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Review.

The ASAS health index: a new era for health impact assessment in spondyloarthritis

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Abstract

The concept of spondyloarthritis (SpA) encompasses a series of entities that share clinical and imaging characteristics and a common genetic basis. These diseases can affect 0.20 to 1.6% of the general population, limiting functioning and affecting the quality of life of patients. Considering the patient perspective in the management of the disease and ensuring patients are sufficiently prepared to participate in decision-making is critical to treatment success as well as for optimal health outcomes. The overall picture of impairments, limitations, and restrictions in activities or social participation of patients with SpA is not adequately assessed in SpA-specific instruments. Therefore, it is quite relevant to measure the broader range of impairments that can affect SpA patients and integrate these into one measure of overall functioning in daily life. The Assessment of SpondyloArthritis international Society-Health Index (ASAS HI) is a recently introduced health instrument for evaluating SpA based on the International Classification of Functioning, Disability and Health, also known as ICF, that could cover a good part of the health metric needs in SpA. This review addresses its origins, its measurement properties, its use in routine clinical practice, as well as its prospects for future use.

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1.- Disease burden in spondyloarthritis: the need for new health metrics

The concept of spondyloarthritis (SpA) encompasses a series of entities that share clinical and imaging characteristics and a common genetic basis. This conceptual umbrella includes entities such as ankylosing spondylitis (AS), non-radiographic axial SpA (nr-axSpA), as well as predominantly peripheral forms (1). The 2009 Assessment of SpondyloArthritis international Society (ASAS) classification criteria have greatly contributed to giving a cohesive view of these entities that has facilitated their study from multiple standpoints (2).

Axial SpA (axSpA) is characterized by inflammatory spinal pain and spinal stiffness and includes AS (radiographic axSpA) and nr-axSpA (2). A recent meta-analysis reported a global prevalence of these conditions with ranges from 0.20% in South East Asia to 1.61% in arctic circumpolar areas (3). As these conditions usually start in young individuals, when many of them are starting their working life, SpA may often condition the professional prospects of many of them. The inability of these patients to continue in their work considerably affects their social life as well as having economic repercussions for patients and societies (4). When compared to rheumatoid arthritis (RA), patients with axSpA and psoriatic arthritis (PsA) experienced more pain and fatigue than did those with RA, and patients with axSpA had more overall and nocturnal spinal pain than did PsA and RA (5). Some studies have shown that the overall unemployment rate in axSpA is 25%, with 20.6% attributable to the disease itself, with this level being conditioned by being female, having a low educational level, living in rural areas as well as high rates of disease activity (6).

Symptoms of pain, stiffness, and fatigue associated with progressive bony fusion of the spine are major contributors to disease burden and limit physical functioning, including

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the ability to perform daily activities (7-11). Many patients with axSpA also experience sexual disfunction, depression, anxiety, and sleep alterations (11). Therefore, patients with axSpA show significantly lower health-related quality of life (HRQoL) compared with the general population, and physical components of HRQoL tend to be more affected than psychological ones in both sexes (11-13).

The European Map of Axial Spondyloarthritis (EMAS) has been the largest survey carried out to date for people with axSpA, across 2846 respondents from 13 European countries (14). The EMAS focus was on understanding the patient perspective through a holistic approach and utilizing a questionnaire designed for patients and by patients. As such, EMAS collected not only clinical characteristics of the disease but also the impact this had on patient's psychological health, daily activities, and working and social life as well as how the disease relates to their hopes and fears, all of which are considered relevant and important aspects to patients with axSpA (14). The final patient questionnaire included 108 items related to 12 different areas: socio-demographic and anthropometric characteristics, disability assessment, work life, daily life, lifestyle habits, diagnostic journey, healthcare resource use, treatment, comorbidities (including extraarticular manifestations), psychological health, disease outcomes, and patient disease-related attitudes and treatment goals (14). Data from this survey indicated important unmet needs in axSpA, including long diagnostic delay, deterioration of QoL, and high burden of disease for patients. Mean diagnostic delay was calculated at over 7 years, confirming similar results drawn from other studies (15). The results of EMAS showed a high burden of disease for patients. Most participants reported moderate to severe limitation during disease flares, which was especially evident while performing daily activities including physical exercise,

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cleaning, getting out of bed, or getting dressed (14). The EMAS sample showed a high prevalence of mental health difficulties. Thus, 61.5% of patients were at risk for psychological distress, with 33.8% and 38.6% respectively reporting depression and anxiety. Participants also reported difficulties finding a job due to their condition (74.1%), that the disease influenced their job choice (45.7%), while workplace adaptation was required by many of them (43.9%) (14).

