Chapter

10

Outcome Measures in Rheumatic Diseases

INTRODUCTION AND GENERAL PRINCIPLES

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Why the need arose? A peek into the History

Old is gold but new is welcome. Which is better? Especially with relevance to therapeutics. Individual health care givers would have their own experiences, coupled with patient heterogeneity, different brands, socio-economic issues, habits of patients, health care givers own core competence—there are innumerable variables that could affect the decision of choice as regards which is better—the old or the new? Outcome assessment is the measurement of these in a standardized and validated manner—the way by which consequences of diseases and health care management decisions are evaluated.[1] Process measures include histological, biochemical or imaging procedures, whereas outcome measures reflect the suffering or loss of health experienced by patients as a consequence of the disease.

As newer armamentarium gathered for treating RA, reports kept piling up on the use of these by several centers and rheumatologists from the world on their utility and results—mainly in the 1980s.[2] There was marked variability in the methodology each used both to carry out the trial and producing the results. The measures used lacked validity and were insensitive to change.

Thus arose the need for a group that brought together rheumatologists of the world and allied specialists, statisticians to uniformly lay out measures that should be used to assess response and disease status. This gave birth to the OMERACT—initially called outcome measures in RA clinical trials but now is the outcome measures in rheumatology.[3] The first OMERACT meet was held in Maastricht in 1992 under the auspices of the WHO, ILAR, EULAR and several other rheumatology bodies.[4] This is where the 'core set' of outcome measures of the WHO/ILAR and later adopted by the ACR took birth. The meet also emphasized on the need for developing measurement methodology. Subsequently the OMERACT has been meeting every two years. Other diseases like osteoarthritis, gout, connective tissue diseases also have been included since. It was after about the 5th OMERACT meet that the significance of having patients in the groups was realized. Fatigue is a classic example of an outcome measure that only a patient can figure out and it was later included in the list.[5]

Outcome measures can also be divided into two categories—observer dependent (rated by the evaluator, e.g. swollen joint count, tender joint count, grip strength, etc.) or observer independent (self-reported, e.g. visual analogue scales VAS for pain, global disease, etc.) or qualitative/quantitative. The various domains within the core set defined for different diseases relied on the Fries' paradigm (5Ds—Death, Disability, Discomfort, Drug and Dollar). Put simply, they define disease consequence in terms of mortality or survivorship and morbidity or impact of disease and the symptom severity on

health related quality of life. The PROMIS (Patient Reported Outcome Measurement Information Systems Initiative) is an NIH initiative using computer adaptive testing to question patients where answers to initial questioning give rise to subsequent questions.

Standardisation: Towards Filtering the Measures!

There are some common attributes that an outcome measure must meet. These are ethicality (risk involved must be weighed against any new information that would be gained), validity (measures what it is supposed to measure), reliability (measure yields same result on repeated usage) and responsiveness (detects minimal change). The OMERACT members also realized these attributes would need to be tested in terms of truth, discrimination and feasibility—what they called the OMERACT filter.[6] Over years, with increasing number of patients and broadening range of conditions being considered, they realized both the core domains and the instruments included within these domains needed to be explicitly defined so that there is some standardization in clinical trials. This brought about the OMERACT Filter 2 which gave a clear statement of what the organization means by core outcome domains and instruments[7] (Tables 10.1 and 10.2).

What do you need to include as Outcome Measures in your Clinical Trials and what are the Techniques used in General?

There are almost 100 different rheumatologic disorders. Disease specific outcome measures would differ but there are common ones that need to be assessed, e.g. pain, disability, handicap, etc. Organisations like the OMERACT, ACR, IMMPACT (Initiative on Methods, Measurement and Pain Assessment in Clinical Trials) have come out with consensus on the core sets, domains, instruments and even responder criteria to be included in trials. Over the last decade, with the advent of EHR (Electronic Health Records), patient responses to PROMS is being captured in an electronic format.

Pain can be measured in terms of Likert scale, VAS, ladder scale, chromatic continuous scale, pain face scale, etc. but VAS is by far the one most commonly used. Other domains included are impairment (e.g. SJC/TJC), disability (can be physical, social or emotional, e.g. HAQ, WOMAC, hand grip), handicap (e.g. Disease Repercussion Profile), global assessments—both patient's (one has to mention what is being gauged—overall disease or symptom and also the time frame—last one week or one month) and physician's or evaluator's or assessor's (generally has greater insight into disease status due to available lab tests, imaging results, etc.), psychosocial issues (depression using validated scales like the Beck depression inventory, etc.—contributes to pain and has to be differentiated from inflammatory pain) and fatigue and sleep (validated fatigue scales and sleep scales, e.g. Pittsburgh Sleep Quality Index—these are patient reported scales which are easier to perform in rheumatology patients than sleep studies due to difficult ambulation in many). Composite indices like DAS 28 in RA are useful to assess disease activity at that point of time and take into consideration all three—patient related, evaluator related and laboratory parameters of the patient. Treatment related OM like adverse reactions (very relevant to drug trials—systems like COSTART and WHOARD grade adverse effects as none, possible, probable and definite),[8] concomitant therapy (rescue therapy, pill counts, keeping a diary, etc.), self management interventions (psychoeducational: patients are taught to learn to self mangage) and economic issues (both direct, e.g. labs, imaging, consultations, etc. and indirect—work loss) have also been included

Table 10.1: The original OMERACT filter

- Truth. Is the measure truthful, does it measure what is intended? Is the result unbiased and relevant? The word captures issues of face, content, construct, and criterion validity.
- Discrimination. Does the measure discriminate between situations of interest? The situations can be states at one time (for classification or prognosis) or states at different times (to measure change). The word captures issues of reliability and sensitivity to change.
- Feasibility. Can the measure be applied easily, given constraints of time, money, and interpretability? The word captures an essential element in the selection of measures, one that may be decisive in determining a measure's success.

Table 10.2: Characteristics of OMERACT filter 2.0

Structure

- There are two concepts to outcome incorporating the impact of health conditions and their pathophysiological manifestations.
- There are four Core Areas of outcome: Death; life impact; resource use* and pathophysiological manifestations. Every clinical trial must include at least one measure under each of these headings.
- Within each Core Area are Domains of interest to particular conditions. Experts and stakeholders should determine at least one domain to be a core outcome within each Core Area. This is the Core Domain Set. Trial designs are not limited to the Core Domain Set but should include them in all clinical trials in that condition in addition to any other domains that might be relevant to their investigation.
- Within each Core Domain at least one valid outcome measure should be identified. Validity is assured by meeting the requirements of truth, discrimination and feasibility (as described in the original OMERACT filter).
- The resultant Core Outcome Measurement Set, which includes at least one instrument from each Core Domain, and at least one domain from each Core Area, should be included in the outcomes of all clinical trials in that condition. Trial designers may also incorporate any other outcomes of interest, including a designated primary outcome which is not part of the Core Outcome Measurement Set but is relevant to their investigation.

Process

Identify the Core Domain Sets

- A literature review of domains and instruments previously used in the condition
- A review of the setting and any contextual factors that need to be taken into account
- Structured enquiry with stakeholders on their views on domains of importance
- Full participation of all stakeholders (including patients) in a consensus process to determine agreement on *what* to measure—the Core Domain Set.

Identify the Core Outcome Measurement Set

- Full literature review to identify validated and applicable outcome instruments for each Core Domain
- Validate instruments in the condition of interest if this has not been done
- Develop and validate new instruments for a Domain that does not have an outcome measurement instrument
- Full participation of all stakeholders (including patients) in a consensus process to determine agreement on how to measure—the Core Outcome Measurement Set

*At present strongly recommended only.

in the list for drug trials. The patients' perspective is gaining more and more importance over the years. For example, fatigue was listed into the list of outcome measures only after the involvement of patients. The 10th OMERACT conference had conducted four workshops on incorporating patients perspective in defining outcome measures and since then has been instrumental in including patients and patient groups in almost all the workshops/conferences held in this context.

How do these Differ in a Private Practice Scenario?

There are differences between real world OPD practices and clinical trials: Patients have heterogenous disorders, numbers may vary, they may be taking concomitant therapies especially alternative, they may have co-morbidities (which are exclusions in trials), they may be from different socio-economic classes and different educational backgrounds especially in a country like ours and the follow up may be unreliable. Also, the goal may be just to track the patient's response over time and treatment efficacy/safety. Patient self-reported questionnaires are best suited in such situations where they can fill up while in the waiting area. The latter have been found to correlate well with other validated outcome measures. These could be general or disease specific combined with patient and physican global assessments and also health related quality of life measures. Flowcharts are particularly useful to document clinical status and drug tolerability.

India Specific Pitfalls and Remedies

In his editorial in the Indian Journal of Rheumatology, Dr Vinod Ravindran has very ably listed the problems with our patients/our infrastructure Table 10.3.

How do we solve these issues? The same supplement with the very experienced authors from our country has suggested solutions for these.[9] Some of these could be—representation of Indian patients/patient groups in the ethics committees and international workshops, adaptations to the OM to suit our needs and as per our socio-economic melieu, short less time consuming questionnaires to be validated since the burden is huge and using Likert scale more often that our patients are able to use. At the organization level, we need to hold workshops at our national meets addressing these issues, collaborate with international organisations like the OMERACT and get some of our interested colleagues trained for participation in their conferences. With increasing use of biologics and affordabililty rising in the Indian populace, answerability in the form of objective assessments and therefore OM, is going to be more and more relevant. As with the ITAS,[10] we need to pull up our socks and work together to add to scientific evidence from our country by applying the outcome measures in relation to rheumatologic diseases.

