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The Clinical Disease Activity Index and the Routine Assessment of Patient Index Data 3 for Achievement of Treatment Strategies

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ABSTRACT. ***Objective.*** To compare the Clinical Disease Activity Index (CDAI) with the Routine Assessment of Patient Index Data 3 (RAPID3) from 2 large United States registries.

Methods. Using a cross section of clinic visits within 2 registries, we determined whether the outcome of each metric would place the patient in remission (REM), low (LDA), moderate (MDA), or high disease activity (HDA) using the CDAI, with the assumption that a patient in MDA or HDA would be a candidate for acceleration of treatment.

Results. We identified significant disparities between the 2 indices in final disease categorization using each index system. For patients identified in LDA by CDAI, RAPID3 identified 20.4% and 28.3% as LDA in Corrona and the Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS), respectively. For patients identified as MDA by CDAI, RAPID3 identified 36.2% and 31.1% as MDA in Corrona and BRASS, respectively, with the greatest disparities within each system identified for LDA and MDA activity by the CDAI (20.4% and 36.2% agreement of RAPID3 with CDAI, respectively, in Corrona and 28.3% and 31.1% agreement in BRASS). Overall comparison between CDAI and RAPID3 in the 4 disease categories resulted in estimated $\kappa = 0.285$ in both. The RAPID3 scores indicated the potential for treat-to-target acceleration in 34.4% of patients in REM or LDA based on CDAI in Corrona and 27.7% in BRASS, respectively.

Conclusion. The RAPID3, based on patient-reported outcomes, shows differences with CDAI categories of disease activity. The components of CDAI are not highly correlated with RAPID3, except for patient global assessment. These differences could significantly affect the decision to advance treatment when using a treat-to-target regimen.

Key Indexing Terms: CDAI, disease metrics, outcomes, RAPID3, rheumatoid arthritis

Metrics are essential for evaluating disease activity in patients with rheumatoid arthritis (RA). Given that rheumatologists have accepted the widely held approach of "treating to target,"[1,2] it is apparent that measures accurately reflecting disease activity in RA are critical for management decisions regarding maintaining, changing, or adding treatment regimens in order to achieve the desired target of low disease activity (LDA) or remission.[1,2]

The Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) and DAS28 based on C-reactive protein (DAS28-CRP) are accepted as a gold standard, along with the American College of Rheumatology (ACR) 20, 50, and 70 responses.[3] However, it is widely recognized that these measures required for regulatory approval are not widely utilized in routine clinical practice in the United States given their complexity and the diligence needed to perform them in the course of routine care. In addition, the acute-phase reactant is not available at the time of the clinic visit.

The Clinical Disease Activity Index (CDAI) is another validated metric that can actually be calculated at the same time as a clinical encounter as it is the simple sum of the number of tender and swollen joints along with the numerical value of both a patient and physician global activity on a visual analog scale.[4,5] Another metric that has become widely used is the Routine Assessment of Patient Index Data 3 (RAPID3),[6,7] which employs values obtained directly from the patient without physician input.

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However, several publications have questioned the contribution of the patient-derived pain and global activity,[8–18] with the latter measure found in both metrics. The RAPID3 will of course derive its final score from patient evaluations as this metric is not associated with either a physician examination or an acute-phase reactant, but only a patient pain and global arthritis activity score along with a Health Assessment Questionnaire. The CDAI is derived from a simple summary of a 28-joint tender (TJC) and swollen joint count (SJC) along with a physician (PGA) and patient global assessment (PtGA).

It is relevant that a significant disparity has been found between patient assessment of pain and global arthritis activity and other measures of disease activity.[8–17] Several publications have found that factors other than disease activity affect these core components of the RAPID3 metric. These elements include depression, life satisfaction, and anxiety that may be ongoing and independent of control of inflammation.[18,19,20,21,22] It has been suggested that patient pain and global disease activity scores measure different domains of patient welfare.[23–30]

We thus sought to compare the CDAI and RAPID3 scores on patients along with analyses of the individual components of each metric to better understand their contribution to the final score within each system. We used 2 different registries in the US, including one from primarily geographically diverse community rheumatologists and one from an academic practice collecting these prospective metrics at the time of a clinical encounter. We focused on how the different measures would inform treatment decisions if they were used in everyday clinical practice while also determining which components of each final metric are potentially problematic for making decisions to treat ongoing inflammation.

METHODS

All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor approval and continuing review was obtained through a central institutional review board (IRB; New England Independent Review Board, NEIRB No. 120160610). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRBs and documentation of approval was submitted to the sponsor prior to initiating any study procedures. All registry subjects were required to provide written informed consent prior to participating.

