Impact of disease outcomes on the Assessment of SpondyloArthritis International Society Health Index (ASAS HI) a Bayesian network analysis of the DESIR cohort

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ORIGINAL RESEARCH

Impact of disease outcomes on the Assessment of SpondyloArthritis International Society Health Index (ASAS HI): a Bayesian network analysis of the DESIR cohort

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ABSTRACT

Objective The objective of this study is to build a structural model visualising and quantifying the interrelationships of different disease outcomes with the Assessment of SpondyloArthritis International Society Health Index (ASAS HI) in patients with axial spondyloarthritis (axSpA).

Methods Cross-sectional data collected at month 72 of the Devenir des Spondylarthropathies Indifférenciées Récentes cohort was analysed. Combining prior knowledge and observed data, probabilistic Bayesian network modelling was used to study how the interplay of different disease outcomes affects the ASAS HI, which measures disease-specific overall functioning and health. Disease outcomes comprised, among others, the Ankylosing Spondylitis (AS) Disease Activity Score (ASDAS) and the Bath AS Functional Index (BASFI).

Results Data of 384 patients were analysed. The obtained structure suggests that ASAS HI is determined by both patient-reported physical function (BASFI) and disease activity (ASDAS). The parameters of the structural model show that an increase of ASDAS or BASFI by 1 unit corresponds to an increase of ASAS HI by 0.70 or 1.25 units, respectively. Moreover, the model suggests that disease activity has an indirect impact on ASAS HI via BASFI. No relationship between spinal mobility or structural damage and ASAS HI was found.

Conclusions This is the first structural model developed to better understand the construct and the interplay between clinically relevant outcomes related to ASAS HI in axSpA patients. It shows that disease activity and physical function have a strong impact on ASAS HI, confirming it to be a valid construct of overall functioning and health in axSpA patients.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The Assessment of SpondyloArthritis International Society Health Index (ASAS HI) is a frequently used assessment tool that evaluates overall functioning and health in patients with axial spondyloarthritis (axSpA). Health-related quality of life in axSpA is determined by several factors including disease activity and physical function.

WHAT THIS STUDY ADDS

⇒ This is the first structural model visualising and quantifying the interplay between outcomes related to ASAS HI in patients with axSpA from a multidependent perspective.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The ASAS HI was confirmed to be a valid construct of overall functioning and health in patients with axSpA by showing that disease activity and physical function have a strong impact on ASAS HI. This data supports the use of the index as a primary outcome in clinical trials—as in a recent treat-to-target study.

INTRODUCTION

Patients with axial spondyloarthritis (axSpA) suffer from a variable disease course in which axial involvement, peripheral arthritis, enthesitis and involvement of other organs can occur and may influence the burden of the disease.[1] Pain, stiffness and mobility limitations are the most prominent health concerns.[2 3] As a consequence, patients face restrictions in working life and social participation.[4] Current knowledge on the health status of patients with axSpA mainly focuses on physical function and disease activity. A health model for patients with radiographic axSpA (r-axSpA) proposed that health-related quality of life (HR-QoL) is determined by physical function and disease activity.[5] The model has been built on data of patients with

r-axSpA including patients with long-standing disease who had been included in the Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy trial.[6] Using the 36-Item Short Form (SF-36) health survey questionnaire as a generic measure for HR-QoL, a hierarchical relationship between spinal damage, spinal mobility, disease activity, physical function and HR-QoL has been demonstrated in patients with r-axSpA using traditional regression analyses.[5] It is not known to what extent such a relationship holds true when a disease-specific measure for the HR-QoL is used and when patients with non-radiographic axSpA (nr-axSpA) are included.

Overall functioning and health is a construct introduced in the International Classification of Functioning, Disability and Health and describes an interaction between body functions, body structures and thereof impairments in activities and social participation.[7] Disease-specific overall functioning and health can be assessed in patients with axSpA using the Assessment of SpondyloArthritis International Society Health Index (ASAS HI), which encompasses impairments in physical and mental functions, limitations in activities and restrictions in social participation.[8] The 17 dichotomous items of the ASAS HI address aspects of pain, emotional functions, sleep, sexual functions, mobility, self-care and community life, representing a wide spectrum of functioning, disability and health in patients with axSpA. The relationship between ASAS HI, disease activity, structural damage and socioeconomic factors is not well known. In fact, most available instruments referred to as HR-QoL actually assess functioning and health but not QoL.

