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# ASAS/EULAR recommendations for the management of ankylosing spondylitis - the patient version

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**Objectives.** The ASAS/EULAR recommendations for the management of ankylosing spondylitis have been developed by rheumatologists for a target population of health professionals.. ASAS and EULAR agreed to extend their cooperation by translating the recommendations to a language that can be easily understood by patients in order to further disseminate and evaluate the recommendations.

**Methods.** In cooperation with patient organizations 17 European and one Canadian AS patients were invited to attend a meeting in February 2008. As a starting point the original publication and a version created by Canadian AS patients were used. To improve the understanding of potential problems data on the evaluation of a recent German translation were presented. After intensive discussions the wording was adjusted and a vote was held on the novel wording of the recommendations aiming for > 80% agreement on each sentence. Finally, patients were asked to indicate their level of agreement with the content of the recommendations.

**Results.** Ten recommendations were successfully translated into a patient understandable version. The original text was changed in most cases. In all but one case (recommendation No. 4) there was broad agreement with the proposed translation. The overall agreement with the content of the recommendations was high: 8.7 ± 0.6.

**Conclusion**. For the first time, EULAR recommendations were successfully converted into a patient understandable language version by a large international group of patients in collaboration with rheumatologists. The evaluation showed broad agreement. Translations into different languages and further dissemination in individual countries will be performed.

**Abbreviations:**
Ankylosing spondylitis (AS); Ankylosing Spondylitis International Federation (ASIF); Assessment of SpondyloArthritis International Society (ASAS); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Disease-modifying antirheumatic drugs (DMARDs); European League Against Rheumatism (EULAR); Magnetic resonance imaging (MRI); Non steroidal anti-inflammatory drugs (NSAIDs); People with Arthritis/Rheumatism in Europe (PARE); Rheumatoid arthritis (RA); Spondyloarthritis (SpA); Strength of recommendation (SOR); Standard deviation (SD); Tumor necrosis factor (TNF); United Kingdom (UK); Visual analog scale (VAS); World Health Organization (WHO).

## Introduction:

Ankylosing spondylitis (AS), the main entity of the spondyloarthritides (SpA), is a chronic inflammatory disease characterized by specific musculoskeletal features: inflammation and ankylosis of the axial skeleton, peripheral arthritis, enthesitis and involvement of other organs such as the eye [1]. Major advances in the management of AS have been recently reached by introduction of magnetic resonance imaging (MRI) and the tumor necrosis factor (TNF)-α inhibitors [2,3]. To assist all health professionals involved in the care of patients with AS, evidence based recommendations for the management of this disease were developed [4].

The Assessment of SpondyloArthritis International Society (ASAS) has recently published recommendations for the use of anti-TNF therapy in AS [5], and together with the European League Against Rheumatism (EULAR) recommendations for the management of AS in 2006 (Supplement 1 and 2) based on a systematic literature search [6, 7]. These were drafted by a combination of evidence and expert consensus. Treatment recommendations for AS have also been released by the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada working group [8, 9].

The ASAS/EULAR recommendations were an important step forward in generating an international consensus on the appropriate management of AS. However, they have been developed by rheumatologists and orthopedic surgeons for a target population of mainly health professionals and payers, and the language of the publication is largely medical. In a chronic disease, sustainable patient knowledge is beneficial and patient input into the decision-making process of recommendations is a requirement by various institutions. The importance of patients' view and preference is also included in the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument for evaluation of guidelines [10]. However, the mechanism by which this is best accomplished has not been well defined.

ASAS and EULAR have agreed to extend their cooperation by translating recommendations into a language that can be easily understood by patients. At a consensus meeting of rheumatologists and deputies of national patient organizations, the ASAS/EULAR recommendations for the Management of AS were translated into a language that can be understood by AS patients in order to further disseminate and evaluate the recommendations among patients.

## Methods:

*Participants:* In cooperation with EULAR (PARE, People with Arthritis/Rheumatism in Europe), the Ankylosing Spondylitis International Federation (ASIF), the Deutsche Vereinigung Morbus Bechterew (DVMB), the National Ankylosing Spondylitis Society (NASS) and other national patient organizations, 18 AS patients (including one rheumatologist) of 10 different countries (Belgium, Canada, Germany, Ireland, the Netherlands, Portugal, Romania, Switzerland, Turkey, United Kingdom) were invited to attend a consensus meeting at the EULAR house near Zurich in February 2008. A planning committee was formed from within ASAS (J. Braun as convener, D. van der Heijde as clinical epidemiologist, H. Mielants as an experienced clinician and ASAS member), EULAR (M. de Wit) and ASIF (E. Feldtkeller). Demographic characteristics, partial history and current health status of the participants were collected. This included questions to be answered by a visual analog scale (VAS), the Bath AS Disease Activity Index (BASDAI) and the Bath AS Functional Index (BASFI).