Data sources. The registry, known as the Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS), began recruitment in 2003. Subjects older than 18 years of age were recruited from the arthritis center practices of attending rheumatologists and fellows. All diagnoses of RA were either verified according to the 1987 ACR criteria by a rheumatologist or met the rheumatologists' criteria for a diagnosis of RA. Subjects were evaluated by their rheumatologists yearly, where information about demographics, medication use, disease activity, functional status, and comorbidities were obtained. Currently, 1343 subjects enrolled in the study have baseline data. Details related to the participation and protocol in the BRASS Registry have been reported elsewhere.[31]

The Corrona RA registry, founded in 2000, includes a network of > 700 participating academic and community rheumatologists at over 180 sites in > 40 states within the US. All patients with a diagnosis of RA treated by participating rheumatologists are eligible to be included in the Corrona registry. Data are gathered at clinical visits from patient and provider forms, as has previously been described.[32]

Data from the most recent visits of 48,255 patients were extracted from 184 Corrona registry sites (83% private and 17% academic) in 42 states to perform a cross-sectional analysis. The visit dates ranged from October 2, 2001, to August 30, 2019.

The Corrona RAPID3 (cRAPID3) is a modified RAPID3 scale used for this study. It does not include the following 2 items that are not collected by the Corrona registry: (1) Are you able to "walk 2 miles or 3 km, if you wish"; and (2) Are you able to "participate in recreational activities and sports as you would like, if you wish?" The scoring of the remaining 8 items ("Over the last week, were you able to...") of the RAPID3 were weighted to ensure the cRAPID3 score was on the same scale as the RAPID3 (0–10). The patient pain and patient global health components of the RAPID3 were not reweighted, and the cRAPID3 score ranged from 0 to 30. The cRAPID3 was also computed in the BRASS registry for comparative purposes.

The rate of moderate disease activity (MDA)/high disease activity (HDA) by cRAPID3 for those in CDAI remission (REM)/LDA were compared between biologic-experienced and -naïve using a logistic regression model and adjusted for duration of disease (early ≤ 2 yrs) vs late (> 2 yrs) at time of the measurement.

Disease activity categories. RA disease activity was measured using CDAI and cRAPID3 in Corrona. A CDAI of ≤ 2.8 was classified as REM, > 2.8 but ≤ 10 was classified as LDA, > 10 but ≤ 22 was classified as MDA, and > 22 was classified as HDA. Similarly, a RAPID3 and cRAPID3 of ≤ 3 was classified as REM, > 3 but ≤ 6 was LDA, > 6 but ≤ 12 was MDA, and > 12 was HDA.

Statistical methods. Spearman correlation coefficients (no assumptions of normality) were calculated to assess the correlation between CDAI, cRAPID3, and RAPID3, as well as individual measurements of clinical characteristics and disease activity levels. κ statistics were calculated to determine the relationship between CDAI and cRAPID3 classifications (REM, LDA, MDA, and HDA). Additionally, κ statistics were also calculated to determine the relationship between the potential treat-to-target groups (REM/LDA vs MDA/HDA) measured by CDAI and cRAPID3.

RESULTS

There are 48,255 Corrona RA patients with CDAI and cRAPID3 measures, and 1343 BRASS RA patients with CDAI and RAPID3 measures. Patient demographics and clinical disease measures are shown in Table 1. BRASS patients with RA are younger (55.9 yrs vs 61.7 yrs) and have higher mean CDAI (19.5 vs 11.2), but slightly lower cRAPID3 (7.3 vs 8.2). PGAs are higher in BRASS (30.6 vs 19.3), but PtGAs are lower (31.7 vs 32.6).

We found that the RAPID3 and cRAPID3 have a high correlation (r_s = 0.998) and overall agreement across disease activity categories is 94% (Supplementary Table 1, available with the online version of this article), as measured by a κ statistic that accounts for chance agreement (κ = 0.92).

Comparison of CDAI and cRAPID3 disease categories in both registries is illustrated in Figure 1 and Table 2 with κ = 0.24 for both Corrona and BRASS. Both registries show a high proportion of cRAPID3 REM within CDAI remission group (78% Corrona, 87% BRASS) but more disagreement at other disease activity levels. For example, only 32% (Corrona) and 41% (BRASS) of CDAI MDA are classified as MDA by cRAPID3. As seen in Figure 1, Table 2, and Table 3, results are similar for comparison of CDAI and RAPID3 in BRASS.

