Measuring fatigue in Axial Spondyloarthritis (axSpA): refinement, application and evaluation of a new electronic patient-reported outcome measure (the Warwick Axial Spondyloarthritis Fatigue and Energy questionnaire (e-WASTEd)) in rheumatology clinical practice.

Date and Version: 11th May 2023, version 1.4

IRAS ID: 310098

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Sponsor: Warwick Medical School, University of Warwick

Funder: NIHR Research for Patient Benefit

Chief investigator signature: 

Conflicts of interest

The research team have no conflicts of interest to report.

Confidentiality statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

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1. Rationale

1.1 Background

The burden of the health problem:
Axial Spondyloarthritis (axSpA) is a progressive, incurable, and disabling rheumatic disease.[1,2] Symptoms typically begin in adolescence or early adulthood and advance slowly, leading to insidious decline in physical and social abilities.[1,2] Outcome is largely unpredictable, with the degree of disability ranging from minimal to devastating,[3,4] often posing problems for a person's career, family and social life.[1,4-6] Management is through life-long physical and drug therapies tailored to patients' needs.[7] Affecting up to 30 per 10,000 UK adults,[8] axSpA has a significant impact on patients, their families and the NHS.[9,10]

Pain, stiffness and reduced mobility are important features, along with sleep disturbance, psychological distress and worry about the future.[9,11,12] However, patients have identified fatigue as a major concern,[11,13] with up to 75% experiencing severe fatigue.[148] We need to improve the assessment of fatigue in axSpA and the treatment offered. To do this, we need a well-developed patient-reported outcome measure (PROM) to measure the impact of axSpA-specific fatigue and the effectiveness and cost-effectiveness of treatment.

Evidence gap: A wide variety of PROMs are used in UK rheumatology clinical services and randomised controlled trials to capture evidence of the impact of illness and treatment effectiveness in axSpA.[15,16] However, those used to assess fatigue are largely of poor quality with limited relevance to axSpA patients.[16] Moreover, digitised formats, supporting remote completion and implementation into practice are not available.

Working collaboratively with axSpA patients and health professionals, we have completed the initial five (of six) phases in the co-production of a patient-centred PROM to measure fatigue impact – the Warwick Axial Spondyloarthritis faTigue and Energy (WASTEd)[17,18] (figure 1). The current version is in a paper format, containing 18 questions across four core aspects (domains) of fatigue: energy, fatigue, symptoms, and control. We now need to complete the final phase in PROM development. This phase will finalise the PROM and provide proof that it is ready for immediate implementation into rheumatology clinical practice and research settings. We will confirm the content of the WASTEd and develop an electronic version to support on-line completion (e-WASTEd). We will test this with patients to ensure relevance and acceptability. We will then test completion of the e-WASTEd with a large group of patients, undertaking a comprehensive evaluation to produce a high quality, relevant and acceptable PROM.

This research will help clinicians to improve patient-oriented assessment and monitor treatment, thus enhancing personalised clinical care and the quality of axSpA treatment research. It will also provide patients with a self-monitoring tool against which to map their progress and self-management.

1.2 The importance of the research towards improving the health and wellbeing of patients

The importance of the research and significance of the research area:
AxSpA typically affects young adults during their reproductive life span[19] and, given the features of the disease, it is perhaps unsurprising that it is responsible for substantial direct and indirect socioeconomic costs,[10] work disability[5,6] and adverse impacts on quality of life.[1,2,6,9,11,12]. Withdrawal from work is three times more common in people with axSpA than in the general population, increasing from 5% during the first year of diagnosis to over 20% at 10 years and 30% at 20 years.[21]. A UK study has found that employment rates were 14% lower than the UK national average with 39.5% of patients of working age being

unemployed, 44% of whom related this to poor health.[5] It is suggested that treatments to improve feelings of helplessness, improving psychological wellbeing and controlling disease activity – of which fatigue is a key feature - could help to reduce work disability and loss of productivity, thus improving quality of life.[22]

Anticipated outputs, outcomes and impact:
This research will provide clinicians and researchers with an accessible, reliable, valid, and responsive method of assessing fatigue in adult patients with axSpA. The WASTEd is a patient-derived, relevant, comprehensive, and accessible PROM, which will be available in both paper and electronic formats. The WASTEd includes the outcomes that are important to patients, and hence its use has the potential to improve shared decision-making, enhancing communication between patients and their clinicians, individualising treatment, and care planning.[23]

Anticipated timescale for the benefits:
At the end of this project, the WASTEd (paper and electronic versions) will be fully operational and ready for immediate implementation into clinical practice. Further, it will be ready for use in axSpA trials and observational studies. The impact from this work is dependent on the dissemination of research findings and is often achieved over the medium to longer term (5 to 10 years). However, the COVID pandemic has accelerated the uptake of ePROMs, with the BSR ePROM initiative providing a speciality-specific open access platform for dissemination of rheumatology ePROMs. This opportunity should reduce the time to incorporation of the e-WASTEd into clinical practice.

1.3 Review of existing evidence

The need for research in this area:
Although identified as a patient priority by patients with axSpA who completed a national survey,[13] evidence suggests that health professionals often overlook symptoms of fatigue.[24]

We have demonstrated the significant limitations of recommended assessment approaches for axSpA fatigue, and their failure to detect patients' experiencing major fatigue-related impairment.[18] Growing recognition of the importance of fatigue to patients resulted in its eventual inclusion axSpA outcome reporting guidance. However, the recommended assessment utilised a single-item scale of fatigue severity.[25] The methodological inadequacies and poor relevance of fatigue measures in axSpA was further highlighted in a systematic review of PROM quality and acceptability.[20] Such measures are likely to underestimate the significant impact of fatigue.

Recent technological advances have increased interest in the use of electronic PROMs (ePROMs) in the routine management of patients with long-term conditions. Numerous electronic platforms - including personal computers, smartphones, and tablet devices – enhance the convenience of ePROM self-completion. They support the reporting of detailed symptoms and health-related quality of life data in clinic settings or between scheduled appoints, facilitating clinical decision-making and informing the provision of tailored and timely care.[26] Additional benefits include greater patient preference, improved data quality and reduced costs.[33] This has become even more relevant with the increase in on-line consultations during COVID-19.

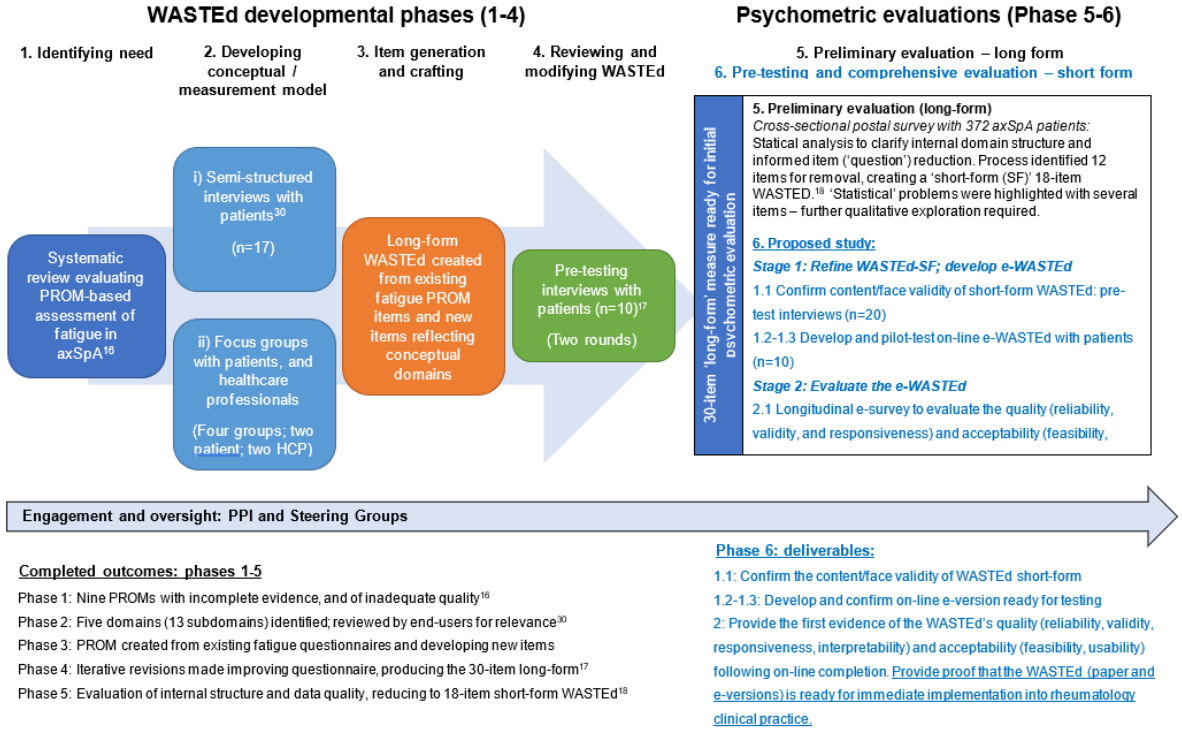
However, knowledge pertaining to the feasibility of completion and barriers to their integration into routine practice remains limited.[27] A recent survey of German rheumatologists (n=118) highlighted that, despite interest in the potential offered by

ePROMs – and a growing demand for the automatic presentation of scores within medical records - the lack of appropriate software solutions, perceived time required, and the need for staff and patient training were key implementation barriers.[27] Similar challenges, including data protection, technical challenges, lack of investment in essential infrastructures and concerns over the 'digital divide' (alienating illiterate and older people) have been described in a recent systematic review of 32 papers reporting the benefits and barriers to ePROM collection.[26] A review of ePRO integration in oncology highlighted poor assessment flexibility, inadequate clinical integration, and poor quality data collection and reporting as important barriers.[28]

