Vanderbilt University School of Medicine
Division of Continuing Medical Education
Clinical and Experimental RHEUMATOLOGY

Sponsorship Statement
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Target Audience
Rheumatologists in the United States, Canada, and Europe.

Purpose and Learning Objectives

In rheumatoid arthritis as in other disease states, quantitative evaluation and documentation of disease status of patients provides critical data for clinical decision-making. Busy clinicians have found it difficult to collect the quantitative data in a format that is convenient to use in their practices. This issue of *Clinical and Experimental Rheumatology* has been designed to provide an overview of the theory and practice of quantitative patient assessment in rheumatic diseases.

If you read all of the articles in this issue, you should be able to describe and discuss:

1. Approaches to quantitative clinical assessment of patients with rheumatic diseases.
2. Patient self-report questionnaires for clinical research and clinical care.
3. Indices for quantitative clinical assessment of specific rheumatic diseases.
4. Databases in standard clinical care of patients with rheumatoid arthritis in different countries.

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Clinical and Experimental RHEUMATOLOGY

Supplement: Quantitative Clinical Assessment of Rheumatic Diseases

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CME Multiple Choice Questions

A.1. *T. Pincus, A. Kavanaugh, D. Aletaha, J. Smolen*:
Complexities in defining remission in rheumatic diseases

1. In population-based studies and early arthritis clinics, spontaneous remission may be seen in at least what percentage of people who appeared to have an inflammatory arthritis?
- **a.** 5%
- **b.** 10%
- **c.** 15%
- **d.** > 20%

2. In one carefully analyzed study of a series of patients reported in the early 1980s, a clinical remission was sustained for longer than 3 years in about what percentage of patients?
- **a.** < 5%
- **b.** 10%
- **c.** 25%
- **d.** 50%

3. Important complexities in a definition of remission in rheumatic diseases include
- **a.** The absence of a single "gold standard" measure
- **b.** A need for continuing medications
- **c.** The possibility of organ damage despite the absence of inflammatory activity
- **d.** All of the above

A.2. *J.S. Smolen, D. Aletaha*:
What should be our treatment goal in RA today?

1. Remission can be assessed by the following criteria
- **a.** ACR criteria requiring all of six items to be fulfilled
- **b.** FDA criteria requiring ACR remission criteria to be fulfilled for six weeks
- **c.** SDAI and CDAI criteria, which do not allow more than two residual swollen joints to be present
- **d.** DAS28 criteria, which do not allow more than two residual swollen joints to be present

2. A definition of remission should include patients who
- **a.** Have not had treatment for at least 6 months
- **b.** Are in clinical remission regardless of therapy
- **c.** Are without disease-modifying anti-rheumatic drugs for 6 months but continue nonsteroidal anti-inflammatory drugs and glucocorticoids
- **d.** Are treated only with analgesics or nonsteroidal anti-inflammatory drugs

3. All of the following states of clinical activity may lead to radiographic progression except
- **a.** Remission
- **b.** Low disease activity
- **c.** Elevated CRP levels
- **d.** None of the above

A. 3. *V.K. Ranganath, D. Khanna, H.E. Paulus*:
ACR remission criteria and response criteria

1. Remission in rheumatoid arthritis was noted by Short to be more common in RA patients who
- **a.** Were younger
- **b.** Had longer disease duration
- **c.** Had more severe disease activity at onset
- **d.** Had longer hospital stays

2. The ACR Remission Criteria include the following elements
- **a.** Morning stiffness ≤ 15 min
- **b.** Absence of fatigue
- **c.** Absence of swollen and tender joints
- **d**. All of the above

3. DAS remission and ACR Remission do not include the following
- **a.** Joint counts
- **b.** Functional status
- **c.** Fatigue
- **d.** Acute phase reactant

A. 4. *H. Mäkinen, P. Hannonen, T. Sokka*:
Various definitions of remission for rheumatoid arthritis and review of selected clinical cohorts and randomized clinical trials for the rate of remission

1. What is the most-widely accepted cut point of remission according to DAS28?
- **a.** DAS28 < 1.6
- **b.** DAS28 < 2.6
- **c.** DAS28 < 3.2
- **d.** DAS28 < 5.1

