# Proposed Severity and Response Criteria for Routine Assessment of Patient Index Data (RAPID3): Results for Categories of Disease Activity and Response Criteria in Abatacept Clinical Trials

THEODORE PINCUS, PATRICIA HINES, MARTIN J. BERGMAN, YUSUF YAZICI, LISA C. ROSENBLATT, and ROSS MacLEAN

***ABSTRACT.*** ***Background.*** An index is needed to assess the status of patients with rheumatoid arthritis (RA), as none of the existing measures are applicable to all individual patients. The 28-joint Disease Activity Score (DAS28) is the most specific and widely used index. Routine Assessment of Patient Index Data (RAPID3) is an index containing only the 3 patient self-report core dataset measures, without a laboratory test or formal joint count, and with simple scoring. RAPID3 is correlated significantly with DAS28, but calculated in 5–10 seconds on a Multidimensional Health Assessment Questionnaire (MDHAQ), compared to 114 seconds for DAS28.

***Methods.*** DAS28 (0–10 scale) categories for high, moderate, and low activity, and remission (≤ 2.6, 2.6–3.2, 3.21–5.1, and > 5.1, respectively) and proposed RAPID3 (0–30 scale) categories for severity (0 ≤ 3, 3.1–6, 6.1–12, and > 12) were compared in patients taking abatacept and control-treated patients at the endpoint of the Abatacept in Inadequate Response to Methotrexate (AIM) and the Abatacept Trial in Treatment of Anti-TNF INadequate Responders (ATTAIN) clinical trials, using cross-tabulations and kappa statistics.

***Results.*** Overall, 92%–99% of patients classified as having high DAS28 activity had high or moderate RAPID3 severity, while 64%–83% in DAS28 remission had RAPID3 low severity or remission; 50%–82% of patients with good or poor EULAR responses had good or poor RAPID3 responses. Kappa values ranged from 0.25 to 0.48, and weighted kappas from 0.32 to 0.52, indicating fair to moderate agreement for the 2 indices.

***Conclusion.*** Proposed RAPID3 severity and response categories yield comparable results to DAS28 and EULAR criteria in AIM and ATTAIN. DAS28 is more specific for clinical trials. RAPID3 does not preclude also scoring DAS28, and may be informative in the infrastructure of routine care. (First Release Nov 15 2011; J Rheumatol 2011;38:2565–71; doi:10.3899/jrheum.110262)

*Key Indexing Terms:*
RHEUMATOID ARTHRITIS ABATACEPT 28-JOINT DISEASE ACTIVITY SCORE
ROUTINE ASSESSMENT OF PATIENT INDEX DATA
MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE

Assessment of patients with rheumatoid arthritis (RA) requires a pooled index of various measures[1], as no single measure is adequate to characterize clinical status in all individual patients. The most widely used index is the 28-joint Disease Activity Score (DAS28)[2,3], which includes a tender joint count (TJC), a swollen joint count (SJC), an acute-phase reactant laboratory test [erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)], and patient global estimate of status.

The DAS28 is the most specific measure to assess patients with RA, but it has several limitations for usual care[4,5]: (1) a laboratory test (ESR or CRP) is needed, which often is not available at the time of the patient visit, and is normal in about 40% of patients[6,7,8]; (2) complex scoring is required, albeit with an excellent available Website (www.das-score.nl/www.das-score.nl/index.html); (3) a formal 28-joint TJC and SJC must be scored, which is not performed at most visits in usual care[9] as it involves about 90 seconds[10]; formal joint counts cannot be assessed in a general medical setting, home, or outside a specific rheumatology setting, and

*From the Division of Rheumatology, Department of Medicine, New York University (NYU) School of Medicine and NYU Hospital for Joint Diseases, New York, New York; Bristol-Myers Squibb (BMS), Hopewell, New Jersey; and Arthritis and Rheumatology, Taylor Hospital, Ridley Park, Pennsylvania, USA.*

*Supported by a research grant from Bristol-Myers Squibb to T. Pincus. Dr. Pincus has received research support from Amgen, Bristol-Myers Squibb, and UCB; and has acted as a consultant to Bristol-Myers Squibb, Centocor, and UCB. Y. Yazici and M. Bergman have acted as consultants to Bristol-Myers Squibb.*

*T. Pincus, MD; Y. Yazici, MD, Division of Rheumatology, Department of Medicine, NYU School of Medicine and NYU Hospital for Joint Diseases; P. Hines, AS; L.C. Rosenblatt, MD; R. Maclean, MD, MBA, Health Services, Bristol-Myers Squibb; M.J. Bergman, MD, Arthritis and Rheumatology, Taylor Hospital.*

*Address correspondence to Dr. T. Pincus, Division of Rheumatology, Room 1608, NYU Hospital for Joint Diseases, 301 East 17th Street, New York, NY 10003, USA. E-mail: tedpincus@gmail.com*

*Accepted for publication August 3, 2011.*

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

results vary considerably when performed by different rheumatologists[11,12].

