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A Publication for Rheumatology
Nurse Practitioners and Physician Assistants

Rheumatoid Arthritis: Ongoing Management and Clinical Assessment

Martin J. Bergman, MD, Senior Editor

Joint damage progresses throughout the course of rheumatoid arthritis (RA) and is associated with functional disability.¹ Radiographic damage is evident within 3 years of disease onset in 70% of patients with RA.² However, joint erosions can occur early in the disease course. In one study, magnetic resonance imaging (MRI) detected joint erosion in 45% of patients with RA of 4 months' duration.³

The goals of RA management are to prevent or control joint damage, prevent loss of function, and decrease pain.⁴ Recent evidence suggests that early, aggressive treatment can improve outcomes in RA.⁵⁻⁷ The American College of Rheumatology (ACR) recommends initiation of disease-modifying antirheumatic drug (DMARD) therapy within 3 months of disease onset.⁴ In its updated recommendations for nonbiologic and biologic DMARD therapy for RA, published in 2008, the ACR also stresses the importance of frequent clinical assessments of disease activity to evaluate disease severity and determine whether treatment adjustments or alternative treatments are warranted.⁸

This issue of PCE Updates in Rheumatology summarizes the ACR's 2008 recommendations for the use of DMARD therapy in RA, strategies for clinical assessment, and the evidence supporting switching therapy when efficacy is lost or adverse events warrant. Nicole Furfaro, MSN, ARNP, presents a case study of a patient with RA, with clinical commentary (page 8).

Needs Assessment

Because joint damage begins early in rheumatoid arthritis (RA), the American College of Rheumatology (ACR) recommends initiating disease-modifying antirheumatic drug (DMARD) therapy within 3 months of disease onset.¹ In its 2008 update on nonbiologic and biologic DMARDs, the ACR also emphasizes that rational therapeutic choices must be based on clear definitions of disease activity and a conception of what constitutes treatment success or failure and that frequent clinical assessments of disease activity are warranted to evaluate disease severity and assess the need for alternative treatments.² Clinicians in rheumatology practices need to be aware of the evidence supporting initial therapies and treatment switching for RA, and the disease evaluation tools available to them.

References

1. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum.* 2002;46:328-346.

2. Saag KG, Teng GG, Patkar NM, et al; American College of Rheumatology. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59:762-784.

Target Audience

Nurse practitioners (NPs), physician assistants (PAs), and physicians in the practice of rheumatology.

Learning Objectives

After completing this activity, participants should be better able to:

1. Apply clinical assessment tools to monitor RA severity and evaluate the need for treatment adjustments.
2. Formulate evidence-based treatment plans for patients with newly diagnosed RA.
3. Translate clinical evidence on biologic DMARD therapy and treatment switching into effective management plans for patients with refractory RA.

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RA Assessment Tools

Measuring Disease Activity

To guide clinicians in making rational therapeutic choices in disease management, several indices for measuring RA activity have been developed.

Perspectives From *Nicole M. Furfaro, MSN, ARNP*

What clinical assessment tools do you find most useful in your clinical practice?

There is no one perfect tool for assessment. With so many options and different components to consider, it is difficult for clinicians to know what is best for their practice. I see value in several different measures, but tend to rely on the DAS28 because of familiarity and its clearly defined parameters. Unfortunately, the DAS can fool clinicians into thinking that all is well if a patient scores in the “remission” or even “low disease activity” range, but still has a few active “critical” joints despite low ESR/CRP levels. In addition, DAS scoring cannot be completed at the time of the office visit because of the need for laboratory testing. I find that tools that incorporate patient and evaluator components, but do not require laboratory assessments can be helpful. I am currently exploring the use of RAPID4 and RAPID5. I am as guilty as the next person of being slow to make changes in my practice, but having just returned from the meeting of the Rheumatology Nurses Society Inaugural Annual Conference in Orlando, Florida, I am feeling motivated and energized to make positive changes. At the meeting I met several extremely motivated and interested nurses who want to incorporate tools in their patient assessments—a tidal wave is starting!

What are the most important challenges facing NP/PAs in managing RA?

Choosing the best treatment from among the many new disease management



The major pooled indices used in clinical trials to assess RA are the ACR core data set,⁹ the Disease Activity Score (DAS),¹⁰ and the Health Assessment Questionnaire (HAQ).¹¹

options is the most important challenge we face today. We must decide which patient will benefit from the new targeted biologic treatments and be prepared to justify the use of expensive medications if that is what is best for our patient. Unfortunately, emerging therapeutic decision making has not kept up with the rapid development of new RA treatments—most practicing clinicians assess and make treatment decisions based on “gut instinct.” We know that if aggressive RA is not properly managed the result will be catastrophic outcomes of disability, illness, and even death. Therefore, we must meet the challenge of recognizing and developing methods for assessing disease outcomes to fully maximize treatment options and standardize the way we choose to treat. We need to assess which medication to try first, second, third, and in what sequence, based on science—not just instinct.

What factors do you consider when switching therapies in RA patients?

Development of an intolerable side effect or reaction to the medication is the first consideration. Then, loss of efficacy or primary lack of response to an agent after 3 or 4 months will mandate a change in my practice. If there is a change in disease activity from low to more than moderate or there is a change of more than a couple of points toward worsening, consideration of a change in therapy should be discussed with the patient. Although the ACR has practice guidelines, they must be individualized to each patient. Switching therapies has not been well studied in randomized, placebo-controlled studies; therefore, we do not have clear-cut data that dictate when and how to switch drugs if a patient requires a change. As more data are accumulated, decision making can be based on science and not instinct.

ACR20/50/70: The ACR core data set includes 7 measures: 3 assessed by clinicians (swollen joint count [SJC], tender joint count [TJC], and physician's global assessment), 3 by patient self-report (physical function, pain, and global status on patient questionnaire), and 1 acute-phase reactant (erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]).⁹ To reach a 20% improvement (ACR20 response), a patient with RA must improve by at least 20% in the tender and swollen joint count and by at least 20% in 3 of the 5 other core set measures. Likewise, the ACR50 and ACR70 responses require 50% and 70% improvement, respectively, in the core measures.⁴ The ACR response value is a "change score" from one time point to another¹² and is used to differentiate responders to therapeutic intervention from nonresponders in clinical trials.