Table 10.3: Limitations of the existing rheumatology outcome measures and barriers in their effective use in the Indian setting

- Not culturally and socially sensitive.
- Importance of some measures not understood by other specialities.
- Patients have difficulty in understanding the concept of visual analogue scale.
- Patients cannot measure their disease in absolute terms.
- Non-affordability of certain therapeutic agents renders the measurement of "outcome" futile.
- Costs of investigations necessary for certain outcome measures may not be acceptable to patients.
- Low education background of patients makes it difficult to administer patient reported outcome measures.
- In a patient with comorbidities, 'global health' might also indicate burden it.
- Poor patient participation at the study design level.
- Self-reported disability and pain have multiple influences.
- Validation in several different Indian languages might be necessary.
- Lack of patient self help/advocacy groups.
- Inadequate international collaboration.
- Focus only on the therapeutic aspect of management of diseases mainly necessitated by a heavy case load.
- An "inward looking" approach.
- Inadequate trained manpower in rheumatology; Time consuming and lack of motivation to work in this field limited by infrastructure and finance.

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10A. OUTCOME MEASURES IN RHEUMATOID ARTHRITIS

Puja Srivastava

Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder, and joint synovitis is its main manifestation. Different patients have different degrees of impairments in general health and functional limitations due to arthritis which is further influenced by other co-morbid illness, economic and societal burdens. Because of this heterogeneity in disease expression, it is difficult for a single parameter to assess all facets of disease, therefore composite indices are used.

In an individual patient, the immediate target of therapeutic intervention is "disease activity (the reversible component)", while the long-term goal is to prevent "disease related damage (the irreversible component)" and to improve the "quality of life (functional disability)". The proxy for disease related damage is the radiographic evidence of joint destruction, which can be quantified by varied quantitative scores. Over last few decades, approach to treatment of RA has undergone spectacular evolution. Current concept is to "Treat to Target", and these targets are defined using composite disease outcome measures.[1]

1. Instruments for measuring disease activity in RA: Core Domains for assessment of RA includes assessment of the main organ involved, i.e. the joint in form of count of number of swollen and tender joints. Other important domains include assessment of pain, global impression of disease activity by the patient and evaluator and laboratory measures of inflammation using acute phase reactants like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).[2]

- *Joint assessment*: It includes count of joints with tenderness and swelling with limited range of motion. Depending upon number of joints included for assessment, different indices have been developed (Table 10A.1). While early measures included 78 joints, the latest one (28 joint count)[3] excludes feet and ankle joints, as they are often painful and tender for the reasons other than RA. Tender joint counts (TJCs) are more sensitive and correlate with pain. Swollen joint counts (SJCs) correlate well with progression of joint damage and acute phase reactants, suggesting that they reflect the pathogenic event of RA more accurately. It has been noted that expanded joint counts do not convey any extra information than the reduced ones.
- *Pain assessment*: It is assessed on a 10 cm horizontal visual analog scale (VAS), with "no pain" at one end and "worst possible pain" at the other, without intermediate categories. This domain evaluates the pain experienced over period of last one week.
- *Patient and evaluator global assessment*: Patient global assessment of disease is more subjective and is liable to be affected by social, economic and multiple other non-related factors while evaluator global assessment is more objective and integrative. Both are used in combination as patients tend to overestimate their illness while physicians provide an optimum average. The responsiveness of measures of global disease activity is good, and such measures discriminate well between the levels of response among different treatment groups.
- *Acute phase reactants*: These are biomarkers of inflammation (e.g. ESR, CRP), and are raised in multiple other conditions like infection, malignancy, etc. Although not specific for RA, they correlate well with swollen joint counts. Further, in composite indices like DAS28, they improve the content validity of the score by measuring an objective laboratory parameter and are heavily weighted.

Composite indices of core variables: Such indices capture the disease activity and functional impairment in a uniform pattern, despite wide variations in disease manifestation in different individuals.

- *Disease activity score (DAS)*: It is a composite measure of disease activity[2,3] and includes 5 core domains (Table 10A.2). The instrument uses a complex formula with different weightage to variables, e.g. relative weightage to TJC/SJC is less than ESR/CRP. The latest DAS uses consolidated 28 joint counts (DAS 28). Both DAS and DAS28 have been modified to include CRP instead of ESR (DAS-CRP and DAS28-CRP) or to exclude assessment of global health

Table 10A.1: Various joint counts used in rheumatoid arthritis

	Ritchie index	*ACR joint count*	*44 joint counts*	*28 joint counts*
Year	1968	1965	1992	1989
No. of joints assessed	78	68/66	46/44	28
Graded	Yes	No	No	No
Joints involved				
DIPs		+		
PIPs	+	+	+	+
MCPs	+	+	+	+
CMCs				
Carpus				
Wrist	+	+	+	+
Elbow	+	+	+	+
Shoulder	+	+	+	+
DIP (feet)				
PIP (feet)		+	+	
MTP	+		+	
Tarso-metatarsal	+			
Tarsus	+	+	+	
Ankle	+	+	+	
Knee	+	+	+	+
Hip	+	+		
Acromio-clavicular	+	+	+	
Sternoclavicular	+	+	+	
Temporomandibular	+	+	+	
Cervical spine	+			

ACR: American College of Rheumatology
DIP: Distal inter-phalangeal joint
PIP: Proximal inter-phalangeal joint
MCP: Metacarpo-phalangeal joint
CMC: Carpometacarpal joint
MTP: Metatarso-phalangeal joint

Adapted from: Aletaha D, Smolen JS. The definition and measurement of disease modification in inflammatory rheumatic diseases. Rheum Dis Clin North Am 2006; 32:9–44.

(DAS-3 and DAS28-3). The cut-off points between high, moderate, low disease activity and remission are 5.1, 3.2, and 2.6, respectively for DAS 28.[3] Table 10A.3 shows the complex mathematical formulae used to calculate DAS. Complex computation is one of the drawbacks of DAS28, which is addressed by other simplified indices.

- *Simplified disease activity index (SDAI)*: It is the simple sum of 5 core domains and does not use complex and weighted mathematical formula like DAS (Table 10A.3). SDAI has been widely validated, and definitions of states of remission and of low, moderate, and high disease activity have been standardized.[4]
- *Clinical disease activity index (CDAI)*: This is purely clinical instrument and does not require the availability of an acute-phase reactant (CRP or ESR), as unavailability of these laboratory results frequently precludes immediate assessment of disease status. It consists of linear sum of 4 core domains (Table 10A.3) and correlates well with the disease activity.[5]

Table 10A.2: Instruments to assess outcome in rheumatoid arthritis

Disease parameters	*Core domains*	*Composite indices/instruments*
1. Disease activity	Tender joint count (TJC) Swollen joint count (SJC) Pain (VAS) Patient global Physician global Acute phase reactant (ESR/CRP)	DAS28 ESR/CRP DAS-3 CDAI SDAI **Patient reported outcomes (PROs)** RADAR RADAI RAPID 3/4/5
2. Improvement criteria	Tender joint count (TJC) Swollen joint vount (SJC) Pain (VAS) Patient global Physician global ESR/CRP HAQ-DI	ACR 20, 50, 70 Hybrid ACR EULAR response criteria
3. Functional improvement	Patient reported Questionnaires	HAQ-DI SF-36 AIMS
4. Radiographic damage	X-rays of hands and/or feet	Larsen method Sharp score Sharp van der Heijde (SvdH) score

Abbreviations: DAS 28, disease activity score based on 28 joint counts; CDAI, clinical disease activity index; SDAI, simplified disease activity index, RADAR, rapid assessment of disease activity in RA; RADAI, RA disease activity index; RAPID 3/4/5, routine assessment of patient index data 3/4/5; HAQ-DI: health assessment questionnaire-disability index; ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; SF-36, Short Form 36; AIMS, arthritis impact measurement scale

Table 10A.3: Composite disease activity indices for rheumatoid arthritis

Index	*Formula*	*Remission*	*Low*	*Moderate*	Severe
DAS28-ESR	$0.56 \times \sqrt{(TJC28)} + 0.28 \times \sqrt{(SJC28)} + 0.70 \times \log_{nat}(ESR) + 0.014 \times GH$	<2.6	2.6–3.1	3.2–5.1	>5.1
DAS28-CRP	$0.56 \times \sqrt{(TJC28)} + 0.28 \times \sqrt{(SJC28)} + 0.36 \times \log_{nat}(CRP + 1) + 0.014 \times GH + 0.96$	<2.6	2.6–3.1	3.2–5.1	> 5.1
SDAI	SJC28 + TJC28 + PGA + EGA + CRP	<3.3	3.4– <11	11.1 – <26	>26
CDAI	SJC28 + TJC28 + PGA + EGA	<2.8	2.9– <10	10.1 – <22	≥22

Abbreviations: DAS 28, Disease Activity Score based on 28 joint counts; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SDAI, simplified disease activity index; CDAI, clinical disease activity index.

- *Patient reported questionnaires (PROs)*: Multiple patient reported measures of disease activity have been developed (Table 10A.2), but are rarely used in clinical practice. Examples: RADAR—six-point questionnaire, RADAI—five item questionnaires, RAPID3, RAPID4 and RAPID5.

