Full-length article

Title: The sensitivity to change of the ASAS Health Index in an observational real-life cohort study

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Abstract

Objective

The ASAS health index (ASAS-HI) measures global functioning and health in axSpA patients covering domains of physical, emotional and social functioning. Main aim was to investigate the sensitivity to change of ASAS-HI in comparison with established parameters of disease activity, function, and mental health.

Methods

AxSpA patients from the disease register RABBIT-SpA with follow-up time of at least 12 months and available ASAS-HI questionnaires were included. Patients received questionnaires addressing disease activity (BASDAI, ASDAS), physical function (BASFI), mental health (WHO-5), and global functioning (ASAS-HI). Standardized response means (SRM) were calculated to compare the sensitivity to change of different parameters.

Results

667 patients were included, 552 treated with bDMARD and 115 with csDMARDs and/or NSAIDs. Between baseline and month 12, the mean ASAS-HI declined from 6.9 to 5.1 in the bDMARD group and from 5.9 to 5.6 in the conventionally treated group.

In the bDMARD group, SRM of ASAS-HI was 0.52, compared to 0.59 for BASFI, 0.65 for WHO-5, 0.73 for BASDAI, and 0.9 for ASDAS.

Following ASAS-HI domains were most frequently affected: pain (78% agreed), maintaining body position (75%), and energy/drive (73%). In the bDMARD patients, there was an improvement in all items. In the control group, the largest improvement was seen in pain.

Conclusion

As expected, ASDAS and BASDAI as disease activity scores showed high sensitivity to change, while changes in physical function (BASFI), mental health (WHO-5), and the broader concept of functioning and health (ASAS-HI) were moderate.

Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease characterized by pain, stiffness, fatigue, and impairments in physical functioning.[1] The treatment of axSpA has been revolutionized by the introduction of TNF-inhibitors (TNFi) and more recently complemented by IL17-inhibitors and JAK-inhibitors.[2-4] Nevertheless, many patients still suffer from severe impairment in their daily activities.[5]

The ASAS (assessment of spondyloarthritis international society) Health Index (ASAS-HI) was developed as a SpA-specific instrument to measure the health status in patients with SpA.[6-8] The ASAS/World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) core set for axSpA served as model and underlying construct to develop the ASAS-HI.[9] The ASAS-HI consists of 17 patient reported items addressing the categories of pain, emotional function, sleep, sexual function, mobility, self-care, community life, and employment. Thus, the ASAS-HI addresses disease-specific aspects of physical, emotional, and social functioning, which are summarized by the term of global functioning.

Psychometric properties of the ASAS-HI have been studied in an observational cohort and in some clinical trials. There are two randomized controlled studies on treatment of patients with radiographic (r-axSpA) and non-radiographic axSpA (nr-axSpA) with ixekizumab in which the ASAS-HI was assessed as secondary outcome parameter.[10,11] About 50% of r-axSpA and nr-axSpA patients on ixekizumab achieved an improvement ≥3 of the ASAS-HI score at weeks 16 and 52, respectively. ASAS-HI was chosen as primary outcome parameter in the first treat to target (T2T) strategy trial in axSpA, the TICOSPA study.[12]

The main aim of this analysis was to investigate the sensitivity to change of the ASAS-HI in comparison with established parameters of disease activity, function, and mental health. We aimed to describe to which extent the improvements of global functioning and health measured by the ASAS-HI are comparable with improvements in disease activity measured either by the Ankylosing Spondylitis Disease Activity Score (ASDAS) or by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI),

functional capacity measured by Bath Ankylosing Spondylitis Functional Index (BASFI), and mental health measured by WHO-5 in axSpA patients treated in routine care. Thus, we analysed the effect size measure standardised response mean (SRM), which allows comparisons between similar outcomes measured with different instruments on a standardised scale. The higher the value of the SRM the higher is the ability of a specific outcome parameter to show a clinically relevant change.

Methods

Data source

The German disease register RABBIT-SpA is a long-term observational cohort study which started in 2017.[13] Patients diagnosed by the treating rheumatologist either with axSpA or psoriatic arthritis who start a new treatment with a biologic disease modifying antirheumatic drug (bDMARD), targeted synthetic (ts) DMARD or a conventional treatment (csDMARDs and/or NSAIDs) can be included. After enrollment data are collected every 6 months covering physician and patient reported parameters. The ASAS-HI is assessed at the baseline visit and then annually.