*Working document:* As a starting point, the original publication and a version created by Canadian AS patients were used. K. Mulholland, an AS patient who was strongly involved in the Canadian project, attended the meeting to explain the development of this patient based version [9]. To improve the understanding of potential problems, data on the evaluation of a recent German translation of the experts version evaluated by patients were presented during the meeting [11].

*Translation process:* Each participant of the consensus meeting was asked to contribute independently proposals relevant to the translation of the patient version of the ASAS/EULAR recommendations for the management of AS. The aim was to create a new manuscript that is produced and understood by patients. To achieve this, the main task was to translate the original text by simplifying the wording and to explain the original text by adding comments to a patient friendly version. However, it was stated at the beginning of the meeting that it was not allowed to modify the meaning of the original recommendations. After the participants had generated ten patient adapted recommendations, comments explaining difficult terms were discussed and a wish-list was developed for possible consideration in the next update of the ASAS/EULAR recommendations for the management of AS.

*Evaluation:* After intensive discussions a vote was held on the new translation of the recommendations aiming for a > 80% agreement on the translation. The participants had the option to agree (positive vote), to disagree (negative vote) or to be neutral (no vote) on translation of the patient version. In case of a negative vote the participants were asked to state the reason for their disagreement. Finally, based on the content of the recommendation, patients were asked to rate the strength of recommendation (SOR) on a numerical rating scale for each recommendation (0=not agree at all, 10=fully agree).

## Results:

*Characteristics of the participants:* The baseline characteristics of the participants are given in Table 1.

**Table 1**: Characteristics of participants (n=18 participants, 17 with available data)

| | | | |
|---|---|---|---|
| **General data** | Men, No (%) | | 14 (76%) |
| | Age (years), mean (SD) | | 51.5 ± 15.5 |
| **Diagnosis** | Disease, No (%) | | Axial AS: 10 (59%)<br>AS with peripheral arthritis: 6 (35%)<br>AS and ulcerative colitis: 1 (6%) |
| | Time since diagnosis (years), mean (± SD) | | 24.5 ± 12.6 |
| | Disease duration since symptom onset (years), mean (± SD) | | 28.6 ± 14.6 |
| **Disease activity** | BASDAI | | 3.3 ± 2.1 |

| | | | |
|---|---|---|---|
| | BASFI | | 3.5 ± 2.0 |
| | VAS pain | | 3.3 ± 2.6 |
| **Pain medication** | overall, No (%) | at least one | 15 (88%) |
| | NSAIDs, No (%) | regular | 7 (41%) |
| | | on demand | 6 (35%) |
| | Analgesics, No (%) | on demand | 3 (18%) |
| | Opioids, No (%) | regular | 2 (12%) |
| **Corticosteroids** | oral, No (%) | regular | 1 (6%) |
| | | on demand | 2 (12%) |
| **DMARDs** | overall, No (%) | | 7 (41%) |
| | Sulfasalazine, No (%) | | 2 (12%) |
| | Methotrexate, No (%) | | 1 (6%) |
| | Anti-TNF therapy | | 4 (23%) |
| **Surgery** | Total hip replacement | | 1 (6%) |
| | Corrective osteotomy | | 1 (6%) |

*Translation and evaluation of the patient version:* Ten recommendations were successfully translated into a patient adapted version. The first 3 recommendations address general concepts in the management of AS, the remaining 7 describe specific treatments in use for AS. The original text was changed in most cases.
Table 2 shows the full recommendations of the patient version; comments to each recommendation are presented in Table 3, while the evaluation of the recommendations (translation and agreement) is shown in Table 4.

## Table 2: Recommendations for the management of ankylosing spondylitis in lay language

**Recommendation 1: General principles for management**

The treatment of Ankylosing Spondylitis (AS) should be specifically adapted for individual patients according to:

- How the disease currently affects the patient (spine, joints, attachments of ligaments and tendons[1], other locations[1]).
- The level of current symptoms, findings on examination, and features that predict how the disease may progress, in terms of:
  - disease activity[1]/inflammation
  - pain
  - function and disability
  - damage to the spine and hip[1, 2].
- The general medical condition (age, sex, other diseases, medication).
- The patient's wishes and expectations.