2. Disease improvement criteria: American College of Rheumatology (ACR) criteria are widely used in clinical trials of RA. The ACR improvement criteria[6] require 20% improvement in SJC and TJC and in three of the five remaining core set variables (Table 10A.2). Minimum of 20% improvement from baseline is called ACR20. This criterion has

also been applied to study more profound responses such as ACR50 and ACR70 for 50% and 70% response, respectively. ACR criteria do not consider the starting level of a patient's disease activity, it only provides us a dichotomas "yes/no" result. To overcome the limitation of dichotomy, a modified numerical ACR-N has been developed which has a continuous scale ranging from 0 to 100%. It has the capability to readout the smallest relative improvement in three measures: SJC, TJC, and the median of the five remaining core set variables.[7] EULAR response criteria is based on change in DAS28 measurement. Moderate to good response is used as marker of efficacy in RA clinical trials.

3. Physical function assessment: Common measures used to assess this parameter include Short Form 36 (SF-36) and Health Assessment Questionnaire (HAQ). While the former score allows the comparison in quality of life parameters of patients with different diseases and normal population, the latter helps in assessment of quality of life of patients with different diseases and different patients with same disease.

Full HAQ includes assessment of disease related discomfort, side effects of drugs, economic burden of disease, acquired disability and mortality associated with the disease. However, it is time consuming and difficult to perform on every outpatient visit. Hence a modified version, called HAQ Disability Index (HAQ-DI) has been devised, which tests patients' ability to perform activities of daily living with the help of a questionnaire.[8] It includes 20 questions divided into eight categories: Arising, hygiene, walking, dressing, eating, reach, grip and usual activities. Each question is weighted on Likert scale from no difficulty to inability to perform (0 to 3). Maximum score in each of the eight categories is divided by eight to calculate the HAQ score (range 0 to 3). HAQ is determined by both disease activity and damage. Minimum change in HAQ should be $\geq$0.22, to observe any clinically significant difference in quality of life of a given patient.

4. Assessment of radiographic damage: This is done using simple X-rays of hands and feet. Different authors have given different scores.[9] Commonly used ones are Larsen score, Sharp score, SvdH score. These measures assess disease severity in terms of radiographic damage (joint space narrowing and erosions), but only sharp score and its modifications are sensitive to change.

Conclusions

Outcome assessment in RA is complex, in view of systemic nature of the disease. Disease activity, radiographic joint damage and functional impairment are three main areas of outcome assessment. All three are interlinked, with one influencing the other and thus, they serve as the determinants of the most important outcome measure, i.e. patient's quality of life.

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10B. OUTCOME MEASURES IN SYSTEMIC LUPUS ERYTHEMATOSUS

Taral Parikh

Introduction

Systemic lupus erythematosus (SLE) is a prototype immune complex mediated disease. It affects multiple organ systems and has a relapsing remitting course, thus making assessment of disease activity and damage more difficult than other rheumatic diseases.

Four core domains are assessed in SLE trials routinely: Disease activity (reversible features), damage (irreversible features), health related quality of life (HRQOL) and adverse events.[1]

The US Food and Drug Administration (USFDA) in the 2010 guidelines have included the following as outcome measures for SLE trials—disease activity, damage, SLE flares, concomitant corticosteroid use, patient-reported outcomes, and biomarkers.[1]

Outcome Measures

Thorough history, physical examination, and laboratory findings help to assess SLE disease activity and efficacy of treatment in the clinic.

Laboratory tests like presence of anaemia, leucopoenia, thrombocytopenia, hypocomplementemia, elevated erythrocyte sedimentation rate, a rise in anti-double-stranded DNA antibody levels, or any combination of these features may be associated with increased SLE disease activity. Proteinuria, hematuria, urinary casts, and a rise in creatinine levels indicate active renal involvement.

Disease Activity Indices

The following disease activity indices (Table 10B.1) and its modifications are used in trials and clinical practice. They capture organ specific or global disease activity. Disease activity indices measure reversible clinical features amenable to therapy and not damage which is usually irreversible.[1,2]

Disease Damage Indices

As SLE has a relapsing remitting nature, damage in various systems accumulate over time, both from the disease and concomitant use of immuno-

Table 10B.1: Composite disease activity measures in SLE

Disease activity measure	
The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)	24 questions assessing the physical findings and laboratory values of SLE Weighted across organ systems
1. SLEDAI	SLEDAI measures manifestations over the past 10 days
2. Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)	SELENA-SLEDAI and SLEDAI-2K score manifestations over the past 28 to 30 days
3. SLEDAI 2000 (SLEDAI-2K)	
4. SLEDAI-2K Responder Index 50% (S2KRI-50)	Is found to reliably detect 50% improvement in the 24 descriptors
The British Isles Lupus Assessment Group (BILAG) Index 1. BILAG classic 2. BILAG 2004 modification	Measures disease activity in individual organ systems based on an intent-to-treat principle The BILAG and BILAG 2004 are the only indices that scores features as: Improved, the same, worse, or new rather than as present or absent Evaluates activity in 9 organ systems occurring within the past 4 weeks versus the previous month Not generally used in clinical practice
The Systemic Lupus Activity Measure (SLAM) SLAM-R modification	Based on signs and symptoms observed over the past 4 weeks, with weighting of more severe clinical manifestations. It is the only measure which scores patient-reported symptoms of fatigue
The European Consensus Lupus Activity Measure (ECLAM)	Scores clinical and laboratory manifestations of SLE over the past 4 weeks

suppression.[1,2] Damage accrual is measured using the SDI (Table 10B.2).

Table 10B.2: Measuring damage in SLE

Damage index	
The Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology Damage Index (SDI)	12 organ systems are assessed to capture damage that has been present for ≥6 months

Health Related Quality of Life (HRQoL)

HRQoL is the impact of disease on the physical, social, psychological and mental aspects of health. Various patient reported outcome measures are shown in Table 10B.3.

Composite Responder Indices[1]

These composite indices (Table 10B.4) have been developed as endpoints for new treatment molecules in SLE. These indices include multiple outcome measures as defined by each trial, thus it increases the power of the study.

Conclusions

- Measuring disease activity, damage and HRQoL is essential in SLE.
- Clinical examination and laboratory tests remain basic to assessing disease activity.
- Damage accrual is major problem in SLE and should be monitored carefully.
- Indices used in clinical trials, help access the treatment efficacy of new drugs.

Table 10B.3: Patient reported outcome measures (HRQoL)

Generic	
The medical outcomes short form 36-item (SF-36) survey	It is important to assess HRQoL in SLE, especially since it has clearly been shown that disease activity, damage, and HRQoL are independent of each other and thus reflect different domains affected by disease.
SLE specific	
Lupus quality of life tool (Lupus QoL) Quality of life in SLE (L-QoL) Systemic lupus erythematosus Quality of life (SLE-QoL) Lupus patient-reported outcome tool (Lupus PRO) Lupus impact tracker	Both generic and disease-specific measures have been used in RCTs in SLE.

Table 10B.4: Responder indices used in randomized controlled trials

Responder index	
Responder index for DHEA trials	Responder indices define patients who have improved with treatment versus those who have not. It usually includes multiple outcome measures.
Response Index for Lupus Erythematosus (RIFLE)	
SLE Responder Index (SRI)	Apart from the specific components defined within each index, "responses" first require that patients are not "treatment failures", as defined prospectively in each trial.
British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) endpoint	

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10C. OUTCOME MEASURES IN SCLERODERMA

Taral Parikh

Measuring Disease Activity and Severity

Scleroderma or systemic sclerosis (SSc) is a connective tissue disease which can affect multiple organ systems.

Since disease activity[1] is defined as those features which are variable over time or has potential to reverse spontaneously or with therapy (e.g. tendon friction rubs, acute-phase reactants, inflammatory polyarthritis, inflammatory myositis), it warrants treatment. While, damage is generally irreversible and increases as the disease progresses (e.g. calcinosis, end-stage pulmonary fibrosis, deformities), here immunosuppression may be less effective.

Thus, assessment of disease activity and severity[2,3] (Table 10C.1) is important in SSc as in any other rheumatic disease, as treatment options are limited and also they carry significant toxicity.

Both activity and damage contribute to disease severity; early in SSc, activity is prominent, but as the disease advances, damage is more likely to accumulate.

Outcome Measures in SSc

Although many novel outcome measures are currently in development those outcome measures that are feasible, reliable, and valid in clinical trials and routine clinical care are listed in Table 10C.2.

Conclusions

These outcome measures, developed for each organ system, helps to decide whether a particular organ is worsening requiring a close surveillance and need for scaling up therapy. For example, if %FVC is less than 70% or HRCT extent of ILD is more than 20%, it indicates need for treatment of the ILD or rapid rise in MRSS would suggest rapidly progressing disease and need for active intervention.

Table 10C.1: Outcome measures to assess—disease activity and severity

A. Disease activity in SSc	*B. Disease severity in SSc*
The European Scleroderma Study Group* Composite Index[2]	Disease severity includes both disease activity and damage.
Includes (clinical examination, patient assessment of activity—last month, laboratory measures, and percent predicted diffusing capacity of the lung for carbon dioxide—%DLCO)	The revised Medsger severity index 3 identifies 9 organ systems (general, peripheral vascular, skin, joint/tendon, muscles, gastrointestinal tract (GIT), lung, heart, and kidney).
It is scored on a 0 (no activity) to 10 (severe activity) basis, with the greatest weight assigned to deterioration of the relevant organ system as evaluated by the patient with respect to the previous month.	Each system is scored from 0 (uninvolved) to 4 (end-stage disease).