The factors positively associated with a poorer HRQoL in patients with SpA depend on inflammatory activity, axial mobility, and physical function. Quality of life instruments, both generic and specific, usually capture the impact related to these factors, however, there are contextual or social factors, as well as specific disease aspects (such as fatigue or sexuality), which are not included in these tools. On the other hand, concepts such as QoL, HRQoL, or disease impact, are not entirely synonymous since the measurement dimensions or the construct content of these approximations are not the same (16). Therefore, there is a growing need for instruments that address the well-being and overall health of these patients in a more holistic way (16).

2.- Development of the ASAS HI

The International Classification of Functioning, Disability and Health, also known as ICF, is an instrument developed by the World Health Organization (WHO) to provide a standard language and framework for the description of health and health-related states (17). In ICF, the term functioning refers to all body functions, activities, and participation, while disability is similarly an umbrella term for impairments, activity limitations and participation restrictions. ICF also lists environmental factors that interact with all these components (17). This more holistic model of disability might be called the biopsychosocial model of disease. In this proposal, disability is viewed as a

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complex phenomenon that is both a problem at the level of a person's body, and a complex and primarily social phenomena. Therefore, disability is always an interaction between features of the person and features of the overall context in which the person lives, but some aspects of disability are almost entirely internal to the person, while other aspects are almost entirely external. In other words, the biopsychosocial model integrates disability as a feature of the person, directly caused by disease, trauma, or other health condition, which requires medical care provided in the form of individual treatment by professionals, along with disability as a socially created problem which requires a political response, since the problem is created by an unaccommodating physical environment brought about by attitudes and other features of the social environment. Therefore, ICF provides a coherent view of different perspectives of health: biological, individual, and social (17).

Figure 1 shows the three levels of human functioning classified by ICF: functioning at the level of body or body part, the whole person, and the whole person in a social context. Disability therefore involves alterations at one or more of these same levels: impairments, activity limitations and participation restrictions (17).

The overall picture of impairments, limitations and restrictions in activities or social participation of patients with SpA are not adequately assessed in SpA-specific instruments (18). Moreover, most of the existing questionnaires are not conceptualized regarding their underlying construct. To overcome this, the ASAS group developed an instrument assessing health as operationalized by the ICF according to ICF categories of functioning (19). The comprehensive ICF Core Set for AS was a disease specific selection of the ICF factors that are typical and relevant for these patients and has served as the underlying construct of the ASAS HI since the whole range of

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functioning, disability, and health of patients with AS was captured (20). The ASAS HI is a linear composite measure containing 17 items with dichotomous response option ("I agree" and "I do not agree") which cover most of the ICF core set (Table 1). The item selection has been carried out based on the Rasch Model. Each positive answer is scored 1 while a negative answer is scored 0. The result is the sum of individual items. Higher values reflect a major degree of impairments, limitations, and restrictions (18,19). Five phases were used to develop the questionnaire and to achieve an index for functioning and health which is easy to administer, easy to fill in and applicable to patients worldwide. The items incorporated into the final questionnaire originated from 251 items pool, which had been developed by linking items from existing questionnaires (either disease-specific or generic instruments) to 44 categories of the comprehensive ICF core set for AS related to the components of body functions, activities, and participation. A total of 76 items covered the 23 ICF categories from the component body functions, 122 items the 24 categories from the component activities and participation, and 53 items covered 14 categories of environmental factors (EF) (18,19). The final 17 items cover a wide range of ICF including pain, emotional functions, sleep, sexual functions, mobility, self-care, and community life. The ASAS HI was originally developed in parallel in English speaking countries (Australia, Canada, Ireland, UK, USA), and it has later been translated and cross-culturally adapted into 18 languages worldwide (19,21).

