as experts in axSpA are now in agreement that the term axSpA is the overall term for the disease. A further differentiation, of which *radiographic* versus *non-radiographic* is only one aspect, may be relevant for research purposes. Another important decision was that the terms AS and radiographic axSpA (r-axSpA) can be used interchangeably, but that the preferred term is r-axSpA. Based on the decision that axSpA is the correct terminology, a proposal was made to officially change the meaning of the ASDAS acronym to 'Axial Spondyloarthritis Disease Activity Score'. In addition, for simplification it was proposed that the term ASDAS (instead of ASDAS-CRP) should be preferred and applied to the ASDAS calculated with C reactive protein (CRP). It is hoped that these changes will be used consequently for education, in textbooks, manuscripts and presentations.

Ankylosing spondylitis (AS) is the historic term used for decades for the HLA-B27-associated inflammatory disease affecting mainly the sacroiliac joints (SIJ) and spine. Additionally, peripheral entheses and joints are involved, and extramusculoskeletal manifestations are present in a substantial proportion of patients.¹ 'Ankylosing' refers to the typical feature of bone formation in the SIJ and bridging syndesmophytes in the spine leading to the characteristic bent over body gestalt in its most severe

phenotype, although the latter occurs only in a minority of patients.

Classification criteria for AS have radiographic sacroiliitis as a dominant characteristic.² However, with the availability of MRI of SIJ, it could be demonstrated that the disease starts long before definite SIJ changes become visible on radiographs. Consequently, the clinical diagnosis can be made (long) before radiographic sacroiliitis is present. In 2004, a manuscript was published in *Annals of Rheumatic Diseases* about early diagnosis of axial spondyloarthritis (axSpA).³ Here, axSpA was defined as either AS or as undifferentiated SpA with predominant axial involvement. In 2009, the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA were published to enable research in the entire group of axSpA patients.^{4,5} These criteria can be fulfilled by one of the two arms: (1) via the so-called 'imaging arm' with sacroiliitis on radiographs or on MRI as the obligatory feature or (2) via the so-called 'clinical arm' with HLA-B27 as a mandatory feature. The AS equivalent of the ASAS axSpA criteria was labelled as 'radiographic' axSpA (r-axSpA) with patients fulfilling the imaging arm based on radiographic sacroiliitis. The remaining patients were labelled as 'non-radiographic' axSpA (nr-axSpA). This nr-axSpA group has been especially embraced by pharmaceutical companies: for drugs that already had an indication for AS, this was the remaining group for which an indication was sought. However, many experts, including members of ASAS, were of the opinion that axSpA is the disease entity covering the entire spectrum. This is in line with rheumatoid arthritis, an umbrella term that covers an entire spectrum, and to which attributes can be added, such as anti-cyclic citrullinated peptides (CCP) positive/negative or erosive/non-erosive.

For the further description of a patient with axSpA, one may add additional descriptors based on the presence or absence of certain features, such as HLA-B27 positivity, structural damage on radiographs or on MRI, inflammation on MRI, as well as



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Table 1 Results of the voting among ASAS members on statements on the nomenclature in axSpA

Statement voted on	Percentage of votes in favour (n=89) (2019)	Percentage of votes in favour (n=93) (2023)	Final decision
Q1: The terms AS and r-axSpA can be used interchangeably as the large majority of patients fulfilling the mNY criteria also fulfil the ASAS	82%	–	Approved by consensus
Q2: The preferred term to use is r-axSpA instead of AS	55%	70%	Approved by consensus
Q3: axSpA is the overall term for the disease; (only for description of a patient/population and research purposes is it important to distinguish between nr-axSpA and r-axSpA)	99%	–	Approved by consensus
Q4: Proposal to officially change the meaning of the acronym ASDAS to 'Axial Spondyloarthritis Disease Activity Score'		94%	Approved by consensus
Q5: Proposal: if ASDAS-CRP, simply state ASDAS; if ASDAS-ESR, state ASDAS-ESR		86%	Approved by consensus

Methods should always describe which acute phase reactant was used.
AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; mNY, modified New York criteria; nr-axSpA, non-radiographic axSpA; r-axSpA, radiographic axSpA.

peripheral or extramusculoskeletal involvement (including anterior uveitis, inflammatory bowel disease and psoriasis). Furthermore, it was proposed that, with the umbrella term of axSpA in mind, it would be more logical to rename AS into r-axSpA, especially because the ASAS axSpA classification criteria are nowadays applied in all studies of patients with axSpA. To substantiate these proposals with data, two research projects were started. First, a systematic literature review (SLR) to investigate if r-axSpA and nr-axSpA belong to the same clinical spectrum. Second, to explore if patients fulfilling the modified New York (mNY) criteria for AS also fulfil the ASAS criteria for r-axSpA and vice versa.