DAS: Unlike the ACR response value, the DAS value is an absolute number. A DAS value can be described for a given patient on a given day in any clinical setting, to be compared with other patients, with past and future scores in the same patient, and/or for analyses in groups for comparison with other groups of patients.¹² The DAS28 commonly used in clinical trials is an abbreviated version of the DAS44.¹⁰ The difference between the DAS44 and the DAS28 involves the number of joints evaluated and the methods of assessment. DAS44 counts 44 tender joints and swollen joints, and uses some subjective assessment methods. DAS28 is limited to 28 specific joints: the metacarpophalangeal and proximal interphalangeal (PIP) joints of the hands, wrists, elbows, shoulders, and knees. The feet are excluded from this joint count. The DAS28 formula includes the TJC

Fast Facts: 2008 ACR Recommendations for Use of Nonbiologic or Biologic DMARDs in RA

DMARDs in RA

In updating its recommendations (Table), the ACR considered RA disease duration, disease severity, and prognostic features. RA disease duration was categorized into 3 groups: <6 months (early disease), 6 to 24 months (intermediate disease duration), and >24 months (long disease duration). Early disease was further subdivided into ≤3 months or

3 to 6 months, when disease activity was high. RA disease severity was categorized as low, moderate, or high. Functional limitation, extra-articular disease, rheumatoid factor (RF) positivity and/or positive anti-cyclic citrullinated peptide (anti-CCP) antibodies, and/or radiographic evidence of bony erosions were considered the most clinically important markers of poor prognosis.⁸

ACR Recommendations for Initiation of DMARD Therapy for RA

Nonbiologic DMARD

- Monotherapy: Methotrexate (MTX) or leflunomide (LFL) for all RA patients
- Dual therapy: MTX + hydroxychloroquine (HCQ) for patients with moderate to high disease activity
- Triple therapy: MTX + HCQ + sulfasalazine (SSZ) for patients with poor prognostic features and moderate to high disease activity

Biologic DMARD

- Routine screening for latent tuberculosis* (TB), including risk factor† assessment and tuberculin skin test, for all patients being considered for biologic therapy
 - Induration ≥5 mm = positive tuberculin skin test result
 - Negative tuberculin skin test result does not exclude latent TB because immunosuppression can cause false-negative results in RA patients; further TB evaluation should be dictated by medical history and other clinical factors
- Anti-tumor necrosis factor- α (anti-TNF- α) agents (etanercept, infliximab, or adalimumab) plus MTX in early RA (<3 months) only for DMARD-naïve patients with high disease activity; in intermediate- and longer-duration RA, for patients with inadequate response to MTX
- Abatacept and rituximab for patients with at least moderate disease activity, poor disease prognosis, and inadequate response to MTX in combination with or in sequential administration with other nonbiologic DMARDs

Contraindications

- MTX, LFL, or biologic agents are contraindicated in patients with active bacterial infection, active herpes-zoster viral infection, active or latent TB, or acute or chronic hepatitis B or C
- Anti-TNF- α agents are contraindicated in patients with a history of heart failure or lymphoma, with multiple sclerosis, or with demyelinating disorders
- MTX, LFL, and minocycline are contraindicated prior to pregnancy and during pregnancy and breastfeeding
- Biologic agents are not recommended in the perioperative period, for at least 1 week prior to and 1 week after surgery

*Latent TB is defined as a positive tuberculin skin test result with no evidence of active TB.

†Risk factors for developing TB include HIV infection, fibrotic changes on chest radiography, organ transplantation, receiving the equivalent of >5 mg/d of prednisone for ≥1 month, use of other immunosuppressive drugs, recent (<5 years) visit to countries where TB prevalence is high, intravenous drug use, residence or employment at high-risk congregate settings (eg, prisons, long-term care facilities for the elderly, healthcare facilities, residential facilities for patients with AIDS, and homeless shelters), mycobacteriology laboratory personnel, silicosis, diabetes mellitus, chronic renal failure, severe hematologic disorders (eg, leukemias or lymphomas), carcinoma of the head/neck or lung, weight loss >10% of ideal body weight, and history of gastrectomy or jejunoileal bypass.

Saag KG et al.⁸

(28-joint count), SJC (28-joint count), ESR, and visual analog scales (VAS) from a patient's general health assessment and is easier to use than DAS44.¹⁰ The composite value obtained from these measures (the DAS28 score) is used to stratify disease activity as remission ($\text{DAS28} \leq 2.6$), low ($\text{DAS28} > 2.6$ and ≤ 3.2), moderate ($\text{DAS28} > 3.2$ and ≤ 5.1), or high ($\text{DAS28} > 5.1$).¹³ DAS is regarded as the most specific measure of inflammation for clinical trials, clinical research, and clinical care but a relatively poor measure of the overall status of patients with RA.¹²

HAQ: The overall functional status of RA patients may be determined by questionnaires such as the HAQ.¹⁴ The HAQ, a disease-specific instrument, asks 20 questions to assess 8 functional categories, with regard to whether or not aids are required to perform these functions. Responses to each question are scored by patients on a scale of 0 (without difficulty) to 3 (unable to do). The worst scores in each category are then summed and divided by the number of categories to give a disability index.¹⁵ A clinically significant improvement of the HAQ index is indicated by a -0.22 change from baseline.¹⁶

Because the ACR core data set, DAS, and HAQ are somewhat complex and time consuming to measure or administer, they are not used routinely in clinical practice. Several simplified disease assessment tools have been developed and validated as reliable measures for busy care settings.