*The European Scleroderma Study Group Composite Index, can be used to assess disease activity in practice, but still awaits validation.

Table 10C.2: Instruments for SSc outcome measures[4]

Instruments	*Remarks*
A. Skin	
Modified Rodnan skin score (MRSS)	Is a measure of skin thickness in SSc Used as the primary outcome measure in clinical trials Surrogate measure of disease severity and mortality in patients with diffuse cutaneous SSc May improve with time even without treatment is a limitation
Durometer	Hand held device—measures hardness of skin Costly

(*Contd.*)

Table 10C.2: Instruments for SSc outcome measures[4] (*Contd.*)

Instruments	*Remarks*
B. Musculoskeletal	
Tendon friction rubs	Associated with a higher likelihood of the development of diffuse cutaneous SSc and more severe disease
Tender joint count	Active arthritis
Serum creatine phosphokinase (CPK)	Myositis
Cochin hand function scale	3 scales—dexterity, rotational movement, and flexibility of the first three fingers
Hand mobility in SSc	9 items that assess hand function
Mouth handicap in systemic sclerosis scale	
C. Cardiac	
Echocardiogram with Doppler imaging	Most widely used for diagnosis and staging of PAH, evaluation of cardiac dimensions and valvular abnormalities Has disadvantages in using for diagnosis, may be used as screening tool
Right-sided heart catheterization (RHC)	RHC remains the gold standard for diagnosing PAH, for trials and clinical practice Helps identify the cause of PAH and response to therapy
6-Minute walk test (6MWT)	6MWT is currently the most widely used primary endpoint for studies investigating SSc-related PAH. Pain and musculoskeletal involvement can influence the 6MWT, and it is not always solely reflective of changes in cardiopulmonary involvement when used in patients with SSc.The 6MWT is not sensitive to change in SSc-ILD. It should not be used as a screening measure but may provide prognostic information in patients with SSc-PAH.
Borg dyspnoea index	
D. Pulmonary	
Pulmonary function test with diffusion capacity (PFT)	% FVC has been used as the main parameter of restrictive lung disease and %DLCO for pulmonary vascular disease % FVC used in clinical trials % DLCO is sensitive but not specific for SSc-ILD or SSc-PAH and can decline in both diseases
High-resolution computed tomography (HRCT)	HRCT of the lungs has two key roles in SSc: 1. Detection and staging of baseline severity 2. As a surrogate endpoint or more accurate measure of serial change.
Validated measure of dyspnoea	The Mahler dyspnoea index is a patient-reported outcome measure and has been used in SSc trials to assesses the level of dyspnoea
Breathing VAS from the SSc HAQ	Allows patients to assess their degree of difficulty in performing daily activities because of shortness of breath on a continuous 100 mm scale

(*Contd.*)

Table 10C.2: Instruments for SSc outcome measures[4] (*Contd.*)

Instruments	*Remarks*
E. Gastrointestinal	
Gastrointestinal VAS from the SSc HAQ	GIT VAS assesses interference in daily activities on a continuous 100-mm scale
UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0	A 34-item instrument, is a validated patient reported outcome measure to assess GIT symptoms and health-related quality of life (HRQOL) in patients with SSc
Body mass index	
F. Renal	
Estimated creatinine clearance	Outcome measures for diagnosis and assessing outcomes in patients with scleroderma renal crisis (SRC)
Systolic and diastolic blood pressure	
Serum creatinine	
G. Raynaud's phenomenon	
Raynaud's condition score (RCS)	RCS is an outcome used in clinical trials and is calculated by summing the daily score over a period of 1 or 2 weeks
Number of attacks as reported by the patient	
Duration of attacks	
Raynaud's VAS from the SSc HAQ	
H. Digital ulcer	
Active digital tip ulcer count on the volar surface	
Digital ulcer VAS from the SSc HAQ	
I. Biomarkers	
Acute-phase reactants	Erythrocyte sedimentation rate and C-reactive protein are associated with disease activity and predict mortality
Serum BNP/NT-Pro BNP	NT-Pro BNP has recently been shown to predict incident cases of PAH
Vascular (von Willebrand factor [vWF]), T-cell (soluble IL-2 receptor [sIL- 2R]), B-cell (autoantibodies), and fibroblast (type III procollagen N-terminal peptide pro-peptide – PIIINP)	Have been proposed as biomarkers for SSc
Transforming growth factor-β-regulated and interferon-regulated genes	
Novel markers include myofibroblast staining, four-gene marker	
J. Patient reported outcome measures	
Short form 36 (SF 36)	
Health Assessment Disability Index (HAQ DI)	
UK Functional Score (UKFS)	
Patient-Reported Outcomes Measurement Information System	
Preference-based measures for health-related quality of life: The short form 6D	

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10D. OUTCOME MEASURES IN SPONDYLOARTHRITIDES

Anuj Shukla

INTRODUCTION

The outcome measure of spondyloarthritis (SpA) can be broadly divided into activity-measure (for example, BASDAI/ASDAS) or damage-measure (for example, BASMI). Arthritic diseases particularly affect the functions of an individual due to pain and limitation of joints, thus demanding for a third important outcome-measure called the functional-outcome-measures (FOMs).

Activity measures a component of disease that can improve with an effective treatment and thus is the best immediate measurement of therapy-responsiveness. Damage measures the components that cannot improve with a treatment and thus cannot assess the immediate effects of the therapy. But it can still assess long-run effects as a measure of accruing damage. Thus, damage measures provide a hard indicator of failure or success of a therapy. Function depends on activity as well as damage, both contributing to the limitation of movement. Thus FOMs partially improve with an effective treatment (activity component) but the damage component does not improve leading to limitation of functions. Thus it cannot precisely assess the response to the treatment. This makes BASMI, a FOM, just a measure of damage after the activity is completely controlled with proper treatment.

The outcome measures can be a single-component-measure or a composite-measure in order to give a single comprehensive value to the disease outcome. Outcome measures have four facets that is patient-based (pain, EMS), physician-based (TJC, SJC, range of movement), laboratory-based (ESR, CRP) and imaging-based (X-rays and MRI). For example, BASFI and BASMI are respectively patient-based and physician-based composite FOMs. Patient-based outcome measures in addition to disease process are affected by individual perception of pain and emotional well-being, which varies among patients. These are soft, subjective and may not exactly reflect the improvement in disease process with an effective therapy but on the other hand cannot be ignored, as the ultimate goal of therapy is patient satisfaction. On the other side, physician-based, lab-based and imaging based measures are increasingly hard, objective measures precisely reflecting the effect of therapy on disease process but may not exactly translate into patient improvement. Thus a good composite outcome measure should have a fine balance of all these four-facets of outcomes. While using all these four-facets of outcomes, the final composite outcome measure must still have good validity, reliability, responsiveness and feasibility (The OMERACT filter) for clinical and research utility.

The spondyloarthritis are currently classified as axial and peripheral. Axial includes classical ankylosing spondylitis (AS) with X-ray evidence of sacroiliac joint involvement and limitation of lumbar and thoracic spine and a major new group of non-radiographic axial-SpA (axSpA) (based on MRI and HLA-B27 with other features). Peripheral SpA (pSpA) includes patients suffering from peripheral arthritis with either HLA-B27 positivity or other typical clinical features of SpA, the major group being undifferentiated spondyloarthritis in the earlier classification. Arthritis associated with psoriasis and inflammatory bowel disease although have many clinical overlapping features, are better classified separately as Psoriatic arthritis (PsA) and enteropathic arthritis. The vast majority of assessment tools have been developed for AS and PsA.

Outcome measures in SpA will be discussed in three categories:

1. Axial spondyloarthritis (axSpA)
2. Non-psoriatic peripheral SpA (pSpA)
3. Psoriatic arthritis (PsA)

Outcome Measure in axSpA

Disease activity in axSpA is a composite measure of clinical features, laboratory parameters and overall impression of patient and the treating physician. The challenge of including all these measures in a single composite index is complicated by the need for ensuring proper validity, reliability, responsiveness and practical feasibility of calculating the index in a busy outpatient department. The Assessment of SpondyloArthritis International Society (ASAS) founded in 1995 has published many landmark papers on outcome measures in SpA.[1,2,3] Major outcome measures of axSpA are summarized in Table 10D.1 and Box 10D.1.

