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SPECIAL ARTICLE

2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures

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Objective. To provide updated American College of Rheumatology (ACR) recommendations on rheumatoid arthritis (RA) disease activity measurements to facilitate a treat-to-target approach in routine clinical care.

Methods. A working group conducted a systematic literature review from the time of the prior ACR recommendations literature search. Properties of disease activity measures were abstracted, and study quality was assessed using the Consensus-Based Standards for the selection of Health Measurement Instruments 4-point scoring method, allowing for overall level of evidence assessment. Measures that fulfilled a minimum standard were identified, and through a modified Delphi process preferred measures were selected for regular use in most clinic settings.

Results. The search identified 5,199 articles, of which 110 were included in the review. This search identified 46 RA disease activity measures that contained patient, provider, laboratory, and/or imaging data. Descriptions of the measures, properties, study quality, level of evidence, and feasibility were abstracted and scored. Following a modified Delphi process, 11 measures fulfilled a minimum standard for regular use in most clinic settings, and 5 measures were recommended: the Disease Activity Score in 28 Joints with Erythrocyte Sedimentation Rate or C-Reactive Protein Level, Clinical Disease Activity Index, Simplified Disease Activity Index, Routine Assessment of Patient Index Data 3, and Patient Activity Scale-II.

Conclusion. We have updated prior ACR recommendations for preferred RA disease activity measures, identifying 11 measures that met a minimum standard for regular use and 5 measures that were preferred for regular use in most clinic settings.

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SIGNIFICANCE & INNOVATIONS

- This is the first update to the American College of Rheumatology's recommended rheumatoid arthritis disease activity measures for regular clinical use.
- We used a systematic approach to identify and evaluate measures meeting a minimum standard for regular use that can be repeated in future updates and provide a path for research on existing or new measures.

INTRODUCTION

A treat-to-target strategy in rheumatoid arthritis (RA) was recommended in the 2015 American College of Rheumatology (ACR) RA Treatment Guidelines (1). In order to adhere to these recommendations, regular RA disease activity assessments must be made during routine care. Although the severity of chronic diseases such as diabetes mellitus or hypertension can be directly measured, no equivalent measurement exists in RA. Numerous RA disease activity measures have been proposed for this purpose, most incorporating data gathered from a combination of sources, including patient-reported measures, provider assessments, laboratory values, and/or imaging modalities. These measures may vary in terms of their performance (e.g., validity, reliability, responsiveness) and feasibility for regular use.

Recognizing the challenge that clinicians face selecting a disease activity measure due to multiple options and varying performance, the ACR convened a working group in 2008 to review the literature and provide recommendations on which RA disease activity measures were best suited for regular use (2). RA disease activity measures were identified through a literature review (3), which were then narrowed by an expert advisory panel. Recommendations were drafted after psychometric properties of the measures were compiled and practicing rheumatologists were surveyed. This process resulted in the recommendation of 6 RA disease activity measures: the Clinical Disease Activity Index (CDAI), Disease Activity Score in 28 joints (DAS28), Patient Activity Scale (PAS), Patient Activity Scale II (PAS-II), Routine Assessment of Patient Index Data 3 (RAPID3), and Simplified Disease Activity Index (SDAI) (2).

Since these original recommendations, additional RA disease activity measures have been reported, further studies characterizing the performance of these and other novel measures have been conducted, and imaging modalities have been developed for assessment of disease activity. Therefore, an update to the prior recommendations for selecting an RA disease activity measure was needed, including a critical evaluation of more recent literature. The ACR convened a working group to update these prior recommendations in conjunction with a separate effort to provide initial recommendations on functional status assessment in RA. The objectives of this RA disease activity measures working group were to provide recommendations for RA disease activity measures meeting a minimum standard for regular use, and preferred RA disease activity measures for regular use. The former objective was added since many measures may be valid, feasibility varies across different practices and healthcare systems, and providers may have experience with and be comfortable using certain disease activity measures.

METHODS

Study design. A working group composed of rheumatologists and rheumatology professionals, including one rheumatology professional diagnosed with RA, was convened by the ACR to update the recommended RA disease activity measures. A protocol was developed and agreed on by the working group for providing updated RA disease activity measure recommendations. The recommendation process and preliminary findings were presented in a special session at the 2017 ACR Annual Scientific Meeting held in San Diego, California and were then opened for public comment (from patients, providers, and other stakeholders) following that presentation.