Collapsing categories combining MDA and HDA for indication of potential treatment acceleration and REM and LDA for indication of no potential treatment acceleration agreement

Table 1. Patient characteristics at index date in each registry.

	Corrona	BRASS
N	48,255	1343
Age, yrs	61.73 (13.91)	55.90 (14.16)
Female sex, %	76.36	82.20
Disease duration, yrs, median (IQR)	9 (4–17)	8 (3–19)
SJC	2.71 (4.42)	6.20 (7.05)
TJC	3.35 (5.46)	7.04 (7.71)
PtGA	32.58 (27.41)	31.67 (25.18)
PGA	19.26 (20.40)	30.58 (21.79)
CDAI	11.24 (11.50)	19.47 (16.45)
Disease activity, %		
Remission (CDAI ≤ 2.8)	25.34	12.51
Low (2.8 < CDAI ≤ 10.0)	34.74	26.81
Moderate (10.0 < CDAI ≤ 22.0)	24.75	24.65
Severe (CDAI > 22)	15.17	36.04
RAPID3	NA	7.62 (5.45)
RAPID3 disease activity categories, %		
Remission (RAPID3 ≤ 3.0)	NA	26.06
Low (3.0 < RAPID3 ≤ 6.0)	NA	19.96
Moderate (6.0 < RAPID3 ≤ 12.0)	NA	31.94
Severe (RAPID3 > 12.0)	NA	22.04
cRAPID3[a]	8.15 (6.55)	7.29 (5.35)
cRAPID3 disease activity categories, %		
Remission (RAPID3 ≤ 3.0)	31.22	28.74
Low (3.0 < RAPID3 ≤ 6.0)	14.82	19.14
Moderate (6.0 < RAPID3 ≤ 12.0)	25.09	31.57
Severe (RAPID3 > 12.0)	28.87	20.55
Patient pain	35.11 (28.84)	34.56 (27.32)
Patient-reported fatigue	38.00 (30.47)	41.41 (29.41)

Values are expressed as mean (SD) unless indicated. [a] cRAPID3 is RAPID3 computed within Corrona registry without 2 of the HAQ questions, and rescaled to 0–30. BRASS: Brigham and Women's Rheumatoid Arthritis Sequential Study; CDAI: Clinical Disease Activity Index; cRAPID3: Corrona Routine Assessment of Patient Index Data 3; HAQ: Health Assessment Questionnaire; NA: not applicable; PGA: physician global assessment; PtGA: patient global assessment; RAPID3: Routine Assessment of Patient Index Data 3; SJC: swollen joint count; TJC: tender joint count.

of CDAI and cRAPID3 are shown in Table 3 ($\kappa = 0.49$ Corrona and 0.39 BRASS). Both registries show close to one-third (34% Corrona and 28% BRASS) cRAPID3 indicating potential acceleration, whereas CDAI indicates REM/LDA.

The correlation of CDAI, cRAPID3, and RAPID3 along with components of the measures are shown in Table 4 for Corrona and BRASS. CDAI and cRAPID3 have estimated Spearman correlation of 0.72 (Corrona) and 0.58 (BRASS). As would be expected given the lesser contribution of this metric to the calculation of the CDAI, PtGA has a higher correlation with RAPID3 and cRAPID3 (0.94 Corrona; 0.91 BRASS for both cRAPID3 and RAPID3) than CDAI with PGA (0.78 Corrona, 0.58 BRASS cRAPID3, 0.57 BRASS RAPID3). PGA, not found in the RAPID3, correlated more highly with CDAI (0.78 Corrona, 0.81 BRASS) than cRAPID3 (0.47 Corrona, 0.56 BRASS) and RAPID3 (0.57 BRASS). TJC and SJC, not found in the RAPID3, correlated more highly with CDAI (TJC 0.80, SJC 0.74 Corrona; TJC 0.90, SJC 0.85 BRASS) than cRAPID3 or RAPID3 (TJC 0.48, SJC 0.31 Corrona cRAPID3; TJC 0.44, SJC 0.29 BRASS cRAPID3; TJC 0.44, SJC 0.30 BRASS RAPID3). However, patient pain, not found in the CDAI but present in the RAPID3 metrics, correlated more highly with cRAPID3 and RAPID3 (0.94 Corrona cRAPID3; 0.92 BRASS for both cRAPID3 and RAPID3) than CDAI (0.67 Corrona, 0.50 BRASS).

