**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Number** (*if previously endorsed*)**:** Click here to enter NQF number

**Measure Title**: Rheumatoid Arthritis: Assessment of Disease Activity

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 2/14/2014

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| **Instructions**  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Maximum of 10 pages (*incudes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.*** * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

|  |
| --- |
| **Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**   1a. Evidence to Support the Measure Focus The measure focus is evidence-based, demonstrated as follows:   * Health outcome: [**3**](#Note3) a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm) and [methods](http://www.uspreventiveservicestaskforce.org/methods.htm), or Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org/publications/index.htm).  **5.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**: (*should be consistent with type of measure entered in De.1*)

Outcome

Health outcome: Rheumatoid Arthritis Disease Activity

Patient-reported outcome (PRO): All have a patient-reported component

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors*

Intermediate clinical outcome (*e.g., lab value*): Click here to name the intermediate outcome

Process: Rheumatoid Arthritis: Assessment of Disease Activity (collection of outcome score)

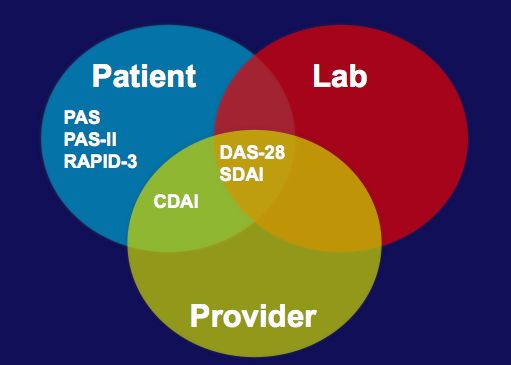
Structure: Click here to name the structure

Other: Click here to name what is being measured

The proposed measure is a *process* measure that requires collection of a key *health outcome* using a standardized score. Collecting this outcome measure in routine clinical care is supported by American College of Rheumatology (ACR) guidelines (*Singh J et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2012 May;64(5):625-39*).

The ACR recently undertook an extensive multi-year project, involving systematic literature reviews, expert consensus ratings, and national surveys to reach consensus on which RA disease activity measures are valid, reliable, and responsive, and feasible to implement in routine clinical practice (*Anderson J et al., Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012 May;64(5):640-7*). This manuscript is included as a supplemental Appendix.

The ACR-endorsed 6 RA disease activity measurement tools, which include overlapping core elements (Figure 1). All include a patient-reported component (PRO). No measure is currently a gold standard; there is good scientific evidence supporting each endorsed measure. Therefore, clinicians can select from a range of valid options appropriate to their practice settings and available resources. This novel approach to measurement has been extensively validated in RA over a period of several decades (*Anderson J et al., Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012 May;64(5):640-7)*.

**Figure 1. Core elements of American College of Rheumatology’s endorsed rheumatoid arthritis**

The 6 proposed outcome measures have cutpoints for low, moderate and high disease activity as well as disease remission to facilitate clinical decision-making. See Table 1.

**Table 1. Disease activity cutpoints for American College of Rheumatology–recommended disease activity measures.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Range | Remission | Low | Moderate | High |
| DAS28 (ESR or CRP) | 0-9.4 | < 2.6 | ≥ 2.6 - < 3.2 | ≥ 3.2 - ≤ 5.1 | > 5.1 |
| CDAI | 0-76 | ≤ 2.8 | > 2.8 - 10.0 | > 10.0 - 22.0 | > 22.0 |
| SDAI | 0-86 | 0.0 - 3.3 | 3.4 - 11.0 | 11.1 - 26.0 | 26.1 - 86.0 |
| RAPID-3 | 0-10 | 0 - 1.0 | > 1.0 - 2.0 | > 2.0 - 4.0 | > 4.0 - 10 |
| PAS | 0-10 | 0.00 - 0.25 | 0.26 - 3.70 | 3.71 - 7.99 | 8.00 - 10.00 |
| PASII | 0-10 | 0.00 - 0.25 | 0.26 - 3.70 | 3.71 - 7.99 | 8.00 - 10.00 |

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**HEALTH OUTCOME/PRO PERFORMANCE MEASURE**  *If not a health outcome or PRO, skip to* [*1a.3*](#Section1a3)

**1a.2.** **Briefly state or diagram the path between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.**

**1a.2.1.** **State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (*i.e., influence on outcome/PRO*).**

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**intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measure**

**1a.3.****Briefly state or diagram the path between structure, process, intermediate outcome, and health outcomes**. Include all the steps between the measure focus and the health outcome.