The SLR plus meta-analysis showed that patients with r-axSpA and nr-axSpA share a similar clinical presentation except for peripheral involvement, which is more prevalent among patients with nr-axSpA.⁶ There was more impaired mobility in the r-axSpA group, but otherwise both groups showed a comparable burden of disease, treatment modalities chosen and treatment effects. The results of this meta-analysis confirm that r-axSpA and nr-axSpA share similar characteristics and burden of disease, supporting the concept of axSpA as one disease.

For the second aim, 8 cohorts including 3882 patients were analysed. Of the patients fulfilling the mNY criteria, 93% also fulfilled the ASAS r-axSpA criteria; inversely, of the patients fulfilling the ASAS r-axSpA criteria, 96% also fulfilled the mNY criteria.⁷ These findings support the interchangeability of the terms r-axSpA and AS. Acknowledging that r-axSpA and AS are in fact interchangeable terms increases comparability across studies, since both terms describe similar patients. This also ensures that results from older research on AS cohorts can be compared one to one with more recent studies on r-axSpA cohorts.

At the 2019 ASAS annual meeting, these data were presented and discussed. Subsequently, three statements were put up for voting. See [table 1](#) for the exact wording. There was an almost unanimous vote (99%) that axSpA should be the overall term for the disease. The fact that the terms AS and r-axSpA can be used interchangeably received also a large majority vote (82%). However, the proposal that the term r-axSpA was preferred over AS received only a small majority (55%).

Nevertheless, the continuous use of both terms has led to confusion. In some publications, authors referred recurrently to both terms (r-axSpA or AS), even in the title of a manuscript.⁸ Moreover, some studies including patients with r-axSpA and nr-axSpA are referring to AS and nr-axSpA.⁹ Both aspects reduce readability and comprehensibility of the content and may mistakenly suggest that these are two distinct diseases, especially for the general rheumatologist and other stakeholders who are less involved in such discussions. In 2023, during the ASAS annual meeting, a new discussion took place and now 70% of

the members were in favour of using r-axSpA instead of AS. This decision was supported by the patient representatives from the Axial Spondyloarthritis International Federation present at the meeting.

This new terminology should now be reflected in outcome measures such as ASDAS (Ankylosing Spondylitis Disease Activity Score), a well validated instrument to assess disease activity, both in patients with r-axSpA and with nr-axSpA.^{10 11} Based on the decision that axSpA is the correct terminology, a proposal was made to officially change the meaning of the ASDAS acronym to 'Axial Spondyloarthritis Disease Activity Score'. This proposal was voted favourably by a large majority of ASAS members (94%) ([table 1](#)). This was supported by the fact that the ASDAS has already been used for many years to assess disease activity in both the clinical and the research setting with data accrued regarding the validity of ASDAS in the entire spectrum of the axSpA population, including r-axSpA and nr-axSpA.¹¹ In addition to the above, for simplification it was proposed that the term ASDAS (instead of ASDAS-CRP) should be preferred and applied to the ASDAS calculated with the C reactive protein (CRP) as this is the preferred way of using ASDAS. The use of CRP should be defined in the methods section. The full-term ASDAS-ESR should be applied when the erythrocyte sedimentation rate (ESR) is used. This proposal was also voted favourably by a large majority of ASAS members (86%) ([table 1](#)).

In conclusion, change takes time and particularly changes in nomenclature traditionally need a long period to be implemented. ASAS, representing a worldwide participation of experts, reached consensus on changes in the nomenclature pertaining to axSpA, such as the terminology of diagnosis and of assessment of disease activity tools. These are important changes in the field, as experts in axSpA are now in agreement that the term axSpA is the overall term for the disease. A further differentiation, of which *radiographic* vs *non-radiographic* is only one aspect, may be relevant for research purposes. Another important decision was that the terms AS and r-axSpA can be used interchangeably, but that the preferred term is r-axSpA. These preferences can only be implemented if used consequently for education, in textbooks, manuscripts and presentations. For the full implementation, it is important that this nomenclature will also be updated in the International Classification of Diseases-coding system. It is hoped and expected that the regulatory agencies will embrace the new nomenclature as soon as possible.

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