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

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

**Measure Title**: Rheumatoid Arthritis: Tuberculosis Screening

**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). |

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| **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*)

Health outcome: Click here to name the health outcome

Patient-reported outcome (PRO): Click here to name the PRO

*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: Tuberculosis screening prior to initiating newly prescribed biologic DMARD therapy for patients with RA.

Structure: Click here to name the structure

Other: Click here to name what is being measured

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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*).**

*Note: For health outcome/PRO performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

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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.

This is a patient safety measure pertaining to commonly used therapies (specific biologic DMARDs) in rheumatoid arthritis. Administrative data suggest that over 1 in 4 individuals with RA receive biologic DMARDs (*Zhang J, Xie F, Delzell E, et al. Trends in the Use of Biologic Therapies among Rheumatoid Arthritis Patients Enrolled in the U.S. Medicare Program. Arthritis care & research. Jun 10 2013*). Over 1.3 million individuals in the United States have RA (*Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis and rheumatism. Jan 2008;58(1):15-25*); therefore this measure is expected to apply to over 300,000 Americans with RA. Biologic therapies can reactivate latent tuberculosis, leading to significant morbidity and even mortality.

The path between the *process* of care and *adverse health outcomes* is illustrated below:

TB risk 🡪 TB screening prior to initiating biologic DMARD therapy 🡪 decreased risk of TB reactivation or worsening of active TB when initiating biologic DMARD therapy 🡪 optimize RA outcomes by avoiding serious adverse event

**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*):

Saag, et al., American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. AC&R 2008;59(6):762-784: (\*\*Grades not assigned to these recommendations)

Singh, 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. AC&R 2012;64(5):625-639. The following recommendations are all Level C Evidence, except for initiation of biologic agents in patients being treated for latent tuberculosis infection (LTBI), where the Level of Evidence is B

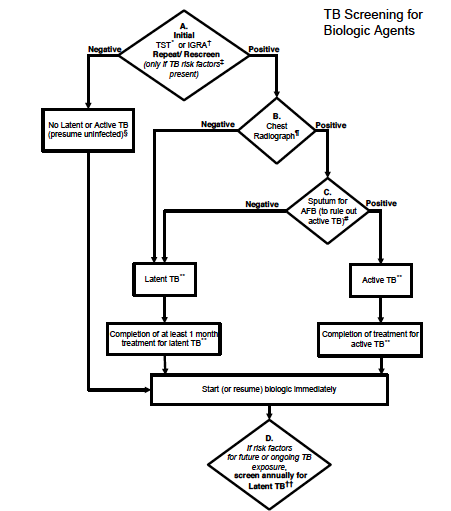
**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

Saag, et al., American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. AC&R 2008;59(6):762-784: (\*\*Grades not assigned to these recommendations)

* In Table 2: “Latent TB infection prior to initiation of latent TB treatment, or active TB disease prior to completing a standard regiment of anti-TB therapy” were “contraindications to starting or resuming therapy with … biologic DMARDs in RA patients”
* Page 776: “The TFP recommended routine TB screening to identify latent TB infection in patients being considered for therapy with biologic agents (Figure 4). The evidence for TB testing is based on a documented higher incidence of TB following anti-TNF-alpha therapy (references 117, 122). To begin, the TFP recommended that clinicians should ask all RA patients being considered for biologic DMARD therapy about their potential risk factors for TB infection (see below) and, irrespective of prior BCG vaccination, should use a TB skin test as a diagnostic aid to assess the patient’s probability of latent TB infection (Figure 4).”
* Page 776: “These ACR recommendations defer the decision to initiate anti-TB therapy to physicians possessing sufficient expertise in TB management. In general, patients with latent TB infection should begin preventive therapy before starting their anti-TNF-alpha therapy (Reference 248). The CDC suggests that the preferred regimen for management of latent TB infection is a 9-month course of daily isoniazid (Reference 245). The CDC also suggests delaying anti-TNF-alpha therapy until isoniazid treatment has been initiated but does not specify an optimal time period of delay (Reference 249). Observational studies suggest anti-TNF-alpha therapy can be safely started 1 month after starting isoniazid treatment (Reference 250,251). The British Thoracic Society also has provided recommendations on this issue (Reference 252). Treatment with isoniazid does not eliminate all cases of anti-TNF-alpha –associated TB, and clinicians should remain vigilant for active TB in any anti-TNF\_–treated patient in whom constitutional or chronic respiratory symptoms develop during anti-TNF-alpha therapy.”