3.- Measurement properties

To review the metrological properties of ASAS HI in patients with SpA, we have searched all the articles referring to this instrument from its original publication to the

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present (2021) in PubMed. Also, some references have been obtained from the databases of the EULAR and ACR congresses, avoiding duplications**.**

3.1. Interpretability:

The ASAS HI is a linear composite measure and higher values reflect a major degree of impairments, limitations, and restrictions (19).

The most important study carried out so far to validate the clinimetric properties of ASAS-HI was a recent cross-sectional international observational study that included 1548 patients from 23 countries (22). The ASAS HI proved to be a valid, interpretable, reliable, and responsive questionnaire to assess overall functioning and health in this global international validation study including 19 languages (22).

The mean total score on the ASAS HI ranged from 3.2 to 8.37 (19, 23-33).

Cognitive debriefing studies have showed that items of the ASAS HI and EF Item Set are clear, relevant, and comprehensive. All translated versions were accepted with minor modifications with respect to item wording and response option. In such studies, only the wording of three items (#7 and #8 of ASAS HI, and #6 of the EF item set) had to be adapted to improve clarity. As a result of cognitive debriefing, a new response option 'not applicable' was added to two items of the ASAS HI to improve appropriateness (21).

3.2. Content validity:

ASAS HI construct validity by Spearman´s correlation coefficient ranged from low (absenteeism: 0.23) to high (BASFI: 0.71 or SF-36 PSC 0.73). Of note, the correlations of ASAS HI with age (r=0.10) and symptom duration were weak. BASDAI, BASFI and ASDAS correlation with ASAS-HI was high with values reported in various studies between (0.51-0.77; 0.62-0.80 and 0.51-0.70 respectively) (19, 22-25, 27-29, 31-33).

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In Min´s study (27), multivariable regression analysis of the axSpA group showed that high NSAID intake and mSASSS were positively associated with higher ASAS HI, whereas higher economic status and alcohol consumption were negatively associated with ASAS HI. Results were consistent in the AS group on subgroup analysis, whereas alcohol consumption was the only factor significantly associated with ASAS HI in the nr-axSpA group. In short, in this cohort study, patients with AS had poorer health status than those with nr-axSpA.

3.3. Internal consistency:

Numerous studies show a high internal consistency of the ASAS HI with a Cronbach's alpha ranging from 0.83 to 0,93. (22-24, 28, 32, 33). Moreover, internal consistency did not vary across different disease groups (0.93 for AS, 0.94 for nr-axSpA, and 0.91 for peripheral SpA) (22).

3.4. Reliability and measurement error:

Reliability was excellent in all the studies analyzed with an ICC with minimum values of 0.84 (95%CI 0.71 to 0.93, p<0.001) and maximum values of 0.97 (95% [CI], 0.95-0.98; p<0.001) (22-25, 28, 29, 33).

Also, ICCs were comparably high in all disease subtypes (AS 0.87 (95%CI 0.84 to 0.89 and 0.94 [95%-CI 0.86 to 0.97); nr-axSpA 0.89 (95%CI 0.85 to 0.93 and 0.97 [95%-CI 0.89 to 0.99); peripheral SpA 0.83 (95%CI 0.75 to 0.88 and 0.92 (95%CI 0.79 to 0.97) (22, 23).

Bland-Altman plot showed good agreement between ASAS HI sum score at first and second assessment. (22, 23, 25). The smallest detectable change (SDC) was calculated as 3.0, which corresponds to the minimum change beyond measurement error that

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can be detected in an individual patient over time (22, 23,33). However, Kwan et al., showed a lower SDC calculated as 1.02 (28).

3.5. Responsiveness:

Several studies analyzed sensitivity to change of ASAS HI in patients who initiated or changed from its original therapy. The standardized response mean (SRM) varied across different studies between -0.27 (low) and 2,58 (large). In general, those patients in which the intervention was a TNFα blocker the SRM was higher than those starting a NSAID or csDMARD (22-24, 33).