In order to assess how patients with rheumatoid arthritis (RA) are responding to therapy or whether they are reaching treatment goals, RA disease activity should be assessed using a validated instrument.

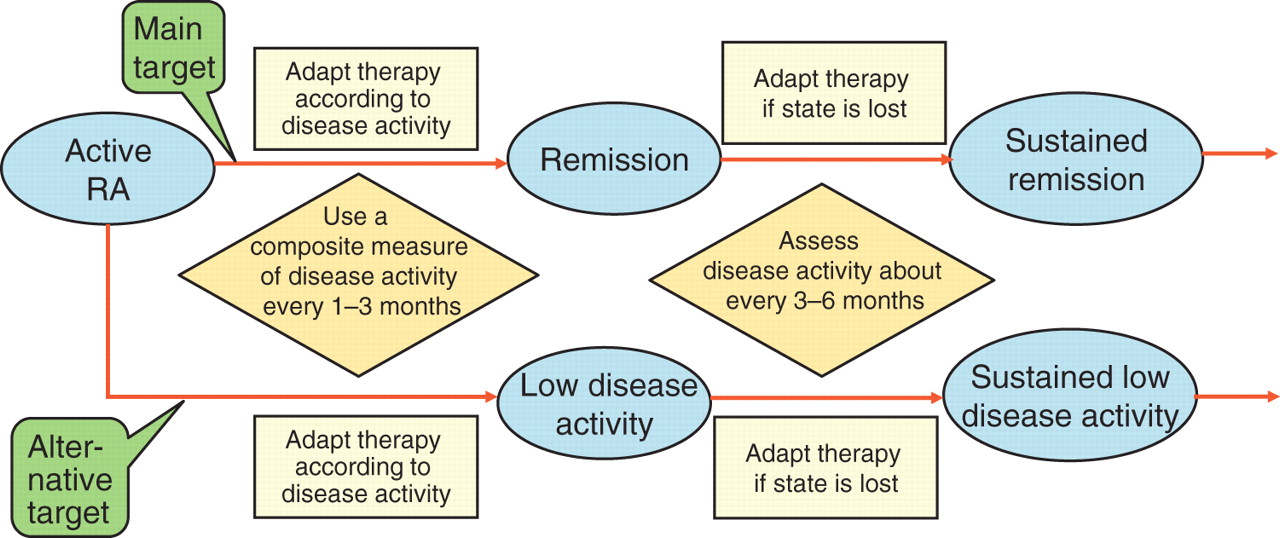
Step 1: Measure disease activity using validated instrument

Step 2: Review disease activity assessment with patient during office visit: is the patient in remission, low, medium (moderate) or high disease activity?

Step 3: If the patient has moderate or high disease activity, consider treatment modification with goal of remission/ low disease activity.

Step 4: At next office visit or 3-6 months after initiation/ change in medication, repeat Steps 1-3 until patient is in remission/ low disease activity or until patient is satisfied with their functional status (patient-reported outcome measure, a separate quality measure).

**Figure 2. Algorithm for using standardized disease activity measures to target therapy in rheumatoid arthritis.**  *From Smolen et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631-637Algorithm for treating rheumatoid arthritis (RA) to target based on the recommendations.*



Standard collection of disease activity outcomes in RA to facilitate a “treat to target” approach, where the target is disease remission or low disease activity, has been shown to improve clinical and radiographic outcomes (*Schipper LG et al. A tight control treatment strategy aiming for remission in early rheumatoid arthritis is more effective than usual care treatment in daily clinical practice: a study of two cohorts in the Dutch Rheumatoid Arthritis Monitoring registry. Ann Rheum Dis. 2012 Jun;71(6):845-50; Smolen JS et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010 Apr;69(4):631-7; Grigor C et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised*

*controlled trial. Lancet 2004;364:263–9.).*

**1a.3.1.** **What is the source of the systematic review of the body of evidence that supports the performance measure?**

Clinical Practice Guideline recommendation – ***complete sections*** [***1a.4***](#Section1a4)***, and*** [***1a.7***](#Section1a7)

US Preventive Services Task Force Recommendation – ***complete sections*** [***1a.5***](#Section1a5) ***and*** [***1a.7***](#Section1a7)

Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)

Other – ***complete section*** [***1a.8***](#Section1a8)

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

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**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** **Guideline citation** (*including date*) and **URL for guideline** (*if available online*):

Singh J et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use ofdisease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2012 May;64(5):625-39.

Smolen JS et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. Mar 2014; 73(3): 492–509.

Smolen J et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631–637.