**Recommendation 2: Disease monitoring**

- Disease monitoring[1] should relate to the patient's current health. It includes patient history (for example, questionnaires), physical examination, laboratory tests, and imaging[1] (for example x-rays), based on the core set[1] of measurements recommended by ASAS[1].
- The frequency of monitoring should be decided for each individual patient based on current symptoms, severity, and medication.

**Recommendation 3: Management strategy**
Optimal management[1] of AS requires the use of both drug and non-drug treatments.

**Recommendation 4: Non-drug treatment**
Non-drug treatment of AS should include patient education[2] and regular exercise. Individual and group physiotherapy[2] under the supervision of a qualified therapist should be considered. Patient associations and self help groups[2] may be useful.

**Recommendation 5: Drug treatment – anti-inflammatory**
- Anti- inflammatory drugs[1] (not including steroids) are recommended as first choice for patients with AS suffering from pain and stiffness.
- For patients with an increased risk of side effects in the stomach there are two options:
    - an additional drug that protects the stomach, or
    - an anti-inflammatory drug with a reduced risk for side effects in the stomach (selective COX-2 inhibitor[1]).

**Recommendation 6: Drug treatment – pain killers**
Pain killers such as paracetamol and opioids[1] might be considered for pain control when anti-inflammatory drugs:
- have not provided sufficient relief,
- have caused unacceptable side effects,
- cannot be used because of other medical reasons.

**Recommendation 7: Drug treatment – steroids**
- Local injections of steroids[1] at the site of inflammation[1] may be considered.
- The benefit of steroids given in other ways is not proven when the disease is only present in the spine.

**Recommendation 8: Drug treatment – DMARDs**
- It is not proven that so-called disease modifying drugs (DMARDs[1]), such as sulfasalazine[2] and methotrexate, are effective for the treatment of AS in the spine.
- Sulfasalazine may be effective in those patients who have inflammation in joints outside the spine.

**Recommendation 9: Drug treatment – anti-TNF**

- If the treatments outlined above do not control disease activity sufficiently, anti-TNF[1] drugs should be given in line with the ASAS recommendations[1].
- It is not necessary to use DMARDs before or along with anti-TNF treatment in those patients who only have disease in the spine.

**Recommendation 10: Surgery**
- Total hip replacement[1] should be considered, regardless of age, in patients with pain or disability not responding to treatment and where there is x-ray evidence of joint damage.
- Spinal surgery may be of value to correct severe deformity[1] or stabilize[1] the spine.

[1] see comments 1-10 (Table 3)
[2] see wish-list (Table 5)

## Table 3: Comments to recommendation 1 – 10

| No. | Text | Comment |
|---|---|---|
| 1 | Ligaments / tendons | Attachment of muscle to bone can become inflamed (enthesitis). |
| | Other locations | Other areas, such as eyes, lungs, bowel, skin and heart can also become inflamed. |
| | Disease activity | Measurement of how affected the patient is. Inflammation is an important part of disease activity. |
| | Damage | In AS there is a coexistence of inflammation, bone destruction and aberrant bone repair with extra bone formation. This causes a condition in the spine by which some or all vertebrae fuse together (ankylosis). Hip joint destruction is primarily characterized by inflammation followed by cartilage loss (coxitis). |
| 2 | Monitoring | Monitoring is continuous observation and measurement of the patient to check AS continuously. It is more than merely patient follow-up. |
| | Imaging | Visualization of body organs using specialized techniques like radiography, ultrasonography or magnetic resonance imaging. |
| | Core set | Group of assessments used to quantify the symptoms of AS patients. |
| | ASAS | Assessment of SpondyloArthritis international Society (ASAS) is an international society of experts in the field of spondyloarthritis. |
| 3 | Management | Guidance of the patient including specific treatment options. |
| 5 | Anti-inflammatory drugs | Non-steroidal anti-inflammatory drugs (NSAIDs) may have a pain-killing and anti-inflammatory effect. Long-term continuous treatment with NSAIDs may be beneficial in reducing radiographic progression in AS. |
| | COX-2 inhibitor | Selective cyclo–oxygenase–2 inhibitors are special types of NSAIDs that block the production of prostaglandins. They differ from NSAIDs by targeting only the pain–signaling prostaglandins. COX–2 inhibitors may act without causing stomach problems (e.g., ulcers) often associated with other NSAIDs. |
| 6 | Opioids | Opioids (e.g. codeine) are powerful painkilling drugs and these morphine-like medications may be used to treat chronic pain. Opioide medications do not cause addiction when used correctly for severe pain under close medical supervision. |
| 7 | Steroids | Corticosteroids are a group of anti-inflammatory drugs similar to the hormone cortisol produced in the body. Steroids work by blocking the production of substances in the immune system that trigger inflammatory reactions. |
| | Site of inflammation | Local inflammation can occur in AS at many different musculoskeletal sites, including spine, joints outside the spine, and enthesitis [see comment 1]. |
| 8 | DMARDs | The term DMARDs subsumes drugs which suppress the overacting immune system, but the exact mechanism of action is unclear. DMARDs work long term and can take several months to produce results. |
| 9 | Anti-TNF | Tumor necrosis factor (TNF) levels are elevated in patients with active AS. Anti-TNF drugs block this molecule and may help reduce inflammation. |
| | ASAS Recommen- | ASAS recommendations for the use of anti-TNF drugs in patients with AS are developed for guidance in clinical decision making (see Suppl 2). |