3.6. Discriminant ability:

ASAS HI discriminated well between patients with different disease activity states (measured by ASDAS and BASDAI) and function (measured by BASFI). The groups with greater disease activity and more impaired functioning had higher mean ASAS HI scores than those with lower disease activity and functional scores. Moreover, ASAS HI was able to differentiate between different stages of disease activity and physical functioning in patients with SpA. Patients with high disease activity and limited physical function had poorer global functional capacity as measured by the sum score of ASAS HI (22-24, 33).

The following is a summary of the main ASAS HI cut-off points that discriminate disease activity**:**

a) 5.0 ± 3.2 as a cut-off point for identifying low disease activity measured by BASDAI<4 (19).

b) 2.9 ± 3.1 as an inactive disease identifier measured by ASDAS and 2.8 ± 2.9 as an identifier of BASDAI remission (22).

c) 4.8 ± 3.2 as a moderate activity identifier measured by ASDAS (23).

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d) 5.9±3.0 as a low activity identifier measured by ASDAS (24).

f) 4 as a cut-off point to define the inactive disease, with respect to ASDAS-CRP and SASDAS (25) and with respect to ASDAS-CRP (34).

g) ≤ 6 aligned well with the states of remission-low activity of ASDAS (31).

h) 4.5± 2 as a low activity identifier measured by ASDAS (33).

With respect to ASAS HI scores related to physical function we found the following cut-off points:

a) 3.7 ± 3.1 as a threshold <2 measured by BASFI (22).

b) 3.5 ± 2.9 as a threshold <2 measured by BASFI (23).

c) 4.1 ± 3.4 as a threshold <2 measured by BASFI (32).

3.7. Thresholds of meaning and cut off values:

There are few studies that have determined specific ASAS HI cut-off that discriminate health states. The following figures have been proposed as cut-off points to define health status:

a) Kiltz et al. (22), design a thresholds per se for evaluation the discriminant ability of the ASAS-HI by calculating the mean ASAS HI scores for predefined status groups (ASDAS status groups (inactive, moderate, high, and very high), BASDAI and BASFI thresholds (<2.0, 2.0-3.99, 4.0-5.99, ≥6.0) by ANOVA. To distinguish between relevant health states (an additional relevant aspect of interpretability), two different methods were applied: fixed 90% specificity and the closest point to (0,1). They used the patient global assessment at predefined levels (6 on numerical rating scale and cut-off between good and poor on Likert scale) as external constructs for “poor”, “moderate” and “good” health status. They used a global rating of change question (Likert scale) as

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external construct to assess change perceived by the patient. A cut off between "improved" versus "no change" or "worse" was used to determine minimal clinically important improvement.

In order to balance sensitivity and specificity a threshold of ASAS HI which differentiated patients with "good/very good" health from those with "moderate" health state, was identified as being 5.0. In contrast, the 90% specificity criterion was considered to be the most clinically relevant threshold of ASAS HI for "moderate" versus "poor/very poor" health identified as a score ≥ 12.0 (22).

b) Min et al., using the health states proposed by Kiltz et al. (22), found that most patients analyzed were in `good health status´ (75.9%). Among nr-axSpA, 84.4% were in a `good health status´ compared to 72.8% of patients with AS (27).

c) Akgul et al., performed a ROC analysis to calculate health status thresholds. Based on ASDAS-CRP and patient´s global assessment (PGA) as external anchors, they established ASAS HI ≤ 4 to distinguish the 'good health status' from 'moderate health status', and ≥12 to identify 'poor health status' (32).

Therefore, ASAS HI sum score ≤ 5 may be a good cut-off for discriminating good versus other health status and sum score between 4 and 6 may be good discriminators for disease activity status.

3.8 Score (floor/ceiling effects):

Floor (percentage of the respondents who had the lowest possible (total) score) or ceiling effects (percentage of the respondents who had the highest possible (total)

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score) of the ASAS HI were acceptable (0%-9.2% and 0.8%-1,2%, respectively) (22, 32, 33).