SDAI: The Simplified Disease Activity Index (SDAI) is the numerical sum of 5 sensitive assessment measures from the DAS and ACR core data set: tender and swollen joint count (28-joint count), patient and physician global assessment of

disease activity (VAS), and level of CRP. An SDAI score ≤ 3.3 denotes remission, > 3.3 and ≤ 11 denotes low activity, > 11 and ≤ 26 denotes moderate activity, or > 26 denotes high disease activity.^{13,17}

CDAI: The Clinical Disease Activity Index (CDAI) is an abbreviated version of the SDAI and does not include the CRP value, as this laboratory value often is not available at the time of the office visit.¹⁸ A CDAI of ≤ 2.8 denotes remission, values > 2.8 and ≤ 10 denote low disease activity, values > 10 and ≤ 22 denote moderate disease activity, and values > 22 denote high disease activity.¹³

RADAI: The Rheumatoid Arthritis Disease Activity Index (RADAI), Patient Activity Scale (PAS), and Routine Assessment of Patient Index Data (RAPID) are entirely patient-assessed disease activity measures. RADAI is a 5-item questionnaire that asks the patient about global disease activity during the last 6 months and current disease activity in terms of swollen and tender joints, amount of arthritis pain, duration of morning stiffness, and amount of pain in each of several joint areas (tender joints). To arrive at a single index of patient-assessed disease activity, the scores from each item are added and the total divided by the number of items.¹⁹

PAS: PAS is a composite index of VAS for pain, a patient global VAS, and the HAQ (or the HAQII for PASII). To compute PASII, the HAQII is multiplied by 3.3 and the sum of the 3 components is divided by 3. Although PAS has not been compared with the ACR core data and DAS, it has been shown to perform as well as the SF-36 composite scale.²⁰

RAPID: RAPID3 uses the 3 patient measures from the ACR

core data set—physical function measures, VAS for pain, and global VAS—on a Multidimensional Health Assessment Questionnaire (MDHAQ).²¹ The MDHAQ includes only 8 of the original 20 activities on the HAQ, 1 from each of the 8 HAQ categories, but adds 2 additional “complex” activities to decrease the “floor effect” (ie, having normal scores despite functional limitations) and to allow quick review of relevant patient information.²²

Evaluating Bone Structure

In addition to the clinical, biochemical, and functional assessments for evaluating disease activity, the assessment of bone destruction and change is an important part of the disease evaluation process in RA. Bone destruction and change can progress despite an apparent clinical remission.²³ Radiography, MRI, ultrasonography, and computed tomography (CT) are options for evaluating bone structural changes in RA.

Radiography has been the gold standard in assessing joint erosion in RA. It routinely is used in clinical practice and in clinical trials to evaluate joint space narrowing and bone erosions.⁴ Although it can detect structural joint damage in patients with established disease, its utility is limited in early RA. During the first year after disease onset, joint erosions are not evident on x-ray films in about 50% of patients.²⁴ Moreover, radiography is insensitive to early stages of bone damage and soft tissue changes including synovitis,²⁵ and is not effective in identifying patients who will not have increasing structural joint damage (ie, future nonprogressors).²⁶

In contrast to radiography, MRI allows the assessment of all structures involved in arthritic disease:

synovial membrane, intra- and extra-articular fluid collections, cartilage, bone, ligaments, tendons, and tendon sheaths.²⁷ Moreover, because of its sensitivity, inflammatory changes, including synovitis, tendonitis, bone edema, and bone erosion, can be detected as early as 4 months after onset of RA symptoms. The severity of these early changes has been shown to be predictive of radiographic damage and clinical parameters 6 years later.²⁸ Absence of MRI erosions during early RA also is clinically useful because it helps identify nonprogressors for whom aggressive therapy may not be necessary.²⁷

Comparable to MRI in detecting early inflammatory and destructive changes in RA, ultrasonography can detect synovial thickening and Doppler ultrasound can detect synovial vascularity.²⁷ The disadvantage of ultrasonography is that it cannot penetrate bone. Thus, many complicated joint surfaces (eg, the wrists and hands) are inaccessible for evaluation.²⁹ However, its portability, relative ease of use, and lower cost compared with MRI make its use in clinical practice attractive.

CT is favored over radiography for its tomographic viewing perspective. The projectional superimposition seen on x-ray films can obscure erosions and mimic joint space narrowing. This can be avoided with CT.³⁰ However, because of its insensitivity to soft tissue changes in RA, CT is considered inferior to MRI and ultrasonography and rarely is used in clinical practice.²⁷

New Paradigm for RA Management: Early, Aggressive Treatment With Tight Monitoring

Results from 3 studies, Tight Control of RA (TICORA), BeSt (Dutch acronym for Behandel-

Strategieën, “treatment strategies”), and Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA), demonstrate that intensive RA management, initiated early in the disease course, with clinical decisions based on rigorous and routine clinical measurements can lead to improvements in physical function, radiographic progression, and disease activity, including remission.

TICORA

A single-blind randomized study in patients with active disease (DAS44 >2.4) of <5 years' duration, TICORA compared an intensive care protocol to a routine care protocol.⁵ Patients in the intensive care protocol were assessed monthly for disease activity and received intra-articular steroid injections into any swollen joint not injected during the last 3 months. At every assessment after 3 months, patients with a DAS44 >2.4 received escalation of oral treatment according to a structured protocol: sulfasalazine (SSZ) monotherapy increasing weekly to target dose→triple therapy with SSZ, methotrexate (MTX), hydroxychloroquine (HCQ)→dose escalation of MTX and then SSZ to maximum doses→addition of oral prednisone→switching to MTX/cyclosporine combination→switching to an alternative DMARD (eg, leflunomide [LFL] or sodium aurothiomalate). The routine care protocol consisted of DMARD monotherapy, switching to an alternative monotherapy or addition of a second or third DMARD in the event of treatment failure, and 3-month reviews with no formal composite measure of disease activity used in clinical decision making.

At 18-month assessment, patients in the intensive care group were significantly more likely than those in

the routine care group to show improvement: good response (82% vs 44%); remission (65% vs 16%); ACR20 (91% vs 64%); ACR50 (84% vs 40%); ACR70 (71% vs 18%) ($P < .0001$). The mean decrease in DAS44 also was significantly greater in the intensive care group than the routine care group (−3.5 vs −1.9) ($P < .0001$) and was sustained throughout the trial. Radiographic progression was reduced to a greater degree in the intensive care group; however, the difference between groups was less striking ($P = .02$), and the benefit was less impressive than that achieved with anti-TNF- α therapy.⁵

BeSt

A multicenter, randomized study in patients with active disease of ≤ 2 years' duration, BeSt compared 4 treatment strategies⁷:

- Sequential DMARD monotherapy (group 1): MTX initially and, if there was no improvement, switching to SSZ, LFL; then MTX + infliximab, if necessary
- Step-up combination therapy (group 2): MTX initially; then adding as necessary SSZ; then HCQ; then prednisone; then switching to MTX + infliximab
- Initial combination therapy with tapered high-dose prednisone (group 3): MTX, SSZ, and a tapered high-dose prednisone; then, if necessary, switching SSZ for cyclosporine; then switching to MTX + infliximab
- Initial combination therapy with infliximab (group 4): MTX + infliximab initially; then, if necessary, switched to monotherapy with SSZ, then LFL; then combination therapy with MTX + cyclosporine + prednisone, then gold + methylprednisolone, then azathioprine + prednisone.