With the recent, rapid growth in ePROM application, understanding the needs and experiences of patients and healthcare professionals will contribute to improvements in ePROM implementation. Moreover, understanding the accessibility needs and usefulness of ePROMs in patient self-directed management, clinical practice and research settings can support future resource allocation, and influence patient outcomes through expedited, tailored care. However, evidence describing the impact on economic and patient outcomes is limited.[27]

Rationale: We have sought to fill this evidence gap by co-producing a new, patient-derived PROM – the Warwick Axial Spondyloarthritis faTigue and Energy (WASTEd). We have completed the first five (of six) phases in PROM development (figure 1). This application focuses on the final phase– phase 6. Further psychometric and qualitative evaluation is now required to finalise the WASTEd, develop an electronic version (e-WASTEd) to support on-line completion, and evaluate its essential measurement and practical properties before its immediate implementation into clinical practice.

Figure 1: Developing the WASTEd – activities completed, and activities proposed (blue text)



We have sought to address some of the potential barriers to ePROM implementation by collaborating with the BSR ePROM initiative (https://www.rheumatology.org.uk/News-Policy/Details/BSR-launches-new-ePROMs-platform). The BSR is a recognised and trusted professional body, providing technical support and a free to access platform for health

professionals and their patients who wish to incorporate ePROMs into clinical practice. We will use focus groups to engage with patients and clinicians who have used the platform to understand their experiences. We will use this information to help us to improve the platform and to ultimately improve patient care.

Past and current research:
In addition to systematic reviews[15,16]and comparative evaluations[14] described above, qualitative exploration with axSpA patients has demonstrated the wide-ranging physical, social and psychological impact of fatigue.[30-33] Existing methods of fatigue assessment lack essential face and content validity – failing to capture important issues such as fatigue frequency, self-management, coping and energy.[16] Incorporating a well-developed PROM into clinical practice can enhance communication and shared decision-making between patients and health professionals. [23,29] Moreover, they contribute to high-quality research through the provision of accurate and relevant end-points.[34]

Work already undertaken by the research team:
We have established that current fatigue-specific methods of assessment are not suitable for axSpA.[14,16] We have completed the first five of six phases to develop a new PROM specific to axSpA fatigue (figure 1).[17,18,30]

Development followed international good practice guidance,[35] working collaboratively with patient partners[36] (figure 1). Qualitative research with patients and health professionals informed a measurement framework of fatigue and energy, highlighting what needed to be assessed[30] and the type of questions ('items') (phase 2). A first iteration of the framework explored item phraseology, recall period, response scales and format (phase 3). The developing measure was pre-tested with axSpA patients using cognitive interviews to explore relevance, memory retrieval, judgement and response mapping (phase 4).[17] This process confirmed the 'long-form' (30 item) version, which was completed by a large UK cohort of patients (phase 5; n=372).[18] Psychometric evaluations informed further item reduction, creating a short-form, 18-item measure.[18]

Phase 6 will provide essential proof that the WASTEd is ready for immediate implementation into clinical practice or research settings. It will: confirm the content and face validity of the short-form 18-item WASTEd; create an on-line version supporting ePROM completion; and confirm the quality and acceptability of the e-WASTEd following completion by a large cohort of UK axSpA patients.[34]

We will build on our existing, award-winning ePROM activities [https://www.rheumatology.org.uk/news-policy/details/2019-prizes-award-winners], collaborative links with rheumatology organisations that have responded to the current COVID-19 requirements to enhance remote access to ePROM completion (https://www.rheumatology.org.uk/practice-quality/eproms), and our research which has evidenced the key features to support PROM implementation into clinical practice.[23,29]

1.4 Aims and Objectives

The overarching aim: is to refine, test and finalise a patient-reported outcome measure (PROM) specific to the experience of fatigue in axSpA. We will provide evidence that it: is high quality, relevant, acceptable and feasible for use in clinical practice; will generate data that is valid and reliable; and has utility in informing the provision of health care on the needs of people with axSpA and for related research.

To achieve this aim, we have the following study objectives:

1.Confirm the content and face validity of the paper-based version of the 'short-form' 18-item version of the WASTEd (Stage 1.1)

2.Develop and pilot an electronic version of the WASTEd (e-WASTEd) to support on-line completion, checking the equivalence of paper and electronic-versions (Stages 1.2 and 1.3).

3. Evaluate the measurement and practical properties of the e-WASTEd following on-line completion by a large UK cohort of axSpA patients using the BSR ePROM platform, thus optimising its use in healthcare and research settings (Stage 2).

4.Explore the experiences of patients and clinicians using the BSR ePROM platform to identify enablers and barriers to its use and help us to make improvements (Stage 3).

2. Experimental Design and Methods

A three-stage, mixed methods study is described.

Stage 1: Refining the WASTEd-Short Form; developing, and piloting the e-WASTEd

Overall strategy:

1.1 *Qualitative interviews (paper version of the WASTEd):* will be conducted with axSpA patients to confirm that the changes made to the long-form WASTEd when creating the short-form version do not detract from the WASTEd's face and content validity.

1.2 *Develop an electronic version of the WASTEd (e-WASTEd)*: supporting on-line completion of the confirmed short-form version.

1.3 *Pilot the e-WASTEd:* system metrics and usability (interface, acceptability) will be collected using written feedback and semi-structured qualitative interviews to test proof of concept.

Justification of sample size:
1.1 From our previous work, we estimate requiring approximately 20 participants, to ensure sufficient data from a range of participants.[17,36]

1.2 N/A.

1.3 The paper and e-formats will be very similar. Guidance, therefore, recommends 10 participants for the pilot evaluation of both delivery methods.[37]

Recruitment strategy:
Participants will be identified from existing clinical databases of patients with axSpA by a nominated clinician within their local rheumatology department. We will purposively sample patients to ensure that gender, age, ethnicity, and level of disease activity is considered.

Eligible patients will be approached by their local clinician who will invite them to take part in the study. If they are interested, they will be provided with a study cover letter, patient information sheet (PIS), and asked to fill in a contact details form. A member of the research team will then contact them and answer any questions prior to patients deciding whether or not to participate. Patients can have at least 24-hours to consider their participation. If they choose to be interviewed about the electronic questionnaire (stage 1.3), they will provide consent to be receive an email with a link to test-version of the BSR e-PROM WASTEd study website by the research team (which will necessitate the patient providing their email address). Within two working days patients will receive an email from the research team inviting them to access the test-version of the website during the interview. Participants will provide verbal informed consent at the time of the interview. The researcher will digitally record the consent and sign and date a form to indicate the participant has agreed to take part.

Due to COVID restrictions, we will offer on-line or telephone options for participating in interviews.

Inclusion criteria: Adults (aged 18+) with a confirmed diagnosis of axSpA and registered with participating rheumatology centres. Participants in pilot interviews exploring the e-WASTEd (1.3) need access to a computer or tablet device to allow for receipt of the e-mail and e-WASTEd completion.

Exclusion criteria: The WASTEd is currently only available in the English language, so the ability to understand written English is a study requirement. The WASTEd has a readability level of 11-13 years; hence, patients with significantly limited literacy levels are excluded. This extends to patients with significant co-morbidities.

We are aware of the potential health inequalities resulting from these criteria. The proposed testing will ensure equivalence between the electronic and paper-versions[37]; validated paper versions will therefore be available after the study for clinical practice settings where patients do not wish to/are unable to complete e-formats. Future work (via Accessibility funding) will seek to translate and explore audio versions or interview-administration of the PROM.