Table 10D.1: Outcome measures for axial-spondyloarthritis (axSpA)

Outcome measure domains	*Outcome measures*	*Year*	*Improvement*	*Issues*
Activity	BASDAI	1994	Time tested, valid, reliable composite index for assessment of disease activity in AS. Does not require any laboratory tests. BASDAI scores are the current employed criteria used to decide for biological drug therapy in AS.	Since they are patient self-reported parameters so scores are affected by patient mood and education, measures only part of disease activity, lacks specificity to inflammatory process, does not weigh individual components.
	ASDAS (ASDAS-CRP is preferred over ESR)	2009	Better construct validity and discrimination than BASDAI, includes lab parameters with less redundancy between individual components and are weighed variably	Requires ESR, CRP. Requires scientific calculator or internet connection*
	SASDAS	2012	Simplified version of ASDAS (summed variables) no need of calculator, same parameters as ASDAS, includes ESR (which is less expensive)	45% patients classified by ASDAS-CRP as moderate disease activity were classified differently by SASDAS. Requires validation in larger cohorts.
Functional	BASFI	1994	Largely supplanted earlier functional indices, underwent rigorous psychometric analysis and has shown good reproducibility	Measures only physical functions, performance for peripheral SpA is poorer compared to HAQ-S
	ASAS-HI	2011	A linear composite patient-reported measure containing 17 dichotomous queries addressing pain, emotional functions, sleep, sex, mobility, self-care, community life and employment	Further studies of its psychometric properties are required prior to its use in clinics and trials It assesses functioning based on objective description and does not assess the subjective appraisal of the problems
Quality of life	ASQoL	2003	A well validated composite patient-reported measure containing 18 dichotomous queries Has excellent scaling and psychometric properties	QoL perspective is based on subjective appraisal of the impact of the disease on life, does not give objective idea of whole range of common difficulties faced by patients
Spinal mobility (Activity + damage)	BASMI	1995	A composite measure including cervical rotation, tragus to wall distance, lumbar side and forward flexion and intermalleolar distance; BASMI-linear (2008) showed better responsiveness than both BASMI-10 step and BASMI-2 step score in the golimumab trial	Not a pure measure of spine mobility as includes intermalleolar distance, does not include chest expansion. There is room to develop new composite scores that may differ from current BASMI

(*Contd.*)

Structural damage (radiological)	mSASSS	2005	Quantification of structural spinal changes in AS using lateral X-ray of cervical and lumbar spine	Very low sensitivity to change, does not include thoracic spine and does not assess inflammation activity. Newer scores being developed are the RASSS which also includes assessment of lower thoracic spine and only osteoproliferative changes are scored, and MRI-based scoring-system.

Abbreviations: AS—Ankylosing spondylitis, SpA—spondyloarthritis, ASAS—Assessment of Spondyloarthritis international Society, ASDAS—AS disease activity score, SASDAS—Simplified ASDAS, BASDAI—Bath AS disease activity index, BASMI—Bath AS metrological index, BASFI—Bath AS functional Index, ASQoL—AS quality of life, ASAS-HI—ASAS health index, mSASSS—Modified Stokes AS Scoring system, HAQ-S Health assessment questionnaire modified for SpA, RASSS—Radiographic AS scoring system

*ASDAS can be calculated on line http://www.asas-group.org/clinical-instruments/asdas_calculator/asdas.html

Box 10D.1 Disease activity slabs, improvement and flare scores for axial-spondylo-arthritis (axSpA)

Disease activity scores

ASDAS-CRP scores

- Inactivity disease—<1.3 (defining remission better than ASAS partial response as it included BASFI)
- Moderate disease activity—1.3 to <2.1
- High disease activity—2.1 to <3.5
- Very high disease activity >3.5

Improvement scores

- Clinically important improvement—at least 1.1 unit change in ASDAS-CRP
- Major improvement—at least 2 units change in ASDAS-CRP
- Other improvement criteria used to define improvement are ASAS20, ASAS40, BASDAI50 and delta BASDAI of at least 2 units

Definition of Flare in axSpA

- An increase of at least 1.3 in ASDAS-CRP or 2.1 in BASDAI has been defined as a flare in axial SpA

Outcome Measures for Non-psoriatic Peripheral Spondyloarthritis (pSpA)

ASDAS-CRP and BASDAI as well as single item measures like Patient Global Assessment (PGA) and Physician Global Assessment (PhGA) all perform equally well and better than the other single measures like ESR and CRP, in detecting disease activity in pSpA and differentiating treatment arm from the placebo arm.[4] But it has been shown that these composite measures fail to assess different aspects of disease in pSpA, for example, enthesitis and dactylitis. This is shown by their poor correlation with PGA and PhGA suggesting that aspects of disease activity considered important by physicians or patients are not captured in these composite measures. This calls for derivation of a new composite measure specific for pSpA excluding PsA.

The ABILITY-2 trial of adalimumab in pSpA used a new disease specific response criteria termed Peripheral SpondyloArthritis Response Criteria (PSpARC-40) as the primary end point. Both response criteria, disease specific PSpARC-50/70 and disease non-specific ACR-20 response criteria performed best in terms of discriminative ability in both the trials of anti-TNF therapy in pSpA. The performance of axial-specific response criteria ASDAS and BASDAI50 was worse compared to the above two. This is likely because the cut-off levels of improvement in ASDAS response and BASDAI50 has been tested in axSpA and not in pSpA and thus failed to capture the improvement.

Outcome Measures for Psoriatic Arthritis (PsA)

Assessment of PsA is complicated by the fact that the disease has heterogeneous manifestations from peripheral arthritis to involvement of skin, spine, enthesis, dactylitis and nail involvement.[5] The most important question that arises is whether to include all these in a single outcome measure or to assess them separately. The variation is not only limited to manifestations but these clinical features also respond varyingly to various immunomodulation. Thus making a single outcome measure including peripheral arthritis, skin and spine involvement increases heterogeneity of responsiveness and decreases discriminative power of the score while

assessing different therapies. This makes a case in favor of assessing peripheral arthritis, spine involvement and skin separately to allow evaluating therapies that are effective for certain but not other manifestations of this heterogeneous disease.

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and *Outcome measures in Rheumatology* (OMERACT) has published 6 mandatory core outcome measures to be included in all clinical trials for PsA. These 6 single variables are peripheral joint activity, patient global and pain assessment, physical function, skin disease and quality of life. Spinal assessment, dactylitis, enthesitis, acute phase reactants, nail changes, fatigue, structural damage and imaging were not included in the core set of obligatory assessment and were included in outer circle and as research agenda.

Most of the current validated and frequently used composite disease activity state measures and response criteria are borrowed from other more common arthritides, for example, *Disease Activity Score-28* (DAS-28) and *European League Against Rheumatism* (EULAR) response criteria from RA. Peripheral arthritis in PsA is also heterogeneous varying from polyarthritis like RA to oligoarthritis, predominant DIP arthritis and monoarthritis. This makes a case against the use of RA based outcome measures using 28-joints involved commonly in RA. Another composite index initially developed for reactive arthritis is *The Disease Activity Index for PSoriatic Arthritis* (DAPSA). It uses 66/68 joint count and is a summation of five disease activity variables: Tender and swollen joint count (TJC, SJC), patient global and pain assessment on visual analogue scale 0–10, and CRP. The other two specific disease activity indices are *The Composite Psoriatic Disease Activity Index* (CPDAI) and *The Psoriatic Arthritis Disease Activity Score* (PASDAS). CPDAI has 5 domains: 66/68 joint count, dactylitis, enthesitis, skin disease and spine disease. Each domain is assessed for activity and quality of life or health assessment questionnaire and given a score of 0 to 3. The single domains are then summarized to give a final score from 0 to 15. In a modified version of CPDAI, spine assessment has been dropped, thus resulting in a maximum score of 12. Another version of CPDAI includes joint count, enthesitis and dactylitis (CPDAI-JED), but excludes skin assessment. PASDAS includes physician and patient global assessment, 66/68 SJC/TJC, physical component score of Survey-Short Form-36, enthesitis, dactylitis as well as CRP. Comparison of various indices is shown in Table 10D.2.

Among the response criteria for PsA, *European League Against Rheumatism* (EULAR) criteria based on DAS-28 improvement performed better than 20/50/70 ACR criteria and both were better than more disease specific *Psoriatic Arthritis Response Criteria* (PsARC). PsARC includes 66/68 SJC/TJC, physician and patient global assessment both on a 0–5 Likert rating scale. 30% improvement in joint count and 1-point reduction in Likert scale is defined as response. PsARC excludes acute phase reactants and pain assessment. Response criteria help to assess change in activity from baseline, thus

Table 10D.2: Outcome measures (disease activity) for psoriatic arthritis (PsA)

Outcome measures	*Advantages*	*Disadvantages*
Disease activity score-28 (DAS-28)	Proven to be highly responsive and discriminative instrument in PsA trials	Does not include joints which are commonly involved in PsA, for example, DIP, foot and ankle
Disease activity for psoriatic arthritis (DAPSA)	Applies 66/68 swollen and tender joint count, exhibits good validity responsiveness and discrimination for PsA patients, shows correlation with ultrasound assessed synovitis	Does not include enthesitis, dactylitis, spine and skin frequently involved in PsA
Composite psoriatic disease activity index (CPDAI)	Disease specific includes all the aspects of PsA, for example, spine and skin involvement	Needs validation in trials
Psoriatic arthritis disease activity score (PASDAS)	PsA specific compound score does not include skin and spinal assessment	Needs validation in trials

improvement with therapy but do not allow the quantification of disease activity.

Indian Perspective for Outcome Measures in SpA and PsA

There are multiple problems with using these outcome measures in Indian routine clinical practice.

1. Low education level with less health related awareness makes it extremely difficult to scale the disease on visual analogue scale of 0–10 by our patients. In fact most of the patients usually scale it as 0, 5 or 10 with 5 being the most common score. This markedly affects the assessment of therapeutic responsiveness of most of these patient-oriented-scores including ASDAS and BASDAI. Patient assessment of global disease activity and pain on visual analogue scale is often the same, as patients are hardly aware of swollen joints or fatigue. Early morning stiffness term is often difficult to understand, which is again confused with pain.
2. SpA in comparison to rheumatoid arthritis (RA) is complicated as it has many components to assess the disease, for example, entheseal assessment, axial and peripheral joint assessment, so it is difficult to make a single composite measure for different aspects of disease activity like DAS-28 in RA. Measuring different aspects of the disease with different outcome measures is difficult in busy Indian outpatient departments.
3. Complicated more for PsA where Psoriasis Area and Severity Index (PASI) for skin involvement is time consuming. Physician training for skin assessment is limited and there is poor interaction between dermatologists and rheumatologists. Due to socio-cultural influences, examining ladies is often incomplete due to reluctance in undressing.
4. In addition to outcome measures there are many other problems related to diagnosis of Axial-SpA, for example, marked delay in diagnosis, use of costly tests like HLA-B27 (PCR) and MRI in diagnosis with limited availability, unsatisfactory management due to cost of anti-TNF therapy. It becomes futile to keep measuring outcome measures in every follow up OPD without giving appropriate therapy.