Patients in groups 3 and 4 benefited with earlier functional improvement compared with patients in groups 1 and 2. After 3 months of therapy, mean D-HAQ (Dutch version of HAQ) scores were 1.0 in groups 1 and 2 and 0.6 in groups 3 and 4 ($P < .001$). After 1 year of therapy, mean D-HAQ scores were 0.7 in groups 1 and 2 and 0.5 in groups 3 and 4 ($P = .009$). Patients in the immediate initial combination therapy groups (groups 3 and 4) also had less radiographic damage than those in sequential monotherapy (group 1) or step-up combination therapy (group 2). The median increases in total Sharp scores were 2.0, 2.5, 1.0, and 0.5 in groups 1, 2, 3, and 4,

respectively ($P < .001$). After 1 year, 32% of all patients had clinical remission of their disease ($\text{DAS44} < 1.6$), likely due to close monitoring and immediate treatment adjustments when DAS44 scores were > 2.4 .⁷

CAMERA

A multicenter, open-label strategy trial in patients with early RA (< 1 year's disease duration), CAMERA compared an intensive treatment strategy with a conventional strategy with the aim of achieving remission.⁶ Patients in both groups received MTX, and cyclosporine if the response to maximal tolerated MTX doses was inadequate. Patients in the intensive treatment group had indi-

vidualized, monthly MTX dosage adjustments based on predefined response criteria in a computerized decision program. Patients in the conventional strategy group were treated according to common practice and were seen once every 3 months. During the 2-year trial, 50% of patients in the intensive strategy group achieved at least 1 period of remission compared with 37% in the conventional strategy group ($P = .03$). In approximately 50% of both groups, RA did not progress radiographically during a 2-year period; in the remaining 50%, the progression rate was higher in the conventional strategy group compared with the intensive strategy group.

Table 1. Switching Between Biologic Agents: Overview of Published Studies

Study	Patients (n)	Switched From	Switched To	Reason for Switching	Response
Ang et al. ³⁴	29	INF ETN	ETN INF	Misc	Efficacy of second agent <i>not</i> predicted by that of first agent
Brocq et al. ³⁵	8 6	INF ETN	ETN INF	Misc	Favorable results in about half of all patients
Favalli et al. ³⁶	14	INF	ETN	Misc	Efficacy in some but not all
Hansen et al. ⁴²	20	ETN	INF	LOE	INF as effective in switchers as in ETN-naïve patients
Haraoui et al. ³⁷	19 3	INF	ETN	LOE AE	Better efficacy with second agent in some patients
Hjardem et al. ⁴⁴	178 39 18	INF ADA ETN	ADA (56%) ETN (44%) ETN (82%) INF (18%) ADA (67%) INF (33%)	LOE (n = 109) AE (n = 72) Other (n = 54)	Better response to second treatment in LOE switchers Response to treatments equal in AE switchers Disease activity reduced after switching regardless of reason for switching or drug sequence
Sanmartí et al. ³⁸	12	INF	ETN	Secondary LOE	ETN as effective as initial INF therapy
van Vollenhoven et al. ³⁹	18 13	ETN INF	INF ETN	LOE AE	Better efficacy with second agent At least equal efficacy with second agent
Wick et al. ⁴¹	27 9	INF ETN	ADA	Secondary LOE	ADA as effective as INF/ETN had been initially
Yazici et al. ⁴⁰	21	ETN	INF	Misc	INF not as effective as in ETA-naïve patients

ADA = adalimumab; AE = adverse event; ETN = etanercept; INF = infliximab; LOE = loss of efficacy; Misc = miscellaneous.

Adapted from Van Vollenhoven RF et al.⁴³

Switching Therapies

Comparative evidence supporting 1 monotherapy treatment strategy or 1 combination treatment strategy over another is limited. A recent systematic review of head-to-head trials found no clinically important differences in efficacy among DMARDs. In this analysis, anti-TNF- α monotherapy resulted in better radiographic outcomes than MTX, but clinical outcomes did not differ substantially.³¹ In its updated recommendations, the ACR generally did not address decisions on switching or adding alternative DMARDs for patients receiving DMARD therapy (whether biologic or nonbiologic). The only exception is its recommendation to switch to biologic DMARDs only after failure of nonbiologic DMARDs.⁸

Anti-TNF- α therapies represent an important advance in the management of moderate to severe RA. Nonetheless, in clinical practice, anti-TNF- α therapies are withdrawn in approximately 30% of patients during the first year of treatment because of lack of efficacy or adverse events (AEs).³² Further management options for these patients are limited.³³

However, growing evidence suggests that patients who do not respond to therapy with 1 anti-TNF- α agent or discontinue it because of AEs may respond well to treatment with a second anti-TNF- α agent (Table 1).³⁴⁻⁴⁴

According to the results from a population-based study of 31 patients from the Stockholm TNF- α Follow-Up Registry (STURE), switching from etanercept to infliximab, mainly because of lack of efficacy, resulted in significantly better DAS28 responses. At the switch from etanercept, the mean DAS28 was 5.2 (close to baseline—consistent with lack of efficacy); the mean best DAS28 after the switch to infliximab was 3.6 ($P < .02$). Switching from infliximab to etanercept, mainly because of AEs, resulted in similar DAS28 response rates. At the time of the switch, however, the mean DAS28 value was considerably above baseline—consistent with treatment efficacy in most patients.³⁹