The comparison of CDAI to cRAPID3 was examined by disease duration and by biologic-naïve vs -experienced (data not shown). Rates of cRAPID3 in MDA/HDA among those with CDAI remission/LDA were slightly higher in the biologic-experienced vs -naïve group (38% vs 30% Corrona, 30% vs 28% BRASS, respectively). Adjusted for duration of disease, the difference by biologic experience was significant ($P < 0.001$ Corrona, $P = 0.046$ BRASS).

DISCUSSION

We found poor correlations in both registries between RAPID3 (or cRAPID3) and CDAI scores for patients in CDAI LDA and MDA, whereas the congruence for both between the metric final scores of REM and HDA were better. When considered together, these data indicate that patient-derived measures contribute differently to the metrics dominating the RAPID3, while SJC, TJC, and PGA dominate the CDAI ($r_s = 0.74, 0.80,$

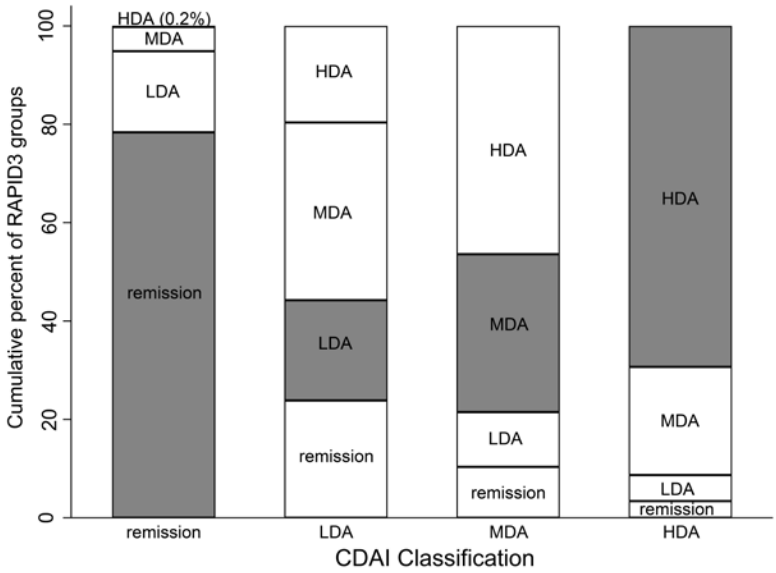

Figure 1. Distribution of cRAPID3 categories within each CDAI category for the Corrona registry. Darker section shows area of agreement. For example, for CDAI remission, 78.4% cRAPID3 also indicated remission. cRAPID3 is RAPID3 computed within Corrona registry without 2 of the HAQ questions, rescaled to 0–30. CDAI: Clinical Disease Activity Index; cRAPID3: Corrona RAPID3; HAQ: Health Assessment Questionnaire; HDA: high disease activity; LDA: low disease activity; MDA: moderate disease activity; RAPID3: Routine Assessment of Patient Index Data 3.

Table 2. Agreement of disease activity levels of cRAPID3 and CDAI from Corrona and BRASS registries.

		Corrona			
		cRAPID3[a] categories			
		REM	LDA	MDA	HDA
CDAI categories	REM	9584 (78.4)	2017 (16.5)	603 (4.9)	25 (0.2)
	LDA	3999 (23.9)	3414 (20.4)	6060 (36.2)	3289 (19.6)
	MDA	1235 (10.3)	1330 (11.1)	3835 (32.1)	5542 (46.4)
	HDA	248 (3.4)	388 (5.3)	1610 (22.0)	5076 (69.3)
		BRASS			
		cRAPID3* categories			
		REM	LDA	MDA	HDA
CDAI categories	REM	146 (86.9)	16 (9.5)	6 (3.6)	0 (0)
	LDA	118 (32.8)	102 (28.3)	112 (31.1)	28 (7.8)
	MDA	69 (20.9)	66 (19.9)	134 (40.5)	62 (18.7)
	HDA	53 (11.0)	73 (15.1)	172 (35.5)	186 (38.4)

Values are expressed as n (%). [a] Row percentages show percent of cRAPID3 categories within each CDAI category. κ statistic of agreement 0.237 (Corrona) and 0.242 (BRASS). * cRAPID3 was calculated in BRASS to exactly match the components of the cRAPID3 in Corrona (full RAPID3 minus the questions regarding ability to engage in sports and walk 2 miles). BRASS: Brigham and Women's Rheumatoid Arthritis Sequential Study; CDAI: Clinical Disease Activity Index; cRAPID3: Corrona Routine Assessment of Patient Index Data 3; HDA: high disease activity; LDA: low disease activity; MDA: moderate disease activity; RAPID3: Routine Assessment of Patient Index Data 3; REM: remission.

and 0.78, respectively, in Corrona, and 0.85, 0.90, and 0.81 in BRASS, respectively; Table 4).