2. The American Rheumatism Association (ARA) (now American College of Rheumatology ACR) remission criteria provided six criteria for remission in RA. How many of those criteria must be met to meet a description of remission?
- **a.** Three of the six criteria
- **b.** Four of the six criteria
- **c.** Five of the six criteria
- **d.** All six criteria

3. The simplified disease activity index (SDAI) consists of five measures, including all of the following except
- **a.** Swollen joint count (28 joints included)
- **b.** Erythrocyte sedimentation rate (ESR)
- **c.** Patient global estimate of disease activity on a 10-cm VAS
- **d.** Pain on a 10-cm VAS

A. 5. *J. Fransen, P.L.C.M. Van Riel*:
DAS remission cut points

1. The cut points for remission on the DAS and DAS28 are
- **a.** DAS <1.6 and DAS28 <2.1
- **b.** DAS <1.6 and DAS28 <2.6
- **c.** DAS <2.1 and DAS28 <2.1
- **d.** DAS <2.1 and DAS28 <2.6

2. If remission is interpreted as the total absence of signs and symptoms of disease activity, the DAS cut points for remission may be regarded as corresponding with
- **a.** "Total remission"
- **b.** "Near-remission"
- **c.** "Partial remission"
- **d.** Not related to remission

3. The structure of the DAS allows people who do not meet ARA criteria to have a DAS <2.6 if they have
- **a.** High number swollen joints and low ESR
- **b.** Low number swollen joints and high ESR
- **c.** High patient global estimate and low ESR
- **d.** High patient global estimate and low swollen joints

A. 6. *B. Saleem, S. Nizam, P. Emery*:
Can remission be maintained with or without further drug therapy?

1. In studies of patients with RA prior to 2000, what percentage of patients with rheumatoid arthritis have irreversible radiographic joint damage within the first 2 years of diagnosis?
a. None
b. < 50%
c. 50% to 80%
d. 100%

2. Which of the following is not included in ACR remission criteria for rheumatoid arthritis?
a. ESR/CRP
b. Early morning stiffness
c. Presence of radiographic erosions
d. Swollen joint count

3. Studies have shown that long-term remission in patients with early rheumatoid arthritis can be achieved following infliximab therapy for
a. 1 month
b. 2 months
c. 4 months
d. 12 months

A. 7. *A.E. Voskyul, B.A.C. Dijkmans*:
Remission and radiographic progression in rheumatoid arthritis

1. In patients with RA who are in remission clinically, functional disability is related to
a. Pain
b. Joint inflammation
c. Radiographic joint damage
d. All of the above

2. Radiographic progression can occur in patients with RA who are clinically in remission after 2 years of follow-up in the following frequency
a. None
b. 5% to 10%
c. 11% to 25%
d. 25%

3. Which imaging techniques can help to evaluate whether joint inflammation is present in RA patients suspected to be clinically in remission?
a. Ultrasonography of joints
b. Magnetic resonance imaging (MRI)
c. Positron emission tomography (PET)
d. All of the above

A. 8. *R. Rau*:
Is remission in RA associated with radiographic healing?

1. Repair of erosions may be regarded as
a. Something that is never seen
b. Invariable with passage of time
c. A normal process comparable to healing of a fracture
d. Independent of control of inflammation

2. Healing of radiographic erosions has been documented with
- **a.** Methotrexate
- **b.** Parenteral gold
- **c.** Combinations of methotrexate and parenteral gold
- **d.** All of the above

3. In an analysis of 93 patients who had persistent remission prior to use of biologic agents, clinically relevant progression was seen in approximately
- **a.** 7% of patients
- **b.** 15% of patients
- **c.** 25% of patients
- **d.** 50% of patients

B. 1. *D. Aletaha, J.S. Smolen*:
Remission of rheumatoid arthritis: should we care about definitions?

1. In rheumatoid arthritis, remission represents
- **a.** The lowest level of disease activity
- **b.** A goal to be achieved in as many patients as possible
- **c.** A state that leads to little or no radiographic progression over time
- **d.** All of the above

2. Which of the following statements is correct?
- **a.** Joint tenderness drives evaluation of disease activity similarly in physicians and patients
- **b.** Patients give more weight to joint tenderness than to joint swelling in evaluation of disease activity
- **c.** Joint swelling drives evaluation of disease activity similarly in patients and physicians
- **d.** None of the above