Overall functioning of patients with axSpA can be influenced by many different factors. The relationship between radiographic damage of the spine and spinal mobility impairment in r-axSpA has been unequivocally demonstrated at the group level. To our knowledge, few studies have examined the interrelationships between ASAS HI and disease outcomes in patients with axSpA.[9 10] The Devenir des Spondylarthropathies Indifférenciées Récentes (DESIR) cohort provides an unselected population of patients with axSpA,[11] including patients with r-and nr-axSpA. This wide variety of severity and disease activity is an ideal patient sample to assess the relationships of different disease outcomes with ASAS HI from a multidependent perspective. Analysis of observational data is traditionally focused on establishing associations resulting in a list of p values or effect sizes without describing the underlying causal structure among variables. Understanding the causal structure, however, provides a deeper comprehension of how one factor under consideration relates to other factors, which is essential to guide interventions.[12] Bayesian networks have become a popular analysis approach to explore complex relationships between input variables.[13]

This study aimed to analyse the interplay of different disease outcomes with ASAS HI in patients with axSpA by adopting a Bayesian network modelling approach.

PATIENTS AND METHODS

A cross-sectional analysis of data at month 72 of the DESIR cohort (ClinicalTrials.gov identifier: NCT01648907)[11] was conducted. The DESIR cohort is a French national prospective multicentre cohort of 708 patients with early inflammatory back pain suggestive of axSpA. Patients were recruited between October 2007 and April 2010. Of those, patients with a definite diagnosis of axSpA at month 72, according to the treating rheumatologist, were selected. Among the axSpA patients, those with non-missing data for the outcome ASAS HI were included in the analysis. A patient inclusion flow chart is provided in online supplemental figure 1. A more detailed description of the DESIR cohort can be found elsewhere (Dougados *et al*[11] and http://www.lacohortedesir.fr/).

Data were retrieved from the visit performed 72 months after inclusion, which was the first time point of ASAS HI collection within DESIR, except for data on imaging, which were gathered from the visit performed 60 months after inclusion, which was the last time before ASAS HI collection where it was available.

Participants gave written informed consent.

Data collection

The ASAS HI ranges from 0 to 17 with higher values indicating worse disease-specific overall functioning and health.[8] Established cut-offs are ≤5 and ≥12 suggesting 'good' (ASAS HI≤5), 'moderate' (5<ASAS HI<12) and 'bad' (ASAS HI≥12) overall functioning and health.[14]

Further information included in the analysis comprised disease activity (Ankylosing Spondylitis Disease Activity Score based on C reactive protein—ASDAS[15]), physical function (Bath Ankylosing Spondylitis Functional Index—BASFI[16]), spinal mobility (Bath Ankylosing Spondylitis Metrology Index—BASMI[17]), lateral spinal flexion (a component of BASMI) and structural damage (modified Stoke Ankylosing Spondylitis Spine Score—mSASSS[18]). These variables were chosen to study a model comparable to the health model for patients with r-axSpA[5] while using the disease-specific outcome measure ASAS HI instead of the generic outcome measure SF-36 and including both nr-axSpA and r-axSpA patients. The previously developed health model further included spinal inflammation which could not be included in the current analysis due to a large amount of missing data for that variable (by protocol, at 60 months, MRIs were only performed in participating centres in Paris, which explains the missing data).

Statistical analysis

First, for any pair of the five disease-specific variables ASDAS, BASFI, BASMI, mSASSS and ASAS HI the Spearman's rank correlation coefficient, which assesses a monotonic relationship that does not need to be linear, was computed.

Second, a Bayesian network analysis approach was used to gain insight into the interplay between ASDAS, BASFI, BASMI, mSASSS and ASAS HI based on their conditional

dependencies and independencies. In an additional analysis, the (total) BASMI was replaced by its component lateral spinal flexion, which may be a better reflection of spinal mobility in early disease.[19]

Bayesian networks are probabilistic graphical models that consist of two components: a directed acyclic graph (DAG) represented by nodes (random variables) joined by directed edges (the directional relationships between variables) and an accompanying joint probability distribution. Specifically, in a causally interpreted graph, the presence of a directed edge between two nodes A and B indicates a causal link between A and B in the direction of the edge. Conversely, the absence of an edge between A and B indicates that there is no causal effect, which is generally regarded as a stronger assumption.[12]