National Institute for Clinical Excellence (NICE). Rheumatoid arthritis: The management of rheumatoid arthritis in adults: NICE clinical guidance 2009;79 [Internet. Accessed February 18, 2014]. Available from: <http://www.nice.org.uk/nicemedia/pdf/CG79NICEguideline.pdf>.

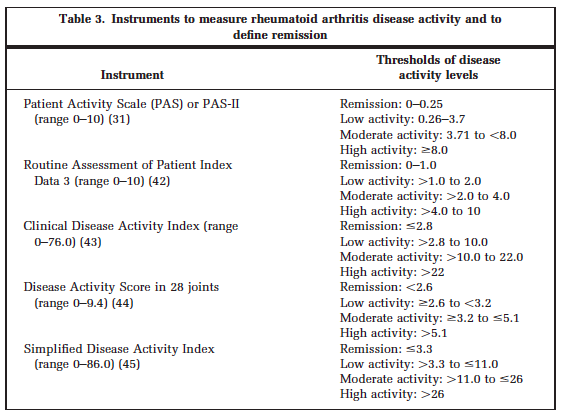
van Hulst LT, Fransen J, den Broeder AA, et al. Development of quality indicators for monitoring of the disease course in rheumatoid arthritis. Ann Rheum Dis. 2009 Dec;68(12):1805-10. (Netherland’s Scientific Institute on the Quality of Health Care)

Anderson J et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012 May;64(5):640-7).

*Additional guidelines available upon request.*

**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

p. 631 *Singh et al (2012)* “Target low disease activity or remission. The panel recommends targeting either low disease activity or remission [Table – pasted below] in all patients with early RA and established RA”



p. 634 *Smolen et al. (2010)* “Measures of disease activity must be obtained and documented regularly, as frequently as monthly for patients with high/moderate disease activity or less frequently (such as every 3–6 months) for patients in sustained low disease activity or remission”

p. 4 *Smolen et al. (2013)* “Treatment should be aimed at reaching a target of remission or low disease activity in every patient…. … low disease activity conveys much better functional and structural outcomes than moderate or high disease activity”, and *Table 1* “Monitoring should be frequent in active disease (every 1–3 months); if there is no improvement by at most 3 months after the start of treatment or the target has not been reached by 6 months, therapy should be adjusted.”

p. 15 *NICE (2009)* “Measure CRP and key components of disease activity (using a composite score such as DAS28) regularly in people with RA to inform decision-making about: increasing treatment to control disease [and] cautiously decreasing treatment when disease is controlled.”

p. 1808 *van Hulst et al.* (2009) “A rheumatologist or a specialised nurse in rheumatology should measure disease activity at baseline and every follow-up visit with the DAS28 in an RA patient.”

Table 3. *Bykrerk VP (2011)* “RA care providers should monitor disease activity as frequently as every 1 to 3 months in patients with active RA (Strength A, Level I). Patients with well controlled disease and patients in remission can be monitored at longer intervals (Strength A, Level IV)”

p. 641 *Anderson et al. (2012)* “We recommend the Clinical Disease Activity Index, Disease Activity Score with 28-joint counts (erythrocyte sedimentation rate or C-reactive protein), Patient Activity Scale (PAS), PAS-II, Routine Assessment of Patient Index Data with 3 measures, and Simplified Disease Activity Index because they are accurate reflections of disease activity; are sensitive to change; discriminate well between low, moderate, and high disease activity states; have remission criteria; and are feasible to perform in clinical settings”

**1a.4.3.** **Grade assigned to the quoted recommendation with definition of the grade:**

In the ACR guideline (Singh et al.), the strength of evidence (**Level C**) was assigned using methods from the American College of Cardiology (*Hunt SA, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2005;112:e154–235*). The evidence was rated by an Expert Panel using the RAND Appropriateness Method, which requires median ratings of 7-9 and no disagreement; disease activity measurement had high agreement. From the guideline, “Level C evidence often denoted a circumstance where medical literature addressed the general topic under discussion but it did not address the specific clinical situations or scenarios reviewed by the panel. Since many recommendations had multiple components (in most cases, multiple medication options), a range is sometimes provided for the level of evidence; for others, the level of evidence is provided following each recommendation.”

Definitions for this grading scheme:

Level A. If data are derived from multiple randomized clinical trials or metanalyses.

Level B. If data are derived from a single randomized trial or non-randomized studies.