| | | |
|---|---|---|
| | dation for anti- TNF treatment | |
| **10** | Total hip replacement | AS may lead to persistent hip damage requiring replacement with an artificial joint (prosthesis). |
| | Severe deformity | In connection with the vertebral fusion of the spine (ankylosis) [see comment 1] the convexity of the thoracic spine can be abnormally increased (kyphosis). This may cause loss of horizontal vision without compensation. In rare cases surgery is used to restore a straighter posture of the spine. |
| | Stabilization | Due to the extra bone formation in the spine [see comment 1] and possible osteoporosis, the risk of instability and fracture is increased in the spine. In rare cases surgery is used to correct the instability. |

## Table 4: Evaluation of the recommendation

| Recommendation | | Translation | | | Evaluation | |
|---|---|---|---|---|---|---|
| | | agree | disagree | neutral | SOR | Range |
| No. 1 | General principles for management | 21 (100%) | 0 | 0 | 9.3 ± 0.9 | 7-10 |
| No. 2 | Disease monitoring | 20 (95%) | 0 | 1 | 8.9 ± 1.3 | 6-10 |
| No. 3 | Management strategy | 20 (95%) | 1* | 0 | 8.2 ± 2.6 | 0-10 |
| No. 4 | Non-drug treatment | 16 (76%) | 4# | 1 | 7.2 ± 2.6 | 1-10 |
| No. 5 | Drug treatment – anti-inflammatory | 20 (95%) | 0 | 1 | 8.3 ± 1.4 | 5-10 |
| No. 6 | Drug treatment – pain killers | 20 (95%) | 0 | 1 | 8.8 ± 2.2 | 1-10 |
| No. 7 | Drug treatment – steroids | 21 (100%) | 0 | 0 | 9.2 ± 0.9 | 7-10 |
| No. 8 | Drug treatment – DMARDs | 21 (100%) | 0 | 0 | 9.0 ± 1.0 | 7-10 |
| No. 9 | Drug treatment – anti-TNF | 21 (100%) | 0 | 0 | 8. 9 ± 1.1 | 7-10 |
| No. 10 | Surgery | 20 (95%) | 1° | 0 | 8.8 ± 1.4 | 6-10 |
| No. 1-10 | overall agreement | 21 (100%) | 0 | 0 | 8.7 ± 0.6 | N/A |

See Table 2 for the text of the recommendations.

SOR, strength of recommendation; N/A, not applicable.

* Participant thinks that AS can be treated without medication in some cases.

# Participants think that the paragraph should be more positive, especially for physiotherapy and self help groups.

° Participant thinks that not always a total hip replacement should be performed.

Table 5 contains the wish-list.