Unlike path models in structural equation modelling, DAGs are entirely non-parametric, enabling the representation of any functional relationship between the variables.[12]

One advantage of Bayesian networks is their ability to capture complex relationships between variables. Another is their ability to encode expert knowledge (prior knowledge about relationships between variables from previous studies or scientific theory) by imposing constraints on Bayesian network structures. This aids the algorithm in the correct orientation of edges and may improve power. A well-known example of such a constraint is that no genetic variable can be influenced by a clinical one. Bayesian networks that are well-supported by a given set of data can be used to identify possible causal relationships and have been argued to be competitive with, and in some cases advantageous to, other causal inference methods.[20 21]

In this study, the structure of the network was learnt using a modern implementation of the constraint-based Peter-Clark (PC) algorithm,[22] which estimates the DAG by conducting a series of conditional independence tests among the variables in the data. In a two-step process it first identifies the undirected edges in the graph (this step is often referred to as 'skeleton identification' by starting off with a complete undirected graph, where there is an undirected edge between any pair of variables, and then removing edges if the involved variables are conditionally independent based on the data.[12] In the second step, the directions of the edges are determined following specific rules.[23] In our study, variables of the network represented by the nodes were continuous and chosen to be modelled with a Gaussian distribution. The following constraints were imposed to aid the algorithm: (1) mSASSS does not depend on BASMI, BASFI or ASAS HI (ie, we assume that these three variables have no effect on structural damage) and (2) mSASSS does not influence ASDAS (ie, we assume that structural damage has no effect on disease activity). Despite of these constraints, it remains challenging to identify the true structure from limited data which gives reason to ask how confident one can be about the existence of an edge identified by the algorithm. To examine the robustness of edges against perturbation of

Table 1 Patient characteristics and disease outcomes at month 72 if not stated otherwise

Characteristic	N	n (%) or mean (SD)
Female gender	384	207 (54%)
Age (years)	384	40.3 (8.7)
Symptom duration (years)	382	7.5 (0.9)
University education or equivalent (at baseline)	382	242 (63%)
Currently employed	381	324 (85%)
BMI (kg/m²)	377	24.9 (4.6)
Current smoking	372	107 (29%)
History of smoking	372	185 (50%)
HLA-B27 positive	383	244 (64%)
Current arthritis	374	18 (5%)
History of arthritis	382	164 (43%)
History of inflammatory bowel disease	384	46 (12%)
History of psoriasis	384	115 (30%)
History of uveitis	384	74 (19%)
History of dactylitis	384	87 (23%)
Enthesitis score*	363	3.0 (5.2)
CRP (mg/L)	325	4.9 (7.5)
ASDAS	322	2.0 (1.0)
BASDAI (0–10)	383	3.4 (2.1)
BASFI (0–10)	382	2.3 (2.1)
BASMI (0–10)	350	2.4 (1.0)
HAQ-AS (0–3)	384	0.5 (0.5)
ASAS HI (0–17)	384	5.8 (4.0)
Good overall functioning (ASAS HI≤5)	384	191 (50%)
Moderate overall functioning (5<ASAS HI <12)	384	155 (40%)
Bad overall functioning (ASAS HI≥12)	384	38 (10%)
Sacroiliitis according to mNY criteria (at month 60)	339	71 (21%)
Active sacroiliitis on MRI (ASAS criteria; at month 60)	132	31 (23%)
mSASSS (0–72; at month 60)	317	1.0 (3.7)
MRI spinal inflammation (Berlin score; at month 60)	134	0.5 (1.0)
TNFi treatment within last 12 months	383	188 (49%)
NSAID intake within last 12 months	382	253 (66%)
csDMARD intake within last 12 months	384	76 (20%)

*Concise Mander Enthesitis Score with gradation.
ASAS HI, Assessment of SpondyloArthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BMI, body mass index; CRP, C reactive protein; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; HAQ-AS, Ankylosing Spondylitis Health Assessment Questionnaire; HLA, human leucocyte antigen; mNY, modified New York; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score; N, number; NSAID, non-steroidal anti-inflammatory drug; TNFi, tumour necrosis factor inhibitor.

the data, a non-parametric bootstrap to network learning was applied.[24] Specifically, the data were resampled 10 000 times using random sampling with replacement and for each of the 10 000 samples, a Bayesian network was learnt. To be included in the final model, an edge (irrespective of its direction) has to appear in more than 90% of the 10 000 bootstrapped networks (strength) and the relative frequency of a directed edge has to be at least 50% (direction).