Level C. If recommendation is based on consensus opinion of experts, case studies, or standard-of-care

In the EULAR guideline (Smolen et al.), the Level of Evidence for frequent monitoring of disease activity in active RA was **2b**, the Grade of recommendation was **A** and the strength of the recommendation was **9.8 out of 10**. Definitions for this grading scheme:

From the Centre for Evidence-Based Medicine, Oxford

1a: Systematic reviews (with homogeneity) of randomized controlled trials

1b: Individual randomized controlled trials (with narrow confidence interval)

1c: All or none randomized controlled trials

2a: Systematic reviews (with homogeneity) of cohort studies

2b: Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)

2c: "Outcomes" Research; ecological studies

3a: Systematic review (with homogeneity) of case-control studies

3b: Individual case-control study

4: Case-series (and poor quality cohort and case-control studies)

5: Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

A High Further research is very unlikely to change our confidence in the estimate of effect.

Several high-quality studies with consistent results

In special cases: one large, high-quality multi-centre trial

B Moderate Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. One high-quality study or

Several studies with some limitations

C Low Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

One or more studies with severe limitations

D Very Low Any estimate of effect is very uncertain.

Expert opinion or No direct research evidence or One or more studies with very severe limitations

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

**1a.4.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.4.1*)**:**

Reference for level of ACC evidence: Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart

References for RAND/UCLA appropriateness method: Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lazaro P, et al. The RAND/UCLA Appropriateness Method user’s manual. Santa Monica (CA): RAND Corporation; 2001.

Reference for Oxford evidence ratings: https://www.essentialevidenceplus.com/product/ebm\_loe.cfm

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

Yes **→ *complete section*** [***1a.7***](#Section1a7)

No **→ *report on another systematic review of the evidence in sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)***; if another review does not exist, provide what is known from the guideline review of evidence in*** [***1a.7***](#Section1a7)

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**1a.5.** **UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1.** **Recommendation citation** (*including date*) and **URL for recommendation** (*if available online*):

**1a.5.2.** **Identify recommendation number and/or page number** and **quote verbatim, the specific recommendation**.

**1a.5.3.** **Grade assigned to the quoted recommendation with definition of the grade**:

**1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: the* *grading system for the evidence should be reported in section 1a.7.*)

**1a.5.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.5.1*)**:**

***Complete section*** [***1a.7***](#Section1a7)

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**1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** **Citation** (*including date*) and **URL** (*if available online*):

**Relevant systematic reviews of RA disease activity measures:**

Anderson J et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012 May;64(5):640-7).

Anderson J et al. Measures of rheumatoid arthritis disease activity: Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, Disease Activity Score (DAS) and Disease Activity Score with 28-Joint Counts (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Patient Activity Score (PAS) and Patient Activity Score-II (PASII), Routine Assessment of Patient Index Data (RAPID), Rheumatoid Arthritis Disease Activity Index (RADAI) and Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5), Chronic Arthritis Systemic Index (CASI), Patient-Based Disease Activity Score With ESR (PDAS1) and Patient-Based Disease Activity Score without ESR (PDAS2), and Mean Overall Index for Rheumatoid Arthritis (MOI-RA). Arthritis Care Res (Hoboken). 2011 Nov;63 Suppl 11:S14-36.

**Additional reviews address the process of care (measurement of disease activity to guide clinical management):**

Smolen J et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010 Apr;69(4):631-7.

Schoels M et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search. Ann Rheum Dis. 2010

Knevel R et al. Current evidence for a strategic approach to the management of rheumatoid arthritis with disease-modifying antirheumatic drugs: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2010 Jun;69(6):987-94.

**1a.6.2.** **Citation and** **URL for methodology for evidence review and grading** (*if different from 1a.6.1*)**:**

***Complete section*** [***1a.7***](#Section1a7)

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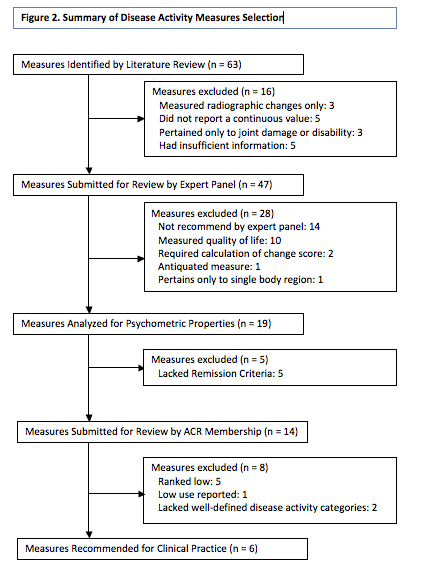
**1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE supporting the measure**

*If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.*

**1a.7.1.** **What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?**

**Selected RA disease activity outcome measures.** The information provided below is an overview of the findings from the systematic review and consensus process performed by Anderson et al., which informed the outcome measures recommended (*Anderson J et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012 May;64(5):640-7;* Figure 2). The process aimed to determine which measurement tools are accurate reflections of RA disease activity; are sensitive to change; discriminate well between low, moderate, and high disease activity states; have remission criteria; and are feasible to perform in clinical settings. The quantity and quality of the evidence supporting the final 6 recommended RA disease activity measurement tools was high. Reviewers are referred to the manuscript for further details.

