Development of an Environmental Contextual Factor Item Set Relevant to Global Functioning and Health in Patients with Axial Spondyloarthritis

Uta Kiltz, Annelies Boonen, Désirée van Der Heijde, Wilson Bautista-Molano, Ruben Burgos Vargas, Praveena Chiowchanwisawakit, Bassel El-Zorkany, Inna Gaydukova, Pál Géher, Laure Gossec, et al.

HAL Id: hal-03894174
https://hal.sorbonne-universite.fr/hal-03894174v1

Submitted on 30 Jan 2023

Development of an environmental contextual factor item set relevant to global functioning and health in patients with axial Spondyloarthritis

PD Uta Kiltz, MD[1,2]; Prof. Annelies E. R. C. H. Boonen, MD[3,4]; Prof. Désirée van der Heijde, MD[5]; University Prof. (Associate) Wilson Bautista-Molano, MD[6]; Dr. Rubén Burgos-Vargas, MD[7]; Prof. (Associate) Praveena Chiowchanwisawakit, MD[8]; Prof. Bassel El-Zorkany, MD[9]; Prof. (Assistant) Inna Gaydukova, MD[10]; Prof. Pal Geher, MD[11]; Prof. Laure Gossec,MD [12,13]; Michele Gilio, MD[14]; Prof. Simeon Grazio, MD[15]; Prof. Jieruo Gu, MD[16]; Prof. Muhammad Asim Khan, MD[17]; Tae-Jong Kim, MD., PhD[18]; Prof. Walter P. Maksymowych, MD[19]; Helena Marzo-Ortega, Honorary Clinical Associate Professor, LMS MRCP PhD[20]; Victoria Navarro-Compán, MD, PhD[21], Prof. Salih Ozgocmen, MD[22], Dimos Patrikos, MD, PhD[23]; Associate Prof. Fernando Manuel Pimentel-Santos, MD, PhD[24], Prof. John Reveille, MD[25], Univ.-Prof. Dr. med. Michael Schirmer[26], Associate Professor Simon Stebbings, MD, PhD[27], Associate Professor Filip Van den Bosch, MD, PhD[28,29], Dr. med. Ulrich Weber, MD[30], Prof. Dr. med. Jürgen Braun[1,2]

[1]Rheumazentrum Ruhrgebiet, Herne Germany; and [2]Ruhr-Universität Bochum, Germany; [3]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Center, the Netherlands; [4]Care and Public Health Research Institute (CAPHRI), Maastricht University, the Netherlands; [5]Leiden University Medical Center, the Netherlands; [6] Rheumatology Department, University Hospital Fundación Santa Fe de Bogotá, and School of Medicine Universidad El Bosque, Bogotá, Colombia; [7]Hospital General de Mexico Universidad Nacional Autónoma, Mexico; [8]Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand; [9]Rheumatology Department, Cairo University, Egypt; [10]North-western medical university, Russia; [11]Semmelweis University, Budapest, Hungary; [12]Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris France, [13]Pitié-Salpêtrière hospital, AP-HP Sorbonne Université, Rheumatology department, Paris, France; [14]Department of Internal Medicine - "San Carlo" Hospital Potenza and Madonna delle Grazie Hospital of Matera, Potenza, Italy; [15]Sestre milosrdnice University Hospital Center, Zagreb, Croatia; [16]University Guangzhou, China; [17]Case Western Reserve University School of Medicine, Cleveland, Ohio, USA, [18]Chonnam National University Medical School and Hospital, Gwangju, South Korea; [19]Department of Medicine, University of Alberta, Canada; [20]NIHR Leeds Biomedical Research Centre, Chapel Allerton Hospital, Leeds, and Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK; [21]Department of Rheumatology, University Hospital La Paz, Madrid, IdiPaz, Spain; [22]Department of Rheumatology, Istinye University, Medicalpark Gaziosmanpasa Hospital, Istanbul, Turkey; [23]Metropolitan Hospital Piraeus, Greece; [24]NOVA Medical School, Universidade Nova De Lisboa, Lisboa, Portugal; [25]Department of Internal Medicine, University of Texas Health Science Center at Houston, USA; [26]Innsbruck Medical University, Department of Internal Medicine, Clinic II, Austria; [27]University of Otago, Dunedin School of Medicine, Dunedin, New Zealand; [28]VIB Center for Inflammation Research, Ghent, Belgium; [29]Department of Rheumatology Ghent University Hospital, Ghent, Belgium; [30]Practice Buchsbaum, Rheumatology, Schaffhausen, Switzerland

Corresponding author:

PD Dr. Uta Kiltz

Rheumazentrum Ruhrgebiet

Ruhr-University Bochum

Claudiusstr 45

44649 Herne

Germany

Tel 0049 2325 592 705

Fax 0049 2325 592 136

uta.kiltz@elisabethgruppe.de

Uta Kiltz: 0000-0001-5668-4497

ORCID IDs:

Uta Kiltz: 0000-0001-5668-4497

Désirée van der Heijde: 0000-0002-5781-158X

Laure Gossec: 0000-0002-4528-310

Helena Marzo-Ortega: 0000-0002-9683-3407

Michael Schirmer: 0000-0001-9208-7809

Wilson Bautista-Molano: 0000-0003-0684-9542

Filip Van den Bosch: 0000-0002-3561-5932

Muhammad Asim Khan: 0000-0003-4704-8311

F.M. Pimentel-Santos: 0000-0002-2816-7705

Simeon Grazio: 0000-0003-3407-0317

Bassel El-Zorkany: 0000-0003-2704-9712

Tae-Jong Kim: 0000-0002-2871-1635

Walter Maksymowych: 0000-0002-1291-1755

Victoria Navarro-Compán: 0000-0002-4527-852

Annelies Boonen: 0000 0003 0682 9533

Word count: 3,731

Abstract

Objective: To describe the development of an Environmental contextual factors (EF) Item Set (EFIS) accompanying the disease specific Assessment of SpondyloArthritis international Society Health Index (ASAS HI).

Method: First, a candidate item pool was developed by linking items from existing questionnaires to 13 EF previously selected for the ICF/ASAS Core Set. Second, using data from two international surveys, which contained the EF item pool as well as the items from the ASAS HI, the number of EF-items was reduced based on the correlation between the item and the ASAS HI sum score combined with expert opinion. Third, the final English EFIS was translated into 15 languages and cross-culturally validated.

Results: The initial item pool contained 53 EF addressing 4 ICF EF-chapters: products and technology (e1), support and relationship (e3), attitudes (e4) and health services (e5). Based on 1754 responses of axial spondyloarthritis patients in an international survey, 44 of 53 initial items were removed based on low correlations to the ASAS HI or redundancy combined with expert opinion. 9 items of the initial item pool (range correlation 0.21–0.49) form the final EFIS. The EFIS was translated into 15 languages and field tested in 24 countries.

Conclusions: An EFIS is available complementing the ASAS HI and helps to interpret the ASAS HI results by gaining an understanding of the interaction between a health condition and contextual factors. The EFIS emphasizes the importance of support and relationships, as well as attitudes of the patient and health services in relation to self-reported health.

Key words: spondyloarthritis, contextual factors, outcome research

Key messages:

1. Environmental context has impact on how an individual will remain active and participate in society

2. This new environmental factor item set (EFIS) helps identifying environmental contextual factors relevant to axSpA patients.

3.

4. Health professionals can use EFIS to identify available resources to support patients in daily life.

Introduction:

Patients with axial spondyloarthritis (axSpA) suffer from a wide range of axial and peripheral symptoms resulting in pain, stiffness, sleep impairment and fatigue.(1) Patients with axSpA may be limited in daily activities and restricted in social participation (2). However, the impact of axSpA on a person's life can be explained only partially by direct health effects such as disease activity, physical function, or comorbidities. It has been shown that interaction of individuals with their particular environmental context may have decisive impact on how these individuals will remain active and participate in society (3).

The International Classification of Functioning, Disability and Health (ICF) emphasizes health results from a complex interaction between the impairments, limitations and restrictions caused by the disease and various contextual factors. One of the major innovations in the ICF is the identification and classification of these factors, distinguishing environmental and personal factors (figure 1) (4, 5). Environmental factors are defined as the physical, social and attitudinal environment in which people live and conduct their lives (6). Although personal contextual factors are relevant for functioning and health, a classification and definitions of personal contextual factors are still lacking (7). Contextual factors can both positively or negatively affect global functioning in daily life and thus act as either barriers to or facilitators of the person's functioning. In general, it is not infrequent that an environmental factor acts both as a facilitator and a barrier. A set of EF categories has been defined in the Assessment of SpondyloArthritis international Society (ASAS) /WHO ICF Core Set for patients with ankylosing spondylitis (AS) and comprises 13 EF categories in the Comprehensive Core Set (8).Research on functioning and health in axSpA patients is mainly focused on investigating the relationship between the different health components of function and disability, while contextual factors are rarely considered. The OMERACT Contextual Factor Working Group developed guidance on how to address contextual factors in clinical trials and explicitly based identification of candidate contextual factors on the ICF(4).

Evidence for the relationship between contextual factors and outcomes of patients remains sparse. Dagfinrud et al. reported that impairment variables (disease activity and pain) explained only one-third of activity and participation restrictions and recommended further examination of contextual factors (2). Gordeev et al. found that contextual factors explained 37% and 47% of the variance in assessment tools like EuroQol five-dimension scale (EQ-5D) and Ankylosing Spondylitis Quality of Life Scale (ASQoL), respectively, and that helplessness and employment were the most important contextual factors (3). Most previous studies have focused on exploring the effect of personal factors exemplified by age and gender, current employment, marital status, education, coping strategies, but few have investigated the effect of environmental context such as support and attitudes towards patients with axSpA (9-11). However, one has to admit that interaction between different factors is complex and that contextual factors not only have an influence on functioning but also functioning may have an impact on the environment.