Another study from the same registry showed that 36 patients switched from infliximab or etanercept to adalimumab because of lack of efficacy had a significantly better clinical response (DAS28) compared with initial agents. The clinical

response of patients whose treatment was switched was comparable to the clinical response of 26 patients initially treated with adalimumab (Figure 1).⁴¹ Likewise, a retrospective study showed that the clinical outcomes (swollen and tender joint count, patient and physician global assessments, morning stiffness, and CRP level) of 20 patients switching from etanercept to infliximab, because of a lack of efficacy, improved substantially and were similar to those of 73 patients initially treated with infliximab.⁴²

Because the studies on switching anti-TNF- α therapies published to date are limited by small sample sizes and inconsistent definitions of what constitutes treatment failure (eg, primary or secondary loss of efficacy or treatment-limiting AEs) or second treatment responses (eg, defined with respect to the baseline for that agent or the baseline for the first agent), it is difficult to draw conclusions about the relative merits of sequential therapies. More studies of sequential agents using appropriate methodologies (eg, comparisons of best results to each as well as comparisons to each baseline) are needed.⁴³

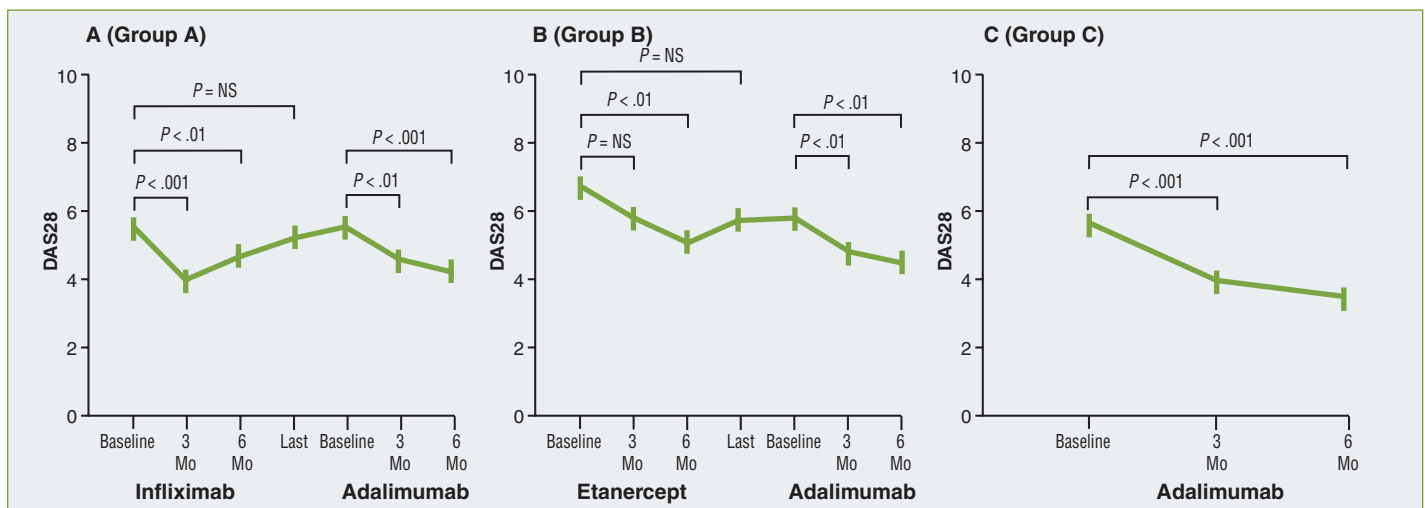


Figure 1. Adalimumab restored good clinical response after secondary loss of efficacy to infliximab or etanercept; responses were similar to those achieved by patients receiving adalimumab as initial anti-TNF- α treatment. Reprinted with permission from Wick MC et al.⁴¹

Case Study: Managing Worsening RA in a Busy Mom

Nicole M. Furfaro, MSN, ARNP

Present Illness

Melinda is a 34-year-old woman with a 5-year history of RA. She recently moved to the area and presents with the following complaints:

- Increasing fatigue during the past 2 months
- Morning stiffness during the past month
- Swollen wrists and fingers during the past 2 weeks, with increasing pain
- Onset of swelling in the toes
- Difficulty sleeping

She reports difficulty in caring for her children (ages 6 and 4 years) because of the increasing pain in her hands and wrists. Fatigue and pressures from her job as a buyer for a department store are making her “more irritable,” and she feels like “there is nothing left for me at the end of the day.” She travels frequently for work and says her sleep has suffered lately because she cannot get comfortable at night. She worries about her future ability to work and care for her family.

Medical History

At her initial presentation to her previous clinician 5 years ago, her laboratory findings included RF negativity but moderately elevated ESR and CRP levels. Radiographs obtained 2 years ago demonstrated 2 small bilateral erosions in the wrists and periarticular osteopenia in the metacarpophalangeals (MCPs) without erosions. She was treated with a combination of MTX (20 mg/wk), HCQ (400 mg daily), and naproxen sodium (500 mg twice a day), and oral corticosteroid tapers for occasional flares. She had a 6-year history of smoking 1 pack per day, but has been a nonsmoker since her RA diagnosis and last pregnancy.

Clinical and Laboratory Findings

- Fatigued appearance
- TJC 28
- SJC 24
- ESR 70 mm/h
- CRP 3.0 mg/dL
- RF 80 IU/mL (positive) (normal value: <20 IU/mL)
- Anti-CCP antibody titer: 60 (moderately positive)
- Mild anemia
- Hemoglobin 11.0 g/dL
- Hematocrit 33%
- Other findings—normal

Radiographic Evaluation

Hand radiographs: multiple erosions of the MCPs and wrists bilaterally; joint space narrowing in several PIP and MCP joints

Foot radiographs: normal

DAS28 Calculation

The patient rated her global health (GH) assessment (on a 100-mm VAS) at 88. Her clinical and laboratory findings and her GH assessment score are used to calculate her DAS28 score with the following formula:

$$\text{DAS28} = 0.56(\sqrt{\text{TJC}}) + 0.28(\sqrt{\text{SJC}}) + 0.70(\ln\text{ESR}) + 0.014(\text{GH})$$

(Note: DAS calculators are available online at: <http://www.das-score.nl/www.das-score.nl/index.html>.)

