Which Domains Should Be Included in a Core Set for Endpoints in Ankylosing Spondylitis? Introduction to the Ankylosing Spondylitis Module of OMERACT IV

The aim of the ankylosing spondylitis (AS) module is the definition of an internationally accepted core set of variables for endpoints in studies on disease controlling antirheumatic therapy (DC-ART). The Assessments in Ankylosing Spondylitis (ASAS) Working Group has worked on this subject since 1995. The Working Group has participants from 21 countries in almost all parts of the world (see Appendix) and comprises clinical experts in the field of AS, clinical epidemiologists, and representatives of the pharmaceutical industry and patient leagues. The results of the first 2 workshops have been published and will be summarized here[1]. To date, the ASAS Working Group has defined core sets for use in 4 settings: DC-ART, symptom modifying antirheumatic drugs (SMARD), and physical therapy, and for clinical record keeping. For every setting the domains (groups of measurements assessing the same concept, e.g., physical function) of the core set have been defined. In later consensus procedures proposals were put forward for one or more specific instruments for each domain. From the OMERACT AS module we reconfirm the selection of the domains by a larger international community of workers in the field of rheumatology. The second aim is to continue with the next steps and start the research on validity of some of the specific instruments for a few domains. These further steps would include only the core set for DC-ART, i.e., the instruments for the domains physical function and acute phase reactants.

METHODS

The aim of the ASAS Working Group was to select core sets of variables to include as endpoints in clinical studies for various types of therapy and for use in clinical practice. Core sets are a minimum set of variables to be included in every study and are not restrictive. It was hypothesized that different core sets might be needed depending on the setting where the core set is used. The general outline for selection of core sets in AS was as follows:
1. Definition of the settings for which the core set will be needed.
2. Collection of all available measures from the literature.
3. Selection of the type of domains (such as a functional measure) appropriate for each setting.
4. Selection of specific measures for each domain [e.g., The Bath Ankylosing Spondylitis Functional Index (BASFI) for the domain functional measure].
5. Review of the literature and, where necessary, additional research to assess the validity of the proposed variables.
6. Selection of the final set based on aspects of validity. Here, the first 3 steps will be described.

Definition of settings
The various settings for which core sets needed to be selected were defined as follows:
1. DC-ART. This therapy changes the course of ankylosing spondylitis, i.e., both (a) improve and sustain function in association with decreased inflammatory manifestations; and (b) prevent or significantly decrease the rate of progression of structural damage. These changes must be sustained for a minimum period of one year (as adapted from work in rheumatoid arthritis[2]).
2. SMARD. These improve the symptoms and clinical features of inflammatory manifestations in AS (as adapted[2]).
3. Clinical record keeping in daily practice. The purpose of this core set is to facilitate uniform clinical record keeping to strengthen research from clinical records and to monitor patient care in a standardized way.
4. Assessment of the effectiveness of physical therapy.
Moreover, the duration of study was divided into long and short term. The definition of longterm was one year or longer, short term has been defined as less than one year. By definition therefore, DC-ART is always longterm. The other 3 settings can be divided into short and longterm. Thus, we originally ended up with 7 settings: DC-ART, short and longterm SMARD, short and longterm clinical record keeping, short and longterm physical therapy.

Survey of available measures
The literature search to 1991 by Bakker, et al[3] was updated by a search from 1991 to 1995. The measures were presented to the ASAS members in a plenary session. Every participant was free to add those measures that were not on the list but were felt to be important. With the new extended list as a basis, all participants were then asked to choose individually those measures that should be included in a core set for a particular setting (e.g., DC-ART). A total number of 100

points (exactly) were to be divided over the preferred measures for each setting to give weight to the importance of the various variables from the point of view of the individual expert. Participants were free to give 100 points to one measure only or to divide 100 points (equally or unequally) over as many variables as required.

Thereafter 4 groups, of 8 to 10 (geographically mixed) participants each, discussed the points given by each member of that group. Some measures were grouped together if they represented the same domain, e.g., ESR and CRP into acute phase reactants. After discussions, participants were free to change the points given. Then the points were summed for every measure and rank ordered. As a final step the small groups chose the variables to be included in the core set. The same process was repeated for all settings. The next step was the presentation of the results of the 4 groups in a plenary session. It was established that all variables chosen by at least 3 groups were definitely included in the core set for that setting; variables chosen by 2 groups were provisionally included; those chosen by one group only were not included.