While it might at first appear to be somewhat circular reasoning, or an obvious predetermined outcome, to derive correlations of components found selectively within only one of the 2 metrics with final scores of both metrics, we believe that it serves a larger purpose. Both the CDAI and the RAPID3 are presently being used to inform treatment decisions. If patients are to be managed based upon the results of these scores, then an understanding of what the components represent, and their relative contribution to the final score, is relevant.

Our approach in comparing the CDAI with the RAPID3 (or cRAPID3) was to compare the different final metrics to each other. We believed that it was appropriate to identify the CDAI

Table 3. Comparison of potential treat-to-target indication in Corrona and BRASS. CDAI and cRAPID3 disease categories dichotomized into REM/LDA and MDA/HDA.

		Corrona	
		cRAPID3[a] No Acceleration (REM/LDA)	Potential Acceleration (MDA/HDA)
CDAI	No acceleration (REM/LDA)	19,014 (65.6)	9977 (34.4)
	Potential Acceleration (MDA/HDA)	3201 (16.6)	16,063 (83.4)
		BRASS	
		cRAPID3[a] No Acceleration (REM/LDA)	Potential Acceleration (MDA/HDA)
CDAI	No acceleration (REM/LDA)	382 (72.35)	146 (27.65)
	Potential Acceleration (MDA/HDA)	261 (32.02)	554 (67.98)

Values are expressed as n (%). [a] cRAPID3 is RAPID3 computed within Corrona registry without 2 of the HAQ questions, and rescaled to 0–30. Row percentages show percent of cRAPID3 categories within each CDAI category. MDA/HDA is labeled as a potential indication patient should have accelerated treatment. κ agreement statistics: 0.492 (Corrona) and 0.388 (BRASS). BRASS: Brigham and Women's Rheumatoid Arthritis Sequential Study; CDAI: Clinical Disease Activity Index; cRAPID3: Corrona Routine Assessment of Patient Index Data 3; HDA: high disease activity; LDA: low disease activity; MDA: moderate disease activity; RAPID3: Routine Assessment of Patient Index Data 3; REM: remission.

Table 4. Spearman rank correlations of CDAI, cRAPID3[a], and components within the Corrona and BRASS registries. *P* values testing correlations equal to zero are all < 0.001.

			Corrona						
	CDAI	RAPID3	cRAPID3	PtGA	PGA	TJC	SJC	Patient Pain	MDHAQ
CDAI	1.000								
RAPID3	NA								
cRAPID3	0.721	NA	1.000						
PtGA	0.711	NA	0.942	1.000					
PGA	0.783	NA	0.468	0.435	1.000				
TJC	0.803	NA	0.477	0.438	0.626	1.000			
SJC	0.741	NA	0.311	0.289	0.578	0.561	1.000		
Patient pain	0.670	NA	0.943	0.843	0.449	0.464	0.297	1.000	
MDHAQ	0.538	NA	0.772	0.641	0.374	0.386	0.252	0.629	1.000
			BRASS						
	CDAI	RAPID3	cRAPID3	PtGA	PGA	TJC	SJC	Patient Pain	MDHAQ
CDAI	1.000								
RAPID3	0.579	1.000							
cRAPID3	0.572	0.998	1.000						
PtGA	0.542	0.911	0.911	1.000					
PGA	0.806	0.566	0.563	0.504	1.000				
TJC	0.902	0.444	0.438	0.385	0.692	1.000			
SJC	0.851	0.296	0.289	0.253	0.603	0.685	1.000		
Patient pain	0.496	0.919	0.923	0.709	0.524	0.401	0.260	1.000	
MDHAQ	0.539	0.766	0.745	0.651	0.506	0.442	0.330	0.630	1.000

[a] cRAPID3 is RAPID3 computed within the Corrona registry without 2 of the HAQ questions, and rescaled to 0–30. BRASS: Brigham and Women's Rheumatoid Arthritis Sequential Study; CDAI: Clinical Disease Activity Index; cRAPID3: Corrona Routine Assessment of Patient Index Data 3; MDHAQ: Multidimensional Health Assessment Questionnaire; PGA: physician global assessment; PtGA: patient global assessment; RAPID3: Routine Assessment of Patient Index Data 3; SJC: swollen joint count; TJC: tender joint count.

as the acceptable core clinical outcome metric, as has previously been established.[4,5] Because we had simultaneous outcome metrics from both registries obtained at the same visit from all patients, there was an unusual juxtaposition of circumstances to facilitate comparison of the real-world performance of the RAPID3 to the CDAI.