The patient's DAS28 is 8.6, correlating with high disease activity.

DAS28 Score Thresholds	Disease Activity Classification
≤2.6	Remission
>2.6 and ≤3.2	Low
>3.2 and ≤5.1	Moderate
>5.1	High

Saag KG et al.⁸ Aletaha D et al.¹³

Clinical Commentary

Nicole M. Furfaro, MSN, ARNP

Many clinicians are reluctant to use clinical assessment tools because they are unfamiliar with them, uncertain about which to choose, or fear that scoring an assessment tool will add too much time to the office visit. However, many assessment measures take a minute or less to score and can be administered by the clinician, an assistant, or a front-office person.

Treatment Decision

Current RA treatment goals are to treat to remission or a disease activity level as low as possible. Melinda's DAS28 score indicates high disease activity, and her RA is likely to progress because she has an elevated anti-CCP antibody titer, RF positivity, worsening of mild erosive disease despite MTX use, and poor functional capacity. Her ESR and CRP level also are high.

The decision is to initiate treatment with the anti-TNF- α agent adalimumab. Her current level of disease activity and need for a treatment that can be self-administered because of frequent travel are discussed with the patient. Because of her extensive travel and smoking history and the need to screen for latent TB, a purified protein derivative tuberculin skin test is administered and a chest radiograph obtained. Her vaccinations are updated according to guidelines from the Centers for Disease Control and Prevention. Upon questioning, she says she is not planning future pregnancy or upcoming surgery.

The patient is counseled to continue MTX therapy because clinical studies indicate that the combination of MTX and an anti-TNF- α agent yields the best outcomes for disease control and lack of radiographic progression. [Goekoop-Ruiterman et al. 2005; Klareskog et al. 2004] She also is advised not to restart smoking because smoking has been associated with worsening disease activity in established RA and may be an initiating event for RA in susceptible people. [Costenbader et al. 2006]

3-Month Follow-up

At her 3-month follow-up, Melinda reports feeling much better. Her morning stiffness as well as her foot swelling and pain have resolved. She has only mild swelling remaining in her wrists and hands. Her fatigue has lessened, and she is more hopeful that her RA can be controlled. Clinical assessment reveals:

- TJC 2
- SJC 1
- ESR 22mm/h
- CRP 1.2 mg/dL
- Patient's GH assessment score 0
- DAS28 3.2 (low disease activity)

Melinda understands that she needs close monitoring of her disease for best outcomes and prevention of further erosive damage. She agrees to fill out the patient assessment questionnaire each time she comes to the office because she understands it will help guide decision making about her RA treatment. She enjoys seeing how her numbers change over time in relation to how she is feeling.

Clinical Commentary

One commonly heard argument for not using measurement tools of disease activity is that the patient will feel "put out" or will not want to do it. However, most patients are eager to please their clinician and are happy to comply once they understand the rationale behind the use of the tool.

The use of validated clinical assessment tools is the way of the future. Not only do these tools facilitate measurement of disease activity and push us as providers toward appropriately managing RA for best outcomes, but they are being increasingly requested by insurance companies to justify need and cost/benefit for biologics. All clinicians should pick a tool and become familiar with its use. By doing so we can develop a common language for patient assessment and improve quality of care through communication and standardization of decision making.

Costenbader KH, Feskanich D, Mandl LA, Karlson EW. Smoking intensity, duration, and cessation, and the risk of rheumatoid arthritis in women. *Am J Med.* 2006;119:503.e1-9.

Goekoop-Ruiterman YPM, de Vries-Bouwstra JK, Allaart CF, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. *Arthritis Rheum.* 2005;52:3381-3390.

Klareskog L, van der Heijde D, de Jager JP, Gough A, Kalden J, Malaise M, et al; TEMPO (Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes) study investigators. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. *Lancet.* 2004;363:675-681.

Although patients who switch anti-TNF- α therapy do better or equally well on the second agent, a percentage do discontinue the second agent. The reasons for discontinuation of the second agent seem to be related to the reasons for stopping the first drug as revealed by 2 large registry studies.^{44,45}

The United Kingdom (UK) national register study followed 856 patients initially on etanercept, infliximab, or adalimumab who had switched to a second agent because of lack of efficacy (503 patients) or AEs (353 patients) during a 15-month period.⁴⁵ At the end of the study period, 73% of patients remained on the second therapy. Discontinuation of the first agent due to lack of efficacy was associated with an increased rate of discontinuation of the second agent due to lack of efficacy (hazard ratio [HR] 2.7, 95% confidence interval [95% CI] 2.1-3.4) but not due to AEs (HR 1.1, 95% CI 0.9-1.5). Similarly, discontinuation of the first agent due to AEs was associated with an increased rate of discontinuation of the second agent due to AEs (HR 2.3, 95% CI 1.9-2.9), but not lack of efficacy (HR 1.2, 95% CI 0.8-1.6).

The Danish registry study followed 235 patients (initially taking etanercept, infliximab, or adalimumab) who had switched therapy over 18 months.⁴⁴ The reasons for switching were lack of efficacy (109 patients), AEs (72), and other reasons (54). On average, patients remained on their second agent significantly longer (92 weeks) than on the first agent (37 weeks) ($P < .001$). Of the patients who switched because of lack of efficacy, 32% withdrew from the second treatment for the same reason and 3% withdrew because of AE. In contrast to the UK study, only 15% of

Table 2. Treatment Response Rates After 3 Months of Anti-TNF- α Therapy

Treatment Response	First-Time Users (n = 1808)	First-Time Switchers (n = 337)	Second-Time Switchers (n = 36)
ACR20	61%	51%	35%
ACR50	37%	27%	18%
ACR70	13%	7%	3%
EULAR, overall	76%	71%	58%
EULAR, good	34%	25%	9%
DAS28 low (<3.2)	38%	30%	9%
DAS28 remission (<2.6)	23%	16%	6%

Karlsson JA et al.⁴⁶

the patients who switched because of AE withdrew from the second drug for the same reason, while 25% withdrew because of lack of efficacy. Nonetheless, both studies tend to indicate that the reasons for anti-TNF- α failure are recurrent.