Altogether there are multiple challenges in diagnosis, management and assessment of outcome measures in SpA and PsA. The classification criteria have recently evolved, the definition of optimum treatment and their targets are likely to evolve with more therapeutic options in the future and so the need for better outcome measures with more construct validity, discriminative capabilities in research trials and feasibility in routine clinical practice.

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10E. OUTCOME MEASURES IN PRIMARY SJÖGREN'S SYNDROME

Nibha Jain, Sapan Pandya

Primary Sjögren's syndrome (pSS) is a systemic disorder extending beyond the exocrine glands. The disease spectrum includes sicca symptoms alone or in combination with systemic extra glandular manifestations.[1]

Clinical features include:

1. Sicca, pain and fatigue affecting almost all
2. Systemic manifestations affecting 20–40%

The natural course of pSS is assessed with respect to three aspects:

1. Disease activity (potentially reversible with intervention) with flares in between
2. Disease damage (irreversible and can increase with time)
3. Subjective findings (patient's perception of the symptoms of the disease).

The need for outcome measures in pSS arose out of interest in conducting clinical trials, including RCTs.[2] Assessments of disease activity was essential for inclusions in clinical trials especially when using biologic or other immunosuppressive therapies, and determining end points was needed. At the same time it ought to be useful for daily clinical practice.

1. Instruments for Measuring Disease Activity (Table 10E.1)

Activity indices are designed for patients with systemic complications of primary pSS. They are based on physician's judgment and include multiple domains (i.e. organ systems). The EULAR Sjögren's syndrome disease activity index (ESSDAI) had domains which encompassed all organ systems involved in the disease, and was agreed upon by a large number of experts.[3] Each domain is rated according to degree of activity with final score calculated as sum of all weighted scores. Domains include fatigue, constitutional symptoms, arthritis, muscle, gland swelling, and skin, pulmonary, renal, neurological and hematological domains.

Constitutional: After excluding infectious causes, symptoms of fever night sweats and weight loss graded according to severity.

Lymphadenopathy: Exclusion of infection followed by assessment of lymph node involvement in any nodal region or inguinal region and/or splenomegaly (clinical or proven by imaging). Current B-cell malignant proliferative disorders are taken as high grade.

Glandular: After exclusion of calculi or infection, salivary gland swelling limited to parotids or submandibular with lacrimal swelling.

Articular: Exclusion of osteoarthritis, involvement of arthralgia or inflammatory arthritis with 28 joint counts.

Cutaneous: Presence of erythema multiforme, cutaneous vasculitis including urticarial vasculitis, or purpura, or subacute cutaneous lupus or ulcers related to vasculitis.

Pulmonary: Evidence of interstitial lung disease with any involvement of breathlessness or cough and lung function tests.

Renal: In the form of tubular acidosis or glomerular involvement with proteinuria, hematuria and reduced GFR or cryoglobulinemia.

Muscular: Assessment of myositis with clinical grading of power, EMG, biopsy and elevated CK levels.

Peripheral nervous system (PNS): Cranial nerve involvement of peripheral origin (except trigeminal (V) neuralgia), pure sensory axonal polyneuropathy shown by NCS, sensory neuropathy with presence of cryoglobulinemic vasculitis, ganglionopathy with symptoms restricted to mild/moderate ataxia, chronic inflammatory demyelinating polyneuropathy (CIDP) with mild functional impairment.

CNS: Rated as cranial nerve involvement of central origin, optic neuritis or multiple sclerosis like syndrome with symptoms or proven cognitive impairment, cerebral vasculitis with cerebrovascular accident or transient ischemic attack, seizures, transverse myelitis, lymphocytic meningitis.

Hematological: In the form of autoimmune cytopenias.

Biological: This domain takes into account the clonal component and/or hypocomplementemia (low C4 or C3 or CH50) and/or hypergammaglobulinemia or high IgG level and presence of cryoglobulinemia.

In 2016 a clinical index (ClinESSDAI) without the biologic domains was devised (Table 10E.1) which was found to correlate well with the ESSDAI.[4] This could be useful especially in the practice setting where patients do not always get investigations done.

2. Measuring Damage in pSS (Table 10E.2)

To assess the accumulated permanent damage in various organs and systems the Sjögren's syndrome damage index (SSDI) was developed.[5] Damage indices become relevant as the duration of illness gets longer due to increasing damage accrual as seen with lupus. The SSDI was developed by the British Sjögren's Group and was based on the SLICC/ACR for lupus. It included 3 main domains—ocular, oral and systemic with the last broken into further organ systems as shown in Table 10E.2.

3. Subjective Measure (Table 10E.3)

The original subjective symptom outcome measure PROFAD[6] (had 8 domains which were scaled on a Likert scale) has been now reduced to just 3 domains (fatigue, dryness and musculoskeletal pain) called the ESSPRI (Table 10E.3 and Fig. 10E.1).[7] Patients with pSS have fatigue and discomfort as major components which can be disabling. Subjective measures take into account this component without

Table 10E.1: Activity index of pSS

Activity index	*Remarks*
SCAI (SS clinical activity index) Exhaustive but too complicated to use in clinical practice	• 10 domains: Fatigue, constitutional symptoms, arthritis, muscle, gland swelling, skin, pulmonary, renal, neurological and hematological domains • Items are recorded as 0(absent) 1(improving) 2(same) 3(worse) and 4(new)
SSDAI (Sjögren's syndrome disease activity index) Simple test but lacks exhaustiveness	• 8-domain global score • Final score >5 suggestive of active disease
(ESSDAI) EULAR SS disease activity index (2009)[3]	• Based on physician's judgment • 12 domains, each is divided in 3–4 levels according to their degree of activity • The final score between 0 and 123 • 0 indicating no disease activity • Any feature stable for 12 months should be taken as damage • Validated in large independent cohort; reproducible • Correlates well with biomarkers like BAFF levels • Thresholds for disease activity and minimal clinically important improvement defined (e.g. ESSDAI ≥5, moderate disease and ≥3 needed for MCII)
ClinESSDAI[4]	• Exclusion of the biological domain of ESSDAI • Comparable ESSDAI with slight lower sensitivity to change • Avoids collinearity of data in biological studies • Can be used in absence of laboratory investigations

Table 10E.2: Measuring damage in pSS

Damage index	*Remarks*
SSDI (Sjögren's syndrome damage index)[5]	• Assess the combined permanent systemic global score on 3 separate scales (ocular, oral and systemic damage). Maximum score was 1 for each item and total items were 27
SSDDI (SS disease damage index)	• A global score including exocrine and non-exocrine features • Not very sensitive to change and generally not used in practice

Table 10E.3: Subjective measure of Sjögren's syndrome

Subjective measure	*Remarks*
PROFAD (Profile of fatigue and discomfort)[6]	• Psychometric instrument • Somatic and mental fatigue domain with the fatigue, arthralgia and vascular dysfunction
PROFAD-SSI (Profile of fatigue and Discomfort: Sicca symptoms inventory)	• 64 questions in eight 'domains' • Scored on an 8-point (0–7) on Likert scale. • Shorter version with 19 questions available.
Xerostomia inventory (XI)	• 11 questions that address xerostomia symptoms in daily activities
ESSPRI (EULAR Sjögren's syndrome patient reported index) (2011)[7]	• Scores 1 to 5 with final score range 11–55 • Patient-administered questionnaire • Evaluates subjective symptoms • Sensitive to change and used in trials—validated in prospective international cohort • Correlates well with quality of life measures • Poorly correlated to ESSDAI

1. How severe has your dryness been during the last 2 weeks?

No dryness	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Maximal imaginable dryness

2. How severe has your fatigue been during the last 2 weeks?

No fatigue	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Maximal imaginable fatigue

3. How severe has your pain (joint or muscular pains in your arms or legs) been during the last 2 weeks?

No pain	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Maximal imaginable pain

Fig. 10E.1: The EULAR Sjögren's syndrome patient reported index (ESSPRI)

any measure of damage. ESSPRI and ESSDAI are complementary as outcome measures in clinical trials and hence a clear definition of which component is being tested is needed while designing them.

4. Responder Indices (Table 10E.4)

Sjögrens syndrome responder index (SSRI) was devised in the TEARS trial (Tolerance and Efficacy of Rituximab in Sjögren's syndrome) and is similar to the SLE responder index.[8] This is particularly useful when assessing treatment response to costly treatments as biologics.

5. Measure of Health Related Quality of Life (HRQoL)

Measure of HRQoL is an important but difficult issue with several factors contributing to the impairment of the HRQoL in pSS. The disease activity, accumulated damage with disease-specific issues such as dryness, chronic pain and fatigue all contribute to it. Since no disease-specific HRQoL index exists, the most widely used tool in pSS has been the short form 36 (SF-36).