Routine Assessment of Patient Index Data (RAPID3) is an index of only 3 patient self-report core dataset measures (physical function, pain, and patient global estimate of status), with simple scoring, and no laboratory test or formal joint count. RAPID3 is calculated on a Multidimensional Health Assessment Questionnaire (MDHAQ) in 5–10 seconds[13], compared to 114 seconds for DAS28 and 106 seconds for a Clinical Disease Activity Index (CDAI)[14]. RAPID3 is correlated significantly with DAS28 in studies in clinical care[15].

RAPID3 is designed to be calculated on an MDHAQ[16,17], but can also be calculated from the standard HAQ[18], from which it was developed (8 items on the MDHAQ are identical[16]). However, RAPID3 from standard HAQ requires 42 seconds versus 5 seconds for RAPID3 on an MDHAQ[13]. RAPID3 incorporating the standard HAQ is correlated significantly with DAS28 in clinical trials of methotrexate[19], leflunomide[19], adalimumab[20], abatacept[21], and certolizumab[22], and distinguishes active from control treatment similarly. While the specificity of DAS28[4] renders it optimal for clinical trials, studies to compare DAS28 and RAPID3 in clinical trials can provide useful information to clinicians in interpretation of RAPID3 scores in usual clinical care[23,24,25].

We extended observations of correlations between DAS28 and RAPID3 with further post-hoc analyses of data from the Abatacept in Inadequate response to Methotrexate[26] (AIM) trial and the Abatacept Trial in Treatment of Anti-TNF INadequate Responders[27] (ATTAIN). We compared 4 categories of DAS28 versus 4 RAPID3 categories for activity severity: high, moderate, and low, and remission. We also compared European League Against Rheumatism (EULAR)-DAS28 improvement criteria to proposed RAPID3 improvement criteria in 3 categories: good, moderate, and poor.

## MATERIALS AND METHODS

*Clinical trials*. Post-hoc analyses were performed on databases from the AIM[26] and ATTAIN[27] clinical trials. All 7 RA core dataset measures[28,29,30] were analyzed at baseline and at endpoint, 12 months in AIM and 6 months in ATTAIN, using last observation carried forward. Further details concerning these clinical trials and post-hoc analyses are found in previous reports[21,26,27].

*Indices*. DAS28 has a score range of 0–10 (Table 1)[3,31]. RAPID3 is designed to be scored in usual care, and includes only the 3 patient-reported RA core data set measures[28] — physical function, pain, and patient global estimate of status. Each is scored 0–10, for a total range of 0–30 (Table 1)[15,21]. In earlier reports, 0–30 RAPID3 scores were recalculated to 0–10, dividing by 3. However, the raw 0–30 score requires about 5 seconds compared to 10 seconds for a recoded score, and is now recommended[13]. In our study, physical function was computed from the standard HAQ Disability Index (HAQ-DI) with standard 0–10 visual analog scale (VAS), although 0–3 HAQ-DI scores were converted to 0–10, as each of the 3 measures is weighted equally. DAS28 and RAPID3 scores were computed using the standard formulas rather than a Website or scoring templates.

The term "activity" is used to describe DAS28 categories, and the terms "severity" and "near-remission" to describe RAPID3 categories, as patient questionnaire scores are sensitive to both activity and damage[32]. Criteria for high, moderate, and low activity, and remission for DAS28 (0–10) are > 5.1, > 3.2–5.1, ≥ 2.6–3.2, and < 2.6, respectively (Table 1)[33]. Proposed criteria for high, moderate, and low severity and near-remission for RAPID3 (0–30) are > 12, > 6–12, > 3–6, and ≤ 3, respectively (Table 1)[15,21].

EULAR-DAS28 response criteria categories are classified as good = decrease > 1.2 units AND endpoint score ≤ 3.2; moderate = decrease > 1.2 units AND endpoint score ≥ 3.2, OR decrease of 0.6–1.2 units AND endpoint score ≤ 5.1; poor = decrease < 0.6 units, OR endpoint score > 5.1 (Table 1)[34]. Proposed RAPID3 response criteria categories are classified as good = decrease > 3.6 units (on a 0–30 scale) AND endpoint score of < 6; moderate = decrease of > 1.8 and ≤ 3.6 units AND endpoint score ≤ 12, OR decrease of > 3.6 units AND endpoint score ≥ 6 to ≥ 12; poor = decrease of < 1.8 units OR endpoint score > 12 (Table 1).

*Statistical analyses*. DAS28 and RAPID3 were compared at baseline and endpoint (52 weeks in AIM, 26 weeks in ATTAIN) in patients who had been randomized to abatacept or control treatment, using cross-tabulations. The proportions of patients in categories of high, moderate, and low activity, and remission for DAS28 and RAPID3 severity were compared in each arm of each trial. Almost all patients had severe status at baseline, and only data at endpoint are presented. EULAR-DAS28 and proposed RAPID3 response criteria were compared with cross-tabulations for the proportions of good, moderate, and poor responses, with statistical significance analyzed according to kappa and weighted kappa statistics[35].