In patients who fail a second anti-TNF- α agent, the question is whether there is a role for a third anti-TNF- α agent or whether it is better to move on to a different class of biologic agent. This was addressed in a recent Swedish prospective, observational study that monitored response rates in 337 patients switched for the first time and 36 patients switched for the second time. These response rates were compared with response rates of first-time anti-TNF- α agent users.⁴⁶ In this study, the 36 patients switched for the second time were restricted to those who had failed 1 antibody-type and 1 receptor-type agent. As shown in Table 2, the responses of patients switched for the first time were somewhat lower, but not markedly lower, than those of first-time anti-TNF- α agent users; the responses of patients switched for the second time, however, were

markedly lower than those of first-time users or patients switched for the first time. Based on the poor response in this study of patients whose therapy was switched for the second time, it appears that in patients who fail a second anti-TNF- α agent other therapeutic options should be considered.

PCE Takeaways

- Several simplified, validated clinical assessment tools have been developed for use in busy rheumatology practices.
- Effective nonbiologic and biologic DMARD therapies for RA are now available.
- Initiation of aggressive DMARD therapy early in the disease process and frequent assessment of disease activity to guide treatment adjustment can lead to improved outcomes, including remission.
- Although comparative clinical data are limited, current evidence suggests that patients who do not respond to therapy with 1 anti-TNF- α agent or who discontinue it because of AEs may respond well to treatment with a second anti-TNF- α agent.

References

- Scott DL, Pugner K, Kaarela K, et al. The links between joint damage and disability in rheumatoid arthritis. *Rheumatology*. 2000;39:122-132.
- van der Heijde DMFM, van Leeuwen MA, van Riel PL, van de Putte LB. Radiographic progression on radiographs of hands and feet during the first 3 years of rheumatoid arthritis measured according to Sharp's method (van der Heijde modification). *J Rheumatol*. 1995;22:1792-1796.
- McQueen FM, Stewart N, Crabbe J, et al. Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals a high prevalence of erosions at four months after symptom onset. *Ann Rheum Dis*. 1998;57:350-356.
- American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum*. 2002;46:328-346.
- 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;364:263-269.
- Verstappen SMM, Jacobs JW, van der Veen MJ, et al; Utrecht Rheumatoid Arthritis Cohort study group. 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;66:1443-1449.
- Goekoop-Ruiterman YPM, de Vries-Bouwstra JK, Allaart CF, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. *Arthritis Rheum*. 2005;52:3381-3390.
- Saag KG, Teng GG, Patkar NM, et al; American College of Rheumatology. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum*. 2008;59:762-784.
- Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum*. 1995;38:727-735.
- Prevo ML, van't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum*. 1995;38:44-48.
- Fries JF, Spitz PW, Young DY. The dimensions of health outcomes: the Health Assessment Questionnaire, disability and pain scales. *J Rheumatol*. 1982;9:789-793.
- Pincus T. The DAS is the most specific measure, but a patient questionnaire is the most informative measure to assess rheumatoid arthritis. *J Rheumatol*. 2006;33:834-837.
- Aletaha D, Smolen J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. *Clin Exp Rheumatol*. 2005;23(5 Suppl 39):S100-S108.
- Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum*. 1980;23:137-145.
- Tomlin GS, Holm MB, Rogers JC, Kwok CK. Comparison of standard and alternative Health Assessment Questionnaire scoring procedures for documenting functional outcomes in patients with rheumatoid arthritis. *J Rheumatol*. 1996;23:1524-1530.
- Wells GA, Tugwell P, Kraag GR, Baker PRA, Groh J, Redelmeier DA. Minimum important difference between patients with rheumatoid arthritis: the patient's perspective. *J Rheumatol*. 1993;20:557-560.
- Smolen JS, Breedveld FC, Schiff MH, et al. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. *Rheumatology*. 2003;42:244-257.
- Shaver TS, Anderson JD, Weidensaul DN, et al. The problem of rheumatoid arthritis disease activity and remission in clinical practice. *J Rheumatol*. 2008;35:1015-1022.
- Fransen J, Häuselmann H, Michel BA, et al. Responsiveness of the self-assessed rheumatoid arthritis disease activity index to a flare of disease activity. *Arthritis Rheum*. 2001;44:53-60.
- Wolfe F, Michaud K, Pincus T. A composite disease activity scale for clinical practice, observational studies, and clinical trials: the Patient Activity Scale (PAS/PAS-II). *J Rheumatol*. 2005;32:2410-2415.
- Pincus T, Sokka T. Quantitative clinical assessment in busy rheumatology settings: the value of short patient questionnaires. *J Rheumatol*. 2008;35:1235-1237.
- Pincus T, Yazici Y, Bergman M. Development of a multi-dimensional health assessment questionnaire (MDHAQ) for the infrastructure of standard clinical care. *Clin Exp Rheumatol*. 2005;23(Suppl 39):S19-S28.
- Molenaar ETH, Voskuyl AE, Dinant HJ, Bezemer PD, Boers M, Dijkmans BAC. Progression of radiologic damage in patients with rheumatoid arthritis in clinical remission. *Arthritis Rheum*. 2004;50:36-42.
- Fex E, Jonsson K, Johnson U, Eberhardt K. Development of radiographic damage during the first 5-6 years of rheumatoid arthritis. A prospective follow-up study of a Swedish cohort. *Br J Rheumatol*. 1996;35:1106-1115.
- Backhaus M, Kamradt T, Sandrock D, et al. Arthritis of the finger joints. A comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. *Arthritis Rheum*. 1999;42:1232-1245.
- Paulus HE, Oh M, Sharp JT, et al. Correlation of single time-point damage scores with observed progression of radiographic damage during the first 6 years of rheumatoid arthritis. *J Rheumatol*. 2003;30:705-713.
- Østergaard M. Imaging in early rheumatoid arthritis: roles of magnetic resonance imaging, ultrasonography, conventional radiography and computed tomography. *Best Pract Res Clin Rheum*. 2005;19:91-116.
- McQueen FM, Benton N, Perry D, et al. Bone edema scored on magnetic resonance imaging scans of the dominant carpus at presentation predicts radiographic joint damage of the hands and feet six years later in patients with rheumatoid arthritis. *Arthritis Rheum*. 2003;48:1814-1827.
- Hoving JL, Buchbinder R, Hall S, et al. A comparison of magnetic resonance imaging, sonography, and radiography of the hand in patients with early rheumatoid arthritis. *J Rheumatol*. 2004;31:663-675.
- Alasaarela E, Suramo I, Tervonen O, et al. Evaluation of humoral head erosions in rheumatoid arthritis: a comparison of ultrasonography, magnetic resonance imaging, computed tomography and plain radiography. *Br J Rheumatol*. 1998;37:1152-1156.
- Donahue KE, Gartlehner G, Jonas DE, et al. Systematic review: comparative effectiveness and harms of disease-modifying medications for rheumatoid arthritis. *Ann Intern Med*. 2008;148:124-134.
- Østergaard M, Unkerskov J, Linde L, et al. Low remission rates but long drug survival in rheumatoid arthritis patients treated with infliximab or etanercept—results from the nationwide Danish “DANBIO” database. *Scand J Rheumatol*. 2007;36:151-154.
- Hyrich KL, Lunt M, Dixon WG, et al. Effects of switching between anti-TNF therapies on HAQ response in patients who do not respond to their first anti-TNF drug. *Rheumatology*. 2008;47:1000-1005.
- Ang HT, Helfgott S. Do the clinical responses and complications following etanercept or infliximab therapy predict similar outcomes with the other tumor necrosis factor-alpha antagonists in patients with rheumatoid arthritis? *J Rheumatol*. 2003;30:2315-2318.
- Brocq O, Plubel Y, Breuil V, et al. Etanercept-infliximab switch in rheumatoid arthritis 14 out of 131 patients treated with anti TNF-alpha. *Presse Med*. 2002;31:1836-1839.
- Favalli EG, Arreghini M, Arnoldi C, et al. Anti-tumor necrosis factor alpha switching in rheumatoid arthritis and juvenile chronic arthritis[letter]. *Arthritis Rheum*. 2004;51:301-302.
- Haraoui B, Keystone EC, Thorne JC, et al. Clinical outcomes of patients with rheumatoid arthritis after switching from infliximab to etanercept. *J Rheumatol*. 2004;31:2356-2359.
- Sanmartí R, Gómez-Puerta JA, Rodríguez-Cros JR, Albaladejo C, Muñoz-Gómez J, Cañete JD. Etanercept in rheumatoid arthritis patients with a poor therapeutic response to Infliximab. *Med Clin (Barc)*. 2004;122:321-324.
- van Vollenhoven R, Harju A, Brannemark S, Klareskog L. Treatment with infliximab (Remicade) when etanercept (Enbrel) has failed or vice versa: data from the STURE registry showing that switching tumour necrosis factor alpha blockers can make sense. *Ann Rheum Dis*. 2003; 62:1195-1198.
- Yazici Y, Erkan D. Do etanercept-naïve patients with rheumatoid arthritis respond better to infliximab than patients for whom etanercept has failed [letter]? *Ann Rheum Dis*. 2004;63:607-608.
- Wick MC, Ernestam S, Lindblad S, Bratt J, Klareskog L, van Vollenhoven RF. Adalimumab (Humira) restores clinical response in patients with secondary loss of efficacy from infliximab (Remicade) or etanercept (Enbrel): results from the STURE registry at Karolinska University Hospital. *Scand J Rheumatol*. 2005;34:353-358.
- Hansen KE, Hildebrand JP, Genovese MC, et al. The efficacy of switching from etanercept to infliximab in patients with rheumatoid arthritis. *J Rheumatol*. 2004;31:1098-1102.
- van Vollenhoven RF. Switching between biological agents. *Clin Exp Rheumatol*. 2004;22 (Suppl 35):S115-S121.
- Hjardem E, Østergaard M, Pødenphant J, et al. Do rheumatoid arthritis patients in clinical practice benefit from switching from infliximab to a second tumor necrosis factor alpha inhibitor? *Ann Rheum Dis*. 2007;66:1184-1189.
- Hyrich KL, Lunt M, Watson KD, Symmons DPM, Silman AJ; for the British Society for Rheumatology Biologics Register. Outcomes after switching from one anti-tumor necrosis factor α agent to a second anti-tumor necrosis factor α agent in patients with rheumatoid arthritis. Results from a large UK national cohort study. *Arthritis Rheum*. 2007;56:13-20.
- Karlsson JA, Kristensen LE, Kapetanovic MC, et al. Treatment response to a second or third TNF-inhibitor in RA: results from the South Swedish Arthritis Treatment Group Register. *Rheumatology*. 2008;47:507-513.

