Defining an optimal referral strategy for patients with a suspicion of axial spondyloarthritis: what is really important? Response to: 'Evaluating the ASAS recommendations for early referral of axial spondyloarthritis in patients with chronic low back pain; is one parameter present sufficient for primary care practice?' by van Hoeven *et al*

We thank van Hoeven *et al*[1] for their interest in our work[2] and for their critical remarks.

The Assessment of SpondyloArthritis international Society (ASAS) referral recommendation[3] has been developed as a flexible tool aimed at improving early diagnosis of axial spondyloarthritis (axSpA), which implies that—dependent on the local conditions—parameters from the list shown in box 1 of the original publication could/should be selected. For instance, it does not make sense to ask for human leukocyte antigen (HLA)-B27 positivity in primary care if primary care physicians do not perform this test for whatever reason.

Although the referral strategy should be applied on the level of primary care physician, the recommendation is, in fact, addressed to rheumatologists who should offer the referral tool to their referring physicians and to decide which referral parameters are of relevance for their practice. We absolutely agree that the proposed referral tool should be tested in a prospective study, optimally with the active participation of primary care physicians. However, at this stage, the project was indeed confined to ASAS members.

We would like to comment on the importance of the positive predictive value (PPV). Van Hoeven *et al*[1] use a reference for a diagnostic test to substantiate their point. However, referral recommendations are used in a different context than diagnostic testing. The aim of the ASAS referral recommendations was to have all patients with axSpA referred (highest sensitivity) and not to miss patients. However, diagnostic testing implies a diagnosis that needs to be confirmed or rejected, and here, a pretest probability is playing a more important role, having direct effects on the PPV, and the false-positive and false-negative results of the test are important. Indeed, PPV needs to be reasonably high, and on the basis of the literature review, this was assured by the use of one referral parameter. We disagree with the statement that referral of 80% of the patients without having axSpA is undesirable: this also depends on the healthcare setting.

In contrast to the statement by van Hoeven *et al*,[1] the recommendations were also based on a careful review of the literature in addition to using a Delphi exercise and a final voting among the ASAS members. As it has been shown in the prospective MASTER and RADAR referral studies performed in primary care settings,[4 5] requiring two positive parameters did not improve the performance of the strategy, probably because of difficulties with application of the strategy by referring physicians due to an increased number of tests or clinical parameters, which have to be evaluated on the primary care level.

The fact that the presence of two parameters resulted in a better PPV than the presence of just one parameter in the retrospective analysis of the CAse Finding Axial SPondyloArthritis (CaFaSpA) population[6] is a confirmation of the retrospective analysis of one of the first referral studies.[7] However, as discussed above, prospective referral studies investigating this specifically could not confirm these data.[4 5] Nonetheless, further studies should investigate whether other potentially suitable combinations of referral parameters have similar performances and whether the PPV can be improved by increasing the referral parameters while keeping 100% sensitivity. If so, this should certainly be implemented.

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