**Table 5: Wish-list of the patients for possible consideration in the generation of the next update of the ASAS/EULAR recommendations for the management of AS**

| No. | Text | Wish-list | Main barrier |
|---|---|---|---|
| 1 | Damage of joints | One should mention not only the hip but also other joints. | Peripheral arthritis is usually oligoarticular and affects mainly the lower limbs. Hip involvement is reported as a bad prognostic sign. |
| 4 | | - Evaluation of non-pharmacological treatment should be given more importance<br>- Non-pharmacological treatment needed further explanation of quality and quantity | Insufficient data of non-pharmacological treatment, only 15% of studies reported effects of non-pharmacological treatment in AS. |
| | Education | - Patient education should be improved<br>- Communication between family doctor and specialist should be enhanced | Effect of isolated education for AS is not clear yet. |
| | Physiotherapy | Appropriate exercise is crucial to managing AS. Regular home exercise is the basis of non-pharmacological treatment. Physiotherapy may be completed with other procedures (balneo- or electrotherapy). | Specific physical modalities have not been studied. |
| | Self help groups | Patients who take an active interest in their condition can positively influence the outcome of AS. Using practical advice of self help groups to manage the condition is strongly recommended by stakeholders. | Self help groups have not been studied for their effect on pain or functional outcomes. |
| 8 | Sulfasalazine | Comment on the role of sulfasalazine for the treatment of uveitis, inflammatory bowel disease, psoriasis. | Additional to the role of sulfasalazine in peripheral arthritis associated with spondyloarthritis, sulfasalazine may play a role in the therapy of uveitis, inflammatory bowel disease, psoriasis, but there are insufficient data on these options. |

*a) Translation:*

In general, common speech was preferred as a translation of Latin terms in the expert's version (e.g. comorbidity -> other diseases, concomitant drugs -> medication (recommendation 1)). But not all medical language can be rendered in lay terms (e.g. COX-2 inhibitor). In such cases, the term is commented on in Table 3. We deleted words in some instances (like "structural" (recommendation 1 and 10) or "persistently" (recommendation 9) where the use or translation of these words did not contribute to a better understanding of the patient adapted version.

To emphasize the heterogeneity of the clinical picture of AS, the term "current manifestation" in recommendation 1 was changed to "other locations" as explained in the 'comments' section. The participants needed an explanation for the understanding of the term "clinical" in recommendations 1 and 2. We consequently decided to change it to "findings on examination" or "medical condition".

The term "function, disability, handicap" in recommendation 1 refers to the model of functioning developed by the World Health Organization (WHO). Most patients accepted dropping "handicap" in the patient adapted version, deciding that handicap is included in the word "disability".

Regarding the division into non-pharmacological and pharmacological treatment options (recommendation 3) it was decided to generally change the word "pharmacological" to "drug" for better understanding. As the majority of the recommendations deal with pharmacological treatment, there was an intense discussion about several problems with understanding of and agreement with recommendations 5-9. Because participants expected that many non-health professionals would have difficulty understanding pharmacological terminology, we used the common term "anti-inflammatory" instead of NSAIDs, stressing explicitly that this does not include corticosteroids in this regard. The experts and participants discussed the translation of "gastrointestinal" intensively. In the patient version the term "stomach" is used ignoring the potential intestinal side effects of NSAIDs. The terms "gut" and "bowel" were also discussed but the majority of the participants found the term 'stomach' easier to understand. The structure of recommendation 5 and 6 was changed extensively for improved understanding.

*b) Evaluation:*

Agreement with recommendation translation was evaluated separately for each recommendation. In all but one case there was broad agreement with the proposed translation. Full agreement of all participants to the translation was achieved in recommendation 1, 7, 8, and 9. Not more than one disagreement was achieved in recommendation 2, 3, 5, 6, and 10. For recommendation No. 4 disagreement was expressed by 4/18 participants (22%). However, this was largely related to the content of the recommendation and not to the actual translation.

The overall agreement with the content of the recommendations was high (mean agreement (± standard deviation (SD)): 8.7 ± 0.6. Agreement was highest for recommendation 1 (general principles for management) and for recommendation 7 (drug treatment – steroids) (mean ± SD 9.3 ± 0.9 and 9.2 ± 0.9, respectively). Agreement was lowest for recommendation 4 (non-drug treatment) with a mean (± SD) value of 7.2 ± 2.6.

## Discussion:

This is the first translation/transformation of EULAR recommendations into a patient adapted version. This effort is a major step forward in the process of evaluation and dissemination to health professionals as well as to non-health professionals as

required in the EULAR standardized operating procedures [12]. The original ASAS/EULAR recommendations for the management of AS published more than 2 years ago have already been evaluated in different countries [4,15-17]. In Canada, a first effort has been undertaken to try this also on the patient level [9]. Support of patient knowledge and participation in the management of chronic diseases is likely to be beneficial since it is well established that one powerful strategy to change behavior of patients is to involve them directly in the development of guidelines or recommendations [18].