Updated systematic literature review. In conjunction with the assistance of a medical librarian, we updated the prior literature review by searching Ovid Medline, Embase, and Cochrane databases from January 1, 2009 to January 25, 2017 for published original articles on RA disease activity measures using combinations of MeSH terms and keywords for rheumatoid arthritis, disease activity measures, and psychometric properties. We did not review components of composite measures individually as prior recommendations selected the composite measures over their individual components (2). A full description of the systematic literature review is shown in Supplementary Appendix 1, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract. Systematic review inclusion criteria were published articles in the English language reporting on a psychometric property of an RA disease activity measure. The exclusion criteria were reports limited to diseases other than RA; reports assessing only cross-cultural validity, radiographic damage, or a single joint area; and measures not providing numerical values. Titles and abstracts were screened in duplicate by 2 authors (BRE and BKT) for relevance, followed by full text review in duplicate by 2 authors (BRE and BKT) to assess eligibility. Discordance after full text review was settled by a third-party reviewer (KM). Publications retrieved were reviewed to identify additional articles eligible for inclusion. RefWorks (ProQuest) was utilized for management of literature search results.

Data abstraction and study quality assessment. Study details and psychometric properties were abstracted and study quality was assessed from included studies, using the Consensus-Based Standards for the Selection of Health Measurement Instru-

ments (COSMIN) 4-point scoring as the template (4). An abstraction tool was developed and was piloted iteratively for data collection, then applied to the studies by an abstractor (BRE or BKT). To ensure abstraction consistency and quality, regular meetings occurred between the abstractors during the abstraction process.

Items abstracted from studies included those pertaining to the publication (author, year, journal), study (patient characteristics, sample size, setting, patient selection), disease activity measures (measures included, score distributions), and psychometric properties. Psychometric properties abstracted were internal consistency, reliability, measurement error, content validity, structural validity, hypotheses testing, and responsiveness (COSMIN properties [4,5]). Criterion validity was not abstracted because considering a distinct RA disease activity measure a "gold-standard" would bias recommendations. Rather, studies reporting criterion validity were abstracted as hypothesis testing (i.e., convergent validity).

Study quality assessment for each psychometric property was assessed using the COSMIN checklist with a 4-point scale (4). Using this method, each psychometric property reported in each study received a quality rating of excellent, good, fair, or poor. The score assigned to each property in each study represented the lowest score of all the criteria for that property.

Level of evidence. Abstracted data on psychometric properties and study quality were synthesized as others have previously reported (6,7). The psychometric properties for each RA disease activity measure received a level of evidence of strong (rating of +++ or - - -), moderate (rating of ++ or - -), limited (rating of + or -), conflicting (rating of ±), or unknown (rating of ?). See Supplementary Appendix 2, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract, for details concerning the level of evidence grading system. Assessments of level of evidence were performed in duplicate (BRE and BKT), and discordance was settled by a third-party reviewer (KM).

Consideration of prior literature. A literature review was previously performed in conjuction with the 2012 ACR RA Disease Activity Recommendations (3). The psychometric properties of RA disease activity measures identified in the prior review were extracted according to the COSMIN groupings utilized in the current systematic review. Additionally, we searched for psychometric properties of studies not previously included in the prior literature review that were published before our search date. As study quality assessment was not part of the prior review, these results were not incorporated into the level of evidence grading with those from the current systematic review. Instead, these prior performance metrics were provided to the working group members for review during the selection (i.e., voting) process.

Feasibility. Validated scoring systems for the feasibility of RA disease activity measures do not currently exist. We scored feasibility on a scale of 0 to 4 (i.e., - to ++++) with scores ≥1 (+ to ++++) denoting measures feasible for regular use and scores of 4 (++++) representing the most feasible measures. The number of items included in the measure, time to complete, need for provider joint counts, need for laboratory testing, commercial availability, and need for advanced imaging were evaluated as part of the grading. All measures not commercially available or requiring advanced imaging (due to additional equipment, training, or consultation being required) were graded as 0 (i.e., - [not feasible for regular use]). Requirement of provider joint counts or laboratory testing both reduced the maximum score by 1 each. Consideration of number of items and completion time served as final modifiers of the feasibility grade. (The score was reduced by 1 if not feasibile in a routine clinic visit or by 2 if not feasible on the same day as the clinic visit.)