3.9 Use in clinical trials:

The effects of Ixekizumab (IXE) on functioning and health were assessed using the ASAS HI on the 303 patients with nr-axSpA enrolled in the COAST–X Trial (35). An improvement ≥3 from baseline in ASAS HI represented a clinically meaningful change and attaining a "good health status" was defined by score ≤ 5. Baseline mean scores (SD) were 9.1 (3.6) for ASAS HI. Patients treated with IXE every 2 weeks (Q2W) reported significant improvements in ASAS HI at Week 16 (-2.74 for IXE Q2W versus -1.76 for placebo, p=0.023) with numerically greater improvements in ASAS HI changes from baseline in both IXE groups compared with placebo through Week 52.

COAST-V and COAST-W are phase III, multicenter, and placebo randomized controlled trials, evaluating the efficacy and safety of IXE in patients with radiographic axSpA. Participants in COAST-V were bDMARD-naïve, whereas in COAST-W, trial participants had failed at least 1 and not more than 2 TNFi (36). At Week 16, bDMARD-naïve patients receiving IXE reported a significantly larger improvement from baseline on ASAS HI versus placebo (-2.36 for Q4W (p=0.01), -2.74 for Q2W). Ixekizumab Q4W bDMARD-naïve patients achieved numerically similar ASAS HI mean change from baseline as patients who received IXE Q2W (-2.7 vs -3.3, at Week 52). Patients treated with the active reference adalimumab also showed consistent significant improvement in ASAS HI mean change from baseline throughout 16 weeks. Patients who received adalimumab or placebo during the blinded treatment dosing period and switched to IXE at Week 16 demonstrated continued numeric improvements in ASAS HI through Week 52. Both IXE regimens (Q2W and Q4W) sustained similar improvements through

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Week 52. Patients in the bDMARD naïve arm experienced a numerically greater improvement of ASAS HI mean change versus TNFi-experienced patients when treated with IXE Q4W (-2.4 vs -1.9 at Week 16 and -2.7 vs - 2.3 at Week 52) or IXE Q2W (-2.7 vs -1.6 at Week 16 and -3.3 vs -2.5 at Week 52). The proportion of patients treated with IXE achieving improvement in ASAS HI ≥3 throughout the 52 weeks were 53.2% for Q2W and 43.0% for Q4W (bDMARD-naïve patients), and 43.3% and 36.8% (TNFi-experienced patients).

Finally, the recently published TICOSPA study evaluated the benefit of a tight control strategy compared to usual practice in patients with axSpA (37). One hundred-sixty patients were randomized (1:1) to the tight control arm (strategy was pre-specified by the scientific committee, based on current axSpA recommendations, visits every 4 weeks and targeted (ASDAS <2.1)) vs usual practice (treatment decisions were made at the discretion of the rheumatologist, with visits every 12 weeks). The percentage of patients with a significant improvement (>30%) in ASAS-HI score during 1-year follow-up was the primary outcome of this study. Although 47.3% vs. 36.1% of patients in the strict control and usual practice arms, respectively, achieved a significant improvement in ASAS-HI at the 1-year visit, the difference was not statistically significant.

Table 3 summarizes the psychometric properties of ASAS HI discussed above.

4.- Applications, potential uses and use in clinical practice

Since the ASAS HI probably captures aspects not only related to the activity of the disease or the functional limitation but also other aspects related to the individual and their social environment, it gathers all measurement properties for its use in clinical routine.

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Quality-adjusted life-years (QALYs) play an important role in reimbursement decisions when one of the criteria is the cost-effectiveness of the health technology. While for many generic QALYs (e.g., based on the EQ-5D) are viewed as the gold standard, there has been a considerable increase in interest in using condition-specific data to generate QALYs (38). Therefore, using patient-reported measures as a basis for indirect health utility valuation may not accurately reflect the effect of interventions on specific impairments and limitations typically experienced by SpA patients (30). The ASAS HI offers an interesting starting point to develop a disease-specific utility index, as it was developed with the specific aim to reflect aspects of health important and typical for patients with axSpA, and to a lesser extent for peripheral SpA (30). Essers et al. (30), have recently developed one generic and six country-specific algorithms which are now available to convert scores of ASAS HI into a utility from the societal cost perspective. This makes it possible to use disease-specific utilities and QALYs in decision-making processes when comparing treatment strategies among patients with SpA (30).