Patients

AxSpA patients with a follow-up time of at least 12 months and with available ASAS-HI questionnaires at baseline and after 12 months were included in this analysis. We selected patients who remained on their treatment for at least 12 months after inclusion (completer analysis) and assigned them according to their treatment to the bDMARD or control group. Switch from the bio-originator to its biosimilar was not considered as treatment change and hence these patients were included and assigned to the bDMARD group. Patients in the control group were treated with csDMARDs and/or NSAIDs. Data base closure was 1^{rst} September, 2021. Prior to enrollment into RABBIT-SpA, all patients gave their informed consent. RABBIT-SpA received approval by the Ethics Committee of the Charité University Medicine, Berlin (#EA1/246/16).

Instruments

The ASAS-HI contains 17 items with a dichotomous response option: “I agree” (1 point) and “I do not agree” (0 points). The sum score of the ASAS-HI ranges between 0 (good functioning) and 17 (poor functioning). Global functioning is categorized based on thresholds as good (ASAS-HI ≤5), moderate (ASAS-HI >5 - 12) and poor (ASAS-HI ≥12).[7] A change from baseline of ≥3 points (smallest detectable change) in an individual patient is considered to be larger than measurement error and thus indicates “true change”. In RABBIT-SpA, the validated German version of the ASAS-HI is used.[8]

The following established instruments were used for comparison: ASDAS is a composite score of physician, patient, and laboratory parameters and is used to assess disease activity.[14] BASDAI is a patient reported score used to measure disease activity.[15] BASFI measures the impairment of physical function in axSpA.[16] WHO-5 score is a depression-screening tool consisting of five questions and is used as patient reported mental health instrument.

Statistical analysis

The parametric analysis of covariance (ANCOVA) was used to compare BASDAI, ASDAS, BASFI, WHO-5 and ASAS-HI changes from baseline to one year of observation for the bDMARD and the control group. Adjustment for possible differences was made for gender, HLA-B27 status, CRP value at baseline and bDMARDs before inclusion into the register as co-variables. Changes over time are shown as adjusted mean scores (Least squared means=LSmeans) with 95% confidence interval (CI). To assess the sensitivity to change in ASAS-HI from baseline to 12 months, the standardised response mean (SRM) was calculated as SRM=(ASAS-HI mean baseline – ASAS-HI mean 12 months)/ASAS-HI standard deviation of differences. In addition, SRM was evaluated for BASDAI, ASDAS, WHO-5 and BASFI.

An SRM <0.4 was considered to represent a low effect, 0.4–0.79 a moderate effect and ≥0.8 a large effect.[7] The SRMs were interpreted in these categories; further statistical analysis of the SRMs was not undertaken. In addition, for both groups ASAS-HI changes from baseline were calculated and proportions of patients who reached the smallest detectable change (SDC) of ≥3.0.[7]

Results

Description of the study sample

Of 988 axSpA patients with a follow-up time of at least 12 months, 82 patients were excluded because of a missing baseline patient questionnaire and 54 patients because of missing treatment information during 12 months follow up time (fig. 1). Excluded patients did not differ significantly in baseline characteristics (gender, disease duration, HLA-B27, CRP) from included patients (data not shown). Further 185 patients were excluded from the analysis due to treatment switch within the first 12 months after enrollment (fig. 1).

The 667 remaining patients were included in the analysis, of whom 552 were treated with a bDMARD (bDMARD group) and 115 patients with csDMARDs and/or NSAIDs (control group) and did not change treatment during the 12 months follow-up time.

Baseline characteristics in bDMARD group compared to control group

Patients in the bDMARD group were slightly younger than the control group (mean age 44 vs. 47 years), the percentage of female patients was lower (40% vs. 50%) and they had a longer duration of symptoms (12.9 vs. 7.7 years) (table 1). The percentage of patients with three and more comorbidities was higher in the bDMARD group (21% vs. 8%). In the control group, 96% were bDMARD-naive compared to 63% in the bDMARD group at inclusion into RABBIT-SpA.