After having obtained the final network model, its parameters were fitted using their maximum likelihood estimate. These correspond to the coefficients of a classic linear regression for each (child) node against its parents (nodes with edges directed into the child node). 95% CIs for the regression coefficients were calculated.

The network was estimated based on complete data under the assumption that the continuous variables follow a Gaussian distribution and imposed constraints must be satisfied. In a sensitivity analysis, the underlying skeleton was identified using an extension of the PC algorithm to non-paranormal data with missing values and no imposed constraints.[25]

Data analyses were performed with R V.4.1.2 and additional packages, including bnlearn (V.4.7.1).

RESULTS

Characteristics of the study population

A total of 384 patients from the DESIR cohort with a definite clinical diagnosis of axSpA at month 72, according to the treating rheumatologist, had non-missing data for ASAS HI and were included in the analysis. Table 1 shows these patients' characteristics and disease outcomes. A total of 46% were male and, 72 months after inclusion, the mean age was 40.3 years with a mean symptom duration of 7.5 years. Patients had, on average, rather low scores for disease activity (ASDAS 2.0), impairment of physical function (BASFI 2.3), impairment of spinal mobility (BASMI 2.4) and structural damage (mSASSS 1.0).

The mean ASAS HI was 5.8 (range: 0–16). Applying existing cut-offs for ASAS HI, 50% had 'good' overall functioning (ASAS HI≤5), 40% had 'moderate' overall functioning (5<ASAS HI <12) and 10% had 'bad' overall functioning (ASAS HI≥12).

Almost half of the patients (49%) received treatment with tumour necrosis factor inhibitors, about two-thirds (66%) received non-steroidal anti-inflammatory drugs and one-fifth received conventional disease-modifying antirheumatic drugs in the last 12 months.

Correlation analysis

Figure 1 shows Spearman's rank correlation coefficient for any pair of ASDAS, BASFI, BASMI, mSASSS and ASAS HI.

The correlation coefficient between BASFI and ASAS HI was highest (0.83), followed by the correlation coefficient between BASFI and ASDAS (0.71) and ASDAS and ASAS HI (0.64), indicating a monotonic relationship between these variables. A weak relationship with mSASSS was found for BASMI (0.24), while other variables had very weak correlation coefficients of at most 0.1 with mSASSS (figure 1).

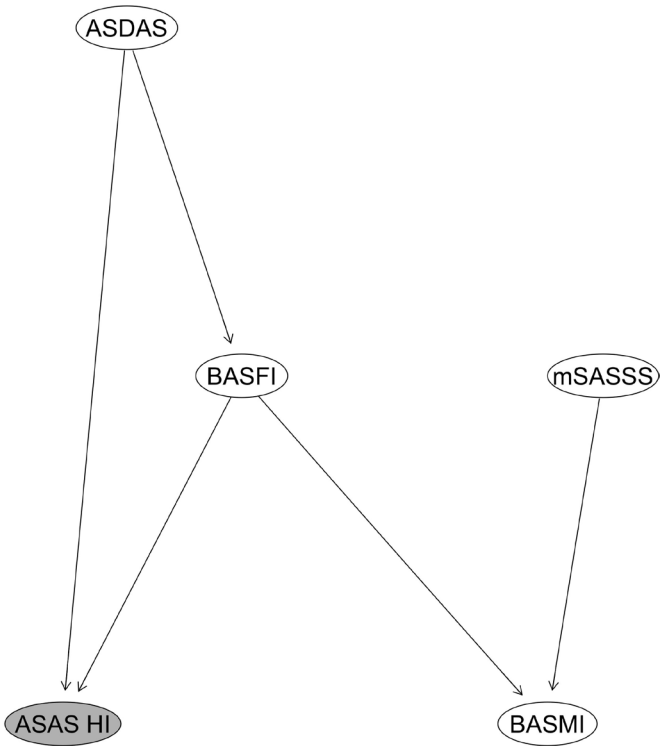

Figure 1 Spearman's rank correlation coefficient for different disease outcomes in patients with axSpA. axSpA, axial spondyloarthritis; ASAS HI, Assessment of SpondyloArthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score based on C reactive protein; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Scatter plots and histograms of ASDAS, BASFI, BASMI, mSASSS and ASAS HI are given in online supplemental figure 2.