The BWS (Best Worst Scaling) method is widely used to measure health preferences. Kiltz et al. conducted a BWS exercise in patients with axSpA from 20 countries worldwide (39). The study was completed by 199 patients. The highest relative importance was assigned to pain, sleep, being exhausted, being standing, and motivation to do anything that requires physical effort. The lowest relative importance was assigned to sexual relationships, toileting, contact with people, driving and washing hair (39). As authors concluded, this information may help to align clinical care to patients' needs.

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In the most important validation study carried out to date, ASAS HI was applicable in all patients with SpA irrespective of the disease subgroup (83.5% axSpA and 16.5% with peripheral SpA). However, the proportion of patients with concomitant psoriasis did not exceed 10%, so the representativeness of patients with PsA was presumably very low in this validation exercise. Morante et al., evaluated the performance of ASAS HI in 90 PsA Spanish patients. Mean ASAS-HI was 5.8 ± 4.3. Convergent validity was high both against the Disease Activity index for Psoriatic Arthritis -DAPSA- and the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire. ASAS HI also showed a high discriminant capacity against DAPSA categories of disease activity. The ASAS-HI items significantly associated with DAPSA active disease were, "I find it hard to stand for long" (β 4.48, $p < 0.0001$), "I find it hard to concentrate" (β 2.94, $p= 0.042$), and "I sleep badly at night" (β 1.86, $p= 0.044$). These results suggest that ASAS HI could be a valid instrument to assess overall functioning and health in PsA (40). Also, recently, the usefulness of ASAS HI has been proven to analyze some differential aspects between patients with PsA and axSpA (41, 42).

5.- Gaps and additional studies needed

Although it is a fast, simple, and accessible tool in clinical practice, we have observed that the dissemination of ASAS HI in clinical practice is still very limited (43). More evidence is also needed to determine cut-off points that better discriminate between health status. Moreover, more information is needed regarding ASAS HI as a potential discriminator of disease activity in SpA. Finally, we also do not know to what extent other concomitant conditions (i.e fibromyalgia) may influence the ASAS HI sum score (44). In short, it is necessary to expand the studies in real clinical practice with this new instrument.

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6.- Conclusions

The ASAS HI is a new SpA-related instrument based on the WHO ICF categories. Its good measurement properties allow it to be a suitable tool for assessing health and functioning in patients with different SpA phenotypes in routine clinical practice, cohort studies, as well as clinical trials. In the next future, it could be a valid questionnaire for the evaluation of other entities such as PsA, and for planning health policies from a societal-cost perspective. Finally, since SpA is frequently accompanied by other conditions that surely have an impact on the way in which patients cope with their day-to-day life, it would be interesting to inquire whether ASAS HI can capture the impact associated with these other SpA-related manifestations (45,46).

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Figure 1 legend.

The biopsychosocial model of disease based on the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (WHO). The model is based on three levels of human functioning: functioning at the level of body or body part, the whole person, and the whole person in a social context. Disability therefore involves alterations at one or more of these same levels: impairments, activity limitations, and participation restrictions.

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Table 1. The 17 items of the ASAS health index

Items	ICF Categories
#1 Pain sometimes disrupts my normal activities	Pain
#2 I find it hard to stand for long	Maintaining a body position
#3 I have problems running	Moving around
#4 I have problems using toilet facilities	Toileting
#5 I am often exhausted	Energy and drive
#6 I am less motivated to do anything that requires physical effort	Motivation
#7 I have lost interest in sex	Sexual functions
#8 I have difficulty operating the pedals in my car	Driving
#9 I am finding it hard to make contact with people	Community life
#10 I am not able to walk outdoors on flat ground	Moving around
#11 I find it hard to concentrate	Handling stress
#12 I am restricted in traveling because of my mobility	Recreation and leisure
#13 I often get frustrated	Emotional functions
#14 I find it difficult to wash my hair	Washing oneself
#15 I have experienced financial changes because of my rheumatic disease	Economic selfsufficiency
#16 I sleep badly at night	Sleep
#17 I cannot overcome my difficulties	Handling stress

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Modified from reference 15. ASAS: Assessment of SpondyloArthritis international Society. ICF: International Classification of Functioning, Disability and Health.