## RESULTS

*Comparisons of RAPID3 and DAS28 activity/severity categories at the conclusion of the AIM trial*. DAS28 remission and low, moderate, and high activity scores at the conclusion of AIM were seen respectively in 17%, 10%, 53%, and 20% of patients randomized to abatacept + methotrexate, versus 2%, 2%, 40%, and 56% randomized to placebo + methotrexate (Table 2). RAPID3 remission, low, moderate, and high severity scores at the conclusion of AIM were seen in 16%, 19%, 33%, and 33% of patients randomized to abatacept + methotrexate, versus 5%, 10%, 28%, and 56% of patients randomized to placebo + methotrexate (Table 2).

Low or remission versus high or moderate severity was seen for abatacept patients in 27% versus 73% according to DAS28, and 35% versus 66% according to RAPID3, and for control patients in 4% versus 96% according to DAS28, and 15% versus 85% according to RAPID3.

Overall, 78%–80% of patients classified as having high disease activity according to DAS28 had high disease severity according to RAPID3, and 95%–99% high or moderate severity according to RAPID3 (Table 2). By contrast, 46%–50% classified as in remission according to DAS28 were in RAPID3 remission, and 64%–75% were in RAPID3 low severity or remission (Table 2). Kappa and weighted kappa statistics ranged from 0.28 to 0.42, indicating fair to moderate agreement between DAS28 and RAPID3 categories.

*Comparisons of RAPID3 and DAS28 activity/severity categories at the conclusion of the ATTAIN trial*. DAS28 remission and low, moderate, and high activity at the conclusion of the ATTAIN trial were seen respectively in 10%, 6%, 34%, and 50% of patients randomized to abatacept + methotrexate, versus 1%, 2%, 16%, and 81% of patients randomized to placebo + methotrexate (Table 3). RAPID3 remission and low, moderate, and high severity at the conclusion of ATTAIN were seen

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

*Table 1.* Features of DAS28 and RAPID3 to assess patients with rheumatoid arthritis (RA).

| Features | DAS28[3,31] | RAPID[15] |
|---|---|---|
| Variables included | | |
| No. tender joints | 0.56 × sq rt (TJC28) | — |
| No. swollen joints | 0.28 × sq rt (SJC28) | — |
| Physician global estimate | — | — |
| ESR (or CRP*) | 0.70 × ln (ESR) | — |
| Patient function | — | 0–10 |
| Patient pain | — | 0–10 |
| Patient global estimate | 0.014 × PTGL | 0–10 |
| Total score | 0–10 | 0–30 |
| Categories of activity/severity | | |
| High | > 5.1 | > 12 |
| Moderate | > 3.2 – ≤ 5.1 | > 6.0 – ≤ 12.0 |
| Low | > 2.6 – ≤ 3.2 | > 3.0 – ≤ 6.0 |
| Remission | 0 – ≤ 2.6 | 0 – ≤ 3.0 |
| Response/improvement categories | | |
| Good | Decrease > 1.2 units AND endpoint score < 3.2 | Decrease > 3.6 units AND endpoint score < 6 |
| Moderate | Decrease > 1.2 units AND endpoint score ≥ 3.2 OR Decrease 0.6–1. 2 units AND endpoint score ≤ 5.1 | Decrease > 3.6 units AND endpoint score ≥ 6 OR Decrease 1.8–3.6 units AND endpoint score ≤ 12 |
| Poor | Decrease < 0.6 unit OR Decrease 0.6–1.2 units AND endpoint score > 5.1 | Decrease < 1.8 units OR Decrease 1.8–3.6 units AND endpoint score > 12 |

*DAS28-CRP uses a different formula than DAS28-ESR. DAS28: 28-joint Disease Activity Score; RAPID3: Routine Assessment of Patient Index Data; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TJC: tender joint count; SJC: swollen joint count.

in 11%, 14%, 21%, and 55% of patients randomized to abatacept + methotrexate, versus 2%, 5%, 12%, and 81% of patients randomized to placebo + methotrexate (Table 3).