Bayesian network analysis

The structural model that was learnt from combining data and prior expert knowledge (by imposing constraints) is shown in figure 2. It resulted from 10 000 bootstrapped networks, of which the relative frequency with which an edge appeared irrespective of its direction (strength) and the relative frequency of a directed edge (direction) are shown in table 2.

The structural model visualises the relationships between disease-specific variables from a multidependent perspective. It suggests that both disease activity (ASDAS) and physical function (BASFI) have a direct impact on ASAS HI. Moreover, the model indicates that disease activity has an indirect impact on ASAS HI via physical function, which in turn has an impact on spinal mobility (BASMI). In addition to physical function, spinal

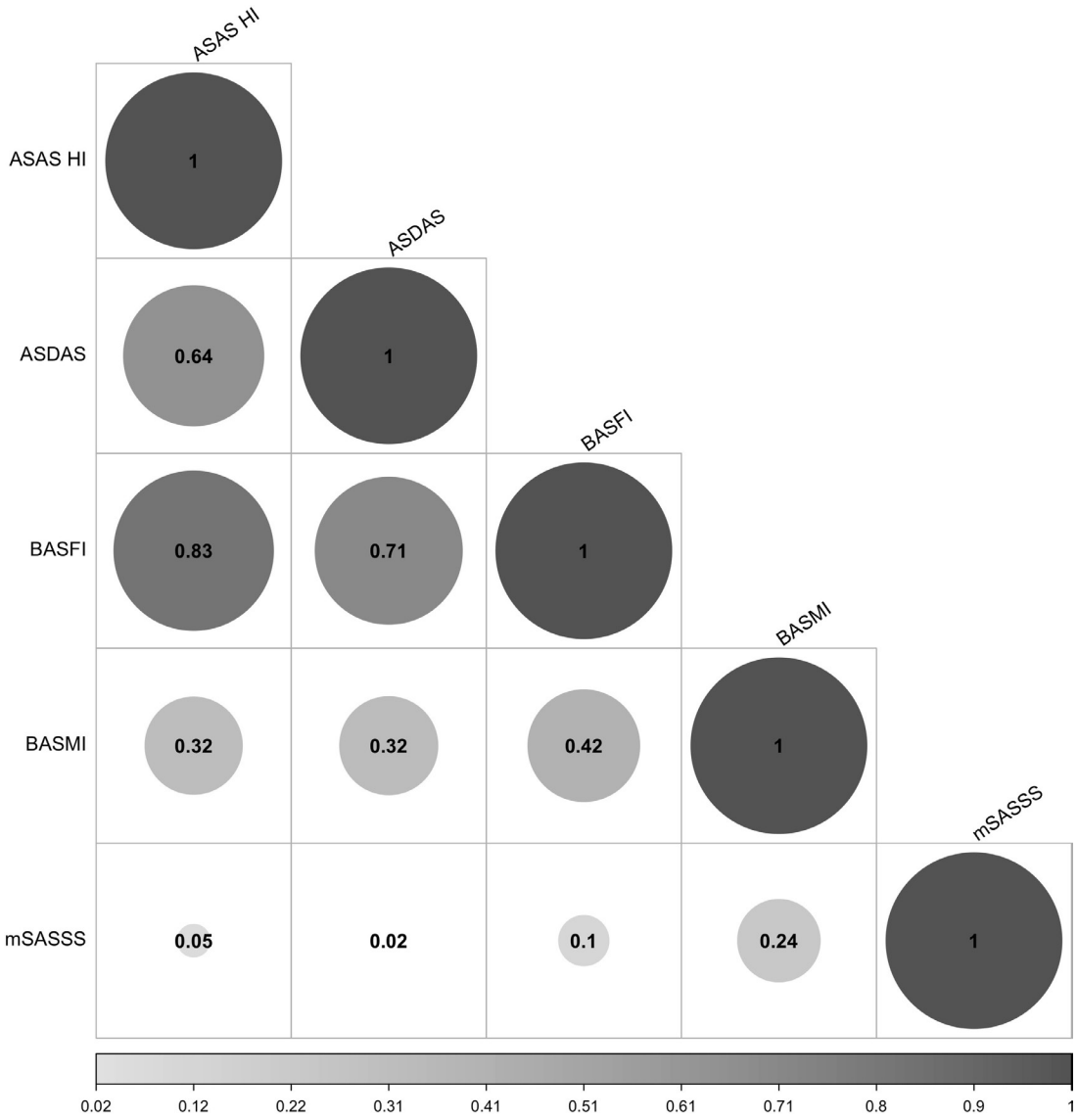

Figure 2 Structural model on inter-relationships of different disease outcomes with overall functioning and health (ASAS HI) in patients with axSpA. axSpA, axial spondyloarthritis; ASAS HI, Assessment of SpondyloArthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score based on C reactive protein; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

mobility is determined by structural damage according to the learnt model. On top of that, the model denies a relationship between spinal mobility or structural damage and ASAS HI.

The fitted parameters of the structural model are given in table 3, according to which an increase of ASDAS by 1 unit (given BASFI) or of BASFI by 1 unit (given ASDAS) corresponds to an increase of ASAS HI by 0.70 units (95% CI 0.30 to 1.11) or 1.25 units (95% CI 1.04 to 1.40), respectively. Furthermore, the model suggests that an increase of ASDAS by 1 unit corresponds to an increase of BASFI by 1.56 units (95% CI 1.39 to 1.78) and that BASMI increases by 0.22 units (95% CI 0.18 to 0.27) when BASFI is increased by 1 unit (given mSASSS) or that BASMI increases by 0.09 units (95% CI 0.07 to 0.12) when mSASSS is increased by 1 unit (given BASFI).