Data collection:
1.1 Qualitative interviews (paper version of WASTEd): We will conduct up to three rounds of semi-structured patient interviews [17] (online/by phone). Questionnaires (the new short-form version of the WASTEd) will be posted/e-mailed out in advance of the interview.

These interviews provide the first opportunity to check the content and face validity of the 'short-form' 18-item WASTEd. Twelve items were removed from the 'long-form' WASTEd following initial psychometric evaluations (phase 5). We will explore if the retained items still capture important issues for patients. Additionally, items identified as 'statistically problematic' during initial psychometric testing will be discussed during the interview, including potential modifications to improve 'fit' to the measurement model. Any modifications will be discussed with participants and our patient partners to ensure that items critical to the face or content validity of the WASTEd are not removed.

Topic guide: A example of the topic guide for the stage 1.1 interviews is available in Appendix 8.1. This stage represents the last opportunity to make any changes to the item content and structure of the new measure. The focus of the interviews is to verify the relevance, acceptability, comprehension and comprehensibility of the new measure to patients with axSpA.

1.2 Develop the e-WASTEd: We will create an electronic (e) version which is compatible for

on-line completion using computers and tablets via the BSR ePROM platform. We will not change PROM item structure or content. Such minor 'modification' supports measurement equivalence (reliability and validity) between paper and e-versions.[37] The core team and patient partners will work collaboratively with the developers before further testing.

1.3 Pilot the e-WASTEd - qualitative interviews: We will conduct up to 10 semi-structured interviews (online/phone) to check usability, acceptability, and feasibility of the eWASTEd.[37] An example of the topic guide for the stage 1.3 interviews is available in Appendix 8.2. The e-WASTEd will be accessed via the BSR ePROM platform; links will be emailed in advance. We will ask participants to open and complete the e-WASTEd whilst engaging with the interviewer.

Participants will provide verbal informed consent at the time of the interview. The researcher will digitally record the consent and sign and date a form to indicate the participant has agreed to take part. We anticipate the interviews will last for between 30-60 minutes. We will digitally audio-record the interviews. Data will be transcribed verbatim via approved transcription services and analysed thematically to identify any key issues.[39] We will discuss and implement proposed changes with our patient partners in advance of each interview round (stage 1.1) and before finalising the final ePROM (stage 1.3).

Choice of analysis:
Qualitative analysis: NViVo software will be used to manage the data. Thematic analysis will be used to identify key issues in the content, comprehension, relevance, acceptability, and accessibility of the measure.[39]

Patient Partners: Refinements will be reviewed by patient partners and research team members between each interview round (stage 1.1), during e-WASTEd development (stage 1.2) and pilot testing (stage 1.3).

Stage 2: Evaluating the e-WASTEd:

Overall strategy:
Longitudinal evaluation: To ensure that the WASTEd is high quality, a large group of axSpA patients will be asked to complete the e-WASTEd using the BSR ePROM platform on three separate occasions (phase 6 - figure 1).

Sample size:
We will recruit 380 patients entering data to the BSR e-PROM website. Assuming 65% completion (consistent with our earlier research[18)] this will provide data from approximately 250 respondents. Item fit statistics (a key component of modern psychometrics) are highly sensitive to sample sizes: a minimum sample size of 250 is recommended.[34]

Recruitment strategy:
Two UK-health professional organisations - the British Society for SpondyloArthritis (BritSpA) and AStretch – and the UK's axSpA patient organisation - National AS Society (NASS) - support this application. They will support the recruitment of collaborative units, clinicians, and patients. Informed by our earlier work, we anticipate requiring participation from up to eight UK centres.

We will invite all respondents to complete the same 'pack' of ePROMs at baseline, two-weeks (to check for test-retest), and three-months (to evaluate responsiveness). We estimate this will provide the minimum of 50 patients required whose health has not changed at two-weeks to inform an assessment of test-retest.[34] It should provide a similar number of

patients reporting that their health has changed (both improved and declined) at three-months to inform evaluation of measurement responsiveness and score interpretation.

Patient recruitment **(inclusion/exclusion):**
Clinicians at participating centres will identify potentially eligible patients with a confirmed diagnosis of axSpA. A poster will also be placed in clinic waiting rooms advertising the study, with contact details for interested individuals. Eligible patients will be advised of the study (either in clinic, by telephone, or by post) and provided with a study cover letter, patient information sheet (PIS), and consent form. Patients who consent to taking part in the study will provide the clinical team with their email address so that they can be given access to the on-line BSR e-PROM website. Within two working days patients will receive an email (from the BSR ePROM website) inviting them to access the study.

All participants will be required to have access to a computer or tablet and the internet to support electronic completion of the ePROMs.

Nature of follow-up: At each completion point, we will send text / e-mail reminders (including the link to the study portal) at 2 and 4-weeks to participants who do not complete the on-line ePROMs.

Data collection:
The ePROM pack will include the e-WASTEd and six additional ePROMs (Appendix 8.3.1 to 8.3.8):

- Generic health (EQ-5D-5L; f
- Fatigue-specific (FACIT-Fatigue questionnaire) https://www.facit.org/measures/FACIT-F;
- Emotional wellbeing (Hospital Anxiety and Depression Scale);
- Pain (single measure of pain severity using an 11-point numerical rating scale) and
- AxSpA-specific health: quality of life (EASI-QoL) disease activity (BASDAI with pain numerical rating scale) and function (BASFI)[19].

Many of these PROMs will be familiar to patients due to their routine collection in UK rheumatology clinics. Previous research has demonstrated the acceptability of a similar package of PROMs,[4,5,18] with completion times approximating 20-30 minutes.

At follow-up only, participants will also complete single-item health transition questions (general and specific to axSpA and fatigue) (Appendix 8.3.9).

Completion of the additional PROMs supports a comparative evaluation of the WASTEd's psychometric properties against established 'validated' measures. Moreover, their inclusion supports an evaluation of measurement validity – that is, how well does the WASTEd measure fatigue, and how well does it detect change in fatigue over time.

Practical properties of the e-WASTEd: Several additional questions (closed and open-format) will be included to explore the usability, feasibility, and acceptability of completing the ePROMs, with specific reference to the e-WASTEd. Such data may highlight where improvements can be made to enhance future use of the ePROMs. These questions will be developed with our patient partners to ensure resonance and clarity and will mirror those used in stage 1.3 (Appendix 8.2).

Choices of analysis:
Statistical evaluation: The psychometric evaluation will utilise both classical and modern test (Rasch modelling) theory approaches to establish evidence of essential measurement

properties: data quality (end-effects; missing data); reliability (internal consistency; test-retest; standard error of measurement (SEM)); validity (structural, construct); and responsiveness (change over time; SEM; interpretation).[34]

Analyses will predominately be conducted using the statistical software R (https://www.r-project.org/) .

Data quality and interpretability: Item-scale characteristics, completion rates (missing data) and percentage of computable scores will be reported. Interpretability will be informed by evidence of end-effects and calculation of the minimal important change (MIC) – the smallest change in score perceived as important by participants[34] -, calculated as the mean change score for patients reporting 'minimal change' in their fatigue at 3-months. Items will be checked for differential item functioning to ensure that there is no item bias between key demographic groups (e.g. gender, disease severity or age).

Structural validity and internal consistency reliability: Confirmatory factor analysis will be used to confirm the four-domain structure of the WASTEd. Internal consistency will be assessed with Cronbach's alpha.

Reliability and measurement error: Two-week test-retest reliability (intra-class correlation coefficient (ICC 2,1)) will be assessed in patients indicating no change in their health, as a measure of temporal stability. We will calculate the standard error of measurement (SEM) to determine the extent of absolute measurement error.[34] The SEM supports score interpretation by accounting for variability, or error, in measurement - only a change greater than measurement error is considered 'real'.[34] The SEM will be subsequently converted into the smallest detectable change (SDC), representing the smallest change in score that is greater than measurement error; the SDC will be calculated for individuals and for groups.[34] The SDC allows one to rule out measurement error (i.e. distinguishing measurement error from true change) when assessing the reliability of a self-reported measure to detect change in health status. Thus, a score change greater than the SDC value is necessary to provide evidence of true change (improvement or deterioration) in health-status.

Construct validity: explores how well the WASTEd measures fatigue. The score correlation between the WASTEd and comparator measures will be assessed to evaluate convergent validity (Pearson's correlation coefficient). Hypothesised theoretical (strength of) associations between the measures will be considered a prior. Items will also be evaluated using an appropriate Rasch model (e.g. a Rating Scale Model) to ensure good item and person fit, as well checking that items cover a sufficient range of the underlying trait That is, items cover and can distinguish between both high and low fatigue levels.