In order to systematically assess overall impact of SpA on functioning and health, the ASAS group set to develop a health index accompanied by a set of EFs aimed to help interpretation of functioning and

health. The ASAS Health Index (ASAS HI) was developed based on the ASAS/WHO ICF Core Set for AS, and contains 17 items addressing problems in body functions, activities and participation (12, 13). The objective of the current study is to describe the development of the accompanying EF Item Set (EFIS) by identifying characteristics, which may influence important aspects of self-reported functioning in patients with axSpA.

Patients and Method:

The development of the EFIS paralleled the development of the ASAS HI and followed the same six phases as the ASAS HI, and in accordance with the study protocol (Table 1) (12, 13). The 13 categories of the component ''Environmental factors'' included in the Comprehensive ICF Core Set for AS served as the starting point (14). The categories covered 4 ICF chapters (subsequently called domains): (e1) products and technology, (e3) support and relationships, (e4) attitudes, and (e5) services, systems and policies (summary of the descriptors in Supplement (Suppl.1) (14). The main difference from the development of the ASAS HI was that in phase I patients were not asked to weigh the importance of items representing the environmental contextual factors. All subsequent phases were conducted in parallel and in the same countries to the development of the ASAS HI throughout the whole process. A steering committee with UK, AB, DvdH, AC, and JB including one AS patient as members was set up for guiding the process methodologically and to select appropriate items based on the results of the cross-sectional surveys.

Patient and public involvement:

Patients participated actively in all phases of this study. They were involved in the evaluation of the item pool as well as in the selection process of the final item set (12). Patients also recommend ways to facilitate study participation while minimising the burden of study visits.

Phases of the study:

1. *Preparatory phase:* An item pool of candidate EF-items was developed in 2008 by linking items from existing questionnaires to the 13 EF categories of the comprehensive ICF Core Set for AS. The origin of the items linked to the categories were either from existing questionnaires currently available in the field of AS (identified by a systematic literature search) or from additional instruments that are not commonly used in AS but which had already been linked to the ICF (data from ICF Research Branch Munich). To be eligible, items had to be short, comprehensible, and address a single concept. Similar to the selection of items for the ASAS HI, items representing EF were quoted directly from the original instrument with some rewording to guarantee a consistent item structure (e.g. use of first person and present tense). The response option was dichotomized to "I agree" and "I do not agree". Linkage was performed following the formal linking rules by two trained investigators (UK and AB)(15). Finally, a face-to-face meeting was conducted with 13 AS patients from 6 countries (Canada, Germany, the Netherlands, Turkey, UK

6

and USA) to evaluate relevance and understandability of items. Patients could propose new items if they felt that a concept had not been adequately addressed in the item pool. Items and conversation were in English.

2. *First international cross-sectional survey:* A cross-sectional international web-based survey in patients with axSpA was undertaken to test the item pool for the EFIS in seven English-speaking countries. Due to the size of the item pool, the questionnaires were split into 5 subsets sharing a common set of 4 EF items. These common EF items were chosen based on content validity, i.e. reflecting basic aspects of the disease such as emotional support from family or side effects of medications. Patients were invited to participate through their national patient organizations and could enter the survey only if they stated that a diagnosis of AS had been made by a physician. Patients provided information on sociodemographic (age, symptom and disease duration) and disease characteristics (Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), nocturnal back pain, total back pain and Bath AS – patient Global Score (BAS-G) last week and over the last week six months, all on a 0–10 NRS scale (16, 17)).

3. *Expert consultation:* After presentation of the results of the first web-based survey, the steering committee reduced the item pool by deleting items by a nominal consensus process (18). This process was informed by the level of correlation between each individual EF item and sum score of the ASAS HI but with the requirement, that all 4 ICF Chapters for EF would remain represented in the final selection. These proceedings aimed to maintain relevant factors while avoiding redundancy within the EFIS. The steering committee assigned a descriptor of being either a facilitator or a barrier to each remaining item based on wording of the items. For example, the item "I modify my living environment" was considered a change to the environment that should facilitate functioning, while the item "My friends expect too much of me" was considered an attitude that would be a barrier for functioning.

4. *Second international cross-sectional survey:* A cross-sectional international study was undertaken among axSpA patients in 6 English-speaking countries.

5. *Consensus:* Selection of final EF items was informed by the level of correlation between each EF item and sum score of the ASAS HI and optimal coverage of items to the variety of ICF domains/ categories of the Comprehensive ICF Core Set for AS. Agreement was achieved by a nominal consensus process.