Overall, 76%–89% of patients classified as having high DAS28 activity had high RAPID3 severity, and 92%–97% high or moderate severity according to RAPID3 (Table 3),

*Table 2.* Number (%) of patients in the AIM trial in RAPID3 versus DAS28 disease activity/severity categories at 52 weeks.

| Abatacept Treatment Group | RAPID3 Severity: High, n (%) | Moderate, n (%) | Low, n (%) | Remission, n (%) | Total, n (%) |
|---|---|---|---|---|---|
| DAS28 Activity | | | | | |
| High | 59 (80) | 14 (19) | 0 | 1 (< 1) | 74 (20) |
| Moderate | 58 (29) | 80 (40) | 42 (21) | 18 (9) | 198 (53) |
| Low | 4 (11) | 14 (38) | 10 (27) | 9 (24) | 37 (10) |
| Remission | 2 (3) | 15 (23) | 18 (28) | 30 (46) | 65 (17) |
| Total | 123 (33) | 123 (33) | 70 (19) | 58 (16) | 374 (100) |
| Kappa = 0.28; weighted kappa = 0.42. | | | | | |
| Control treatment group | | | | | |
| DAS28 Activity | | | | | |
| High | 80 (78) | 17 (17) | 5 (5) | 0 | 102 (56) |
| Moderate | 23 (31) | 33 (45) | 12 (16) | 6 (8) | 74 (40) |
| Low | 1 (33) | 0 | 0 | 2 (67) | 3 (2) |
| Remission | 0 | 1 (25) | 1 (25) | 2 (50) | 4 (2) |
| Total | 104 (56) | 51 (28) | 18 (10) | 10 (5) | 183 (100) |
| Kappa = 0.33; weighted kappa = 0.40. | | | | | |

AIM: Abatacept in Inadequate Response to Methotrexate; RAPID3: Routine Assessment of Patient Index Data; DAS28: 28-joint Disease Activity Score.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

*Table 3.* Number (%) of patients in the ATTAIN trial in RAPID3 versus DAS28 disease activity/severity categories at 26 weeks.

| Abatacept Treatment Group | RAPID3 Severity | | | | |
|---|---|---|---|---|---|
| | High, n (%) | Moderate, n (%) | Low, n (%) | Remission, n (%) | Total, n (%) |
| DAS28 Activity | | | | | |
| High | 68 (76) | 15 (17) | 6 (7) | 1 (1) | 90 (50) |
| Moderate | 26 (43) | 18 (30) | 7 (12) | 9 (15) | 60 (34) |
| Low | 3 (27) | 2 (18) | 3 (27) | 3 (27) | 11 (6) |
| Remission | 1 (6) | 2 (11) | 9 (50) | 6 (33) | 18 (10) |
| Total | 98 (55) | 37 (21) | 25 (14) | 19 (11) | 179 (100) |
| Kappa = 0.25; weighted kappa = 0.40. | | | | | |
| Control treatment group | | | | | |
| DAS28 Activity | | | | | |
| High | 70 (89) | 7 (9) | 2 (3) | 0 | 79 (81) |
| Moderate | 9 (56) | 3 (19) | 2 (13) | 2 (13) | 16 (16) |
| Low | 0 | 1 (50) | 1 (50) | 0 | 2 (2) |
| Remission | 0 | 1 (100) | 0 | 0 | 1 (1) |
| Total | 79 (81) | 12 (12) | 5 (5) | 2 (2) | 98 (100) |
| Kappa = 0.26; weighted kappa = 0.32. | | | | | |

ATTAIN: Abatacept Trial in Treatment of Anti-TNF INadequate Responders; RAPID3: Routine Assessment of Patient Index Data; DAS28: 28-joint Disease Activity Score.

while 33% classified as in remission according to DAS28 were in RAPID3 remission, and 83% in RAPID3 remission or low activity. Kappa and weighted kappa statistics ranged from 0.25 to 0.40, indicating fair agreement between DAS28 and RAPID3 categories.

*EULAR-DAS28 and proposed RAPID3 response criteria in the AIM trial.* In the AIM trial, EULAR-DAS28 criteria indicated good, moderate, and poor responses in 27%, 62%, and 10%, respectively, of abatacept-treated patients compared to 4%, 59%, and 37% of control patients. Proposed RAPID3 response criteria indicated good, moderate, and poor responses in 35%, 45%, and 20% of abatacept-treated patients compared to 16%, 43%, and 42% for control patients (Table 4). Among all patients in the AIM trial, good, moderate, and poor responses were seen in 20%, 61%, and 19%, respectively, for EULAR-DAS28, compared to 29%, 44%, and 27% for RAPID3 (Table 4).

Among 102 abatacept-treated patients with good EULAR-DAS28 responses, 67 (66%), 29 (28%), and 6 (6%) had good, moderate, and poor responses according to RAPID3 ($p < 0.001$; kappa 0.35; weighted kappa 0.40; Table 4). Among patients randomized to control treatment, 68 had poor responses according to EULAR-DAS28 criteria, of whom 46 (68%) had poor responses according to RAPID3 ($p < 0.001$; kappa 0.29; weighted kappa 0.36; Table 4). Among all patients, 109 had good responses according to EULAR-DAS28, of whom 72 (66%) had good, 31 (28%) moderate, and 6 (6%) poor responses according to RAPID3

*Table 4.* Number (%) of patients in the AIM trial in RAPID3 response categories as compared to EULAR-DAS28 response categories.