Markers of disease status and physical function such as physician global assessment, BASFI, and number of affected joints were all higher in the bDMARD group compared to the control group.

75% of patients in the bDMARD group were treated with TNFi (Adalimumab 30%, Golimumab 21%, Etanercept 12%, Certolizumab 11%, Infliximab 1%) and 25% of the patients with the IL-17 inhibitor Secukinumab.

ASAS-HI compared to disease activity, physical functioning, and mental health

In the bDMARD group, the mean ASAS-HI declined between T0 and month 12 from 6.9 (± 3.5) to 5.1 (± 3.9) and in the conventional group from 5.9 (± 3.6) to 5.6 (± 3.9) (fig. 2).

In the bDMARD group, the mean BASDAI, ASDAS, and BASFI decreased over the period of 12 months from 4.7 to 3.1, 2.9 to 1.8, and 3.9 to 2.8, respectively (fig. 2). The WHO-5 increased from 43.8 to 57.6. In the control group, the values decreased from 4.4 to 3.8 (BASDAI), 2.6 to 2.2 (ASDAS), and 3.2 to 3 (BASFI) (fig. 2). The WHO-5 increased from 47.4 to 52.4.

For BASDAI, ASDAS, BASFI, WHO-5, and ASAS-HI, changes from baseline between the two groups were compared (tab. 2). Improvement in ASAS-HI taking the baseline status and covariates (see methods) into account was compared for the two groups using ANCOVA. ASAS-HI at baseline (p=0.0014), CRP value at baseline (p=0.016) and bDMARD treatment before inclusion to RABBIT-SpA (p=0.0001) influenced ASAS-HI change significantly and were used for adjusting, whereas HLA-B27 (p=0.13) and gender (p=0.17) did not.

The percentage of patients in good to very good health status (ASAS-HI ≤ 5) increased in the bDMARDs group from 34% at baseline to 56% at month 12, in contrast to the control group, which remained nearly unchanged with 49% at baseline and 51% at month 12.

The percentage of patients with a smallest detectable change (SDC ≥3) in the ASAS-HI from baseline to follow up at 12 months was 27% in the bDMARD group and 14% in the control group. This was a statistically significant difference between the groups (p=0.007).

Sensitivity to change of ASAS-HI

In order to analyse the sensitivity to change of the ASAS-HI, we evaluated the SRM of ASAS-HI separately for the two groups and in comparison with other instruments measuring disease activity, function and mental health (figure 3). The SRM of ASAS-HI was higher in the bDMARD group than in the control group (SRM 0.52 resp. 0.15). SRM for ASDAS (0.9), BASDAI (0.73), BASFI (0.59) and WHO-5 (0.65) also showed larger treatment effects in the bDMARD group than in the control group. SRMs for

ASDAS, BASDAI, BASFI and WHO-5 were 0.4, 0.29, 0.11 and 0.24 in the group of patients treated with conventional treatment.

ASAS-HI single items

The 17 items of the ASAS-HI are shown in the spider diagram in fig. 4. Following ASAS-HI domains were most frequently affected: pain (78% of the patients agreed), maintaining body position (75%), and energy and drive (73%). In the bDMARD treated patients, there was an improvement in all items. In the control group, the largest improvement was seen in the item pain.

Discussion

The main aim of this study was to investigate the sensitivity to change of the ASAS-HI in comparison with established parameters of disease activity, function, and mental health in axSpA patients treated in routine care. Moreover, we compared these results with BASDAI, ASDAS, BASFI and WHO-5. The sensitivity to change of an outcome parameter is an important value to measure and interpret treatment effects. As expected, in the bDMARD group ASDAS and BASDAI as disease activity scores showed high sensitivity to change. Mental health (WHO-5), function (BASFI) and the broader concept of health (ASAS-HI) showed lower sensitivity to change, however still representing a moderate change. As expected, in control patients, none of the parameters showed a considerable sensitivity to change due to lower treatment effect.