Selection process. The RA disease activity measures working group reviewed the literature search, abstracted data, level of evidence for each identified measure, prior literature for each measure, and feasibility scoring, as well as their own experience with these measures, to provide 2 recommendations on RA disease activity measures feasible for regular use in rheumatology clinics. First, the group identified RA disease activity measures meeting a minimum standard for regular use and second, the group selected measures with the most favorable psychometric properties and feasibility for preferred use.

Fulfilling the minimum standard for an RA disease activity measure in regular use was established by measures 1) providing a numerical value, 2) categorizing to ≥3 disease states that separate low, moderate, and high disease activity, 3) being feasible for regular measurement in the clinic, and 4) possessing adequate psychometric properties. Items were considered to meet the minimum standard for feasibility in regular use if the previously mentioned feasibility score was ≥1. Psychometrics were considered adequate if the level of evidence suggested at least moderate positive results in the COSMIN area of hypothesis testing plus 1 of the following: level of evidence suggesting at least moderate positive results in at least 1 other COSMIN area, level of evidence suggesting at least limited positive results in at least 2 COSMIN areas (one of which must be responsiveness), or a defined minimum important difference/minimum clinically important difference.

A modified Delphi process was utilized to generate the recommendations on RA disease activity measures for preferred use (8). Working group members and an ACR Quality Measures Subcommitee liason rated each measure that fulfilled the minimum standard on a scale of 1 to 9, where 9 = essential this measure be recommended for use. Ratings of 7 to 9 constituted a recommended measure for inclusion, while ratings of 4 to 6 were inconclusive and ratings of 1 to 3 were recommended measures for exclusion. Measures were *recommended* if >80% of members (all but 1) rated the measure in the 7 to 9 range and

Table 1. Characteristics of rheumatoid arthritis disease activity measures*

Measure†	Components	Items, no.	Formula	Range	Rem	Low DA	Moderate DA	High DA	Method of administration	MID, MCID
Clinical Disease Activity Index (CDAI)	28TJC (0–28); 28SJC (0–28); Pt Global VAS (0–10); Pr Global VAS (0–10)	4	28SJC + 28TJC + PtGA + PrGA	0–76	≤2.8	>2.8 to 10	>10 to 22	>22	Patient item, provider assessment	MCID 12 (12 for high DA, 6 for moderate DA, 1 for low DA)
Modified CDAI (Baker)	28SJC; Pr Global	2	28SJC + 2xPrGA	0–48	-	-	-	-	Provider assessment	-
Patient Derived CDAI	Pt 28TJC; Pt 28SJC; Pt Global, Pr Global	4	28SJC + 28TJC + PtGA + PrGA	0–76	≤2.8	>2.8 to 10	>10 to 22	>22	Patient items, provider assessment	-
Disease Activity Score (DAS)	RAI; SJC44; ESR; Pt Global	4	0.53938xSqrt(RAI) + 0.06465xSJC44 + 0.33ln(ESR) + 0.00722(PtGA)	0–10	<1.6	1.6 to <2.4	2.5 to <3.7	≥3.7	Patient item, provider assessment, lab	1.2
Disease Activity Score 28 Joints (DAS28)	28TJC (0–28); 28SJC (0–28); Pt Global VAS (0–10); ESR or CRP	3 or 4	0.56xSqrt(28TJC) + 0.28xSqrt(28SJC) + 0.70xln(ESR) + 0.014xPtGA OR 0.56xSqrt(28TJC)+ 0.28xSqrt(28SJC) + 0.36xln(CRP + 1) + 0.014xPtGA + 0.96	0–9.4	<2.6	2.6 to <3.2	3.2 to ≤5.1	>5.1	Patient item, provider assessment, lab	MID 1.2; MCID 1.2 (DAS28-ESR), 1.0 (DAS28-CRP)
Modified DAS28 (Baker)	28SJC; Pr Global; acute,-phase reactant (ESR or CRP)	3	0.40xln(ESR) + 0.17xSJC28 + 0.26xPrGA -OR- 0.49xln(CRP) + 0.15x28SJC + 0.22PrGA + 1	-	-	-	-	-	Provider assessment, lab	-
Modified DAS28 (no acute-phase reactants) (Bentley)	28TJC; 28SJC; mHAQ; Pain; Pr Global; Pt Global	6	0.53xsqrt(28TJC) + 0.31xsqrt(28SJC) + 0.25xmHAQ + 0.001xPain + 0.005xPrGA + 0.014xPtGA + 1.694	-	-	-	-	-	Patient items, provider assessment	-
Patient Derived DAS28	Pt 28TJC; Pt 28SJC; Pt Global; ESR or CRP	4	0.56xSqrt(28TJC) + 0.28xSqrt(28SJC) + 0.7xln(ESR) + 0.014xPtGA OR 0.56xSqrt(28TJC) + 0.28xSqrt(28SJC) + 0.36xln(CRP + 1) + 0.014xPtGA + 0.96	0–9.4	<2.6	2.6 to <3.2	3.2 to ≤5.1	>5.1	Patient items, lab	-