6. *Translation:* The final English EFIS was subsequently translated together with the ASAS-HI into 15 languages by using forward-backward translation (19). (20). Availability of an ASAS member as country investigator to supervise translation / cultural validation and representation of the main languages worldwide were the main reasons to choose languages or translation of the ASAS HI. Translations as well as the original English version were field tested to assess content validity (including comprehension), applicability (cultural relevance) and feasibility using cognitive debriefing. Interviewees completed the EFIS questionnaire and the response pattern of each

single EF item was calculated. When needed, wording of the items was adapted based on the feedback of the patients.

The study complies with the Declaration of Helsinki and the locally appointed ethics committee of each international participating site has approved the research protocol. Participants gave written informed consent prior to inclusion in the study.

Statistics. The characteristics of the respondents in the sample are presented as mean (SD) for continuous variables or as absolute frequencies and percentages for categorical variables. Correlation between individual items of EFIS and ASAS HI total sum were calculated to inform the selection during the process of item reduction (Pearson). Selection process of EFIS items was informed by extent of correlation without application of a specific threshold. Final selection of EFIS items took extent of correlation coefficient, representation of the 4 relevant ICF chapters, and avoidance of redundancy into account. The items with the lowest correlation (no specific cut off) were removed first.

Results:

Analysis of the six phases:

1. *Preparatory phase*: Fifty-three items related to one of the EF categories of the WHO/ASAS Core Set for AS were found in 24 different questionnaires, none of them commonly used in patients with SpA. These items could be linked to 7 of the 13 EF categories of the ICF Core Set for SpA: Drugs (e1101), Products and technology for personal use in daily living (e115), Products and technology for personal indoor and outdoor mobility and transportation (e120), Design, construction and building products and technology of buildings for private use (e155), Support and relationship (e3), Attitudes (e4), and Health care services, systems and policies (e580). Importantly, all 4 EF domains remained covered. The 6 ICF categories not represented by an available item comprise: products and technology for employment, design, construction and building products (e135), and technology of buildings for public use (e150), transportation services, systems and policies (e540), social security services, systems and policies (e570), general social support services, systems and policies (e575) and labour and employment services, systems and policies (e590). All these categories were rated by the patients either as partially represented by another EF item (e.g. category e155 represents also content of e135 or e150) or as covered by other ICF categories of the ASAS HI (e.g. category d870 represents also content of e590). During the patient meeting, 5 new items were proposed by the patients covering aspects of support given by friends and relatives (e3), attitudes of friends (e4) and receipt of best possible treatment (e5). Items were quoted directly from the original instruments except for 8 items in which transformation into first person and present tense was needed to guarantee a consistent item structure.

2. *First* international *cross-sectional survey:* A total of 1,915 patients accessed the web-survey, 161 patients were excluded because of incomplete data. The characteristics of the remaining 1754

patients are shown in table 2. Correlation coefficients between individual EF and ASAS HI sum score varied between -0.25 and 0.46 and were sorted into an ascending order subsequently (Suppl.2). Eight items were excluded because of the lowest correlation while ensuring that all 4 ICF Chapters remained represented.

3. *Expert consultation:* After consideration and discussion of the results of the first web-based survey, the steering committee decided to select the four items for each ICF domain, which correlated the most to the ASAS HI sum score. Thus, 37 items were further deleted. Of the remaining 16 items, 8 items were assigned to act as a facilitator and 8 items as a barrier based on theoretical considerations of the steering committee.

4. *Second international cross-sectional survey:* 628 patients accessed the second web-based survey and complete data sets of 622 patients were available for analysis. Correlation coefficients between individual items of EFIS and ASAS HI total sum varied between 0.09 and 0.49 (table 3). Of note, for 4 out of 8 (50%) facilitators had a positive correlation with the ASAS HI instead of the theoretically expected negative correlation.

5. *Consensus meeting:* After presentation of the results of the second web-based survey, the steering committee decided to include 9 items into the EFIS. Decision was based on the extent of the correlation coefficient between each individual EF item and the sum score of the ASAS HI as well as considering avoidance of redundancy because of high correlation coefficient individual items of EFIS and ASAS HI total sum and coverage of representative domains of the Comprehensive ICF Core Set for AS (final EFIS version in Suppl.3). Of the final 9 items of the EF Item Set, 3 items were described as being a facilitator and 6 items were described as being a barrier (table 3). The EFIS covers 4 ICF domains of EF: 'e1 (n=1), e3 (n=3), e4 (n=3) and e5 (n=2).