This is the first time that patient-adapted recommendations for the management of AS have been developed with direct participation of patients in a consensus meeting. Hereby the ten key recommendations of the expert's version (Supplement 1) were successfully translated into a patient understandable language (Table 2). Indeed, the notable and most important experience in this meeting was that it was no great problem to agree on this patient adapted version of the recommendations for the management of AS among a rather mixed group of AS patients from 10 different European countries. The involvement of patients with many different native tongues enhances the likelihood that the present language version can be easily understood by many patients and also easily translated in various languages as specific English wording is avoided. Although there was a lot of discussion, it was eventually possible to agree on the basis of a majority vote with > 80% agreement in almost all cases. Participants accepted that the basic content of the original recommendations could not be changed during this translation process. Considerable time was spent on discussions relating to the content of the recommendations (importance of non-pharmacological treatment options, use of opioids and corticosteroids etc.). The patients prepared a wish-list for further consideration in the next update of the recommendations, in which most of the discussion regarding the content is summarized (Table 5). Despite the discussion to discriminate between agreement with the translation versus with the content of the patient version, it is quite obvious that in some cases (e.g. recommendation No. 4) the patients vote to the translation is influenced by disagreement to the content of the recommendation. This difficulty can be reduced if the AS patients will be able to participate in the development of recommendations at earlier steps.

This patient version of the ASAS/EULAR recommendation for the management of AS should serve as a preliminary step for the development of the ASAS/EULAR management recommendation update and also for further evaluation and dissemination in individual countries where a broader array of patients should be included. Thus, the patient version will be forwarded to ASAS members in all EULAR countries with the request to perform a translation in cooperation with national patient organization. Within this national translation process the group of participants should be heterogeneous concerning disease status and educational level. This was not the case in our group of AS patients because the success of creating an international patient version depends on excellent knowledge of the English language of all participants. The dissemination and evaluation of the national patient versions will be checked after one year.

The participants elaborate during the discussion that not only body functions and structures have to be discussed as an important aspect of disease progress (recommendation No. 1). In terms of the composition of the International Classification of Functioning, Disability and Health developed by the WHO for describing functioning of people with an ill health condition the aspects of activity and participation of the patients have to be considered as well [13]. In this framework function is not narrowed to biomedical function but environmental and personal

factors are in a complex interaction of these areas. Recently, this has already been applied to patients with AS [14].
The study on dissemination and evaluation of the health professionals publication of the ASAS/EULAR recommendations for the management of AS among European rheumatologists has already shown that conceptual agreement with the recommendations was very high, as was self-declared application by rheumatologists (8.9 ± 0.9 and 8.2 ± 1.0, respectively) [15]. Potential barriers to the application of the ASAS recommendations include primarily insufficient funding and administrative burden for anti-TNF therapy and patient concern about safety of pharmacological therapy. Barriers to the use of the non-pharmacological treatment are lack of consultation time, insufficient number of qualified physiotherapists, lack of facilities for education and lack of patient compliance with recommendations. Similar to the European evaluation, a broad agreement with the recommendations was achieved to an evaluation in the German language area and in Mexico [16,17].

For the first time, EULAR recommendations were successfully converted into lay terms by a large international task force of patients in collaboration with rheumatologists. This can be seen as a starting point for the dissemination and implementation of the patient version to provide guidance for monitoring and treatment of patients with AS. Further translations into different languages and appropriate evaluations in larger patient groups will be performed.

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Competing interests: There are no competing interests.



Appendix 1: List of participants
John Barnes; Ireland; Campbell Barr, UK; David Blythe, UK; Philippe Carron, Belgium; Cor van Drogen, The Netherlands; Eric Eustance, UK; Ernst Feldtkeller, Germany; Barbara Foster, UK; Hedley Hamilton, UK; Merryn Jongkees, The Netherlands; Uta Kiltz, Germany; Jose Luis Lopes, Portugal; Ken Mulholland, Canada; Joke Nijns, Belgium; Salih Özgocmen, Turkey; Eckhard Pfeiffer, Germany; Peter Staub, Switzerland; Corina Stefan, Romania.

Figure 1 gives the strength of each recommendation as assigned by the participants.