| AIM Trial Treatment Groups | EULAR-DAS28 Response Categories | EULAR-DAS28 No. (%) Patients | RAPID3 Response Categories, No. (%) Patients | | |
|---|---|---|---|---|---|
| | | | Good (improve > 3.6 units) | Moderate (> 1.8 and ≤ 3.6 units) | Poor (improve ≤ 1.8 units) |
| Abatacept (kappa 0.35, weighted kappa 0.40) | Good | 102 (27) | 67 (66) | 29 (28) | 6 (6) |
| | Moderate | 233 (62) | 63 (27) | 130 (56) | 40 (17) |
| | Poor | 39 (10) | 2 (5) | 8 (21) | 29 (74) |
| | Total | 374 (100) | 132 (35) | 167 (45) | 75 (20) |
| Control (kappa 0.29, weighted kappa 0.36) | Good | 7 (4) | 5 (71) | 2 (29) | 0 |
| | Moderate | 108 (59) | 22 (20) | 56 (52) | 30 (28) |
| | Poor | 68 (37) | 2 (3) | 20 (29) | 46 (68) |
| | Total | 183 (100) | 29 (16) | 78 (43) | 76 (42) |
| All patients (kappa 0.35, weighted kappa 0.43) | Good | 109 (20) | 72 (66) | 31 (28) | 6 (6) |
| | Moderate | 341 (61) | 85 (25) | 186 (55) | 70 (21) |
| | Poor | 107 (19) | 4 (4) | 28 (11) | 75 (70) |
| | Total | 557 (100) | 161 (29) | 245 (44) | 151 (27) |

AIM: Abatacept in Inadequate Response to Methotrexate; RAPID3: Routine Assessment of Patient Index Data; EULAR: European League Against Rheumatism; DAS28: 28-joint Disease Activity Score.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

(Table 4). Among 341 patients who had moderate responses according to EULAR-DAS28 criteria, 186 (55%) had moderate, 85 (25%) good, and 70 (21%) poor responses according to RAPID3 (Table 4). Among 107 patients who had poor responses according to EULAR-DAS28 criteria, 75 (70%) had poor, 28 (11%) moderate, and 4 (4%) good responses according to RAPID3 ($p < 0.001$; kappa 0.35; weighted kappa 0.43; Table 4).

*EULAR-DAS28 and proposed RAPID3 response criteria in the ATTAIN trial*. In ATTAIN, good, moderate, and poor responses were seen in 17%, 56%, and 28%, respectively, of abatacept-treated patients for EULAR-DAS28 criteria, compared to 4%, 30%, and 66% in control patients. Proposed RAPID3 good, moderate, and poor responses were seen in 24%, 45%, and 31% of abatacept-treated patients compared to 6%, 32%, and 62% of control patients (Table 5). Among all patients in the ATTAIN trial, good, moderate and poor responses were seen in 12%, 46%, and 41%, respectively, for EULAR-DAS28 compared to 18%, 40%, and 42% for RAPID3 (Table 5).

Of 30 abatacept-treated patients with good EULAR-DAS28 responses, 20 (67%) had good, 6 (20%) moderate, and 4 (13%) poor responses according to RAPID3 ($p < 0.001$; kappa 0.37; weighted kappa 0.44; Table 5). Among patients randomized to control treatment, 65 had poor EULAR-DAS28 responses, of whom 53 (82%) had poor, 11 (17%) moderate, and 1 (2%) good RAPID3 responses ($p < 0.001$; kappa 0.48; weighted kappa 0.52; Table 5). Among all patients in the ATTAIN trial, 34 had good responses according to EULAR-DAS28, of whom 22 (65%) had good, 8 (24%) moderate, and 4 (12%) poor responses according to RAPID3 (Table 5). Among 129 patients with moderate responses according to EULAR-DAS28, 75 (58%) had moderate, 26 (20%) good, and 28 (22%) poor RAPID3 responses (Table 5). Among 115 patients with poor responses according to EULAR-DAS28, 85 (74%) had poor, 29 (25%) moderate, and 1 (1%) good RAPID3 responses ($p < 0.001$; kappa 0.44; weighted kappa 0.51; Table 4).

## DISCUSSION

The results indicate fair to moderate agreement between DAS28 and RAPID3, both for categories of high, moderate, and low activity/severity and remission, as well as for EULAR-DAS28 response criteria and proposed RAPID3 response criteria. Lower levels of both remission and good responses are seen according to RAPID3 compared to DAS28, in both abatacept and control patients. This finding may reflect, in part, that RAPID3 is more sensitive than DAS28 to fibromyalgia or joint damage, resulting in higher scores for pain and global status, in the absence of overt inflammation.