3. A definition of remission is most specific if we use
- **a.** Criteria with multiple variables, in which each has its own threshold value
- **b.** A scale that comprises all important variables in an unweighted manner, such as the SDAI or CDAI
- **c.** A stringent cut point for the most relevant single disease activity variable
- **d.** A weighted scale of all relevant variables, such as the DAS28

B. 2. *G. Wells, M. Boers, P. Tugwell*:
Low disease activity state in rheumatoid arthritis: concepts and derivation of minimal disease activity

1. A patient with rheumatoid arthritis has been started on MTX and has been increased to your usual dose. The profile of the disease activity after 6 months of therapy at that dose is

Measure	Range	Result
Pain	(0-10)	2
Swollen joint count	(0-28)	0
Tender joint count	(0-28)	1
Physical function/HAQ	(0-3)	0
Physician global assessment	(0-10)	2
Patient global assessment	(0-10)	0
ESR	(0-120)	26
DAS28		2.84

Which of the following statements is true?
- **a.** Patient is in minimal disease activity (MDA) according to the ACR Core Set definition and in MDA according to the DAS-based definition
- **b.** Patient is in MDA according to the Core Set Definition but not according to the DAS-based definition
- **c.** Patient is not in MDA according to the Core Set Definition but is in MDA according to the DAS-based definition
- **d.** Patient is not in MDA according to the Core Set Definition and according to the DAS-based definition
- **e.** There is not enough information to make this determination

2. Consider a patient with rheumatoid arthritis who has been started on MTX and has been increased to your usual dose. The profile of the disease activity after 6 months of therapy at that dose is

Measure	Range	Result
Pain	(0-10)	6.5
Swollen joint count	(0-28)	0
Tender joint count	(0-28)	3
Physical function/HAQ	(0-3)	0.75
Physician global assessment	(0-10)	0
Patient global assessment	(0-10)	3.5
ESR	(0-120)	9
DAS28		2.52

Which of the following statements is true?
a. Patient is in MDA according to the Core Set Definition and according to the DAS-based Definition
b. Patient is in MDA according to the Core Set Definition but not according to the DAS-based Definition
c. Patient is not in MDA according to the Core Set Definition but is in MDA according to the DAS-based Definition
d. Patient is not in MDA according to the Core Set Definition and according to the DAS-based Definition
e. There is not enough information to make this determination

3. From the rationale and methodologic perspective for developing a definition of minimal disease activity (MDA), all of the following statements are true except
a. The proposed conceptual definition of low disease activity is that state that is deemed a useful target of treatment by both physician and patient, given current treatment possibilities and limitations
b. For the judgmental approach, opinions could be elicited by direct questioning, by studying patient profiles, by asking physicians to submit cases, and by direct observation of clinical practice
c. The proposed approach to validate a definition of MDA is using the definition as a secondary endpoint in randomized clinical trials and further validated it in other datasets and long-term outcome databases
d. It was determined that an indirect procedure (i.e., polling for desired levels for each core set measure separately) was better than a direct procedure (i.e., have respondents assess descriptions of patients using profiles that provide results of all the core set measures)
e. The need for a definition of MDA arose from the observation that achieving (and maintaining) a satisfactory state of low disease activity is probably more important in the long term than the improvement from a high level of disease activity documented in trials, and that remission is not a frequent occurrence in regular clinical practice

B. 3. *T. Pincus, Y. Yazici, M. Bergman, C. Swearingen, T. Harrington*:
A proposed approach to recognise "near remission" quantitatively without formal joint counts or laboratory tests: a patient self-report questionnaire routine assessment of patient index data (RAPID) score as as a guide to a "continuous quality improvement" strategy

1. Which one of the following features is <u>not</u> a difference between patient questionnaires designed for research versus a patient questionnaire designed for clinical care?
a. Time required for the patient to complete the questionnaire
b. Time required for the physician to review the questionnaire
c. Time required for a health professional to score the questionnaire
d. Time to compare questionnaire score to previous visit