(Continued)

Table 1. *(Cont'd)*

Measure†	Components	Items, no.	Formula	Range	Rem	Low DA	Moderate DA	High DA	Method of administration	MID, MCID
Ultrasound Derived DAS28	Pt 28TJC; Pr 28TJC; US 28SJC; Pt Global; ESR or CRP	4	0.56xSqrt(28TJC) + 0.28xSqrt(28SJC) + 0.7xln(ESR) + 0.014xPtGA OR 0.56xSqrt(28TJC) + 0.28xSqrt(28SJC) + 0.36xln(CRP + 1) + 0.014xPtGA + 0.96	0–9.4	<2.6	2.6 to <3.2	3.2 to ≤5.1	>5.1	Patient items, provider assessment, lab, imaging modality	-
Global Arthritis Score (GAS)	Pain VAS (0–10); mHAQ (0–24); Pt reported 28TJC (0–28)	3	Pain + mHAQ + Pt 28TJC	0–62	-	-	-	-	Patient items	-
Hospital Universitario La Princesa Index (HUPI)	28TJC; 28SJC; Pt Global; acute-phase reactant (ESR or CRP)	4	Each component scored 0–3 based on cutoff values	0–12	-	≤2	>2 to ≤5	>5	Patient items, provider assessment, lab	4 (~DAS 1.2)
Individualized Ultrasound Score	Selects up to 7 or 12 of most affected joints for MSUS	Up to 7 or 12	Sum of individual joint scores (sum of US subscores divided by maximum score at the joint - GS synovial hypertrophy, PD vascularity, tenosynovitis (GS & PD)	-	-	-	-	-	Imaging modality	-
Individualized Composite Ultrasound Score	Selects up to 7 or 12 of most affected joints for MSUS and clinical examination	Up to 7 or 12	Sum of individual joint scores (sum of US subscores and joint subscores divided by maximum score at the joint)	-	-	-	-	-	Provider assessment, imaging modality	-
Kappa/Lambda Hybrid Antibody	Antibody measurement	1	Values generated referent to a standard curve	-	-	-	-	-	Lab	-
Mean Overall Index for Rheumatoid Arthritis (MOI-RA)	28SJC; 28TJC; Pt Global; Pr Global; Pain; HAQ; ESR	7	Mean of standardized values of individual components (each 0-100)	0–100	-	-	-	-	Patient item, provider assessment, lab	-
Multi-Biomarker Disease Activity Score (MBDA)	CRP; EGF; IL-6; Leptin; MMP-1; MMP-3; Resistin; SAA; TNFRI; VCAM-1; VEGF-A; YKL-40	12	(0.56sqrt(TJC) + 0.28SJC + 0.14PtGA + 0.36log(CRP+1) + 0.96) x 10.53 + 1 (Biomarker scores to predict above components)	1–100	≤25	26–29	30–44	>44	Lab	-
Optical Spectral Transmission (OST)	Bilateral PIP (1–5); MCP (1–5); wrist	22	Not reported	-	-	-	-	-	Imaging modality	-
Patient Activity Scale (PAS)	HAQ (0–3); Pain VAS (0–10); Pt Global VAS (0–10)	3	(HAQx3.33 + Pain VAS + PtGA VAS)/3	0–10	≤0.25	>0.26 to 3.70	3.71 to <8.0	≥8.0	Patient items	-