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About PCE Updates in Rheumatology...

Welcome to the first of 4 issues of 2008 *PCE Updates in Rheumatology*, Volume 2 developed for those NPs and PAs who serve patients in rheumatology practices throughout the country. "The demands for rheumatologic services are increasing exponentially with the aging population, while the number of physicians entering the rheumatology specialty is shrinking," according to the Society of Physician Assistants in Rheumatology (SPAR). Rheumatologists treating patients with rheumatoid diseases increasingly rely on specialist NPs and PAs to take an active management role in the frequent clinical contacts these patients require.

As healthcare professionals, NPs and PAs collectively provide a vital and increasing role in the diagnosis and management of acute and chronic illness. As clinicians, you spend more time with patients than most physicians, with your emphasis being patient disease state counseling and preventive care. Most importantly, NPs and PAs report that their roles have evolved from assisting physicians to treating and following their own patients. This increased role includes writing prescriptions,

monitoring patient progress, and seeing patients in your own examination rooms. As NPs and PAs, you are rapidly emerging as key providers of patient care. You practice with greater autonomy and prescribe more medication than ever before.

Approximately 286 NPs and 188 PAs see patients in rheumatology practices that provide ongoing care for patients with rheumatoid diseases. Therefore, you need to be thoroughly familiar with the latest therapeutic advances. This issue of *PCE Updates in Rheumatology* summarizes the ACR's 2008 recommendations for the use of DMARD therapy in RA, strategies for clinical assessment, and the evidence supporting switching therapy when efficacy is lost or adverse events warrant.

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