2. Which of the following patient reported outcome (PRO) measures is not included in an index that distinguishes between active and control treatment in clinical trials as effectively as the entire American College of Rheumatology (ACR) Core Data Set and disease activity score (DAS)?
a. Physical function
b. Fatigue
c. Pain
d. Global status

3. The multidimensional HAQ (MDHAQ) differs from the HAQ in all the following except
- **a.** The MDHAQ includes 10 ADL and the HAQ includes 20 ADL
- **b.** The MDHAQ includes all ADL on one side of one page
- **c.** Scoring each activity on the MDHAQ is 0 to 5 and each activity on the HAQ is 0 to 3
- **d.** The MDHAQ does not include queries concerning aids and devices or help from another person
- **e.** The MDHAQ includes two advanced activities reflecting improved outcomes for patients with rheumatic diseases

C. 1. *T. Sokka, H. Mäkinen, K. Puolakka, T. Möttönen, P. Hannonen*:
Remission as the treatment goal – the Fin-RACo trial

1. In the FIN-RACo study, ability to work was maintained over 5 years if
- **a.** Patients improved less than ACR20% over the first 6 months of treatment
- **b.** Patients improved by at least ACR20% over the first 6 months of treatment
- **c.** Patients improved by at least ACR50% over the first 6 months of treatment
- **d.** Patients were in remission over the first 6 months of treatment

2. After 2 years of treatment in the Fin-RACo study, remission was seen in
- **a.** 27% of combination group and 8% of monotherapy group
- **b.** 27% of combination group and 15% of monotherapy group
- **c.** 37% of combination group and 18% monotherapy group
- **d.** 37% of combination group and 28% monotherapy group

3. A delay of less than 4 months led to a 3-fold reduction in the proportion of patients who were in remission after 2 years in the Fin-RACo study in
- **a.** Both the group randomized to combination and the group randomized to monotherapy
- **b.** Only the group randomized to combination therapy
- **c.** Only the group randomized to monotherapy
- **d.** Neither the group randomized to combination or monotherapy

C. 2. *C.F. Allaart, Y.P.M. Goekoop-Ruiterman, J.K. de Vries-Bouwstra, F.C. Breedveld, B.A.C. Dijkmans, FAAR Study Group*:
Aiming at low disease activity in rheumatoid arthritis with initial combination therapy or initial monotherapy strategies: the BeSt study

1. What percentage of patients with early, active rheumatoid arthritis in the BeST clinical trial achieve clinical remission (DAS < 1.6) with currently available anti-rheumatic therapies, adjusted according to frequent disease activity measurements?
- **a.** 10%
- **b.** 40%
- **c.** 65%
- **d.** 90%

2. After 2 years of treatment, what percentage of patients treated in the BeST clinical trial with initial combination therapy with methotrexate and infliximab permanently discontinued infliximab while maintaining consistent low disease activity (DAS =< 2.4)?
- **a.** 25%
- **b.** 35%
- **c.** 55%
- **d.** 75%

3. After 2 years of treatment of patients with early, active rheumatoid arthritis in the BeST clinical trial, what is the difference in outcome between patients treated with initial combination therapy and patients treated with initial combination therapy?
- **a.** After 2 years, patients treated with initial combination therapy have less joint damage than patients treated with initial monotherapy

b. After 2 years, patients treated with initial combination therapy have better functional ability than patients treated with initial monotherapy
c. After 2 years patients treated with initial combination therapy are more often in clinical remission than patients treated with initial monotherapy
d. After 2 years, patients treated with initial combination therapy have more adverse side effects than patients treated with initial monotherapy

D. 1. *A. Kavanaugh, J. Fransen*:
Defining remission in psoriatic arthritis

1. Common areas of involvement in patients with PsA include all of the following except
a. Skin, with psoriasis and nail changes
b. Pulmonary, with nodular lesions and interstitial changes
c. Enthesitis, for example at the Achilles tendon
d. Spondylitis, with inflammatory back pain

2. Which of the following statements concerning PsA is true?
a. Outcome measures developed for RA are of no value in assessing the peripheral arthritis of PsA
b. Joint disease precedes skin disease in the majority of PsA patients
c. Spinal involvement in PsA is asymmetric more commonly than in patients with ankylosing spondylitis
d. The PASI is a measure of nail disease in psoriasis