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Table 2. Defined health status groups according to the ASAS health index

External equivalents	Good health status ≤ 5	Moderate health status >5 - <12	Poor health status ≥12
ASAS HI	2.1 (1.5)	7.8 (2.0)	13.7 (1.5)
BASFI	1.2 (1.5)	3.8 (2.5)	6.3 (2.3)
BASDAI	2.1 (1.6)	4.8 (2.1)	6.6 (1.9)
ASDAS	1.7 (0.9)	2.6 (2.1)	3.7 (1.1)
SF36 PSC	47.6 (7.1)	35.7 (8.8)	28.7 (6.6)
EQ-5D	0.8 (0.1)	0.6 (0.2)	0.4 (0.2)

The three defined health status groups within ASAS HI discriminate with respect to disease activity (BASDAI, ASDAS), functioning (BASFI), and QoL measures (SF36, EQ-5D). Modified from reference 22. Values are means (SD).

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Table 3. Main worldwide studies carried out to date with the ASAS health index

Author, year	N	Spondyloarthritis type (n)	Treatment	BASDAI Correlation	BASFI Correlation	ASDAS Correlation	ASAS HI average score	Activity discrimination score	Internal consistency (Cronbach α)	Reliability (ICC)	SDC	SRM	Floor/ceiling effects	Mean time consumption
Choi, 2014	43	13 nr-axSpA 30 AS	ND	r= 0.63	r= 0.69	ND	5.3 (SD 4.2)	ND	ND	0.97 (95% CI 0.95-0.98)	ND	ND	ND	75.4 seconds (SD 31.7)
Kiltz, 2015	1754	AS	ND	r=0.60	r=0.70	ND	8.37 (SD 3.9)	5.0±3.2 for BASDAI <4	ND	ND	ND	ND	ND	ND
Kiltz, 2016	215	140 AS 75 nr-axSpA	ND	ND	ND	ND	7.1 (SD 4.4)	ND	ND	ND	ND	ND	ND	ND
Di Carlo, 2016	140	98 AS 42 nr-axSpA	70.7% TNFi. All with NSAID on-demand	r= 0.56	r= 0.67	r= 0.56	7.6 (SD 3.9)	4	ND	0.976 (range 0.966-0.982)	ND	ND	ND	1.92±0.76 minutes (range 0.8-3.5)
Cruz, 2017	10	6 AS 4 nr-axSpA	ND	ND	ND	ND	5.1 (SD 4.0)	ND	ND	ND	ND	ND	ND	2.2±0.4 minutes (range 1.2 to 3.2)
Di Carlo, 2017	140	93 AS 47 nr-axSpA	70.7%TNFi. All with NSAID on-demand	ND	ND	ND	ND	4	ND	ND	ND	ND	ND	ND
Bautista-Molano, 2018	50	30 AS 14 nr-axSpA 6 pSpA	ND	r= 0.66	r= 0.62	r= 0.65	8.2 (SD 5.1)	5.9±3.0 for ASDAS low activity	0.91	0.84 (95% CI 0.71-0.93)		2.94 (2.13 - 4.24) TNFi 2.22 (1.23 - 3.21) NSAID or DMARD	ND	ND
Kiltz, 2018	1548	1292 axSpA (375nr-axSpA/917 AS) 256 pSpA	64.2% NSAID 26.2% DMARD 38.2% TNFi	r= 0.70	r= 0.71	r= 0.61	6.7 (SD 4.3)	5	0.93 for AS 0.94 for nr-axSpA 0,91 for pSpA	0.87 (95% CI 0.84-0.89)	3	-0.44 NSAIDs -0.69 csDMARDs -0.85 TNFi	6.9%/0.8%	ND
Kiltz, 2019	171	90 AS 44 nr-axSpA 37 pSpA	NSAID7 6,6% DMARD 21,6% 30.4% TNFi	r= 0.71	r= 0.74	r= 0.52	7.3 (SD 4,1)	4.8 ±3.2 for ASDAS moderate activity	0.83	0.94 (95% CI 0.90-0.96)	3	-0.27	ND	ND
Kwan, 2019	108	axSpA	70.2% NSAID 16.4% DMARD 14.7%	r= 0.61	r= 0.62	ND	3.2 (range 0-15)	ND	0.83	0.96 (95% CI 0.93-	1.02	ND	ND	1.2 minutes