The additional analysis with lateral spinal flexion instead of the total BASMI led to similar results (the structural model and its fitted parameters are given in online supplemental figure 3 and table 1, respectively). Moreover, the same underlying skeleton was found in the sensitivity analysis.

DISCUSSION

To the best of our knowledge, this is the first large-scale study that used a Bayesian network analysis approach to investigate how the interplay of different disease outcomes affects ASAS HI in patients with axSpA. Our model shows that ASAS HI is determined both by patient-reported physical function (BASFI) and by disease activity (ASDAS).

Table 2 Relative frequency with which an edge appeared irrespective of its direction (strength) and relative frequency of a directed edge (direction) resulting from non-parametric bootstrap

From	To	Strength	Direction
ASDAS	*ASAS HI*	*0.91*	*0.65*
ASDAS	mSASSS	<0.01	1
ASDAS	BASMI	0.03	0.72
ASDAS	*BASFI*	*>0.99*	*0.57*
ASAS HI	ASDAS	0.91	0.35
ASAS HI	mSASSS	0.2	0
ASAS HI	BASMI	0.02	0.72
ASAS HI	BASFI	1	0.41
mSASSS	ASDAS	<0.01	0
mSASSS	ASAS HI	0.2	1
mSASSS	*BASMI*	*>0.99*	*1*
mSASSS	BASFI	0	0
BASMI	ASDAS	0.03	0.28
BASMI	ASAS HI	0.02	0.28
BASMI	mSASSS	>0.99	0
BASMI	BASFI	>0.99	0.38
BASFI	ASDAS	>0.99	0.43
BASFI	*ASAS HI*	*1*	*0.59*
BASFI	mSASSS	0	0
BASFI	*BASMI*	*>0.99*	*0.62*

Edges included in the final model are shown in italic.
ASAS HI, Assessment of SpondyloArthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; axSpA, axial spondyloarthritis; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Table 3 Parameters of the structural model corresponding to coefficients of linear regression analyses

Dependent variable (child node)	Independent variable (parent node)	Regression coefficient with 95% CI
BASFI	ASDAS	1.56 (1.39 to 1.78)
ASAS HI	ASDAS	0.70 (0.30 to 1.11)
	BASFI	1.25 (1.04 to 1.40)
BASMI	mSASSS	0.09 (0.07 to 0.12)
	BASFI	0.22 (0.18 to 0.27)