RESULTS

Over 110 variables used in research in AS were collected from the literature. Participants added 6 other measures, focusing on sick leave and quality of life measures. Participants chose freely from this new list. In total, 51 variables were selected by the 36 participants, ranging from 3 to 19 variables per participant (median 6). The minimum number of points given to a measure was 2, the maximum 50. However, as mentioned, in the discussion groups measures were grouped into domains if they addressed the same concept. For example, number of tender joints, Dougados articular index, number of swollen joints, enthesis index according to Mander were all grouped together as peripheral joints and entheses[4,5].

Selection of the DC-ART core set
Table 1 gives the domains that were selected by the 4 groups for the DC-ART setting. The number behind the domain depicts the number of groups selecting that particular domain. All domains selected by 3 or 4 groups (above the broken line) were included definitively in the core set. Those selected by one group only (below the double line) were not included in the core set. Domains selected by 2 groups (between the broken and the double line) were initially included in the core set. The final decision on the status of these last domains will be made during future meetings.

Selection of core sets for other settings
Exactly the same process was followed for short term studies with SMARD (Table 2). Two groups proposed that no distinction between short and longterm studies be made for

Table 1. Measures selected by the 4 discussion groups for the DC-ART core set. Numbers represent the number of groups that selected the measure. Domains above the broken line are definitely included, those below the double line are excluded, and those between are provisionally included in the core set.

Domain	No. of Groups
Physical function	4
Pain	4
Spinal mobility	4
Peripheral joints/entheses	4
Spine radiograph	3
Patient global assessment	3
Hip radiograph	2
Spinal stiffness	2
Fatigue	2
Acute phase reactant (AUC*)	2
Physician global assessment	1
Socioeconomic consequences	1
Quality of life	1
Drug safety	1
Extraskeletal manifestations	1

*AUC: area under the curve; acute phase reactants assessed as a cumulative measure over time.

Table 2. Measures selected by the 4 discussion groups to include for the SMARD short term core set. The number represents the number of groups that selected this measure. Domains above the double line are definitely included in, and those below are excluded from the core set.

Domain	No. of Groups
Pain	4
Physical function	4
Spinal stiffness	4
Spinal mobility	4
Patient global assessment	3
Peripheral joints/entheses	1
Physician global assessment	1

SMARD, physical therapy, and clinical practice. Further, one group proposed that no distinction be made between SMARD and physical therapy. Both proposals were approved in the plenary session. This reduced the number of remaining different core sets to 3 — one set for DC-ART (see above), one for SMARD/physical therapy, and one for clinical record keeping — for the 4 settings. Due to time constraints, only one group was able to complete the selection of the domains for clinical record keeping. Patient global assessment was initially not included in the proposed set by this group. During the plenary session it was felt that the patient global assessment is one of the most important assessments in clinical practice. This variable was added to the final selection and approved by all members. The 3 preliminary core sets are presented in Table 3, with all sets

Table 3. Preliminary core sets for studies on DC-ART, SMARD/physical therapy, and for clinical record keeping.

DC-ART	SMARD/Physical Therapy	Clinical Record Keeping
Physical function	Physical function	Physical function
Pain	Pain	Pain
Spinal mobility	Spinal mobility	Spinal mobility
Spinal stiffness	Spinal stiffness	Spinal stiffness
Patient global assessment	Patient global assessment	Patient global assessment
Peripheral joints/entheses		Peripheral joints/entheses
Acute phase reactants (AUC)		Acute phase reactants
Spine radiograph		
Hip radiograph		
Fatigue		

AUC: Area under the curve; acute phase reactants assessed as a cumulative measure over time.
Domains in italic print are not definitely included in the core set, but are put on the research agenda.

including physical function, pain, spinal mobility, and patient global assessment. Spinal stiffness is included in the SMARD/physical therapy set and in the clinical record keeping set, but is the subject of further study in the DC-ART set. Also, definite decisions regarding the inclusion of fatigue, acute phase reactants, and x-ray of the hips were deferred to a later stage.

CONCLUSIONS

During the work done so far by the ASAS Working Group, the number of settings has been reduced from the original 7 to just 4 and the domains for these 4 settings have now been selected. The next step is the choice of specific measures in each domain based on aspects of validity. This requires an extensive literature search, analyses of existing databases, and possibly further research.

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