3. Which of the following statements concerning patients with PsA is not true?
a. Psoriatic arthritis affects approximately 5% of the general population
b. TNF inhibitors are contraindicated in PsA patients
c. Erosive changes do not commonly occur in PsA patients with peripheral arthritis
d. Quality of life among PsA patients is far better than among patients with RA

D. 2. *J. Zochling, J. Braun*:
Remission in ankylosing spondylitis

1: Outcome in ankylosing spondylitis is currently measured as
a. Remission
b. ASAS 20% response
c. Partial remission
d. b and c

2. What percentage of patients with ankylosing spondylitis achieve partial remission with anti-TNF therapy?
a. 10%
b. 20%
c. 30%
d. 40%

3. The definition of disease flare in ankylosing spondylitis is currently based on
a. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
b. Bath Ankylosing Spondylitis Function Index (BASFI)
c. Patient global assessment
d. Pain

D. 3. *C. Mukhtyar, B. Hellmich, D. Jayne, O. Flossmann, R. Luqmani*:
Remission in antineutrophil cytoplasmic antibody-associated systemic vasculitis

1. Which of the following is true of Wegener's granulomatosis?
a. The natural history of untreated disease is of survival in over 50% cases
b. In non-renal disease, remission is achieved in more than 70% of cases using methotrexate and glucocorticoid therapy
c. Relapses are always preceded by a rise or reappearance of levels of anti neutrophil cytoplasm antibodies (ANCA)
d. Long-lasting remission (for at least 5 years) is likely following standard use of cyclophosphamide and glucocorticoid in over 90% of patients

2. Which of the following is true concerning organ damage in patients with vasculitis?
- **a.** Damage is associated with an increased risk of mortality
- **b.** Most damage occurs after the first 2 years of disease
- **c.** Damage is part of the definition of disease remission in vasculitis
- **d.** Damage can be measured using the five factor score

3. With regard to the definition of disease states in vasculitis, which is true?
- **a.** Low activity disease state is unlikely to respond to glucocorticoid therapy
- **b.** In Churg Strauss syndrome, the term "active disease" refers only to the presence of active vasculitis, and not other manifestations of the disease such as tissue eosinophilia
- **c.** Response can be defined as a 50% reduction in disease activity together with the absence of new disease activity
- **d.** Minor relapse is defined as non-life threatening but can be organ threatening

D. 4. *M. Mosca, S. Bombardieri*:
Assessing remission in systemic lupus erythematosus

1. The assessment of systemic lupus patients in clinical trials requires the evaluation of
- **a.** Disease activity based on validated indices
- **b.** Disease activity based on the experience of the treating physician
- **c.** Disease activity, damage, quality of life, drug toxicity
- **d.** Disease activity, damage, quality of life

2. The evaluation of remission in SLE could be based on
- **a.** The assessment of specific organ involvement
- **b.** The assessment of global activity
- **c.** The assessment of damage
- **d.** The combination of activity, damage and quality of life

3. Which of the following is true?
- **a.** A definition of remission has been proposed based on the SLEDAI index
- **b.** A definition of remission has been proposed based on the SLAM index
- **c.** A definition of remission has been proposed based on the ECLAM index
- **d.** A definition of remission has been proposed based on the BILAG index

D. 5. *A. Ravelli, A. Martini*:
Remission in juvenile idiopathic arthritis

1. How long should criteria for inactive disease be met after discontinuation of all anti-arthritis medications for a patient with juvenile idiopathic arthritis to be classified as being in clinical remission without medications?
- **a.** 6 months
- **b.** 12 months
- **c.** 18 months
- **d.** 24 months

2. Which of these parameters is not part of the preliminary criteria for inactive disease and clinical remission of juvenile idiopathic arthritis?
- **a.** No joints with active arthritis
- **b.** No fever, rash, serositis, splenomegaly, or generalized lymphoadenopathy attributable to JIA
- **c.** Absence of morning stiffness
- **d.** Normal ESR or CRP

3. What percentage of juvenile idiopathic arthritis patients has been found to be in clinical remission or inactive disease at last follow-up visit in the studies published in the last 10 years ?
- **a.** 15% to 20%
- **b.** 20% to 30%
- **c.** 40% to 60%
- **d.** 70% to 80%