ASAS HI, Assessment of SpondyloArthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; axSpA, axial spondyloarthritis; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Our model agrees with the stratified model proposed by Machado *et al*[5] regarding the association of overall functioning and health with disease activity and physical function, which was also found in previous studies on ASAS HI.[9 10 26] The health status in the former study was assessed using the mental and physical component scores of the SF-36 health survey questionnaire. Our study design differs in several ways: First, we used the ASAS HI, which is a disease-specific patient-reported outcome assessing overall functioning and health in patients with axSpA. Second, we adopted a Bayesian network analysis approach combining prior knowledge with measured data to explore and visualise the interrelationships among variables. Third, patients with r-axSpA and nr-axSpA were included in the analysis. Despite the different study design, a further agreement with the stratified model consists of the association of physical function and disease activity. By contrast, our model diverts from the stratified model by disregarding a relationship between spinal mobility or structural damage and ASAS HI. One reason might be the low proportion of patients with spinal mobility impairment or structural damage in our study possibly due to the fact that DESIR is an inception cohort. Nevertheless, in two recent studies, no association between ASAS HI and structural damage was found,[9 10] while a third recent study found no association between health status and structural damage but an association between health status and spinal mobility.[26] In the latter study, health status was assessed using the Ankylosing Spondylitis Health Assessment Questionnaire.

Moreover, in contrast to the stratified model, our model suggests that physical function determines spinal mobility. The strength of the edge between BASFI and BASMI exceeded 0.99, which implies that in nearly all of the 10 000 bootstrapped networks, an edge connecting BASFI and BASMI was present. Furthermore, this edge was more often directed from BASFI to BASMI rather than from BASMI to BASFI. Consequently, in the final consensus network, the edge from BASFI to BASMI was incorporated. However, from a clinical perspective, the directionality of this edge is not readily apparent and warrants further investigation to determine if it is potentially misoriented. For this, it may be helpful to include MRI spinal inflammation, which has been shown to contribute to the impairment of spinal mobility in patients with r-axSpA[27] but could not be included in the present analysis due to a large amount of missing data (according to protocol, MRI was only performed in all patients at baseline, afterwards only in a small number of centres was MRI performed in all visits). The availability of MRI could also have shed light on the relationship between MRI spinal inflammation and ASDAS, BASFI and ASAS HI.

The main strength of this study is that, instead of focusing on establishing associations resulting in a list of p values, it provides insight into the causal structure, which is necessary for the identification of causal effects using observational data.[28] Furthermore, understanding

the causal structure among variables is advantageous for guiding confounder selection since statistical adjustment for the wrong set of covariates may increase confounding bias.[12 29] Moreover, our findings support scientific evidence of the association of ASAS HI with disease activity and physical function. Notably, we employed a distinct approach, Bayesian network analysis, to enhance the validity of these findings.

Notable strengths of this study further include the population-based design and large sample size, both are beneficial for external validity, that is, the bias from applying the study results to other rheumatology healthcare settings (in Europe) is reduced. Furthermore, prior knowledge of interactions between variables was integrated and non-parametric bootstrap was applied to acquire a model with more robust probabilistic relationships.

This study has several limitations. First, of the 708 initially recruited patients, only 384 could be included in the present analysis at month 72, which might introduce selection bias. However, in terms of patient characteristics and disease outcomes at baseline, these two groups did not differ.

Second, only disease outcomes were included in the model to keep it comparable to the previously developed health model. Other characteristics, such as socioeconomic status, were absent from the analysis but may ultimately impact ASAS HI. Third, a Bayesian network analysis approach most typically underlies the causal Markov assumption and the causal faithfulness assumption, which could not be verified from the data. Thus, drawing causal conclusions from observational data remains a challenging endeavour,[30 31] which causal search algorithms like the PC algorithm do not completely 'solve'.[12] However, estimating the underlying causal structure offers valuable insights that are not attainable through other commonly used methods.[12] Further investigations are needed to validate the model in patients with early axSpA (though DESIR is an inception cohort, the model is based on cross-sectional data from month 72) and to study its evolvement over time.

In conclusion, a Bayesian network analysis approach integrating expert knowledge and observational data were adopted to investigate through graphical probabilistic representation how the interplay of different disease outcomes affects ASAS HI in an axSpA population. This study shows that disease activity and physical function have a strong impact on ASAS HI, confirming it to be a valid construct of overall functioning and health in patients with axSpA. The proposed structure of the network represents a relevant step in better understanding the construct of ASAS HI in patients with axSpA.

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