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The supplemental appendix of this manuscript includes details of the systematic search strategy, ratings by expert panelists, responses to the national survey of U.S. rheumatologists and additional information.

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Process of RA disease activity measurement to guide treatment. The systematic literature review that informed International Recommendations regarding using RA disease activity measures to reach treatment goals (*Smolen J et al.* *Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010 Apr;69(4):631-7*) is contained in *Schoels M et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search. Ann Rheum Dis. 2010 Apr;69(4):638-43*. This review found four studies that randomized patients to routine or targeted treatment. All identified studies showed significantly better clinical outcomes of targeted approaches than routine approaches. Four studies compared radiographic outcomes, two showing significant benefit of the targeted approach.

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**1a.7.2.** **Grade assigned for the quality of the quoted evidence with definition of the grade**:

See grade and definitions, above.

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.**

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**:

January 1, 1966 through January 31, 2007 and from January 1, 1998 through February 14, 2007, respectively, for the 2008 ACR RA treatment guidelines, and through to Sept 22, 2010 for the 2012 ACR RA treatment guidelines.

**QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5.****How many and what type of study designs are included in the body of evidence**? (*e.g., 3 randomized controlled trials and 1 observational study*)

The primary study designs included in the body of evidence are randomized controlled trials. Key trials include:

* Grigor C, Capell H, Stirling A, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. Lancet 2004;364:263–9.
* Verstappen SM, Jacobs JW, van der Veen MJ, et al. Intensive treatment with methotrexate in early rheumatoid arthritis: aiming for remission. Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA, an open-label strategy trial). Ann Rheum Dis 2007;66:1443–9.
* Fransen J, Bernelot Moens H, Speyer I, et al. Effectiveness of systematic monitoring of rheumatoid arthritis disease activity in daily practice: a multicentre, cluster randomised control trial. Ann Rheum Dis 2005;64:1294–8.
* Symmons D, Tricker K, Roberts C, et al. The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis. Health Technol Assess 2005;9:iii–iv, ix–x, 1–78.

**1a.7.6.** **What is the overall quality of evidence across studies in the body of evidence**? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

Randomized controlled trials provide an otherwise unobtainable scientific evaluation of health care interventions and processes, and suggest that use of standardized measurements to reach RA treatment goals outperforms usual care in improving patient outcomes. However, there is significant heterogeneity across trials. For example, trials used different treatment targets (DAS <2.4, Composite Response Criteria, Swollen Joint Counts, etc.), followed patients at different intervals (e.g. clinical assessments were performed monthly to every 4 months; some trials randomized patients to different visit intervals). Most studies have examined individuals with shorter disease duration. Only one trial to date has focused explicitly on late disease (duration >5 years) and found no advantage of tighter disease control on functional outcomes.

The heterogeneity of RA severity in the population, the limitations of available clinical trials discussed above, and the complete absence of studies that have built risk-adjustment models for RA disease activity outcomes limit the ability to develop a risk-adjusted outcome measure. *However, available trial evidence and strong national and international consensus support the process of care (performing standardized RA disease activity assessments) to guide treatment*.

**ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7.** **What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence**? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

Heterogeneity across studies limits our ability to calculate benefits across studies. No meta-analyses have been performed.

**1a.7.8.** **What harms were studied and how do they affect the net benefit (benefits over harms)?**

No studies conducted to date have found harms associated with either RA disease activity measurement or treating to target, although data are limited. For example, in the TICORA study, three patients assigned routine care and one allocated intensive management died during the study; none was judged attributable to treatment (*Grigor C et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. Lancet 2004;364:263–9*). Similarly, in the CAMERA study, rates of adverse events were comparable between groups (*Verstappen SM et al. Intensive treatment with methotrexate in early rheumatoid arthritis: aiming for remission. Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA, an open-label strategy trial). Ann Rheum Dis 2007;66:1443–9*) .

**UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9.** **If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review**.

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**1a.8 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

**1a.8.1** **What process was used to identify the evidence?**

**1a.8.2.** **Provide the citation and summary for each piece of evidence.**