6. *Translation:* The 9 items were translated into 15 languages (available https://www.asas-group.org/clinical-instruments/asas-health-index/). Cognitive debriefing was performed in 24 countries with 214 patients interviewed (table 2). Results of cognitive debriefing of the EFIS have been partly published together with the results of the cognitive debriefing of the ASAS HI (12, 20). Wording of two items was adapted based on the feedback during the qualitative interviews. For EFIS item 1, patients proposed changing the initial wording of "ankylosing spondylitis" to "my rheumatic disease" because nomenclature of patients with axial SpA is heterogeneous worldwide and patients and researchers aimed to make the wording globally understandable for different patients' groups. In the same item, patients also proposed changing the wording of "children" to "my family / relatives" because this wording applies to a wider patient group. For EFIS item 4, patients proposed changing the initial wording of "living environments" to "home and work environments" because this term specifies the content of this item. For EFIS item 5, patients proposed changing the initial wording of "relapsing" to "worsening" because the use of the word relapse is not commonly used in axSpA patients. All suggestions were implemented in the final EFIS version (Suppl. 3).

Consensus on the final Item Set version: The final set of 9 EF items complement the ASAS HI and was endorsed by ASAS members at their annual meeting in January 2013 (38 positive votes, 1 negative vote, 3 abstentions from voting).

Scoring of the EF Item Set: Each of the final 9 statements can be answered with an agreement or disagreement. Due to its multidimensional approach, there is no sum score available for the 9 items of the final EFIS. The response pattern allows identification of those areas in which patients experience limitation and restrictions and thus may need individual support.

Discussion:

In this paper, we describe the successful development of an EFIS, which accompanies the ASAS HI and provides a comprehensive standardized framework to collect environmental contextual factors in patients with axSpA. The EFIS represents environmental factors that have been identified by patients and experts (clinicians and researchers) to be relevant for functioning and health and were shown to have moderate correlation with the ASAS HI. Factors, which address support/relationship, attitudes of the patient and health care services are brought together in one item set. This is the first time in axSpA research that an item set assessing environmental contextual factors was developed in parallel with a health index utilizing the same classification system and methodology. The EFIS will help to interpret the ASAS HI results by gaining an understanding of the interaction between a health condition and contextual factors. The availability of the EFIS will support interpretation of the scores on the ASAS HI and lead to a better general understanding of disability.

The importance of contextual factors for appropriate patient-specific care is widely acknowledged. Thus, health professionals can use this pool to recognize barriers to functioning or to identify available resources to support patients in daily life and address these in a targeted approach. Researchers should undertake further research to understand the magnitude of confounding or effect modification of contextual factors in the setting of observational studies or trials. However, a main limitation is that the classification and definition of personal factors to be included in the ICF are still lacking, leading to the fact that important information cannot be studied.The OMERACT Contextual Factor Working Group identified in a nominal group qualitative study, a list of 28 generic variables characterizing the context of the individual person- and of his physical and social environment, and potentially relevant in all clinical studies in rheumatology. (4). (21). Our set of environment factors based on qualitative as well as quantitative evidence, applies to SpA, is relevant when functioning and health is the outcome domain. In comparison to the work by OMERACT, the EFIS did not specify personal factors. Having defined these EF, it is important to gain further knowledge in understanding the statistical consequences of these contextual factors, as they might influence the outcome directly, or might modify the effect of interventions or disease activity on overall functioning and health(8). Some previous work reported the relevance of personal factors in experiencing health (3, 22). Gordeev et al. reported that personal factors including helplessness, being employed and education had an important and independent impact on

10

health-related quality of life (3). Dagfinrud et al. underscored the importance of education on health outcomes in their case-control study (22). A recent review investigated relationship between contextual factors and various work outcomes such as employment status, sick leave and presenteeism (23). The authors showed that factors like absence of work accommodation, workplace support by colleagues, or regulations of the social security system were environmental factors influencing work outcomes. Item 4 of the current EFIS (I modified my work environment) addressed workplace adaptation and our assignment to the descriptor "facilitator" based on theoretical considerations. However, correlation analysis showed that it was in fact positively associated with functioning of the patients. Likely the "modifications at home or at work" (item 4) were made because of severe disease (confounding by indication) and impact on functioning would even be worse if such modifications had not been made. A similar paradox was seen for item 1 "As a result of my rheumatic disease, my family takes more responsibility for household tasks (item 1)". This clearly shows challenges how to interpret the scores on the ASAS HI in view of the results of the environmental contextual factors. Being theoretically a facilitator, the 'reverse' correlation indicates functioning would be worse without modification or support from family. A potential approach could be to adjust the ASAS HI score, similar as for the HAQ, which is adjusted when persons use aids when performing physical activities. Perhaps even more relevant, additional research is needed to understand the interaction between health condition and contextual factors in (non-pharmacological) interventions.

Response patterns on EFIS may also serve as a starting point to modify these factors in order to improve functioning and health. Although, EFIS is not validated for use in clinical practice, but we think that EFIS may give insights into individual impairments of environmental contextual factors and may help to address individual needs. The EFIS identifies environmental factors such as support and relationship based on the ASAS/WHO ICF Core Set for patients with AS providing the possibility to identify the environmental factor as a potential confounder and/or an effect modifier (4, 14).