Conclusion

Since Sjögren's syndrome is one of the diseases with a lot of subjective overlay with the objective symptoms, use and application of outcome measures which can gauge disease activity (both symptoms and signs) versus damage become very relevant in today's era where more and more biologic therapies are being used early in diseases. At the moment, the ESSPRI and ESSDAI are the most useful measures and both are recommended to be used in clinical trials as they complement each other. In the practice setting, ESSPRI and ClinESSDAI can

Table 10E.4: Responder indices

Responder index	*Remarks*
SSRI (SS responder index)[8]	• Composite index with five outcome measures: VAS fatigue score, VAS oral dryness score, VAS ocular dryness score, unstimulated whole saliva flow and ESR • Includes both subjective and objective measures • SSRI-30 response is defined as a 30% improvement in at least two of the five outcome measures

be easily used. We recommend the latter as a bare minimum in our country if we were to contribute to global Sjögren's data from the subcontinent.

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10F. OUTCOME MEASURES IN VASCULITIDES

Piyush Joshi

INTRODUCTION

Systemic vasculitides can be divided into 7 groups according to the 2012 International Chapel Hill Consensus Conference (CHCC 2012) on the Nomenclature of Vasculitides.[1] An uncommon incidence with protean presentations makes deriving outcome measure a difficult task accomplish. Relapsing nature of the disease, e.g. in Granulomatosis with polyangiitis make it essential to assess disease activity and damage judiciously. Disease activity measures are available only for Takayasu's arteritis and ANCA associated vasculitis.

Large Vessel Vasculitis (LVV)

Takayasu's arteritis and Giant cell arteritis (GCA) are not uncommon diseases. Despite this, no outcome measure is still validated for GCA. Most outcome measures available are for Takayasu's arteritis. Following things are taken into account while formulating outcome measure for LVV like pulse loss, claudication, organ damage (CNS, heart), physician global index, acute phase reactants and imaging modalities. Among laboratory measures ESR (erythrocyte sedimentation rate) and CRP (C reactive protein) can be used as markers of inflammation. Their correlation with disease activity has been poor along with not good negative predictive value.[2] No mortality outcome measures are available.

In a study from the National Institute of Health (NIH) by Kerr et al. (presence of constitutional symptoms, new bruits, APR, or new angiographic features), is commonly applied in studies of Takayasu's arteritis.[2] The Birmingham Vasculitis Activity Score (BVAS) documents evidence of active vasculitis with a 1-page form.[3] Although designed to apply to all vasculitides, BVAS is mostly used in therapeutic trials of ANCA-associated vasculitis and is validated for use in small- and medium-vessel vasculitis. However, most of the 11 organ systems in BVAS are not involved in Takayasu's arteritis.

Disease Activity Measures

1. DEI-TAK (Disease Extent Index for Takayasu's arteritis): This score quantifies extent of disease at assessment, considering features present in the past 6 months, whether new or persistent, with a maximum score of 75. Various domains assessed include: systemic, cutaneous, mucous membranes, eyes, ENT (ear, nose, and throat), chest, abdomen, renal (including hypertension), nervous system, genitourinary, and cardiovascular. Aydin et al. compared the DEI.Tak to the NIH criteria and found an agreement of 94% between the two criteria for detecting patients with active TA.[4] When compared with the physician global assessment (PGA) for activity, NIH criteria had an agreement of 74% compared to 68% for the DEI.Tak. because of inclusion of radiology. The DEI.Tak, like the NIH criteria, is sensitive enough to reflect changes in disease activity over time. The DEI.Tak has been validated in a cohort of Turkish patients.[4]

2. ITAS 2010 and ITAS 2010-A (Indian Takayasu's clinical activity score): It is an Indian modification of DEI.TaK score. Features of large vessel vasculitis were derived from the erstwhile DEI.Tak. ITAS2010 score features, which are new or worse in the past 3 months in the following domains: Systemic (malaise, weight loss greater than 2 kg, fever, myalgia, arthralgia, arthritis, headache), abdomen (severe abdominal pain), genitourinary (abortions), renal (systolic hypertension greater than 140 mm Hg, diastolic hypertension greater than 90 mm Hg), nervous system (stroke, seizures, syncope, and dizziness) and cardiovascular system. Cardiovascular features account for 33 of the 44 features considered.[5] The cardiovascular features include bruits, pulse inequality, new loss of pulses, claudication, carotidodynia, aortic regurgitation, congestive cardiac failure, cardiomyopathy, myocardial infarction, or angina. Features of diastolic hypertension, stroke, new pulse loss, bruits, pulse inequality, claudication, and carotidodynia are weighted to reflect a higher score. A maximum score of 51 is possible. ITAS2010 score of 4 or more is considered active. The ITAS-A is a modification of the ITAS 2010 to reflect acute phase reactants with additional score of 0–3 given based on acute phase reactants (ESR, if not available CRP is used). ESR (mm/h) [0–20 is 0, 21–39 score 1, 31–59 score 2 and >60 score 4] and CRP [<6 mg/dl is 0, 6–10 is 1, 10–20 is 2 and >20 is 3 points]. The score was

validated in 143 Indian patients from two different centres. The score was significantly higher in patients with active TA compared to those with grumbling or inactive disease as rated by the physician global assessment. ITAS-A predicted onset of new vessel involvement better than ESR or CRP alone.[6] This score suffers from certain limitations. Considering the fact that TA is a slow grumbling disease, it is reasonable to suppose that the disease may have been active for a number of years before it becomes clinically apparent.

3. Physician global index: It is a good measure to know disease activity but inter-rater correlation is poor.

4. CDUS (colour Doppler ultrasonography score)—Kolkata: It is one of the few imaging measures available for disease activity assessment. 19 sites are evaluated while doing this measure. Wall thickening, stenosis and flow pattern decides regarding activity of disease.

Other measures like VDI (vasculitis damage index), SF-36 (short form 36) and MAF (multifunctional assessment of fatigue) are good measures for disease damage, health related quality of life and fatigue assessment respectively, but still not validated in LVV.

Medium and Small Vessel Vasculitis

Disease activity in vasculitis measure severity and extent of inflammation in arterial tree. Various serum markers like ESR, CRP, MPO and PR3 levels (myeloperoxidase and proteinase-3), TNF (tumour necrosis factor) and vWF (von Willebrand factor) has been tried but without consistent results. Numerous markers such as haemoglobin, ESR, C-reactive protein, von Willebrand factor, ANCA titer, cytokines (e.g. TNF, IL-6) and soluble adhesion molecules have been studied, but none of them are able to provide a suitable measure of overall disease activity.[7] Any disease outcome measure should be able to differentiate low, medium and high disease activity, persistent disease and damage due to vasculitis. SO a composite tool comprising of history, clinical examination, laboratory investigations and imaging is ideal for such complex disease.

1. **Birmingham vasculitis assessment score (BVAS):** It is most commonly used and most widely studied outcome measure in systemic vasculitis and has been used in almost all prospective clinical trials.

   BVAS (original version)[8]

   It is developed by consensus expert opinion. It has 59 individual items in 9 categories that include history and/or examination, laboratory and radiology data. Every positive item should be due to vasculitis only and not any other cause. Items are weighed according to severity (e.g. mouth ulcers are given a score of 2, whereas alveolar hemorrhage is weighted 6). It has been validated in a group of 213 patients with vasculitis.[8]

   BVAS v.2

   It is a modification of original BVAS to generate two separate scores for new/worse disease and persistent disease. It has been used in validated to be used in EUVAS (European Vasculitis Society) trials.[9, 10]

   BVAS v.3

   It is a modification in v.2 with a reduction in the total number of items by omission or merging (although retaining the same overall maximum score).[3] It also combines new/worse versus persistent for all items rather than for each individual item. It has been validated and used in EUVAS clinical trials.[11, 12]

   BVAS-WG (BVAS for granulomatosis with polyangiitis)

   It is a BVAS modification specifically for granulomatosis with polyangiitis (Wegener's) but has also been used and validated in patients with microscopic polyangiitis in the RAVE trial.[13] In this version, total items are reduced to 34 instead of 56 in v.3 by removing less specific items for GPA like myalgia, weight loss, pulse loss, cardiomyopathy, valvular heart disease, loss of vision. Retro orbital mass and salivary gland swelling has been added.

   BVAS has construct and content validity. It has shown good intra- and inter-observer reliability, correlation with CRP, physician global assessment and old measures of disease activity like vasculitis assessment index (VAI). It helps in differentiating disease severity and making treatment decisions. Completion of all forms of the BVAS takes less than 3 min.

2. **Disease extent index (DEI):** It is a vasculitis disease activity measure index which comprises 11 categories. Each system is scored as combined and no individual weight given to more severe symptoms.

3. **Vasculitis damage index (VDI):** Evaluating extent of damage is very important in systemic vasculitis specifically to differentiating it from being persistently scored as disease activity in activity scores. OMERACT has endorsed 'damage' as part of the "Core set" of outcome measures trials in AAV. VDI is most widely used and validated instrument for this.[14] It was developed by consensus of international expert opinion and consists of 64 items grouped into 11 categories.[14] Any organ affection which is >3 months persistent and irreversible will be considered as damage. VDI has construct and content validity based on the fact that it was developed by expert opinion.[14] It takes less than two minutes to complete.
4. **FFS (five factor score):** Five-factor score (FFS) for systemic necrotizing vasculitides (polyarteritis nodosa [PAN], microscopic polyangiitis [MPA], granulomatosis with polyangiitis [GPA] and Churg-Strauss syndrome [CSS]) is used to evaluate prognosis at diagnosis.[15] It comprises renal insufficiency, proteinuria, cardiomyopathy, CNS and GI involvement. 5 years survival is 88% (FFS = 0), 74% (FFS = 1) and 54% (FFS >= 2).