A rich recent literature has described the psychological and life satisfaction factors that contribute so strongly to patient-derived measures of the RAPID3, including the patient global and pain scores.[9–23] It is apparent that the RAPID3 can provide a clinician with potentially complementary information on the welfare of their patient. But, as has been demonstrated in these recent publications, because the RAPID3 is dominated by variables with strong psychological and psychosocial derivations, the scores should not be used in isolation to either evaluate ongoing RA inflammation or to adjust treatment. Ferreira and colleagues have suggested a "dual-target approach" in which psychological outcomes are derived from patients, whereas inflammation-related variables are derived from physician joint counts as found in the CDAI.[33]

We believe that it is thus important to recognize that even though certain key variables such as tender and swollen joints on examination as well as a physician global evaluation are not found in the RAPID3, their absence should not release this metric from the burden of achieving the goal of reflecting inflammatory disease activity as captured in a validated metric such as the CDAI. As several authors have described, these patient-reported outcomes reflect different domains of patient welfare.[23–30] Additional compelling evidence from a Dutch society published by Boone and colleagues has described similar disparities between the RAPID3 and both the CDAI[34] and the DAS28.[35]

The high correlation and agreement of RAPID3 and cRAPID3 provides evidence that the cRAPID3 used in Corrona is a good proxy for RAPID3. We thus employed the cRAPID3 in Corrona to derive correlations with the CDAI after confirming the very high correlation with the full RAPID3 in BRASS (Supplementary Table 1, available with the online version of this article). The metrics from the Corrona registry were collected from 706 rheumatologists at 184 sites in 42 different states with a distribution of private vs academic sites (83% vs 17%). The results for each metric were compared both within and across registries. The BRASS registry represents data that are entirely derived from a single academic center. We found that there were differences in the evaluation of disease activity between registries. The PtGAs are quite similar whereas the PGAs differ (19.26 [SD 20.40] Corrona, and 30.28 [SD 21.79] BRASS), as do the CDAI scores (11.24 [SD 11.50] Corrona, and 19.47 [SD 16.45] BRASS). The reasons for the differences are speculative but may reflect either the likelihood that a tertiary academic center might attract more challenging patients or the fewer numbers of evaluators in BRASS. We did not have an *a priori* expectation that the disease activity would be overwhelmingly similar in both Corrona and BRASS given the differences in the makeup of the registry sites, and we believed that this was a virtue when comparing the CDAI with the RAPID3. Nevertheless, the reason(s) for the differences in the PGA remain speculative. The differences in these ratings may indeed be site-specific and reflect a shared approach for disease assessment of providers at a single site. Differences in PGA might be a topic for future research.

While the RAPID3 is convenient and saves physicians' time compared with a 28-joint count and PGA, it is apparent that the outcome scores are frequently divergent from the CDAI. In addition, it has previously been published that the same RAPID3 can be used to reflect osteoarthritis (OA) disease activity.[36] Given that patients with RA often have concomitant OA, it would not be possible to determine the contribution of OA to the patient's rating of pain and global arthritis activity when the same metric is used for RA.

This study has several strengths. We studied a very large number of patients and compared the CDAI and cRAPID3 measures obtained at the time of the same clinic visit. We compared data across 2 different registries, including one from an academic health science center (BRASS) and one from predominantly private practitioners (Corrona). In addition, we were able to examine the correlation of the patient global and pain measures with each metric and confirm the discordance with an array of clinical disease measures obtained by a physician. For what we believe is the first time, we extend earlier findings on patient pain and global evaluations as they apply to a commonly used patient-derived metric, the RAPID3, in comparison with a CDAI.

There are also some potential weaknesses. Physician TJCs and SJCs were typically performed by the same clinician but not always. The Corrona registry consists of multiple sites with inevitable variability across sites, whereas BRASS is a single academic site with fewer evaluators. It is possible that differences in results between the registries reflect these differences in site composition. These analyses are derived from a cross-sectional, retrospective review of prospectively collected observational data. Nevertheless, the inclusion of the possibility of different investigators evaluating the same patient might actually add to the representativeness of the observations across different physicians, thus hypothetically buttressing the external validity of the data. We believe that the heterogeneity of the data sources and very large number of clinical evaluations from 2 different registries serve to support the clinical conclusion. It is also possible that these US-based findings may not be representative of other societies, although we believe that this is not likely as much of the data we cite on the discordance of the PtGA with actual disease activity are derived from European authors.[9–12,14–17,19,20–23]