Content validity: semi-structured interviews (stage 1.1) will explore measurement relevance, acceptability, clarity, and comprehensiveness.

Responsiveness: reflects the ability of a measure to detect real change in health that is greater than measurement error. We will calculate the absolute measurement error at 3-months (standard error of measurement (SEM) and the smallest detectable change (SDC)), to represent the smallest change in score that is greater than measurement error in patients reporting change in health at 3-months. We will calculate the minimal important change (MIC) as the mean change in those reporting minimal improvement or deterioration at 3-months. We will calculate the minimal important clinical difference (MICD) as the mean change in score in those who are 'somewhat better' minus the mean change in those who are the same at 3-months.[34] Additionally, we will calculate receiver operating characteristic (ROC) curves to assess the ability of measures to discriminate between people whose health has improved or deteriorated (on axSpA-specific health transition question) at 3-months (criterion-based responsiveness).[34] An area under the curve (AUC) score of > 0.70

is considered sufficiently discriminatory; an AUC of 0.5 suggests no discriminatory power. Finally, the effect size (ES) and standardised response mean (SRM) will be calculated for subgroups of patients in each health transition category (axSpa is better / same / worse). The main hypotheses to be tested will include: ES and SRM will be <0.2 for patients who reported no change in axSpa-specific health; >0.2 for patients reporting a slight improvement / deterioration; >0.5 for patients reporting greater levels of improvement / deterioration (much better / much worse).

Practical properties of e-WASTEd completion: Qualitative responses will be analysed thematically to identify key issues in patients' experiences. Closed-format questions will be presented as frequencies.

Stage 3: *Exploring the experiences of patients and clinicians using the BSR ePROM platform*:

Overall strategy: To explore patient and clinician experiences of using ePROMs accessed via the ePROM platform to provide information to help to improve the ePROM platform and ultimately to improve patient care.

Sample size:
We estimate requiring up to 10 patients and 10 health professionals (clinicians, physiotherapists, nurses) to participate in focus groups. From our previous work we estimate that this number will provide a breadth of experience of ePROM usage. Recent experience suggests smaller groups (3 to 5 participants) provide better quality data when using virtual media, so we will hold up to six focus groups.

Recruitment:
Patient participants in stage 2 will be asked to consider taking part in a focus group to discuss their experiences of e-PROM completion and use of the BSR e-PROM platform. If interested, they will be provided with hard or digital copies of the study information and patient information sheet (PIS), and to confirm that they are happy to be contacted about this stage of the study. A member of the research team will then contact them and answer any questions. Patients will have at least 24-hours to consider their participation.

Health professionals will be made aware of the study via adverts on clinician-facing websites (BSR e-PROM platform. BritSpA, AStretch, NASS). Interested clinicians will be advised to e-mail the research team, who will provide them with a study information sheet. They will then arrange to contact them and answer any questions. Potential participants will have at least 24-hours to consider their participation.

We will be seeking participants who are willing to discuss both positive and negative experiences of using the BSR ePROM platform.

Data collection:
All participants will provide verbal informed consent at the time of the focus group. The researcher will digitally record the consent and sign and date a form to indicate the participant has agreed to take part.

Focus groups will be conducted separately for patients and clinicians using video-conferencing facilities (Microsoft Teams). We anticipate that focus groups will last for up to 2-hours, with a comfort break. The topic guide will be informed by the literature exploring barriers to ePROM implementation in clinical practice (examples of questions are illustrated in Appendix 8.4). Focus groups will be digitally audio-recorded. Data will be transcribed verbatim and analysed thematically.[39]

Choice of Analysis:
The data will be analysed thematically to identify key elements of participant experience.[39] Similar codes based on meanings within the data will be drawn together to develop categories and then themes. Interpretation will include similarities and differences within transcripts and across the whole data set. NVivo 12, a software package for qualitative data, will be used to help manage the data.

Project timetable (figure 2):

Set up:
Months 1-2: Ethical and R&D approval will be sought in advance of the study. Patient research partners and core group discussions.

Stage 1: Refining the WASTEd-SF, developing and piloting the e-WASTEd
Months 1-4 (4-months): 1.1 Refining and confirming the WASTEd content - qualitative interviews and analysis.

Months 4-6 (2-months): 1.2 Develop e-WASTEd and ePROM package for BSR ePROM platform.

Months 6-8 (2-months): 1.3 Pilot the e-WASTEd: qualitative interviews and analysis.

Months 7-8 (1-month): Finalise e-WASTEd ready for stage 2; meeting with core research team and patient research partners.

Stage 2: Evaluating the e-WASTEd
Months 8–24 (18 months): 2. Longitudinal evaluation – 2.1 Baseline data collection

Months 14-19 (6 months): 2.1.1 Psychometric analysis (baseline)

Months 12–19 (8 months): 2.2 Two-week follow-up

Months 14-21 (8 months): 2.2.1 Psychometric analysis (test-retest)

Months 14–21 (8 months): 2.3 Three-month follow-up

Months 16-23 (8 months): 2.3.1 Psychometric analysis (responsiveness)

Stage 3: Focus groups exploring use of the BSR ePROM platform
Months 14-21 (8-months): Six Focus groups with 10 patients and 10 clinicians.

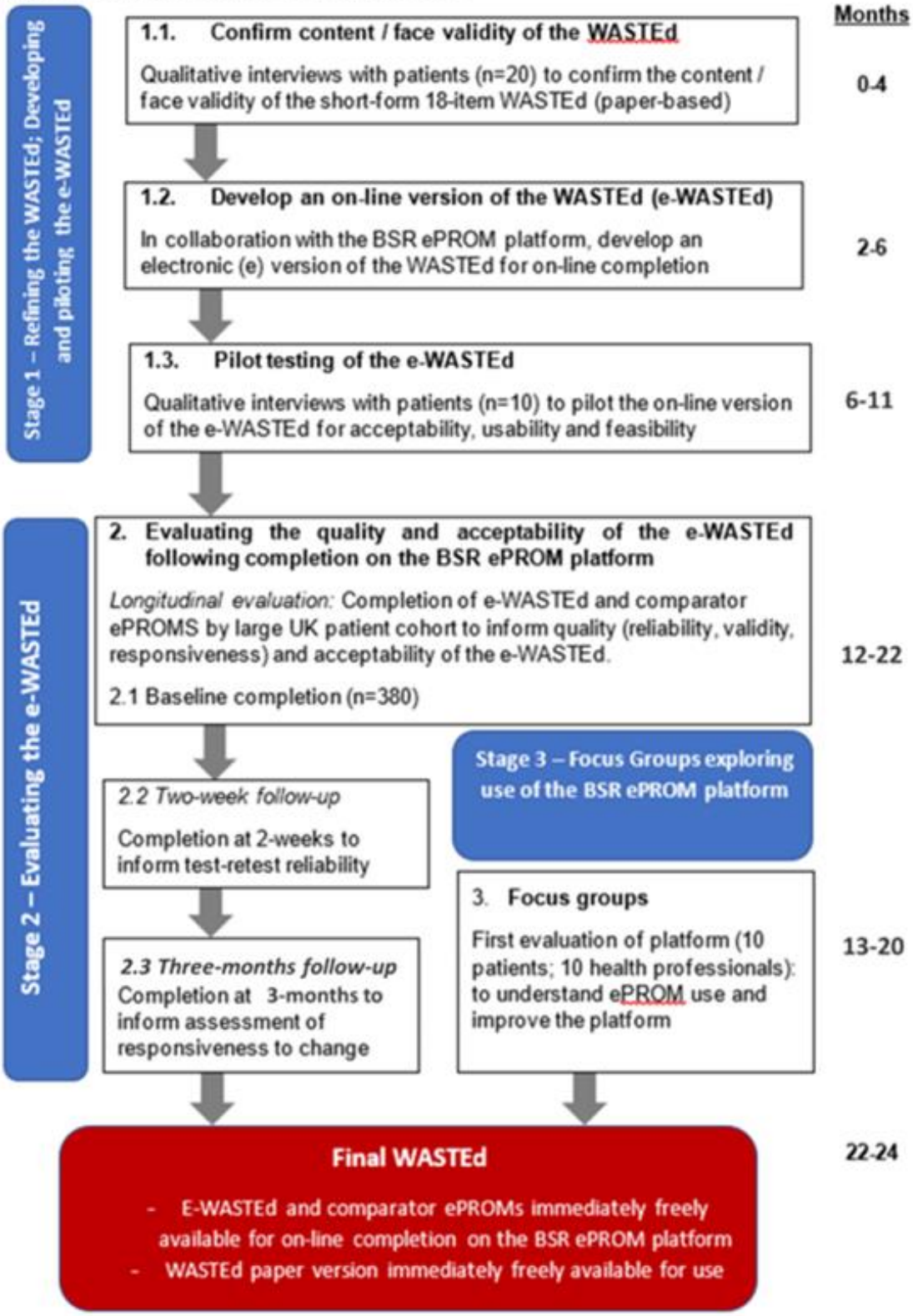
Stage 4: Final analysis
Months 18-24 (8-months) 4.1 Develop users' guide.