The sensitivity to change measured by the SRM naturally depends on the treatment. It has been established to use thresholds for the interpretation of the sensitivity to change with an SRM <0.4 representing a low effect, 0.4–0.79 a moderate effect and ≥0.8 a large effect.[17] In the publication on measurement properties of the ASAS-HI, the SRM of the ASAS-HI was 0.44 for NSAIDs, 0.69 for csDMARDs and 0.85 for TNFi.[7] In our analysis, it was 0.54 in bDMARD treated patients and 0.19 in the control group. In a meta-analysis on the efficacy of TNFi in patients with radiographic axSpA and non-radiographic axSpA, the effect size for BASDAI and BASFI in the randomised clinical trials that were included were compared.[18] Although the effect size (standardised mean difference (SMD) that was used

in the meta-analysis slightly differs from our effect size measure SRM, BASDAI also showed a higher effect size than BASFI, which is similar to our results.

Although ASAS-HI is a rather new outcome parameter, it is becoming an important tool in axSpA research. For example, ASAS-HI was chosen as primary outcome parameter in the first treat to target (T2T) strategy trial in axSpA, the TICOSPA study.[12] The main outcome was defined as percentage of patients reaching ≥30% improvement in ASAS-HI. The T2T strategy was numerically superior but not statistically significantly superior to usual care (47.3% vs. 36.1%). Furthermore, most secondary efficacy outcomes were in favor for T2T. The authors and others discussed the results and besides the fact, that the trial might have been underpowered also the outcome parameter ASAS-HI has been questioned.[19-21] Our data add to this debate in showing a smaller sensitivity to change for ASAS-HI in comparison to ASDAS and BASDAI.

As expected in an observational cohort, patients treated with conventional therapies showed less severe disease compared to patients assigned to bDMARDs at inclusion into the register. After one year of treatment, the disease activity, functioning and health status were similar in both groups, reflecting adequate treatment for both groups.

We showed that global functioning measured by ASAS-HI improved in patients with bDMARDs whereas it remained stable in control patients. In addition, the percentage of patients in a good to very good health status increased in the bDMARD group, in contrast to the control group, which remained unchanged. The patients treated with bDMARDs showed greater improvement in ASDAS, BASDAI, BASFI, and ASAS-HI compared to the patients in the conventional treatment group. Consistently, the percentage of patients with a smallest detectable change (SDC ≥3) was larger in the bDMARD group compared to the control group. As this is a completer analysis, these results cannot be interpreted in terms of effectiveness of the treatment groups.

In addition to our global evaluation of the ASAS-HI, we analysed the 17 single items of the ASAS-HI score separately. The pattern of affirmed items is similar to a recent analysis of the performance of the

ASAS-HI in a cross-sectional single center analysis from Spain.[22] We compared the treatment groups and the change of the ASAS-HI results between baseline and 12 months of follow up. The treatment groups show large differences in the response pattern. While the sum score declines in both groups, in the control group this change was mainly driven by an improvement in pain. However, in the bDMARD group, numerical improvements were seen in all 17 items. In the control group, most patients were treated by NSAIDs only. As is generally known, NSAIDs have a good analgetic capacity but their effect on other aspects that impair the health status of axSpA patients such as mobility or emotional functions is minimal or not existing.

This is an analysis of an independent cohort analysing the new questionnaire ASAS-HI in a real live setting. ASAS-HI can easily be implemented in routine care; the results of the questionnaire can help the treating rheumatologist in understanding the health functioning of his axSpA patients.

Limitations

The cohort especially in the conventional group is rather small. Nevertheless, this cohort is independent from the previously published studies analysing ASAS-HI. The comparison of the two treatment groups (bDMARDs vs conventional treatment) shows differences in baseline characteristics. These differences are typical for observational cohort studies and reflect confounding by indication. They were taken into account in the statistical analysis. Unfortunately, the radiographic status of the patients could not be included in the model because of the high portion (46%) of missing values in this variable. We focused on SRMs for different outcomes in patients staying on one treatment (either bDMARDs or conventional treatment) for a period of 12 months. This completer-analysis approach hampers direct comparisons of the treatment groups. However, it allows analysing the sensitivity to change of the outcome parameters of interest.

Conclusion

We conclude that the ASAS-HI is a useful tool for routine clinical care of patients with axSpA. In patients with a new start of bDMARD, improvement was seen in all 17 ASAS-HI items while in conventionally

treated patients this was only the case for the pain item. Since the ASAS-HI covers a broad concept of physical and mental health, it is not surprising that its sensitivity to change is lower than that of measures of disease activity. However, changes in important domains of global health and burden of illness can be shown by this instrument and are of interest to the treating rheumatologist.