Nevertheless, there is increasing awareness of the fact that the experience of health is the product of complex relations between a health condition on the one hand and a series of contextual factors in the person and the environment on the other (5). Therefore, we developed a set of disease-specific items based on a universal classification system, which describes these possible interactions in patients with axSpA.

To our knowledge, the ASAS HI is the first instrument for which an environmental contextual factor item set has been defined along its development, As an underlying concept, the ICF provided a list of environmental factors that are comprehensive in their coverage of the external features of the physical, social and attitudinal world in which people conduct their lives. Using this approach clarifies different experiences of disability and helps the understanding of why some people may experience discrimination and disadvantage while others do not. This difference can be seen between a person who requires minimal or no environmental interventions to retain or develop full functioning, and another who requires not only many environmental accommodations but also faces the stigmatizing attitudes of others. The EFIS was developed based on a disease-specific core set and thus, enable the researchers to investigate the interaction in patients with axSpA. However, since the EFIS addresses superordinate

categories of environmental contextual factors (such as attitudes and support), it can be discussed to what extent the factors could be applied in generic context.

There are a number of issues that must be considered in understanding the person-environment relationship. EF may often impact functioning not as single categories but as complex arrays of multiple EFs. The interactive approach taken recognized the multi-dimensional phenomenon, but requires further research to enlarge the understanding of the influence of EF on health status in patients with axSpA. In particular, three issues should be considered (i) influence of the EF on health states might depend on the underlying disease, (ii) influence of the EF on health states might operate differently in the life span and (iii) interaction between personal factors and environmental factors as well as interaction between contextual factors and psychological profile of the individual patients. Moreover, cultural and/or geographical differences were not addressed in this study but should be investigated further on because we think that these factors might influence occurrence and expression of contextual factors (24, 25). In addition, the relation and interaction between different EF needs to be studied and further research is needed to understand the integrative approach of the ICF. Knowledge about this integrative approach is needed in respect to a more general understanding of disability as well as focusing on interventions to improve influence of contextual factors on health outcomes. This is not only important from an individual perspective; but also when considering a worldwide perspective.

To conclude, the suggested EFIS provides the scientific community with focal points that support the understanding of functioning in a comprehensive and systematic manner and may serve as guidance to identify relevant environmental contextual factors for patients with axSpA. Importantly, it helps understand and collect in a standardized manner the attitudes of the patients and health services in relation to perceived health. Since knowledge about the influence of contextual factors on health outcomes is evolving, the use of the EFIS will for now be restricted to the research settings. Further work will aim to explore when and how to utilize the EFIS in clinical practice.

Competing interests none declared.

Ethics: The study complies with the Declaration of Helsinki, the locally appointed ethics committee of each international participating site has approved the research protocol and informed consent has been obtained from the subjects (or their legally authorized representative).

Data sharing statement No additional data are available.

Contributorship Statement:

Study concept and design: U Kiltz, D. van der Heijde, A Boonen, J Braun

Acquisition of data: all authors

Analysis and interpretation of data: All authors

Writing of the manuscript: U. Kiltz, D. van der Heijde, A Boonen, J Braun

Critical revision of the manuscript for important intellectual content: All authors

All authors had access to the data, commented on the report drafts, and approved the final submitted version.

Disclosures:

All authors declared no conflict of interest for this study.

References

1.   Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet. 2017;390(10089):73-84.

2.   Dagfinrud H, Kjeken I, Mowinckel P, Hagen KB, Kvien TK. Impact of functional impairment in ankylosing spondylitis: impairment, activity limitation, and participation restrictions. J Rheumatol. 2005;32(3):516-23.

3.   Gordeev VS, Maksymowych WP, Evers SM, Ament A, Schachna L, Boonen A. Role of contextual factors in health-related quality of life in ankylosing spondylitis. Ann Rheum Dis. 2010;69(1):108-12.

4.   Finger ME, Boonen A, Woodworth TG, Escorpizo R, Christensen R, Nielsen SM, et al. An OMERACT Initiative Toward Consensus to Identify and Characterize Candidate Contextual Factors: Report from the Contextual Factors Working Group. J Rheumatol. 2017;44(11):1734-9.

5.   (WHO) WHO. The International Classification of Functioning Disability and Health. Geneva2001 2001.

6.   Organization WH. How to use the ICF: A practical manual for using the International Classification of Functioning, Disability and Health (ICF). . Exposure draft for comment. Geneva: World Health Organization; 2013.

7.   Geyh S, Peter C, Muller R, Bickenbach JE, Kostanjsek N, Ustun BT, et al. The Personal Factors of the International Classification of Functioning, Disability and Health in the literature - a systematic review and content analysis. Disability and rehabilitation. 2011;33(13-14):1089-102.