At the same time, the RAPID3 criteria may be more stringent, and patients who have a pain score or global estimate > 3 may not consider their disease in remission, even if they have no swollen and tender joints. A patient who has a TJC and SJC of 0, an ESR of 20, but a patient global estimate of 3 will have a DAS28 of 2.5, indicating remission. Conversely, a patient with no swollen joints, ESR of 18 (indicative of no inflammation), but patient global estimate of 10 and 28 tender joints (indicative of fibromyalgia) would have a DAS28 of 6.4 and CDAI of 38 (as well as RAPID3 of 20), all suggesting high disease activity.

Any clinical measure or index must be regarded as one component of the data needed for clinical decisions, and should not be the only variable that triggers a response from a clinician. Consider ESR, which, for example, might be elevated to 75 mm/h from a normal value 3 months earlier. This finding could signify a flare of RA, but also an infection or

*Table 5*. Number (%) of patients in the ATTAIN trial in RAPID3 response categories as compared to EULAR-DAS28 response categories.

| ATTAIN Trial Treatment Groups | EULAR-DAS28 Response Categories | EULAR-DAS28 No. (%) Patients | RAPID3 Response Categories, No. (%) Patients | | |
|---|---|---|---|---|---|
| | | | Good (improve > 3.6 units) | Moderate (> 1.8 and ≤ 3.6 units) | Poor (improve ≤ 1.8 units) |
| Abatacept (kappa 0.37, weighted kappa 0.44) | Good | 30 (17) | 20 (67) | 6 (20) | 4 (13) |
| | Moderate | 100 (56) | 23 (23) | 57 (57) | 20 (20) |
| | Poor | 50 (28) | 0 | 18 (36) | 32 (64) |
| | Total | 180 (100) | 43 (24) | 81 (45) | 56 (31) |
| Control (kappa 0.48, weighted kappa 0.52) | Good | 4 (4) | 2 (50) | 2 (50) | 0 |
| | Moderate | 29 (30) | 3 (10) | 18 (62) | 8 (28) |
| | Poor | 65 (66) | 1 (2) | 11 (17) | 53 (82) |
| | Total | 98 (100) | 6 (6) | 31 (32) | 61 (62) |
| All patients (kappa 0.44, weighted kappa 0.51) | Good | 34 (12) | 22 (65) | 8 (24) | 4 (12) |
| | Moderate | 129 (46) | 26 (20) | 75 (58) | 28 (22) |
| | Poor | 115 (41) | 1 (1) | 29 (25) | 85 (74) |
| | Total | 278 (100) | 49 (18) | 112 (40) | 117 (42) |

ATTAIN: Abatacept Trial in Treatment of Anti-TNF INadequate Responders; EULAR: European League Against Rheumatism; DAS28: 28-joint Disease Activity Score; RAPID3: Routine Assessment of Patient Index Data.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

neoplasm, which must be excluded prior to initiating new RA therapy. Similarly, DAS28, RAPID3, or any index may provide valuable information to help guide management of RA, but should not be a sole determinant of therapeutic decisions. A complete medical history, physical examination, appropriate laboratory assessment, and ancillary studies should be performed at every clinical encounter to provide an optimal database for clinical decisions.

Discordance of DAS28 and RAPID3 is seen in certain patients, reflected in kappa levels in the range of 0.2–0.4, indicating fair to moderate agreement. This is common with most measures in clinical medicine. For example, both ESR and CRP are valid measures of inflammation, but these measures are not invariably congruent, being correlated with one another at about rho = 0.5[15]. About 15% of patients with a high ESR have a normal CRP, while about 15% have a high CRP and normal ESR[8]. RAPID3 is correlated with DAS28 and CDAI at about rho = 0.6–0.7[15], higher levels than the correlation of ESR with CRP, although nonetheless reflecting incomplete concordance.

RAPID3 certainly is not regarded as replacing a careful joint examination. On the contrary, such an examination is necessary for a diagnosis of RA and should be included in every visit to a rheumatologist. Nonetheless, a formal quantitative joint count may not be necessary to guide clinical decisions. Involvement of, say, 12–14 versus 1–2 swollen joints may be very important in treatment decisions, but whether a patient has 12 versus 14, or 1 versus 2 swollen joints generally will not affect clinical decisions. A careful examination without a formal, quantitative joint count is generally adequate to recognize 12–14 versus 1–2 swollen joints.

We describe clinical trial data concerning RAPID3 based on a HAQ, rather than on an MDHAQ[13,15,36]. The MDHAQ was adapted from the HAQ for usual clinical care over 25 years[16,17,37,38], and has evolved to differ in many respects: (1) 10 (vs 20) items for physical function, adding complex activities that better reflect status of patients at this time than 3 decades earlier; (2) scoring templates for physical function; (3) 21-circle visual analog scale for pain and patient global estimate of status, as well as fatigue (rather than 10-cm lines, so that a ruler is not needed); (4) self-report RA disease activity index (RADAI)[39] joint count; (5) review of systems; (6) medical history self-report; (7) queries regarding depression, anxiety, sleep quality, morning stiffness, exercise status, and smoking status; and (8) demographic measures. Nonetheless, the HAQ and MDHAQ physical function scores are highly correlated, as 8 of the 10 physical function scale items on the MDHAQ are identical to 8 of the 20 HAQ items[16,17]. The similarity of results to distinguish active from control treatment in clinical trials according to RAPID3 or DAS28 is presented here to reassure clinicians that RAPID3 data reflect the more traditional DAS28[13,15].