Months 18-24 (8-months): 4.2 Final analysis; write up and dissemination.

Milestones: Month 4 confirm WASTEd content/face validity. Month 7 confirm e-WASTEd; Month 20 longitudinal evaluation complete; Month 24 experiences of using the BSR ePROM platform complied; Month 22 psychometric analysis complete.

Deliverables: A high-quality, relevant, and acceptable measure of fatigue for the axSpA community, ready for implementation (paper and electronic) into rheumatology clinical practice and research.

Figure 2: Flowchart of planned research activities



3. Data management

3.1. Access to data

Direct access will be granted to authorised representatives from the Sponsor or host institution for monitoring and/or audit of the study to ensure compliance with regulations.

3.2. Data recording and record keeping

Digital audio recordings (stages 1 and 3) will be transcribed verbatim by a university-approved transcription service. University-approved transcription service providers have agreed to a framework agreement for the Supply of Transcription Services with the University of Warwick. All suppliers have been through the University's Information Security checks and have overarching Data Processing Agreements in place. Recordings will be deleted once the study has been published. Transcripts will be pseudonymised as soon as possible and kept on a password protected university desktop computer or encrypted, password protected laptop. Any information stored on portable media (e.g., audio recorder) will be encrypted and locked away (as soon as practicable to do so) in a locked room in a locked filing cabinet at Warwick Medical School, University of Warwick, in compliance with the Data Protection Act (2018). Patient lists (containing identifiable information) will be recorded digitally on a password protected spreadsheet and stored separately from anonymised data on the secure university server.

As per the University of Warwick's Research Code of Conduct, data will be retained intact in paper or electronic format as appropriate, for a period of 10 years from the date of any publication which is based upon it. Research data will be fully anonymised, containing no personal or identifying information, and will be stored securely for 10 years. Only the research team will have access to the original data (Dr's Kirstie Haywood, Elizabeth Tutton, Nathan Pearson, Helen Parsons, Jon Packham, Jane Martindale, James Galloway, Mrs Melanie Martin, and the study Research Fellow (tbc)).

Data collected for stage 2 will be collected electronically via the British Society of Rheumatology's (BSR) ePROM portal. The information collected will be anonymised and stored in a research database. The team at King's College London (KCL) will remove all personal and identifiable data. The process of making this new dataset fully anonymous includes:

- All patient identifiers except for a unique case id will be removed. A linkage key will be stored in a different location to the original dataset but will only be shared with the core research team (Drs Haywood, Parsons, Packham, Tutton, Galloway, Research Fellow).
- Postcodes will be converted into an index of multiple deprivation rank, and the original postcode removed.
- The name of the hospital where the patient was assessed will be removed.
- Date of birth will be converted to age at study entry. Exact date of birth will be removed.
- All data fields in the entire database will be offset by a random number that is unique to each dataset created for research. The number will be constant within an individual dataset to ensure times between events remain unchanged. The random number used to create the offset will be stored with the identification key but will only be shared with the core research team (Drs Haywood, Parsons, Packham, Tutton, Galloway, Research Fellow).

- Unusual events will be found and removed; using statistical software we will identify any patient record which contains an extreme value (e.g., age) and censor that record.

King's College London is responsible for the manner in which the data is processed. The information entered by patients will be stored in a digital format only. Information will be held in an encrypted format in a secure Microsoft SQL server. The Centre for Rheumatic Diseases processes the data using a secure cloud-based data storage within Microsoft SharePoint at King's College London. All data repositories are encrypted, and password protected. All people with access to the data will sign confidentiality agreements and will be trained in the responsibilities of data protection. For the purpose of this study only core members of the research team will have access to the data (Dr's Haywood, Tutton, Pearson, Parsons, Packham, Galloway, Martin, Martindale, Research Fellow (tbc)).

4. Ethical considerations

4.1. Confidentiality

The study will adhere to the General Data Protection Regulation (2018) which requires data to be anonymised as soon as it is practical to do so. Participant names will not be used; instead unique identifiers will be assigned. This will be consecutively assigned numbers which infer nothing of the individual's gender (which could be inferred if pseudonyms were used). Consent forms will be scanned, encrypted, and stored on the secure university server (separate from transcripts) and the hard copies, shredded.

4.2. Data security

All consent forms will be scanned, encrypted, and stored on a secure university server as soon as practicable to do so. Hard copies will then be shredded. Patient lists (containing identifiable information) will be recorded digitally on a password protected spreadsheet and stored separately from anonymised data. Digital audio recordings will be done using an encrypted device. Recordings will be transferred to the secure university server as soon as practicable to do so, and the recording device wiped. Following publication of the study, the recordings will be deleted. As per the University of Warwick's Research Code of Conduct, transcripts will be retained intact in paper or electronic format as appropriate, for a period of 10 years from the date of any publication which is based upon it. Only the research team will have access to the original data (Dr's Haywood, Tutton, Pearson, Parsons, Packham, Galloway, Martin, Martindale, Research Fellow).

For stage 2 (ePROM completion), King's College London will be responsible for the manner in which the data is processed. The information entered by patients will be stored in a digital format only. Information will be held in an encrypted format in a secure Microsoft SQL server. The Centre for Rheumatic Diseases processes the data using a secure cloud-based data storage within Microsoft SharePoint at King's College London. All data repositories are encrypted, and password protected. All people with access to the data will sign confidentiality agreements and will be trained in the responsibilities of data protection. For the purpose of this study only core members of the research team will have access to the data (Dr's Haywood, Tutton, Pearson, Parsons, Packham, Galloway, Martindale, Mrs Martin, Research Fellow (tbc)).

4.3. Benefit and risks

Participants may not receive a direct benefit as a result of participating in an interview, focus group, or completing the ePROM questionnaires. However, experience suggests that patients are often pleased to have an opportunity to share their experience with a researcher and contribute to research.

Participation in the interviews or focus group, or completion of the on-line questionnaires may be burdensome. Some patient participants may find that completion of the questionnaires and discussion around the relevance to their experience of axSpA distressing; should this occur, they will be advised to contact their rheumatologist.

5. Benefits of the study

The proposed research will benefit a large number of patients with axSpA and the rheumatology clinical services that treat them. It is only by accurately reflecting and recording individuals' experiences of fatigue that clinicians become aware of the impact of fatigue on their patients, which then directly influences interventions and treatment choices. This is the first PROM developed to holistically reflect the effect of fatigue and is a complete step change in fatigue measurement, away from the currently unsatisfactory assessment options available.

Severe fatigue prevalence in axSpA is extremely common. Fatigue is a crucial determinant of impaired quality of life (QOL) across many inflammatory rheumatic diseases including axSpA, and a predictor of work disability. Over 75% of patients identify fatigue as the main barrier to remaining in employment. Despite these profound consequences, patients feel this symptom is clinically ignored and rheumatologists admit ignorance regarding its management.

A recently completed trial of physical and CBT therapies in inflammatory arthritis aimed at lessening the impact of fatigue (LIFT trial; Versus Arthritis grant number 21175 Trial registration number: NCT03248518)(*in press*) has clearly shown clinical and health economic benefit of these interventions. This provides an evidence base to unlock widespread access to these much-needed therapies. If clinicians can recognise which patients require treatment for fatigue, by using validated PROMs such as WASTEd, then the right patients can be referred for fatigue-specific therapy at the right time in their patient journey.

6. Resources and costs

Financial support for this study is provided by a NIHR Research for Patient Benefit (Tier 3) grant [NIHR202800].

6.1 Value for money of the research

The research provides value for money because the multidisciplinary research team consists of a unique blend of world leading experts who will ensure that all components of the application are completed to the highest standard and delivered on time. Informed by the requirements of the application, the team includes experts in the development, testing and implementation of PROMs (Haywood, Parsons, Pearson, Galloway), qualitative methods (Tutton, Haywood, Pearson, Martindale), clinical rheumatology/ axSpA expertise (Packham, Martindale, Martin, Galloway), ePROMs and digital health (Martin, Galloway) and clinical service leadership (Packham). Our patient partners (Strickland, Thompson) have worked

collaboratively with the team in the co-development of the WASTEd, facilitated by a dedicated PPI lead (Martindale). Pearson completed the first five (of six) stages in the development of the WASTEd for his doctoral studies.