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References

1. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet 2017;390:73-84.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978-91.
3. van der Heijde D, Song IH, Pangan AL, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled, phase 2/3 trial. Lancet 2019;394:2108-17.
4. Deodhar A, Sliwinska-Stanczyk P, Xu H, et al. Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study. Ann Rheum Dis 2021;80:1004-1013.
5. Macfarlane GJ, Rotariu O, Jones GT, Pathan E, Dean LE. Determining factors related to poor quality of life in patients with axial spondyloarthritis: results from the British Society for Rheumatology Biologics Register (BSRBR-AS). Ann Rheum Dis 2020;79:202-8.
6. Kiltz U, van der Heijde D, Boonen A, et al. Development of a health index in patients with ankylosing spondylitis (ASAS HI): final result of a global initiative based on the ICF guided by ASAS. Ann Rheum Dis 2015;74:830-5.
7. Kiltz U, van der Heijde D, Boonen A, et al. Measurement properties of the ASAS Health Index: results of a global study in patients with axial and peripheral spondyloarthritis. Ann Rheum Dis 2018;77:1311-7.
8. Kiltz U, Winter J, Schirmer M, Baraliakos X, Braun J. [Validation of the German translation of the ASAS health index : A questionnaire to assess functioning and health in patients with spondyloarthritis]. Z Rheumatol 2019;78:352-8.
9. Boonen A, Braun J, van der Horst Bruinsma IE, et al. ASAS/WHO ICF Core Sets for ankylosing spondylitis (AS): how to classify the impact of AS on functioning and health. Ann Rheum Dis 2010;69:102-7.
10. Kiltz U, Wei JC, van der Heijde D, et al. Ixekizumab Improves Functioning and Health in the Treatment of Radiographic Axial Spondyloarthritis: Week 52 Results from 2 Pivotal Studies. J Rheumatol 2021;48:188-97.
11. Walsh JA, Magrey MN, Baraliakos X, et al. Improvement of Functioning and Health With Ixekizumab in the Treatment of Active Nonradiographic Axial Spondyloarthritis in a 52-Week, Randomized, Controlled Trial. Arthritis Care Res (Hoboken) 2022;74:451-60.
12. Molto A, Lopez-Medina C, Van den Bosch FE, et al. Efficacy of a tight-control and treat-to-target strategy in axial spondyloarthritis: results of the open-label, pragmatic, cluster-randomised TICOSPA trial. Ann Rheum Dis 2021;80:1436-44.
13. Regierer AC, Weiss A, Baraliakos X, Zink A, Listing J, Strangfeld A. [RABBIT-SpA: a new disease register for axial spondyloarthritis and psoriatic arthritis]. Z Rheumatol 2020;79:135-42.
14. van der Heijde D, Lie E, Kvien TK, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:1811-8.

15. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286-91.
16. Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 1994;21:2281-5.
17. Middel B, van Sonderen E. Statistical significant change versus relevant or important change in (quasi) experimental design: some conceptual and methodological problems in estimating magnitude of intervention-related change in health services research. Int J Integr Care 2002;2:e15.
18. Callhoff J, Sieper J, Weiss A, Zink A, Listing J. Efficacy of TNFalpha blockers in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Ann Rheum Dis 2015;74:1241-8.
19. Kiltz U, Wendling D, Braun J. ASAS Health Index: The "All in One" for Spondyloarthritis Evaluation? J Rheumatol 2020;47:1457-60.
20. Cai G, Peng X. Correspondence on 'Efficacy of a tight-control and treat-to-target strategy in axial spondyloarthritis: results of the open-label, pragmatic, cluster-randomised TICOSPA trial'. Ann Rheum Dis 2021;Epub ahead of print.doi:10.1136/annrheumdis-2021-220904.
21. Wang W, Lee YH, Wei JCC. Correspondence on 'Efficacy of a tight-control and treat-to-target strategy in axial spondyloarthritis: results of the open-label, pragmatic, cluster-randomised TICOSPA trial'. Ann Rheum Dis 2021;Epub ahead of print.doi:10.1136/annrheumdis-2021-220938.
22. Alonso-Castro S, Pardo E, Charca L, et al. Performance of the ASAS Health Index for the Evaluation of Spondyloarthritis in Daily Practice. J Rheumatol 2020;47:1483-9.