Other Types of Vasculitis

No specific disease activity or damage indices are available for other types of vasculitides. DEI has been tried in cryoglobunemic vasculitis. BVAS for activity and VDI for damage can be used, but they are not validated for use in other vasculitides. SF-36 can be used for patient related outcomes. For patients with polyarteritis nodosa, FFS can be used to predict mortality.

Table 10F.1: Summary of outcomes measures in the vasculitides

Type of vasculitis	*Disease activity measures*	*Disease damage measures*	*Mortality measures*	*Others*
Large vessel vasculitis	DEI-Tak ITAS 2010 ITAS 2010A PGI CDUS	VDI		SF 36 MAF
Medium vessel and ANCA associated vasculitis	BVAS v.3 VAI DEI	VDI	FFS	SF-36
Other vasculitis	BVAS DEI	VDI	FFS	SF-36

Abbreviations: DEI-Tak, disease extent index for Takayasu's arteritis; ITAS 2010, Indian Takayasu clinical activity score 2010, PGI, physician global index; CDUS, colour Doppler ultrasonography score; VDI, vasculitis damage index; BVAS v.3, Birmingham vasculitis activity score version 3; FFS, five factor score; SF 36, short form 36; MAF, multifunctional assessment of fatigue; VAI, vasculitis assessment index; DEI, disease extent index

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10G. OUTCOME MEASURES IN OSTEOARTHRITIS

Piyush Joshi

Osteoarthritis (OA) is the most common arthritis worldwide. Degenerative nature of the disease leads to a poor response to treatment from any of the drugs including hyaluronic acid injections or slow acting symptomatic osteoarthritic drugs (diacerein, glucosamine sulfate, chondroitin sulfate, etc.), making it necessary to find a good outcome measure which can evaluate treatment responsiveness in osteoarthritis.

Understanding the derivation and validation of outcome measures and minimal clinically important differences (MCID) helps clinicians interpret data from published RCTs (randomized control trials). OARSI (Osteoarthritis Research Society International) and OMERACT (outcome measures in rheumatology) both advocated the use of core outcome measures which access pain and function in people with OA. Both patient-reported and performance-based outcome measures have been used to assess physical function but currently there is no gold standard measure in the assessment of OA. Absence of a consensus on the best performance-based tests makes it difficult to select the most feasible and reliable outcome measures for clinical and research purposes.[1]

Outcome measure included by OMERACT should show truth, reliability and discrimination.[2] Reliability is measured by evaluating the extent to which the same or similar scores are assigned the same valuation over multiple replications, reported as internal consistency coefficients (ICCs) (kappa coefficient value of >0.8 suggests good test retest reliability). "Truth" is assessment of an instrument according to its content, criterion, and construct validity. Content validity is extent to which instrument measures what it should with meaningful information. Criterion validity is how instrument fare to gold standard and construct validity is the extent to which an instrument correlates with other measures with which it should be related (convergent evidence) and is able to distinguish between groups (e.g. *between patients with or without a condition*—discriminate evidence). "Discrimination" is the ability of an instrument to detect changes over time.[1, 3]

For commonly used outcome measures, it is useful to understand whether improvements represent clinically important differences perceptible to patients or not. Determination of MCID (minimal clinically important difference) helps in setting goals and sample size calculations.

Table 10G.1 shows all the outcome measures for osteoarthritis available, while in the following discussion only important ones are discussed further. Outcome measures can be divided among patient reported and performance based outcome measures.

Patient Reported Outcome Measures

1. **Pain assessment:** Pain is often considered the most important symptom of OA. Pain can be accessed based on VAS (Visual analogue scale) (0–100 mm); Likert scale (5 point scale) and SF 36 (short form 36) bodily pain subscale can be used for objective measurement of pain. VAS scales are potentially more sensitive to change. People also advocate the use of a numeric rating scale for patients with language, cultural, or cognitive difficulties comprehending VAS scales. Short form-36 (SF-36) bodily pain subscale is considered as a brief measure of pain severity because of its reliability, validity, and the extensive normative data available for this instrument.
2. **Global disease activity by patient:** Patient global assessment question can be answered by the use of a Likert scale (very good, good, fair, poor, or very poor), or a 100-mm VAS. In general, VAS scores are more sensitive to change, physician's global assessment is not part of the obligatory OMERACT III core set, in part because of the disparity between patient and physician reported outcomes, but is recommended only as a supportive measure.
3. **Physical function assessment**

FOR KNEE AND HIP OA

WOMAC (Western Ontario and McMaster Osteoarthritis Index)[4, 5]: The WOMAC includes 24 questions in the following three sections: pain (five questions), stiffness (two questions), and

Table 10G.1: Outcome measures in osteoarthritis

	Outcome measures
Pain scale	1. Visual analogue scale (VAS) 2. Likert scale 3. SF-36 bodily pain subscale
Physical function scales	**Hip and Knee:** 1. Western Ontario and McMaster Osteoarthritis Index (WOMAC) 2. Hip injury and osteoarthritis score (HIOS) 3. Knee injury and osteoarthritis score (KIOS) 4. Oxford hip score 5. Oxford knee score 6. Le Quesne **Index Shoulder:** 1. American Shoulder and Elbow Surgeons (ASES) Standardized Shoulder Assessment Form **Hand OA:** 1. Australian/Canadian (AUSCAN) Osteoarthritis Hand Index 2. Disabilities of the Arm, Shoulder, and Hand (DASH) 3. Dreiser and Cochin Indices
General measures	1. Patient global assessment (PGA) 2. Health assessment questionnaire (HAQ) 3. Arthritis Impact management scale (AIMS and AIMS-2) 4. Osteoarthritis Global Index 5. Patient Reported Outcome Measurement Information System (PROMIS-29) 6. Short form-36 (SF-36) 7. Health related quality of life (HRQoL) 8. Work limitation questionnaire (WLQ)

physical function (17 questions). The WOMAC is completed using Likert 5-point (none, mild, moderate, severe, or extreme) or VAS (0 [no difficulty] to 100 mm [extreme difficulty]) scales and has been well validated. Test-retest reliability is 0.8 for physical function and 0.7 for pain. Overall truth, reliability, and discrimination were well demonstrated for the pain and physical function subscales across patient groups and types of interventions. Completion of the WOMAC requires approximately 5 minutes.

Hip Injury and Osteoarthritis Score (HIOS)

It is a WOMAC modification for hip. It is a 40 item self-report questionnaire with 5 subsets (pain, stiffness, QoL, daily activities and sports) on Likert scale.

Knee Injury and Osteoarthritis Score (KIOS)

It is a modification of WOMAC score for knee. A 42 item self-administered assessment of five outcomes: Knee related QoL (quality of life), activities of daily living, sports and recreation function, symptoms and pain on Likert scale 0–4.

Oxford Hip Score

12 point score on patient's pain and function on scale of 0–5, making a total score of 60.

Oxford Knee Score

12 point score on patient's pain and function on scale of 0–5, making a total score of 60.

Le Quesne Index[6]

The Le Quesne Index measures pain (five questions) and physical function, specifically maximal walking distance and activities of daily living (four items). In post arthroplasty patients, on comparing WOMAC with Le Quesne Index, WOMAC was more responsive. Total WOMAC and pain subscale scores had SRMs (Standardized response means) of 2.0 (knee) and 2.4 (hip) compared with 1.5 and 2.1, respectively.

Shoulder Osteoarthritis

American shoulder and elbow surgeons (ASES)[7]—standardized shoulder assessment form: It is a specific scoring system for shoulder OA. The ASES is a 100-point scale that consists of two dimensions: Pain and activities of daily living each worth 50 points.

Hand Osteoarthritis

Australian/Canadian osteoarthritis hand index[8]: The AUSCAN is formatted similarly to the WOMAC, including 15 questions regarding pain (five questions), stiffness (one question), and physical function (nine questions) answered by the Likert scale or VAS.[18] The AUSCAN was derived from face-to-face interviews with 50 patients with hand OA and is reliable, valid, and responsive. When evaluated against the health assessment questionnaire (HAQ), the Dreiser index (described later), and patient global assessment, significant correlations were evident.

Disabilities of the arm, shoulder, and hand (DASH): The DASH is a 30-item questionnaire assessing difficulties in performing activities specific to the upper extremity (21 items), symptom severity (five items), and impact on social activities, work, sleep, and self-image (four items). Items included in the DASH were chosen based on patient responses to sample queries in the US, Canada, and Australia.

Dreiser Index and Cochin Index: Dreiser index (for hand OA) and Cochin index (for rheumatoid arthritis) can be used for physical function assessment in osteoarthritis. The Cochin correlated well with the Dreiser index (r = 0.87) and less with patient perceived handicap reported by VAS (r = 0.67), indicating good construct validity (ICCs of 0.96).

Low Back Pain

Roland-Morris Disability Questionnaire (RDQ) and Oswestry Disability Index (ODI): RDQ (24 items) and ODI (10 items) scores are health-status measures specific for low back pain, regardless of cause. Responses by RDQ and ODI correlate well with each other, as well as the physical component score of SF-36.

Performance Based or Objective Outcome Measures

They help in objectively evaluating function in osteoarthritis.

For hand OA: Hand held dynamometer, Jabson hand function assessment, Sollerman hand function test.

Knee and Hip OA: 30 second chair to stand test, stair climbing test, 40 m fast packed walk test and 6 minutes walk test are a few among varieties of tests available.

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