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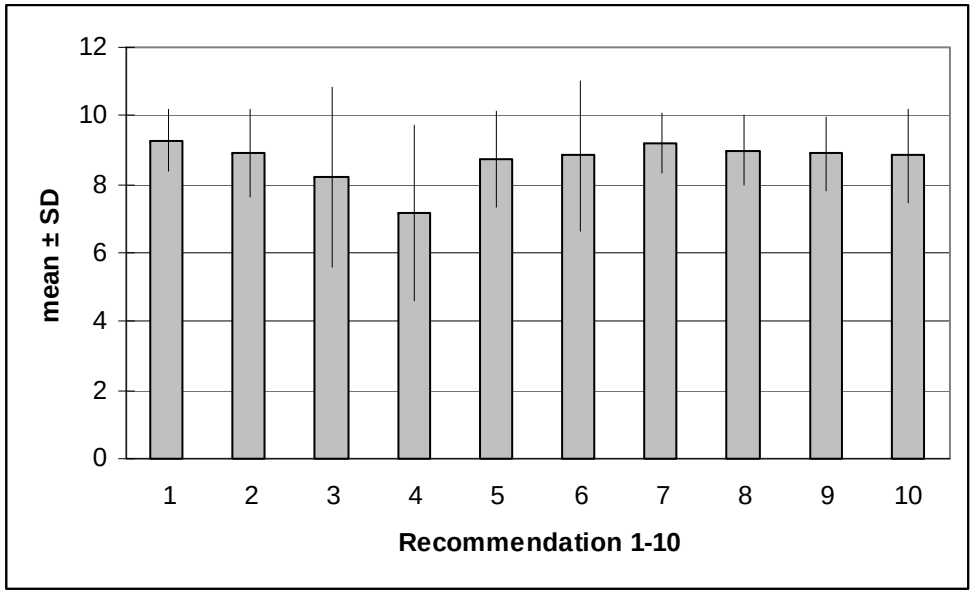


Figure 1: Strength of recommendation 1 – 10

**Supplement 1 ASAS/EULAR recommendations for the management of ankylosing spondylitis (health professional's publication)**

Zochling et al. Ann Rheum Dis 2006;**65**:442-452

| No. | Recommendation |
|---|---|
| 1 | Treatment of AS should be tailored according to:<br>• Current manifestations of the disease (axial, peripheral, enthesal, extra-articular symptoms and signs)<br>• Level of current symptoms, clinical findings, and prognostic indicators<br>- Disease activity/inflammation<br>- Pain<br>- Function, disability, handicap<br>- Structural damage, hip involvement, spinal deformities<br>• General clinical status (age, sex, comorbidity, concomitant drugs)<br>• Wishes and expectations of the patient |
| 2 | Disease monitoring of patients with AS should include: patient history (for example, questionnaires), clinical parameters, laboratory tests, and imaging, all according to the clinical presentation as well as the ASAS core set. The frequency of monitoring should be decided on an individual basis depending on symptoms, severity, and drug treatment |
| 3 | Optimal management of AS requires a combination of non-pharmacological and pharmacological treatments |
| 4 | Non-pharmacological treatment of AS should include patient education and regular exercise. Individual and group physical therapy should be considered. Patient associations and self help groups may be useful |
| 5 | NSAIDs are recommended as first line drug treatment for patients with AS with pain and stiffness. In those with increased GI risk, non-selective NSAIDs plus a gastroprotective agent, or a selective COX-2 inhibitor could be used |
| 6 | Analgesics, such as paracetamol and opioids, might be considered for pain control in patients in whom NSAIDs are insufficient, contraindicated, and/or poorly tolerated |
| 7 | Corticosteroid injections directed to the local site of musculoskeletal inflammation may be considered. The use of systemic corticosteroids for axial disease is not supported by evidence |
| 8 | There is no evidence for the efficacy of DMARDs, including sulfasalazine and methotrexate, for the treatment of axial disease. Sulfasalazine may be considered in patients with peripheral arthritis |
| 9 | Anti-TNF treatment should be given to patients with persistently high disease activity despite conventional treatments according to the ASAS recommendations. There is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease |
| 10 | Total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage, independent of age. Spinal surgery – for example, corrective osteotomy and stabilisation procedures, may be of value in selected patients. |

## Supplement 2 Recommendations for anti-TNF therapy in AS.

Braun J et al. Ann Rheum Dis 2006;**65**:316-320.