RAPID3 appears to be a useful, feasible index for busy clinical settings. It approximates information found in DAS28 for categories of activity/severity and response criteria. The MDHAQ and RAPID3 do not replace a standard medical history and physical examination, including a careful joint examination. The MDHAQ enhances capacity to focus on concerns of the patient more directly, and can save time for the rheumatologist. A review of systems and recent medical history within 2 pages on the MDHAQ help improve doctor-patient communication, saving time and focusing the patient on a more productive visit[40]. We suggest that all rheumatologists consider distribution of an MDHAQ at every visit of every patient with any rheumatic disease, and calculating RAPID3 as an adjunct to clinical decisions in the infrastructure of usual rheumatology care.

## REFERENCES


1. Goldsmith CH, Smythe HA, Helewa A. Interpretation and power of pooled index. J Rheumatol 1993;20:575-8.
2. van der Heijde DMFM, van 't Hof MA, van Riel PLCM, Theunisse LM, Lubberts EW, van Leeuwen MA, et al. Judging disease activity in clinical practice in rheumatoid arthritis: First step in the development of a disease activity score. Ann Rheum Dis 1990;49:916-20.
3. Prevoo MLL, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LBA, van Riel PLCM. 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;38:44-8.
4. 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;33:834-7.
5. Lindsay K, Ibrahim G, Sokoll K, Tripathi M, Melsom RD, Helliwell PS. The composite DAS Score is impractical to use in daily practice: evidence that physicians use the objective component of the DAS in decision making. J Clin Rheumatol 2009;15:223-5.
6. Wolfe F, Michaud K. The clinical and research significance of the erythrocyte sedimentation rate. J Rheumatol 1994;21:1227-37.
7. Wolfe F. Comparative usefulness of C-reactive protein and erythrocyte sedimentation rate in patients with rheumatoid arthritis. J Rheumatol 1997;24:1477-85.
8. Sokka T, Pincus T. Erythrocyte sedimentation rate, C-reactive protein, or rheumatoid factor are normal at presentation in 35%-45% of patients with rheumatoid arthritis seen between 1980 and 2004: Analyses from Finland and the United States. J Rheumatol 2009;36:1387-90.
9. Pincus T, Segurado OG. Most visits of most patients with rheumatoid arthritis to most rheumatologists do not include a formal quantitative joint count. Ann Rheum Dis 2006;65:820-2.
10. Yazici Y, Bergman M, Pincus T. Time to score quantitative rheumatoid arthritis measures: 28-joint count, Disease Activity Score, Health Assessment Questionnaire (HAQ), Multidimensional HAQ (MDHAQ), and Routine Assessment of Patient Index Data (RAPID) scores. J Rheumatol 2008;35:603-9.
11. Sokka T, Pincus T. Joint counts to assess rheumatoid arthritis for clinical research and usual clinical care: advantages and limitations. Rheum Dis Clin North Am 2009;35:713-22.
12. Pincus T. Limitations of a quantitative swollen and tender joint count to assess and monitor patients with rheumatoid arthritis. Bull NYU Hosp Jt Dis 2008;66:216-23.
13. Pincus T, Swearingen CJ, Bergman MJ, Colglazier CL, Kaell A, Kunath A, et al. RAPID3 on an MDHAQ is correlated significantly with activity levels of DAS28 and CDAI, but scored in 5 versus


Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org

more than 90 seconds. Arthritis Care Res 2010;62:181-9.
14. 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:S100-8.
15. Pincus T, Swearingen CJ, Bergman M, Yazici Y. RAPID3 (Routine Assessment of Patient Index Data 3), a rheumatoid arthritis index without formal joint counts for routine care: Proposed severity categories compared to DAS and CDAI categories. J Rheumatol 2008;35:2136-47.
16. Pincus T, Swearingen C, Wolfe F. Toward a Multidimensional Health Assessment Questionnaire (MDHAQ): Assessment of advanced activities of daily living and psychological status in the patient-friendly Health Assessment Questionnaire format. Arthritis Rheum 1999;42:2220-30.
17. Pincus T, Sokka T, Kautiainen H. Further development of a physical function scale on a Multidimensional Health Assessment Questionnaire for standard care of patients with rheumatic diseases. J Rheumatol 2005;32:1432-9.
18. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137-45.
19. Pincus T, Strand V, Koch G, Amara I, Crawford B, Wolfe F, et al. An index of the three core data set patient questionnaire measures distinguishes efficacy of active treatment from placebo as effectively as the American College of Rheumatology 20% response criteria (ACR20) or the Disease Activity Score (DAS) in a rheumatoid arthritis clinical trial. Arthritis Rheum 2003;48:625-30.
20. Pincus T, Chung C, Segurado OG, Amara I, Koch GG. An index of patient self-reported outcomes (PRO Index) discriminates effectively between active and control treatment in 4 clinical trials of adalimumab in rheumatoid arthritis. J Rheumatol 2006;33:2146-52.
21. Pincus T, Bergman MJ, Yazici Y, Hines P, Raghupathi K, Maclean R. An index of only patient-reported outcome measures, Routine Assessment of Patient Index Data 3 (RAPID3), in two abatacept clinical trials: Similar results to Disease Activity Score (DAS28) and other RAPID indices that include physician-reported measures. Rheumatology 2008;47:345-9.
22. Pincus T, Furer V, Keystone E, Yazici Y, Bergman MJ, Luijtens K. RAPID3 (Routine Assessment of Patient Index Data) severity categories and response criteria: Similar results to DAS28 (Disease Activity Score) and CDAI (Clinical Disease Activity Index) in the RAPID1 (Rheumatoid Arthritis Prevention of Structural Damage) clinical trial of certolizumab pegol. Arthritis Care Res 2011;63:1142-9.
23. Pincus T. Is a self-report RAPID3 score a reasonable alternative to a DAS28 in usual clinical care? J Clin Rheumatol 2009;15:215-7.
24. Pincus T. Can RAPID3, an index without formal joint counts or laboratory tests, serve to guide rheumatologists in tight control of rheumatoid arthritis in usual clinical care? Bull NYU Hosp Jt Dis 2009;67:254-66.
25. Pincus T, Yazici Y, Bergman MJ. RAPID3, an index to assess and monitor patients with rheumatoid arthritis, without formal joint counts: Similar results to DAS28 and CDAI in clinical trials and clinical care. Rheum Dis Clin North Am 2009;35:773-8.
26. Kremer JM, Genant HK, Moreland LW, Russell AS, Emery P, Abud-Mendoza C, et al. Effects of abatacept in patients with methotrexate-resistant active rheumatoid arthritis: A randomized trial. Ann Intern Med 2006;144:865-76.
27. Genovese MC, Becker JC, Schiff M, Luggen M, Sherrer Y, Kremer J, et al. Abatacept for rheumatoid arthritis refractory to tumor necrosis factor alpha inhibition. N Engl J Med 2005;353:1114-23.
28. Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum 1993;36:729-40.
29. Tugwell P, Boers M. OMERACT Committee. Proceedings of the OMERACT Conferences on outcome measures in rheumatoid arthritis clinical trials, Maastricht, Netherlands. J Rheumatol 1993;20:527-91.
30. van Riel PL, van Gestel AM. Clinical outcome measures in rheumatoid arthritis. Ann Rheum Dis 2000;59 Suppl 1:i28-31.
31. van der Heijde DMFM, van 't Hof M, van Riel PLCM, van de Putte LBA. Development of a disease activity score based on judgment in clinical practice by rheumatologists. J Rheumatol 1993;20:579-81.
32. Aletaha D, Smolen J, Ward MM. Measuring function in rheumatoid arthritis: Identifying reversible and irreversible components. Arthritis Rheum 2006;54:2784-92.
33. Fransen J, van Riel PLCM. DAS remission cut points. Clin Exp Rheumatol 2006;24 Suppl 43:S29-32.
34. Fransen J, van Riel PLCM. The Disease Activity Score and the EULAR response criteria. Clin Exp Rheumatol 2005;5 Suppl 39:S93-9.
35. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.
36. Pincus T, Bergman M, Sokka T, Roth J, Swearingen C, Yazici Y. Visual analog scales in formats other than a 10 centimeter horizontal line to assess pain and other clinical data. J Rheumatol 2008;35:1550-8.
37. Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. Arthritis Rheum 1983;26:1346-53.
38. Pincus T, Yazici Y, Bergman M, Maclean R, Harrington T. A proposed continuous quality improvement approach to assessment and management of patients with rheumatoid arthritis without formal joint counts, based on quantitative Routine Assessment of Patient Index Data (RAPID) scores on a Multidimensional Health Assessment Questionnaire (MDHAQ). Best Pract Res Clin Rheumatol 2007;21:789-804.
39. Stucki G, Liang MH, Stucki S, Brühlmann P, Michel BA. A self-administered rheumatoid arthritis disease activity index (RADAI) for epidemiologic research. Arthritis Rheum 1995;38:795-8.
40. Pincus T, Oliver AM, Bergman MJ. How to collect an MDHAQ to provide rheumatology vital signs (function, pain, global status, and RAPID3 scores) in the infrastructure of rheumatology care, including some misconceptions regarding the MDHAQ. Rheum Dis Clin North Am 2009;35:799-812.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2011. All rights reserved.



Downloaded on April 17, 2024 from www.jrheum.org