Packham is a trustee of the British Society of Rheumatology (BSR) executive board and an executive member of the British Spondyloarthritis (BRiTSpA) group. Martin and Martindale also have strong links with BritSpA and AStretch. All co-applicants have strong links with the National AS Society (NASS), the UK's primary patient organisation. These links will support the recruitment of collaborating sites and patients. They will also support our proposed dissemination activities. This provides value for money because these recruitment and dissemination pathways have already been created, tested and proven in earlier research.

Galloway is clinical academic lead for the BSR ePROM platform. Martin is a founding member of the BSR information technology committee which provides oversight for the ePROM platform. She is now working within NHSX, the digital transformation directorate of NHS England, bringing additional expertise which will further inform our thinking around ePROM implementation and reach. The ePROM platform is freely available to UK clinicians providing care for rheumatology patients. It is already in use across a large number of NHS trusts, with more than 700 patients completing ePROMs using the system. The research provides value for money because we are using a parallel system to collect on-line research data to one that is already established collecting routine remote clinical data. Our collaboration with the BSR ePROM platform will ensure that the ePROMs produced with this research will be freely available to UK rheumatology practitioners to incorporate into routine (including remote) rheumatology clinical care and that the output from the research can be seamlessly disseminated to all UK rheumatology centres and sustained long term.

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8. Appendices

Appendix 8.1: Topic guide for Cognitive Interviews for WASTEd refinement – paper version (Stage 1.1).

This is a draft topic guide to cover **stage 1.1** cognitive interviews with AxSpA/AS patients.

This stage represents the last opportunity for significant revision to the modified or new PROM. The focus of the cognitive interviews is to verify the relevance, acceptability, comprehension and comprehensiveness of the PROM with patients with AxSpA/AS who are representative of the target population.

Four stages of cognitive processing underpin the interviewing process in stage 3:

- comprehension – the process of making sense of the question and developing a response.
- memory retrieval – of relevant information to enable a response.
- judgement – to determine if memory retrieval is accurate and complete; and
- response mapping – the process by which an appropriate response option is selected

Interviewees will be invited to 'think aloud' whilst completing the questionnaire – expressing aloud their thought processes whilst answering the questions. This will be followed by 'verbal probing' – respondents are invited to retrospectively paraphrase or rephrase items.

Examples of question probes include:

1. Narrative

- What do you think about the questionnaire?

2. Readability

- Is the question / questionnaire easy to read? If not, where are the difficulties?
- Are any of the questions difficult to understand? How could they be improved?

3. Acceptability and relevance

- Do the questions include 'what really matters' to you when you think about your experience of fatigue?
- Are the questions easy to respond to? If not, which ones are more difficult and why? How could this be improved?
- Are there any important things that are missing?
- Are there any questions that are not helpful?

4. Ease of completion

- Is the questionnaire easy to complete?

5. Content and structure

- How would you improve the questionnaire?

Appendix 8.2: Topic guide for Cognitive Interviews for WASTEd development – electronic version (Stage 1.3).

This is a draft topic guide to cover **stage 1.3** cognitive interviews with AxSpA/AS patients.

This stage represents the opportunity to check the electronic adaptation of the paper-based version of the WASTEd into an electronic format. The focus of the cognitive interviews is to verify the relevance, acceptability, and comprehension of the electronic (e-)PROM with patients with AxSpA.

Interviewees will be invited to 'think aloud' whilst completing the questionnaire – expressing aloud their thought processes whilst answering the questions. This will be followed by 'verbal probing' – respondents are invited to retrospectively paraphrase or rephrase items.

Examples of question probes include:

1. Narrative

- What do you think about the electronic questionnaire?

2. Readability

- Is the e-question / questionnaire easy to read? If not, where are the difficulties?
- Are the response options easy to use? If not, where are the difficulties? How could they be improved?

3. Acceptability and relevance

- Is it easy to open the e-questionnaire? If not, how could this be improved?
- Are the questions easy to respond to? If not, which ones are more difficult and why? How could this be improved?
- Are there any important things that are missing?

4. Ease of completion

- Is the e-questionnaire easy to complete?

5. Content and structure

- How would you improve the e-questionnaire?

Appendix 8.3: Questionnaire package for PROM completion (Stage 2).

8.3.1 WASTEd (18-items over 6-pages)

Warwick Axial Spondyloarthritis Fatigue and Energy questionnaire (WASTEd)

Instructions

We would like to know how your fatigue and energy levels associated with your Axial Spondyloarthritis (axSpA) have affected you, ***on average,*** over the ***past 7-days***.

We understand that your fatigue and energy levels may have changed day-to-day, but we would like you to answer the questions about how you have been feeling ***on average*** over the ***past 7-days***. This will let us understand how you feel and are affected by your axSpA-fatigue and help us decide how best we can support you.

The questionnaire is separated into two sections:

Section 1 – Fatigue: here, we ask 10 questions about your experience of fatigue associated with your axSpA and how it has affected you, ***on average, over the past 7-days***.

Section 2 – Energy: here, we ask 8 questions about your energy levels associated with your axSpA and how they have affected you, ***on average, over the past 7-days***.

Please read each question carefully and answer each question with a single cross.

Section 1: Fatigue

Please read the following statement before completing this section.

Fatigue: Everyone gets tired or even worn-out at times, but after a few good night's rest they usually feel refreshed. It is known that people with this condition experience fatigue which is not like normal tiredness. Fatigue can last for weeks at a time and no amount of sleep or rest will relieve it.

On **AVERAGE** over the **PAST 7-DAYS**

1. **How often have you felt fatigued?**

☐ Not at all ☐ Rarely ☐ Often ☐ All the time

2. **How severe was your fatigue?**

☐ Not at all severe ☐ A little ☐ Very ☐ Extremely severe

3. **Has your fatigue made it difficult to concentrate or remember things? (e.g. concentrating on driving or puzzles, more forgetful than normal)**

☐ Not at all difficult ☐ A little ☐ Very ☐ Extremely difficult

4. **Have you found it difficult to engage in conversations with other people because of your fatigue? (e.g. friends, family, work colleagues)**

☐ Not at all difficult ☐ A little ☐ Very ☐ Extremely difficult

On **AVERAGE** over the **PAST 7-DAYS**

5.	**Has your fatigue made it difficult to do the things you enjoy? (e.g. listening to music, watching a TV programme)**

☐	☐	☐	☐
Not at all difficult	A little	Very	Extremely difficult

6.	**Has your mood been affected by your fatigue? (e.g. feeling low, worried, frustrated, guilty)**

☐	☐	☐	☐
Not at all affected	A little	Very	Completely affected

7.	**Have you felt the need to be left alone because of your fatigue? (e.g. not interacting with friends or relatives)**

☐	☐	☐	☐
Not at all	A little	A lot	All the time

8.	**I feel I have been able to manage my fatigue.**

☐	☐	☐	☐
Not at all	A little	A lot	All the time

9.	**I feel I have been able to cope with my fatigue.**

☐	☐	☐	☐
Not at all	A little	A lot	All the time

On **AVERAGE** over the **PAST 7-DAYS**

10.	**Do you feel that your fatigue has made you more dependent on others? (e.g. having to ask for help to do everyday tasks from family, friends or carers)**

☐	☐	☐	☐
Not at all	A little	A lot	All the time

Section 2: Energy levels

Please read the following statement before completing this section.

Energy: Everyone usually has the energy levels to do things in their day, but with this condition it could be a real struggle to find that 'get up and go' to do the things you want or need to do. You may feel 'drained' and need to stop for a quick rest which might help you generate some energy.

