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To Lump or Split When Assessing Psoriatic Arthritis- Not Mutually Exclusive?

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PASDAS for Psoriatic Arthritis

Arguably, the most important advances in modern clinical care have arisen not through the development new drugs but instead through a recognition the Gestlat approach to disease assessment is simply not adequate when it comes to selecting and assessing response to therapy. Accurate and regular assessment with an appropriate measurement instrument gives the clinician and patient reliable information to track disease trajectory and make treatment decisions. Achieving consensus on a single disease specific instrument has considerable advantages, facilitating adoption of international treatment guidelines, and interpretation of data from trials, cohorts and registries to make translation in to routine care seamless.(1) In the context of Rheumatoid Arthritis (RA) Disease Assessment Score- 28 (DAS28) has been widely adopted as the most frequently used generally continuous measure of activity. The DAS28 has established cut points for high, moderate, low disease activity and remission, clinicians are used to the measure and what the numbers mean clinically and this has allowed a smooth translation of research findings in to clinical practice, including the implementation of treat to target and adoption of clinical guidelines. It has been harder to achieve this consensus in the field of Psoriatic Arthritis with no current agreement on the most appropriate instrument to adopt. We briefly discuss why is this the case and what are the key barriers?(2)

The greatest challenge in the adoption of a composite measure for routine care in PsA has been philosophical: should we incorporate multiple domains of disease in a single measure to capture the totality of disease or should we focus on one domain at a time for accurate assessment and avoid diluting responsiveness? As we know, PsA may manifest in a variety of different ways with combinations of peripheral joint disease, skin psoriasis, enthesitis, dactylitis and axial disease. The argument for 'lumping' domains together has been the desire to try and capture the totality of disease in a single numeric value. There is a perceived need for this in PsA because peripheral joint disease is generally less destructive than RA but the impact of disease on quality of life and work is similar, due to the accumulation of disease activity in multiple domains. It is only through the incorporation of multiple domains of disease in to a single composite measure that we can quantify the total level of disease. A number of candidate composite measures have been developed to capture multiple domains of disease including (but not limited to) the Psoriatic Arthritis Disease Activity Score (PASDAS), the Composite Psoriatic Disease Activity Index (CPDAI) and the GRACE.(3) The concern with 'lumping' domains together is that it may not be philosophically desirable to condense such diverse aspects of a disease in to a single numerical value. A further disadvantage

may be that a resulting score may be less responsive and may remain static if one aspect or domain of disease improves whilst the other deteriorates. The Disease Activity in Psoriatic Arthritis (DAPSA) score is largely an articular measure (comprised of a 66/68 joint count, patient pain and global activity ratings and C-reactive protein) and thus can be argued to be one-dimensional.(4) If the DAPSA is used other domains of disease need to be evaluated separately. Whilst the approach of focussing on articular disease in a single measure avoids the issue of 'lumping' domains together the concern has been that the DAPSA will underestimate the totality of disease activity by focussing solely on peripheral articular disease. To add to this debate Perruccio and colleagues provide further evidence in this issue of *The Journal*, so what does their data contribute?

The PASDAS is an example of a continuous composite measure of disease activity in PsA as opposed to a response criterion such as achieving Minimal Disease Activity (MDA) which is a binary state that you are either in or not.(5, 6) The PASDAS is an eight item score comprised of the 66 swollen and 68 tender joint counts, physician and patient global visual analogue scales, the Leeds Enthesitis Index (LEI), tender dactylitis count, physical function component of the SF36 (or SF12) and C reactive protein.(7) The final PASDAS score is derived from a weighted formula that gives a single numeric value of disease activity; the score ranges between 0 (no disease) and 10 (severe disease). The mathematical model only included outcomes that optimised the ability of the PASDAS to detect change, therefore the PASDAS is not an 'all inclusive' or comprehensive composite – for example the skin is excluded. This approach has parallels with the Disease Activity Score 28 (DAS28) that does not include assessment of the feet in rheumatoid arthritis (RA) as the foot joints were found not to contribute any extra information.

The aim of the study by Perruccio *et al* was to externally validate the PASDAS disease activity states of high, moderate and low disease activity states as well as define cut offs for remission and low disease activity. Clinical and patient reported outcomes were collected from 178 patients attending the University of Toronto PsA clinic. The PASDAS, MDA (a state of low disease activity) and Very Low Disease Activity (VLDA, 7 out of 7 MDA, as a state of near remission) were subsequently calculated. Receiver Operating Characteristic Curve (ROC) analysis identified a PASDAS score of 3.2 and 2.1 maximised the sensitivity and specificity for MDA and VLDA respectively. These estimates correlate well with the analyses from the GRACE dataset (PASDAS 3.2 for low disease activity and 1.9 for very low disease activity) which gives external validity to previously defined cut offs (figure 1). The study is elegantly simple with few limitations to its interpretation. The cohort is representative of those

commonly seen in rheumatology clinics. The mean disease duration was well established at 17 years. However a fifth of those included had disease duration of <5 years giving confidence that the results are generalizable across the spectrum of disease duration. Similarly, it is desirable that a composite score should perform well amongst those with oligo-articular as well as poly-articular disease and 15% of participants had oligo-articular disease, which is representative of the proportion seen in clinical practice. So how should we interpret these data, and should we now use the PASDAS in routine practice?

The PASDAS was developed specifically for PsA in the GRACE study (as opposed to borrowed and adapted from another disease) so has good face validity; there is also evidence for its reliability, feasibility, and responsiveness in trial and observational cohort studies.(3, 8, 9) . Perhaps unsurprisingly, given its method of development, the PASDAS out performs other composite measures in RCT and observational datasets and predicts radiographic progression.(10, 11) With the new data from Perruccio *et al* in this issue of *The Journal* we now have external validation for clinically usable cut points for disease activity. (6) Subsequent analysis proposed a PASDAS score of 1.9 or less corresponded with remission as defined by VLDA (12) The study by Perruccio *et al* now provides external validation for these clinically relevant disease states for use in the clinical setting. Therefore, it seems the only barrier to the wider adoption of the PASDAS remains the philosophical question we posed in the title of this editorial, should we lump outcomes together (as in the PASDAS) or split (and measure individual domains separately, as has been done in the DAPSA)? We suggest herein the two are not mutually exclusive and it is helpful to look to the DAS28 again to explain why. As clinicians when we use the DAS28 in RA we assess the joints, global visual analogue scales and C-reactive protein to get a global measure of disease, but we examine the individual elements as they are recorded. If there are no swollen joints and the CRP is normal we instinctively interpret the numeric value differently and consider imaging and assessing for other causes of pain. It is second nature to treating clinicians to interpret the component parts of the DAS28 in addition to the total score (13). So the single numeric value of a composite score is only interpreted in the context of its component parts, in other words the component parts of a composite measure and final score are not mutually exclusive.

The core purpose of a composite measure of disease activity is to provide a measure of disease state in a single numeric value that has clinical meaning. Such a composite score has greater power in discerning outcomes and gives us a metric by which to convey information to our colleagues and

patients. Further, in a disease such as PsA the individual components themselves may not rate as 'severe' (by any metric, including the payers) yet the composite score may achieve that description. For the PASDAS, the data from the study by Perruccio *et al* gives external validity to the clinically relevant disease states of low disease and near remission, which can be applied in clinical practice. By utilising the PASDAS as we have become used to using the DAS28, by clinically reflecting on the component parts as the score is calculated, we also preserve the advantages of lumping outcomes together, without the philosophical disadvantages.

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