Figure legends

Figure 1: Flowchart of inclusion of patients. Abbreviations: AE: adverse event; T0: baseline; T3: 12 months follow-up

Figure 2: ASAS-HI, BASDAI, ASDAS, and BASFI at baseline (T0) and after 12 months of follow-up. Abbreviations: ASAS-HI: ASAS health index; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index

Figure 3: Standard response means of ASAS-HI, ASDAS, BASDAI, BASFI and WHO-5.

Figure 4: Single item analysis of ASAS-HI at baseline (black lines) and after 12 months (grey lines) shown as spider diagram. Solid lines show the results for bDMARD group, dotted lines for control group.

Tables

Parameter	**Control group N=115**	**bDMARD group N=552**
Age, mean (SD)	46.7 (13.1)	44.2 (12.8)
Female, n (%)	58 (50)	222 (40)
Symptom duration, years, mean (SD)	7.7 (9.5)	12.9 (10.5)
Disease duration, years, mean (SD)	4 (8)	7.6 (9.1)
HLA-B27, n (%)	65 (63)	413 (78)
CRP in mg/l, mean (SD)	12.8 (20.1)	12.5 (17.3)
CRP positive (≥5mg/l), n (%)	33 (51)	282 (57)
Enthesitis (based on clinical judgement), n (%)	16 (14)	90 (16)
Number of sites with enthesitis (0-16), mean (SD)	3.3 (2.8)	2.7 (2.1)
Peripheral arthritis, n (%)	40 (35)	125 (23)
Number of joints with arthritis (0-44), mean (SD)	3.1 (1.7)	3.4 (4)
BMI, mean (SD)	27 (5.1)	26.9 (5.1)
BMI ≥30, n (%)	27 (24)	137 (25)
Comorbidities ≥3, n (%)	9 (8)	117 (21)
Physician global (NRS 0-10), mean (SD)	4.2 (1.6)	5.7 (2)
BASDAI (0-10), mean (SD)	4.4 (1.9)	4.7 (2)
ASDAS, mean (SD)	2.6 (1.1)	2.9 (1)
BASFI (0-10), mean (SD)	3.2 (2.2)	3.9 (2.4)
WHO-5 (0-100), mean (SD)	47.4 (22.1)	43.8 (20.2)
ASAS-HI (0-17), mean (SD)	5.9 (3.6)	6.9 (3.5)
Patient global (NRS 0-10), mean (SD)	5.3 (2.3)	5.7 (2.3)

Table 1: Baseline characteristics of included patients

	mean changes from baseline				adjusted mean changes			
Parameter	**bDMARD**		**controls**		**bDMARD**		**controls**	
	mean (SEM)	**95% CI**	**mean (SEM)**	**95% CI**	**mean (SEM)**	**95% CI**	**mean (SEM)**	**95% CI**
BASDAI	1.5 (0.09)	(1.28; 1.65)	0.6 (0.21)	(0.16; 1.01)	1.5 (0.09)	(1.28; 1.65)	0.7 (0.31)	(0.06; 1.27)
ASDAS	1.1 (0.06)	(0.94; 1.18)	0.3 (0.2)	(-0.12; 0.71)	1.1 (0.05)	(0.98; 1.18)	0.5 (0.2)	(0.08; 0.87)
BASFI	1.1 (0.09)	(0.91; 1.26)	0.3 (0.2)	(-0.07; 0.73)	1.1 (0.09)	(0.92; 1.28)	0.4 (0.3)	(-0.2; 0.99)
WHO5	-13.7 (0.99)	(-15.61; -11.71)	-5.7 (2.25)	(-10.15; -1.2)	-13.5 (1.04)	(-15.53; -11.44)	-6.9 (3.35)	(-13.43; -0.26)
ASAS-HI	1.7 (0.16)	(1.39; 2.03)	0.3 (0.27)	(-0.24, 0.85)	1.7 (0.17)	(1.37; 2.04)	0.4 (0.55)	(-0.66; 1.48)

Table 2: Changes from baseline unadjusted and adjusted for baseline status after one year of observation in RABBIT-SpA