In conclusion, the RAPID3 should not be used as an exclusive measure to evaluate clinical status and inform treatment decisions, as the individual components of this metric are highly associated with noninflammatory conditions such as depression, anxiety, and quality of life[19,20,21,22,23] and are discordant with CDAI evaluations. Nevertheless, the RAPID3 can add valuable information on patient psychometrics, which complement the CDAI outcomes that are more reflective of inflammatory outcomes. We believe that it is important for treating clinicians to recognize and acknowledge the core clinical themes that are actually being measured within each metric. A patient who is

doing well on a CDAI, but not on a RAPID3, should be further evaluated for the contribution of both psychosocial factors and OA to this score. Further, the RAPID3 should not be relied upon to inform decisions when treating to target.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Smolen JS, Landewe R, Bijsma J, Burmester G, Chatzidionysiou K, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017;76:960-77.
2. Singh JA, Saag KG, Bridges SL Jr, Aki EA, Bannuru RR, Sullivan MC, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. Arthritis Care Res 2016; 68:1-25.
3. Martins FM, da Silva JA, Santos MJ, Vieira-Sousa E, Duarte C, Santos H, et al. DAS28, CDAI and SDAI cut-offs do not translate the same information: results from the Rheumatic Diseases Portuguese Register Reuma.pt. Rheumatology 2015;54:286-91.
4. 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;5 Suppl 39:S100-8.
5. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569-81.
6. Pincus T, Sokka T. Quantitative measures for assessing rheumatoid arthritis in clinical trials and clinical care. Best Pract Res Clin Rheumatol 2003;17:753-81.
7. 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 disease activity score and clinical disease activity index categories. J Rheumatol 2008; 35:2136-47.
8. Ferreira RJ, Duarte C, Ndosi M, de Wit M, Gossec L, da Silva JA. Suppressing inflammation in rheumatoid arthritis: does patient global assessment blur the target? A practice-based call for a paradigm change. Arthritis Care Res 2018;70:369-78.
9. Studenic P, Radner H, Smolen JS, Aletaha D. Discrepancies between patients and physicians in their perceptions of rheumatoid arthritis disease activity. Arthritis Rheum 2012;64:2814-23.
10. Khan NA, Spencer HJ, Abda EA, Alten R, Pohl C, Ancuta C, et al; QUEST-RA group. Patients global assessment of disease activity and patient's assessment of general health for rheumatoid arthritis disease activity. Ann Rheum Dis 2012;71:1942-9.
11. Nikiphorou E, Radner H, Chatzidionysiou K, Desthieux C, Zabalan C, van Eijk-Hustings Y, et al. Patient global assessment in measuring disease activity in rheumatoid arthritis: a review of the literature. Arthritis Res Ther 2016;18:251.
12. Hirsh J, Wood P, Keniston A, Peng M, Ramaswami S, Caplan L, et al. Limited health literacy and patient confusion about rheumatoid arthritis patient global assessments and model disease states. Arthritis Care Res 2019 May;71:611-9.
13. Studenic P, Smolen JS, Aletaha D. Near misses of ACR/EULAR criteria for remission: effects of patient global assessment in Boolean and index-based definitions. Ann Rheum Dis 2012;71:1702-5.
14. Ferreira RJ, Dougados M, Kirwan J, Duarte C, de Wit M, Soubrier M, et al; CoimbRA investigators, RAID investigators and COMEDRA investigators. Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients. Rheumatology 2017;56:1573-8.
15. Masi KR, Shaver TS, Shahouri SH, Wang S, Anderson JD, Busch RW, et al. Validity and reliability problems with patient global as a component of the ACR/EULAR remission criteria as used in clinical practice. J Rheumatol 2012;39:1139-45.
16. Barton JL, Imboden J, Graf J, Glidden D, Yelin EH, Schillinger D. Patient-physician discordance in assessments of global disease severity in rheumatoid arthritis. Arthritis Care Res 2010;62:857-64.
17. Santos EJF, Duarte C, Ferreira RJO, Pinto AM, Geenan R, da Silva JAP, et al; 'Promoting Happiness Through Excellence of Care' Group. Determinants of happiness and quality of life in patients with rheumatoid arthritis: a structural equation modeling approach. Ann Rheum Dis 2017;77:1118-24.
18. Matcham F, Norton S, Scott DL, Stear S, Hotopf M. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. Rheumatology 2013;55:268-78.
19. Van Dyke MM, Parker JC, Smarr KL, Hewett JE, Johnson GE, Slaughter JR, et al. Anxiety in rheumatoid arthritis. Arthritis Rheum 2004;51:408-12.
20. Marrie RA, Hitchon CA, Walld R, Patten SB, Bolton JM, Sarren J, et al; Canadian Institutes of Health Research Team in Defining the Burden and Managing the Effects of Psychiatric Comorbidity in Chronic Immunoinflammatory Disease. Increased burden of psychiatric disorders in rheumatoid arthritis. Arthritis Care Res 2018;70:970-8.
21. Hammer HB, Uhlig T, Kvien TK, Lampa J. Pain catastrophizing, subjective outcomes, and inflammatory assessments including ultrasound: results from a longitudinal study of rheumatoid arthritis patients. Arthritis Care Res 2018;70:703-12.
22. Lee YC, Frits ML, Iannaccone CK, Weinblatt ME, Shadick NA, Williams DA, et al. Subgrouping of rheumatoid arthritis patients based on pain, fatigue, inflammation and psychosocial factors. Arthritis Rheumatol 2014;66:2006-14.
23. Kievat W, Welsing PMJ, Adang EMM, Eijsbouts AM, Krabbe PFM, van Riel PLCM. Comment on the use of self-reporting instruments to assess patients with rheumatoid arthritis: the longitudinal association between the DAS28 and the VAS general health. Arthritis Rheum 2006;55:745-50.
24. Ferriera RJO, Carvalho PD, Ndosi M, Duarte C, Chopra A, Murphy E, et al. Impact of patient's global assessment on achieving remission in patients with rheumatoid arthritis: a multinational study using the METEOR database. Arthritis Care Res 2019;71:1317-25.
25. Steunebrink LMM, Oude Voshaar MAH, Taal E, Vonkeman HE, Ziflstra TR, van de Laar AFJ. Determinants of perceived health nonimprovement in early rheumatoid arthritis patients with favorable treatment outcomes. Arthritis Care Res 2018;70:510-5.
26. Jacobs JW, Ten Cate DF, van Laar JM. Monitoring of rheumatoid arthritis disease activity in individual patients: still a hurdle when implementing the treat-to-target principle in daily clinical practice. Rheumatology 2015;54:959-61.
27. Putrik P Ramiro S, Hilfinger M, Keszei AP Hmamouchi I, Dougados M, et al. In wealthier countries, patients perceive worse impact of disease although they have lower objectively assessed disease activity: results from the cross-sectional COMORA study. Ann Rheum Dis 2016;75:715-20.
28. Boers M. Let's stop fooling ourselves. In RA, only ACR/EULAR criteria define remission and equate with absence of disease! Ann Rheum Dis 2016;75;e68.