On **AVERAGE** over the **PAST 7-DAYS**

1. **How often have you felt drained of energy?**

☐ Not at all ☐ Rarely ☐ Often ☐ All the time

2. **Have your energy levels made it difficult for you to maintain your personal care? (e.g. showering, brushing your teeth, eating your usual meals)**

☐ Not at all difficult ☐ A little ☐ Very ☐ Completely difficult

3. **Have your energy levels made it difficult for you to keep to your routine? (e.g. usual work, hobbies, leisure activities)**

☐ Not at all difficult ☐ A little ☐ Very ☐ Extremely difficult

4. Have your energy levels made it difficult to make plans?

☐ Not at all difficult ☐ A little ☐ Very ☐ Extremely difficult

On **AVERAGE** over the **PAST 7-DAYS**

5.	**Have your energy levels caused you to change your plans? (e.g. cancel or reschedule)**

☐ Not at all ☐ A little ☐ A lot ☐ All the time

6.	**Have you been able to maintain your energy levels to achieve what you wanted to do?**

☐ Not at all ☐ A little ☐ A lot ☐ Completely

7.	**Have you lacked physical energy?**

☐ Not at all ☐ A little ☐ A lot ☐ All the time

8.	**Have you lacked mental energy?**

☐ Not at all ☐ A little ☐ A lot ☐ All the time

Thank you for completing the WASTEd questionnaire

8.3.2 Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) (13-items; 1page)

FACIT Fatigue Scale (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

		Not at all	A little bit	Some-what	Quite a bit	Very much
H7	I feel fatigued	0	1	2	3	4
H12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

8.3.3 EuroQoL EQ-5D-5L and EuroQol-Thermometer

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

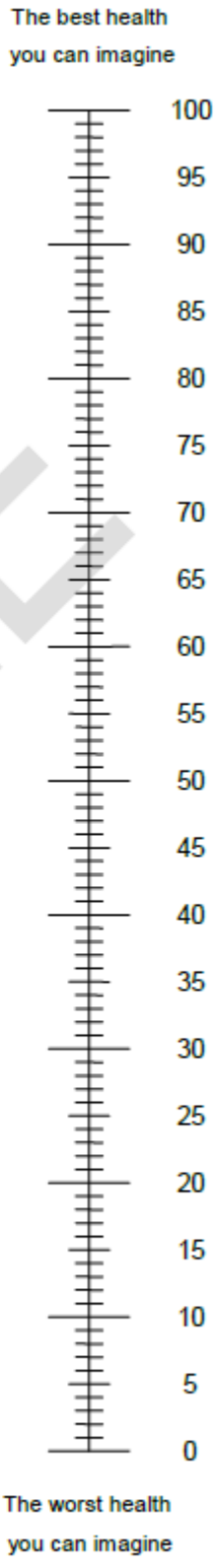
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



8.3.4 Hospital Anxiety and Depression Scale (HADS)

Hospital Anxiety and Depression Scale (HADS)

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more.

This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

I feel tense or 'wound up'
- Most of the time
- A lot of the time
- From time to time, occasionally
- Not at all

I still enjoy the things I used to enjoy
- Definitely as much
- Not quite so much
- Only a little
- Hardly at all

I get a sort of frightened feeling as if something awful is about to happen
- Very definitely and quite badly
- Yes, but not too badly
- A little, but it doesn't worry me
- Not at all

I can laugh and see the funny side of things
- As much as I always could
- Not quite so much now
- Definitely not so much now
- Not at all

Worrying thoughts go through my mind
- A great deal of the time
- A lot of the time
- Not too often
- Very little

I feel cheerful
- Never
- Not often
- Sometimes
- Most of the time

I can sit at ease and feel relaxed
- Definitely
- Usually
- Not often
- Not at all

I feel as if I am slowed down
- Nearly all the time
- Very often
- Sometimes
- Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach
- Not at all
- Occasionally
- Quite often
- Very often

I have lost interest in my appearance
- Definitely
- I don't take as much care as I should
- I may not take quite as much care
- I take just as much care as ever

I feel restless as if I have to be on the move
- Very much indeed
- Quite a lot
- Not very much
- Not at all

I look forward with enjoyment to things
- As much as I ever did
- Rather less than I used to
- Definitely less than I used to
- Hardly at all

I get sudden feelings of panic
- Very often indeed
- Quite often
- Not very often
- Not at all

I can enjoy a good book or radio or television programme
- Often
- Sometimes
- Not often
- Very seldom

Now check that you have answered all the questions

8.3.5 Evaluation of AS Quality of Life (EASIQoL)(20 items, 3 pages)

LIMITATIONS DUE TO YOUR ANKYLOSING SPONDYLITIS

The following questions ask about the problems that your **Ankylosing Spondylitis** has caused you. Please answer every question with a cross.
If you are unsure about how to answer a question, please give the best answer you can.

These questions ask about activities you might do during a typical day.
Does your **Ankylosing Spondylitis** limit you in these activities **today**? If so, how much?

For each question, please cross the **one** response that **applies to you today.**

Please cross one box on each line

	Not limited at all	A little limited	Moderately limited	Very limited	Totally limited / unable to do
1. Lifting a child or **heavy objects** such as shopping or furniture	☐	☐	☐	☐	☐
2. Walking **one mile**	☐	☐	☐	☐	☐
3. Standing for **30 minutes**	☐	☐	☐	☐	☐
4. **Getting up** from a sitting position	☐	☐	☐	☐	☐
5. Finding a **comfortable** position in which you can relax	☐	☐	☐	☐	☐
6. **Dressing or undressing** yourself	☐	☐	☐	☐	☐

We would now like to ask you questions about the ***past week***. We understand that your Ankylosing Spondylitis may have changed from day to day but we would like you to give a response that shows how you have been ***feeling on average*** over the ***past week***.

Please answer every question with a cross. If you are unsure about how to answer a question, please give the best answer you can.

7. During the **past week**, how much pain or discomfort did your Ankylosing Spondylitis cause you?

☐ **None** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extreme**

EASi-QoL 20

8. During the **past week**, how much did your Ankylosing Spondylitis interfere with your sleep?

☐ Not at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extremely

9. During the **past week**, how much of the time have you felt tired or lacking in energy because of your Ankylosing Spondylitis?

☐ None of the time ☐ A little of the time ☐ Some of the time ☐ Most of the time ☐ All of the time

10 During the **past week**, how much morning stiffness did your Ankylosing Spondylitis cause you?

☐ None at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extreme

11. During the **past week**, how much of the time have you felt embarrassed or self-conscious because of your Ankylosing Spondylitis?

☐ None of the time ☐ A little of the time ☐ Some of the time ☐ Most of the time ☐ All of the time

12. During the **past week**, how much of the time has your Ankylosing Spondylitis caused you to worry about the future (including work, caring for others, your social life and staying active)?

☐ None of the time ☐ A little of the time ☐ Some of the time ☐ Most of the time ☐ All of the time

13. During the **past week**, how much did your Ankylosing Spondylitis interfere with your ability to concentrate (including reading, listening to someone talking or watching the television)?

☐ Not at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extremely

14. During the **past week**, how much of the time have you lacked drive or motivation because of your Ankylosing Spondylitis?

☐ None of the time ☐ A little of the time ☐ Some of the time ☐ Most of the time ☐ All of the time

EASi-QoL 20

Please answer every question with a cross. If you are unsure about how to answer a question, please give the best answer you can.

15. During the **past week**, how much of the time have you felt downhearted or low because of your Ankylosing Spondylitis?

☐ **None of the time** ☐ **A little of the time** ☐ **Some of the time** ☐ **Most of the time** ☐ **All of the time**

16. During the **past week**, how much of the time has your Ankylosing Spondylitis interfered with your normal work (including work both outside the home and housework)?

☐ **None of the time** ☐ **A little of the time** ☐ **Some of the time** ☐ **Most of the time** ☐ **All of the time**

17. During the **past week**, how much did your Ankylosing Spondylitis interfere with family life or friendships?

☐ **Not at all** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extremely**

18. During the **past week**, how much did your Ankylosing Spondylitis interfere with traveling either by car or public transport (including buses or trains)?

☐ **Not at all** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extremely**

19. During the **past week**, how much did your Ankylosing Spondylitis interfere with your ability to keep physically active?

☐ **Not at all** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extremely**

20. During the **past week**, how much of the time did you feel that your Ankylosing Spondylitis was interfering with the quality of your life?

☐ **None of the time** ☐ **A little of the time** ☐ **Some of the time** ☐ **Most of the time** ☐ **All of the time**

EASi-QoL 20

8.3.6 Bath AS Disease Activity Index (BASDAI)
and
8.3.7 Bath AS Functional Index (BASFI)

The BASDAI Score

Please read each question and circle the box you feel is the most appropriate to describe how severe your condition has been in this area. **Each question relates to how you have felt in the past week**. Please only circle one box for each question. There is no wrong answer.

1. How would you describe the overall level of fatigue/tiredness you have experienced? Score out of 10

None 0 1 2 3 4 5 6 7 8 9 10 *Very severe* ☐

2. How would you describe the overall level of AS neck, back or hip pain you have had?

None 0 1 2 3 4 5 6 7 8 9 10 *Very severe* ☐

3. How would you describe the overall level of pain/swelling in joints other than the neck, back or hips?

None 0 1 2 3 4 5 6 7 8 9 10 *Very severe* ☐

4. How would you describe the overall level of discomfort you have had from any tender areas to touch or pressure?

None 0 1 2 3 4 5 6 7 8 9 10 *Very severe* ☐

5. How would you describe the overall level of morning stiffness you have had from the time you wake up?

None 0 1 2 3 4 5 6 7 8 9 10 *Very severe* ☐

6. How long does your morning stiffness last from the time you wake up?

None 0 1 2 3 4 5 6 7 8 9 10 *2 or more hours* ☐

1 hour

The BASFI Score

Please read each question and circle the box you feel is the most appropriate to describe how severe your condition has been in the last week. Please only circle one box for each question. There is no wrong answer.