| **Patient Selection** | |
|---|---|
| ▪ Diagnosis | ▪ Patients normally fulfilling modified New York Criteria for definitive AS<br>▪ Modified New York criteria 1984 (van der Linden et al.)<br>▪ **Radiological criterion**<br>▪ Sacroiliitis, grade ≥ II bilaterally or grade III to IV unilaterally<br><br>▪ **Clinical criteria** (2 out of the following 3)<br>▪ Low back pain and stiffness for more than 3 months that improves with exercise but is not relieved by rest<br>▪ Limitation of motion of the lumbar spine in both the sagittal and frontal planes<br>▪ Limitation of chest expansion relative to normal values correlated for age and sex |
| ▪ Active disease | ▪ Active Disease for at least 4 weeks<br>▪ BASDAI ≥ 4 (0-10) and an expert* opinion**<br>*The expert is a physician, usually a rheumatologist, with expertise in inflammatory back pain and the use of biologics. Expert should be locally defined.<br><br>**An expert opinion is comprised of both, clinical features (history and examination) and serum acute phase reactant levels and/or imaging results, such as radiographs demonstrating rapid progression or MRI scans indicating ongoing inflammation. |
| ▪ Treatment failure | ▪ All patients should have had adequate therapeutic trials of at least 2 NSAIDs. An adequate therapeutic trial is defined as :<br>▪ Treatment for at least 3 months at maximal recommended or tolerated anti-inflammatory dose unless contraindicated<br>▪ Treatment for < 3 months where treatment was withdrawn because of intolerance, toxicity, or contraindications.<br>▪ Patients with pure axial manifestations do not have to take DMARDs before anti-TNF therapy can be started.<br>▪ Patients with symptomatic peripheral arthritis should have an insufficient response to at least one local corticosteroid injection if appropriate<br>▪ Patients with persistent peripheral arthritis must have had a therapeutic trial of sulfasalazine*<br>▪ Patients with symptomatic enthesitis must have failed appropriate local treatment.<br><br>* Sulfasalazine: Treatment for at least 4 months at standard target dose or maximally tolerated dose unless contraindicated or not tolerated. Treatment for less than 4 months, where treatment was withdrawn because of intolerance or toxicity or contraindicated. |
| ▪ Contraindication | ▪ Women who are pregnant or breastfeeding; effective contraception must be practiced<br>▪ Active infection<br>▪ Patients at high risk of infection including:<br>▪ Chronic leg ulcer<br>▪ Previous tuberculosis (note: please follow local recommendations for prevention or treatment)<br>▪ Septic arthritis of a native joint within the last 12 months |

| | |
|---|---|
| | ▪ Sepsis of a prosthetic joint within the last 12 months, or indefinitely if the joint remains *in situ*<br>▪ Persistent or recurrent chest infections<br>▪ Indwelling urinary catheter<br><br>▪ History of Lupus or Multiple Sclerosis<br>▪ Malignancy or pre-malignancy states excluding:<br>▪ Basal cell carcinoma<br>▪ Malignancies diagnosed and treated more than 10 years previously (where the probability of total cure is very high) |
| **Assessment of Disease** | |
| ASAS core set for daily practice | ▪ Physical function (BASFI or Dougados functional index)<br>▪ Pain (VAS, last week, spine at night, due to AS *and* VAS, last week, spine due to AS)<br>▪ Spinal mobility (chest expansion *and* modified Schober *and* occiput to wall distance *and* lateral lumbar flexion)<br>▪ Patient's global assessment (VAS, last week)<br>▪ Stiffness (duration of morning stiffness, spine, last week)<br>▪ Peripheral joints and entheses (number of swollen joints [44 joints count], enthesitis score such as developed in Maastricht, Berlin or San Francisco)<br>▪ Acute phase reactants (ESR *or* CRP)<br>▪ Fatigue (VAS) |
| BASDAI | ▪ VAS overall level of fatigue/tiredness past week<br>▪ VAS overall level of AS neck, back, or hip pain past week<br>▪ VAS overall level of pain/swelling in joints other than neck, back or hips past week<br>▪ VAS overall discomfort from any areas tender to touch or pressure past week<br>▪ VAS overall level of morning stiffness from time of awakening past week<br>▪ Duration and intensity (VAS) of morning stiffness from time of awakening (up to 120 minutes) |
| **Assessment of Response** | |
| Responder criteria | BASDAI :50% relative change or absolute change of 20 mm and Expert Opinion : Continuation yes/no |
| Time of evaluation | Between 6 and 12 weeks |