29. Bykerk VP, Massarotti EM. The new ACR/EULAR remission criteria: rationale for developing new criteria for remission. Rheumatology 2012;51: Suppl 6:vi16-20.
30. Nakagami Y, Sugihara G, Takei N, Fujii T, Hashimoto M, Murakami K, et al. Effect of physical state on pain mediated through emotional health in rheumatoid arthritis. Arthritis Care Res 2019;71:1216-23.
31. Bykerk VP, Shadick N, Frits M, Bingham CO 3rd, Jeffery I, Iannacone C, et al. Flares in rheumatoid arthritis: frequency and management. A report from the BRASS registry. J Rheumatol 2014 Feb;41:227-34.
32. Kremer JM. The Corrona US registry of rheumatic and autoimmune diseases. Clin and Exp Rheum 2016;5 Suppl101:S96-9.
33. Ferreira RJO, Ndosi M, de Wit M, Ferreira Santos EJ, Duarte C, Jacobs JWG, et al. Dual strategy: a proposal to mitigate the risk of overtreatment and enhance patient satisfaction in rheumatoid arthritis. Ann Rheum Dis 2019;78:e109.
34. Boone NW, Seprieno A, van der Kuy P-H, Janknegt R, Peeters R, Landewe RB. Routine assessment of Patient Index3 (RAPI3) alone is insufficient to monitor disease activity in rheumatoid arthritis. RMD Open 2019;5:e001050.
35. Boone NW, Teenwisse P, van der Kuy P-H, Jankneg R, Landewe RB. Evaluating patient reported outcomes in routine practice of patients with rheumatoid arthritis treated with biological disease modifying anti rheumatic drugs (b-DMARDs). Springerplus 2015;4:462.
36. Chua JR, Jamal S, Riad M, Castrejon I, Malfait M, Block JA. Disease burden in osteoarthritis is similar to that of rheumatoid arthritis at initial rheumatology visit and significantly greater six months later. Arthritis Rheumatol 2019;71:1276-84.