8.   van Echteld I, Cieza A, Boonen A, Stucki G, Zochling J, Braun J, et al. Identification of the most common problems by patients with ankylosing spondylitis using the international classification of functioning, disability and health. J Rheumatol. 2006;33(12):2475-83.

9.   Webers C, Vanhoof L, Leue C, Boonen A, Kohler S. Depression in ankylosing spondylitis and the role of disease-related and contextual factors: a cross-sectional study. Arthritis Res Ther. 2019;21(1):215.

10.   Boonen A, Boone C, Albert A, Mielants H. Contextual factors influence work outcomes in employed patients with ankylosing spondylitis starting etanercept: 2-year results from AS@Work. Rheumatology (Oxford). 2018;57(5):791-7.

11.   van Lunteren M, Scharloo M, Ez-Zaitouni Z, de Koning A, Landewe R, Fongen C, et al. The impact of illness perceptions and coping on the association between back pain and health outcomes in patients suspected of axial spondyloarthritis: data from the SPACE cohort. Arthritis Care Res (Hoboken). 2018.

12.   Kiltz U, van der Heijde D, Boonen A, Cieza A, Stucki G, Khan MA, 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(5):830-5.

13.   Kiltz U, van der Heijde D, Boonen A, Akkoc N, Bautista-Molano W, Burgos-Vargas R, 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(9):1311-7.

14.   Boonen A, Braun J, van der Horst Bruinsma IE, Huang F, Maksymowych W, Kostanjsek N, 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(1):102-7.

15.   Cieza A, Geyh S, Chatterji S, Kostanjsek N, Ustun B, Stucki G. ICF linking rules: an update based on lessons learned. Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine. 2005;37(4):212-8.

16.   Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, 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(12):2281-5.

17.   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(12):2286-91.

18.   Karine Manera CSH, Talia Gutman, Allison Tong. Consensus Methods: Nominal Group Technique. P. L, editor. Singapore: Springer, Singapore; 2019.

19.   Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000;25(24):3186-91.

20.   Kiltz U, van der Heijde D, Boonen A, Bautista-Molano W, Burgos-Vargas R, Chiowchanwisawakit P, et al. Measuring impairments of functioning and health in patients with axial spondyloarthritis by using the ASAS Health Index and the Environmental Item Set: translation and cross-cultural adaptation into 15 languages. RMD Open. 2016;2(2):e000311.

21.   Nielsen SM, Uggen Rasmussen M, Boers M, D AvdW, de Wit M, T GW, et al. Towards consensus in defining and handling contextual factors within rheumatology trials: an initial qualitative study from an OMERACT working group. Ann Rheum Dis. 2021;80(2):242-9.

22.   Dagfinrud H, Mengshoel AM, Hagen KB, Loge JH, Kvien TK. Health status of patients with ankylosing spondylitis: a comparison with the general population. Ann Rheum Dis. 2004;63(12):1605-10.

23.   Stolwijk C, Castillo-Ortiz JD, Gignac M, Luime J, Boonen A, Group OWP. Importance of Contextual Factors When Measuring Work Outcome in Ankylosing Spondylitis: A Systematic Review by the OMERACT Worker Productivity Group. Arthritis Care Res (Hoboken). 2015;67(9):1316-27.

24.   Putrik P, Ramiro S, Molto A, Keszei AP, Norton S, Dougados M, et al. Individual-level and country-level socioeconomic determinants of disease outcomes in SpA: multinational, cross-sectional study (ASAS-COMOSPA). Ann Rheum Dis. 2019;78(4):486-93.

25.   Rodrigues Manica S, Sepriano A, Ramiro S, Pimentel Santos F, Putrik P, Nikiphorou E, et al. Work participation in spondyloarthritis across countries: analysis from the ASAS-COMOSPA study. Ann Rheum Dis. 2018;77(9):1303-10.

Table 1: Phases of development for the EF Item Set (EFIS)

	Phase	Aims	Methods
I	*Preparatory*	Development of candidate EF-items representing the EF-categories of the Comprehensive ICF Core Set for AS	Linkage of items from various assessment tools for functioning and health to 13 EF-categories covering 4 domains
II	*1st international cross-sectional survey*	Data collection and analyses for item reduction (within and across EF)	Correlation of each individual EFIS with sum score of ASAS HI was used to inform selection process
III	*Expert consultation(Steering Committee)*	Agreement on item reduction	Nominal Consensus Process based on level of correlation, redundancy and representation of ICF domains
IV	*2nd international cross-sectional survey*	Data collection and analyses for validation of the draft version and further item reduction	Correlation of each individual EF-item to the sum score of the ASAS HI was used to inform consensus
V	*Consensus Meeting (Steering Committee)*	Agreement on a final version	Nominal Consensus Process based on level of correlation, redundancy and representation of ICF domains
VI	*Translation and field test*	Provide a country-specific language version for each participating country	Forward-backward translation and cognitive debriefing according to Beaton et al. (19) resulting in some minor adaptations when needed by country PI