1. Putting on your socks or tights without help or aids (eg, sock aid). Score out of 10

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

2. Bending forward from the waist to pick up a pen from the floor without an aid.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

3. Reaching up to a high shelf without help or aids (eg, helping hand).

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

4. Getting up out of an armless dining room chair without using your hands or any other help.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

5. Getting up off the floor without help from lying on your back.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

6. Standing unsupported for 10 min without discomfort.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

7. Climbing 12 to 15 steps without using a handrail or walking aid. One foot at each step.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

8. Looking over your shoulder without turning your body.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

9. Doing physically demanding activities (eg, physiotherapy, exercises, gardening or sports).

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

10. Doing a full day's activities, whether it be at home or at work.

None 0 1 2 3 4 5 6 7 8 9 10 *Impossible* ☐

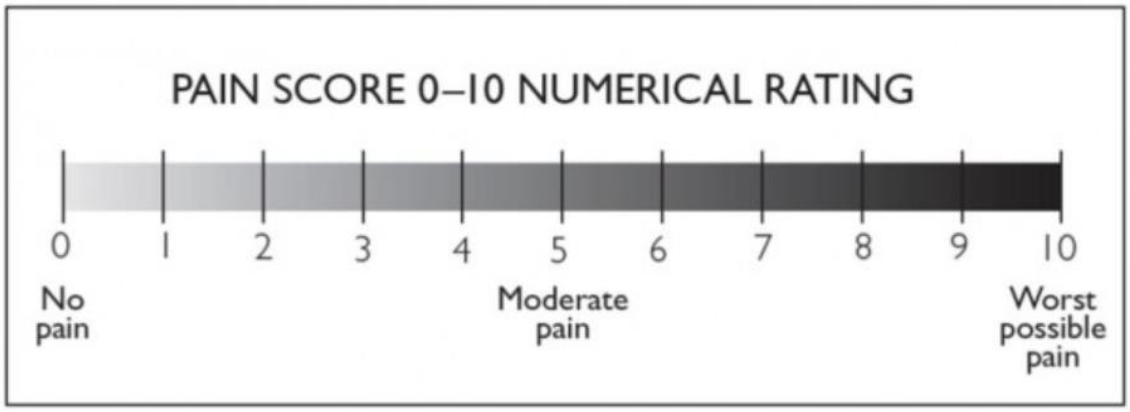
For clinician use only *BASFI Score* ☐

BASFI Score Calculation
Add all scores from questions 1 -10 and divide by 10.
The higher the BASFI score, the more severe the patient's limitation of function due to their AS.

Adapted from Calin et al. J Rheumatol. 1994 Dec;21(12):2281-5.

8.3.8 Single Item Pain Severity – 11-point Numerical Rating Scale

How would you rate your usual level of pain during the last week?



8.3.9 Health transition items (generic and axSpA specific)

8.3.9.1 General Health Transition Question

In comparison to when you last completed this questionnaire, would you describe your **general health** as:

☐	☐	☐	☐	☐
Much worse	Somewhat worse	About the same	Somewhat better	Much better

8.3.9.2 Axial Spondyloarthritis-specific Transition Question

In comparison to when you last completed this questionnaire, would you describe your **Axial Spondyloarthritis (axSpA)** as:

☐	☐	☐	☐	☐
Much worse	Somewhat worse	About the same	Somewhat better	Much better

Appendix 8.4: Topic guide for focus groups to explore views on ePROM completion and use of the BSR ePROM platform

This is a suggested topic guide to cover **stage 3** focus groups with AxSpa/AS patients and healthcare professionals who have completed ePROMs via the BSR ePROM platform. Example points for discussion have been included for each topic area.

Topics:

1. Ground rules
2. Introduction and background to the study
3. Exploring the experience of using the BSR ePROM platform
4. Exploring the experience of ePROM completion
5. Close

Example questions

1. Ground rules

The focus group is anticipated to take up to 2 ½ hours – including a 30-minute comfort break. As far as the focus group is concerned, there are some "ground rules" that we all should agree to follow:

- To be clear, we are not here to provide any medical advice.
- As we have limited time, any questions or comments that are off topic will be answered after the focus group.
- I would like everyone to have a chance to speak and be heard.
- We should listen to one another and not speak over another person or dominate the discussion.
- Please respect each other's opinion(s). It's okay to have a different opinion or experience, and there is no right or wrong answer to any of the questions or discussion points.
- If you discuss what was said in the focus group after the session, please talk about the points in general terms without naming who said what.
- The focus group will be reported without using names.

2. Introduction and background to the study

Welcome to everyone and many thanks for agreeing to come along today and to join with our group discussion.

Introduce RF and facilitators.

Our reason for asking you to come along today is to enable us to better understand your experience of completing ePROMs and/or of using the BSR ePROM platform.

Questionnaires are widely used to help patients in telling health professionals about how they are feeling, what they can and cannot do, and how their life is being affected by their health condition and/or treatment. Well-developed questionnaires provide a record, or assessment, of how you are feeling so that both patients and health professionals can see what the major problems are at any particular time, and how these problems change (improve, get worse, or stay the same) over time. This is important to ensuring that patients get the treatment that they need at the right time. These questionnaires are often called

'PROMs' – that is, patient-reported outcome measures. Hence, the name of the new BSR ePROM platform.

Using an electronic platform to complete the questionnaires or PROMs helps the questionnaires to be 'scored' more quickly so that they results can be more readily incorporated into clinical decision-making. We would like to discuss with you your experiences of completing the electronic, or e-questionnaires or e-PROMs, and of using the BSR ePROM portal. (For clinicians: We would like to discuss with your experiences of using the BSR ePROM portal for ePROM completion).

We are interested in both positive and negative experiences – what was good, and what was not so good and could be improved.

We thank you for volunteering to participate in this group discussion. We hope that you will all be able to freely contribute your thoughts and views and we will aim to ensure that you can do this; but please don't wait to be invited before joining in with the discussion. Please also be re-assured that there are no 'right or wrong' answers, everyone's views are important, and we hope to hear as many different thoughts as possible. Also, please note that the views and concerns of each member of the group are confidential and should not be repeated outside of this meeting.

We will be audio-recording the discussion in order to provide a full account of everything that is said. We would therefore ask you please to try and avoid talking over each other. XX will be taking notes to assist us with our analysis. Once analysed, the results of the discussions will help us in further refining the BSR ePROM platform and towards providing guidance for patients and healthcare professionals in the use of ePROMs.

We have a total of 2 hours for the discussion, and we plan to have a short comfort break after about an hour, but please do feel free to stand and move around as necessary. Please feel free to ask for clarification at any point during the meeting.

Are there any questions?

3. Exploring access to and use of the BSR ePROM platform (50 mins)

The BSR ePROM platform will be displayed via a large screen so that it is visible to all participants. The process of accessing and navigating the site will be discussed and explored. Participants will be asked to share their positive and negative experiences of site navigation and use, highlighting, where necessary, where improvements are required.

Questions may include:

Which aspects of the ePROM platform work well? Why?

Which aspects of the ePROM platform don't work so well? Why?

What would be the top three things that you think could improve the experience of PROM completion via the BSR ePROM platform?

COMFORT BREAK (10 mins)

4. Exploring completion of ePROMs via the BSR ePROM platform (50 mins)

The seven ePROMs included in the study (Stage 2) will be displayed via a large screen so that they are visible to all participants. The process of accessing and completing the specific PROMs will be discussed and explored. We are interested to know which PROMs work well and which don't work so well in an electronic format. We would like to know how completion could be improved.

Questions may include:

Which e-questionnaires do you think work well? Why?

Which e-questionnaires don't work so well? Why?

If we were to choose an e-questionnaire, which one would be the best/worst?

Healthcare professionals will be invited to share their broader experiences of PROM completion via the BSR ePROM platform, beyond those included in the study.

Before we finish, is there anything else that you would like to say or add or that people feel they haven't had a chance to say?

5. CLOSE (5 mins)

Many thanks to you all for agreeing to take part in this group discussion; we hope that you have enjoyed the experience. Your contribution has been really very helpful.

We will be running several group discussions and then looking at the information you provide to see which issues are most important for people when completing ePROMs, particularly when using the BSR ePROM platform.

If you would like to know more about this study, please leave your name and contact details with me and I will endeavour to keep you informed of progress.

Many thanks – have a safe trip home!