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			biologic therapy							0.98) week 1 0.95 (95% CI 0.91-0.98) week 2				
Esser s, 2019	19 9	130 AS 69 nr-axSpA	ND	ND	ND	ND	7.2 (SD 4.5)	ND	ND	ND	ND	ND	ND	ND
Min, 2019	35 7	261 AS 96 nr-axSpA	54.6 % NSAID 34.3% sulfasalazine 47.8% TNFi	r= 0.58	r= 0.65	r= 0.56	3.5 (SD 3.4)	5	ND	ND	ND	ND	ND	ND
Alonso, 2020	11 1	74 AS 37 nr-axSpA	80.2% NSAID 60.3% biologic therapy	r= 0.77	r=0.80	r= 0.70	5.4 (SD 3.8)	6	ND	ND	ND	ND	ND	ND
Agkul, 2020	99 1	851 AS 140 nr-axSpA	ND	r=0.50	r= 0.57	r= 0.51	6.16 (SD 4.37)	4	0.84	ND	ND	ND	9.2%/1.9%	ND
Rodrigues-Manica, 2020	91	63 axSpA (49 r-axSpA and 14 nr-axSpA) 28 pSpA	74% NSAIDs 44% csDMARDs 18% TNFi	r=0.77	r=0.76	r=0.66	6.4 (SD 3.6)	4.5 (2.0) for ASDAS low activity	0.88 r-axSpA 0.90 nr-axSpA 0.86 pSpA 0.50	0.76 (95%CI 0.09-0.91)	3	-0.53	0%/1.1%	ND

ASAS: The Assessment of Spondyloarthritis International Society; n: number of patients; SpA: spondyloarthritis; AS: ankylosing spondylitis; nr-axSpA: non-radiographic axial spondyloarthritis; pSpA: peripheral spondyloarthritis; ND: not described; NSAID: non-steroidal anti-inflammatory drugs; DMARD: Disease modifying antirheumatic drugs; TNFi: tumor necrosis factor α inhibitor; BASDAI: Bath ankylosing spondylitis disease activity index; BASFI: Bath ankylosing spondylitis functional index; , ASDAS: Ankylosing Spondylitis Disease Activity Score; r= rho de Spearman; SD: standard deviation. ICC: intraclass correlation coefficient. CI: confidence interval. SDC: smallest detectable change. SMR: standardized response mean.

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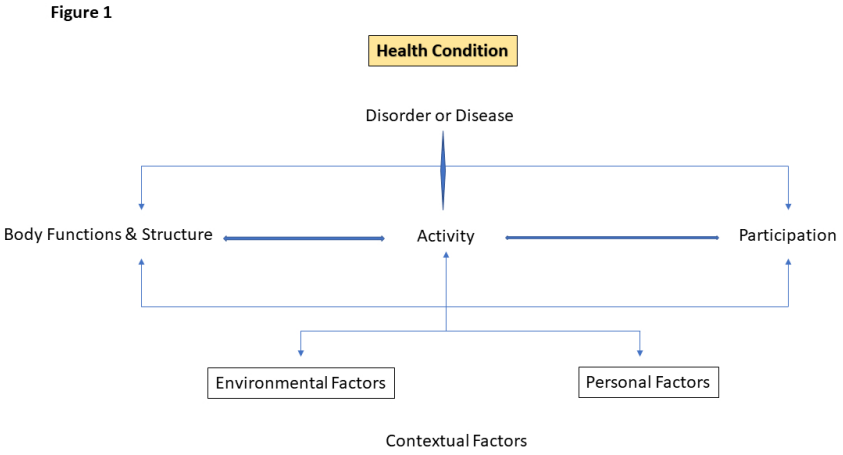

Figure 1

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