ASAS HI=Assessment of Spondyloarthritis International Society Health Index; EF=environmental factor; PI=Principal Investigator

Table 2: Demographic and disease characteristics of participants for both surveys and the cognitive debriefing study

Variables$	1st web-based survey (n=1754)*+	2nd web-based survey (n=622)*#	Cognitive debriefing study (n=214)§
Male (%)	929 (53.0)	372 (59.8)	142 (66.3)
Age (years)	48.3 (13.4)	48.3 (14.1)	40.5 (14.8)
Duration of symptoms (years)	22.8 (14.0)	20.4 (13.8)	11.9 (11.6)
BASDAI	5.5 (2.4)	5.4 (2.4)	4.3 (5.1)
BASFI	4.6 (2.6)	4.5 (2.6)	NA
Total back pain (NRS 0 – 10)	6.0 (2.8)	4.7 (2.8)	NA

$Variables given as mean (SD) unless otherwise indicated

*Analysis based on complete data set regarding demographic questionnaires

+ Patients from 7 English speaking countries (Australia (n=24), Canada (n=255), Ireland (n=91), New Zealand (n=36), Singapore (n=40), UK (n=706) and USA (n=602)) represented 4 continents (Europe, America, Asia, Australia/New Zealand).

Patients from Canada (n=94), Ireland (n=81), New Zealand (n=39), Singapore (n=35), the U.K. (n=190) and the U.S. (n=183))

§ Patients from Australia, Austria, Canada, Colombia, Croatia, Egypt, France, Germany, Greece, Hungary, South Korea, Mexico, the Netherlands, Portugal, Russia, Switzerland, Thailand, Turkey and U.S (each country with 10 participants) as well as Belgium (n=9), China (n=2), Italy (n=5), and Spain (n=7).

NA=not assessed; NRS=numerical rating scale; SD=standard deviation

Table partly published in: Kiltz et al. (12)

Table 3: EF Item Set with results of 2nd web-based survey and rating of consensus meeting

ICF chapter and category of ICF	Items linked to the ICF category	Facilitator ∞	Barrier ≠	Agreement with item of EFIS (n n=622)	Correlation between item and ASAS HI sum score	Selection for EFIS
e1	**PRODUCTS AND TECHNOLOGIES**					
e155	I modify my living environments.	X		327 (52.6%),	0.49	Included (item 4), wording adapted
e115	I might need some assistance during an attack.		X	411 (66.1%)	0.39	Excluded
e120	I need help to walk about outside (e.g., a walking aid or someone to support me).		X	78 (12.5)	0.37	Excluded
e1101	I take tablets to help me sleep.	X		239 (38.4%)	0.36	Excluded
e3	**SUPPORT AND RELATIONSHIP**					
e 3	As a result of my AS#, the children take more responsibility for household tasks.	X		119 (44.1%)$	0.48	Included (Item 1), wording adapted
e 3	I usually feel as if my family is pushing me.	X		123 (19.8%)	0.40	Excluded
e 3	I don't like the way my friends act around me.		X	62 (10%)	0.30	Included, (Item 2)
e 3	I can't count on my relatives to help me with my problems.		X	186 (29.9%)	0.21	Included, (Item 3)
e4	**ATTITUDES**					
e 4	My friends expect too much of me.		X	109 (17.5%)	0.39	Included, (Item 7)
e 4	No one pays much attention to me at home.		X	101 (16.2%)	0.24	Included, (Item 8)
e 4	My friends understand me.	X		413 (66.4%)	-0.25	Included, (Item 9)
e 4	My family usually considers my feelings.	X		477 (76.7%)	-0.09	Excluded
e5	**HEALTH CARE SERVICES, SYSTEMS AND POLICIES**					
e580	I have difficulties getting relapses acknowledged by a health care professional.		X	169 (27.2%)	0.32	Included, (Item 5), wording adapted
e580	Treatment of AS is taking up time.		X	322 (51.7%)	0.27	Included, (Item 6), wording adapted
e580	The therapy I received helped me functionally.	X		420 (67.5%)	-0.17	Excluded
e580	I am getting the best possible treatment for my condition.	X		392 (63%)	-0.17	Excluded

∞ assignment done before conducting the survey based on theoretical considerations

≠ (assignment done before conducting the survey based on theoretical considerations)

*Number of participants is based on the total cohort of 628 patients. Number of participants per item is less than 628 because of splitted pool

Disease axSpA was historically called ankylosing spondylitis (AS) in the items of the initial item pool

$ n = 270, as this item was not not applicable for the remaining 352

Figure legend:

Figure 1: Structure of the International Classification of Functioning, Disability and Health (ICF)

Contextual factors (both the Personal Factors and the Environmental factors (EF)) influence the biopsychosocial domains body functions, activity and participation which are covered by the already published ASAS Health Index