Singh, et al., AC&R 2012;64(5):625-639: This is an update to the 2008 ACR RA treatment Guidelines. The following recommendations are all Level C Evidence, except for initiation of biologic agents in patients being treated for LTBI, where Level of Evidence is B

* Page 634: “The panel recommends screening to identify LTBI in all RA patients being considered for therapy with biologic agents, regardless of the presence of risk factors for LTBI (diamond A of Figure 3) (Reference 14). It recommends that clinicians assess the patient’s medical history to identify risk factors for TB (specified by the CDC) (Table 2).”
* Figure 3 illustrates the recommendations for TB screening methods
* Page 636: “If the RA patient has active or latent TB based on the test results, the panel recommends appropriate antitubercular treatment and consideration of referral to a specialist. Treatment with biologic agents can be initiated or resumed after 1 month of latent TB treatment with antitubercular medications and after completion of the treatment of active TB, as applicable (Figure 3; below).”



* Page 638: “Because these recommendations were heavily informed by CDC guidance and minimal additional information was found in the broader literature search, our TB screening and vaccination recommendations are concordant with the CDC recommendations.”

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

The recommendations are all Level C Evidence, except for initiation of biologic agents in patients being treated for LTBI, which are Level of Evidence B. The strength of evidence 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; Tb screening recommendations 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

**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.*)

See above.

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

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.

Shekelle P. The appropriateness method. Med Decis Making 2004;24:228–31.

Shekelle PG, Park RE, Kahan JP, Leape LL, Kamberg CJ, Bernstein SJ. Sensitivity and specificity of the RAND/UCLA Appropriateness Method to identify the overuse and underuse of coronary revascularization and hysterectomy. J Clin Epidemiol 2001;54:1004–10.

Reference for level of 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 Rhythm Society. Circulation 2005;112:e154–235.

**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*):

**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?**

The evidence review examined studies quantifying the risk of TB reactivation and infection in individuals taking RA drug therapies and also evaluated screening procedures.

The review also specifically examined new data pertaining to screening methods for TB in RA patients. MESH terms “”Tuberculosis”, “TST”, Tuberculin skin test”, “QuantiFERON”, QuantiFERON‐Gold”, “BCG”, “IGRA”, “Bacillus Calmette‐Guérin”, “T‐SPOT”, AND “ Rheumatoid arthritis” were applied. Many studies compared the sensitivity and usefulness of Tuberculin skin test (TST) with Interferon Gamma Release Assays (IGRAs) like T‐SPOT.TB test and QuantiFERON‐TB Gold (QFT‐GT) in detection of LTBI. 18 studies provided data on TB screening tests. Evidence tables are available upon request.

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

See above.

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

Levels of evidence were assigned according to the Oxford Centre for Evidence-based Medicine levels of evidence (<http://www.cebm.net/index.aspx?o=1025>, accessed 29 March 2010).

**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 RA treatment guidelines, and through to Sept 22, 2010 for the 2012 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*)

Evidence tables are available upon request. Trials and observational data. 295 studies in Saag et al (2008); 128 studies in Singh et al (2012).

**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*)

In Saag, et al. (2008), the median Jadad score was 5 (IQR 3-5) for biologic DMARDs for RCTs; the median Newcastle-Ottawa Scale (NOS) score was 7 (IQR 5-8) for observational studies.

**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*)

No specific estimation of benefit has been made in these treatment recommendations. Because this measure was recommended as appropriate, it reflects the quantity, quality, and consistency of the existing data. Given the morbidity and mortality associated with TB reactivation, screening and appropriate treatment prior to initiation of biologic DMARD therapy is expected to decrease morbidity and mortality associated with TB reactivation.

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

Harms have not been specifically estimated in these publications. There are risks associated with TB therapies (e.g., adverse drug effects). Under appropriate physician supervision in which safety precautions are undertaken, such adverse events can be monitored and minimized, thereby supporting net benefit of TB screening.

**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.**