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Table 1. *(Cont'd)*

Measure†	Components	Items, no.	Formula	Range	Rem	Low DA	Moderate DA	High DA	Method of administration	MID, MCID
Patient Activity Scale-II (PAS-II)	HAQ-II (0–3); Pain VAS (0–10); Pt Global VAS (0–10)	3	(HAQ-IIx3.33 + Pain VAS + PtGA VAS)/3	0–10	≤0.25	>0.26 to 3.70	3.71 to <8.0	≥8.0	Patient items	-
Patient Based Disease Activity Score (PDAS1)	Pt Global; Pt 50TJC; HAQ; ESR	4	0.19xPtGA + 0.842ln(ESR+2) + 0.432xln(PtTJC +2) + 0.271xHAQ	-	<3.5	3.5-4.5	4.5-4.8	>4.8	Patient items, lab	0.8 good response
Patient Based Disease Activity Score (PDAS2)	Pt Global; Pt 28SJC; HAQ; morning stiffness duration	4	2.667 + 0.021xPtGA + 0.483xHAQ + 0.033xPtSJC + 0.002xAM stiffness	-	<3.8	3.8–4.6	4.6–5.0	>5.0	Patient items	1.2 good response
Patient Reported Clinical Arthritis Activity (PRO-CLARA)	Recent Onset Arthritis Disability questionnaire (ROAD 0–10); Pt 16TJC (0–10); Pt Global (0–10)	3	ROAD + PtTJC + PtGA/3	0–10	-	-	-	-	Patient items	-
Rheumatoid Arthritis Disease Activity Index (RADAI)	Pt Global (0–10); Current swollen/tender joints (0–10); Pain (0–10); Duration morning stiffness (0–10 transformed); Tender joint list: (0–10 transformed)	5	(PtGA + swollen/tender + pain + AM stiffness + TJC)/5	0–10	-	<2.2	≥2.2 to ≤4.9	>4.9	Patient items	1-1.4
Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)	Pt Global 6 months (0–10); Pt active joint swollen/tender today (0–10); Pain (0–10); Pt general health (0–10); AM stiffness (0–10)	5	(PtGA + Pt swollen/ tender joints + Pain + Pt GH + AM stiffness) / 5	0–10	≤1.4	1.6–3.0	3.2–5.4	≥5.6	Patient items	-
Rheumatoid Arthritis MRI Scoring (RAMRIS)	Synovitis (7 areas scored 0–3); Osteitis/bone edema (23 areas scored 0–3), Erosion (23 areas scored 0–10)	3	Subcomponents or total score (sum)	-	-	-	-	-	Imaging modality	-
Routine Assessment of Patient Index Data 3 (RAPID3)	MDHAQ (0–10); Pain VAS (0–10); Pt Global VAS (0–10)	3	MDHAQ + Pain VAS + PtGA VAS	0–30	≤3	4–6	7–12	≥13	Patient items	MID 3.2-3.6
Routine Assessment of Patient Index Data 4 (RAPID4)	MDHAQ (0–10); Pain VAS (0–10); Pt Global VAS (0–10); RADAI Tender Joint List (0–10)	4	MDHAQ + Pain + Pt Global + RADAI-tender joint list	0–40	≤4	5–8	9–16	≥17	Patient items	-
Routine Assessment of Patient Index Data 5 (RAPID5)	MDHAQ (0–10); Pain VAS (0–10); Pt Global VAS (0–10); RADAI Tender Joint List (0–10); Pr Global (0–10)	5	MDHAQ + Pain + Pt Global + RADAI-Tender Joint List + Pr Global	0–50	≤5	6-10	11–20	≥21	Patient items, provider assessment	-
Simplified Disease Activity Index (SDAI)	28TJC (0–28); 28SJC (0–28); Pt Global VAS (0–10); Pr Global VAS (0–10); CRP (0–10)	5	28SJC + 28TJC + PtGA + PrGA + CRP	0–86	≤3.3	>3.3 to ≤11.0	>11.0 to ≤26	>26	Patient item, provider assessment, lab	16 ~ DAS MID1.2; MCID 13

(Continued)

Table 1. *(Cont'd)*

Measure†	Components	Items, no.	Formula	Range	Rem	Low DA	Moderate DA	High DA	Method of administration	MID, MCID
Modified SDAI (Baker)	28SJC; Pr Global; CRP	3	CRP + 28SJC + PrGA	-	-	-	-	-	Provider assessment, lab	-
Patient Derived SDAI	Pt 28TJC; Pt 28SJC; Pt Global VAS; Pr Global VAS; CRP	5	28SJC + 28TJC + PtGA + PrGA + CRP	0–86	≤3.3	>3.3 to ≤11.0	>11.0 to ≤26	>26	Patient items, provider assessment, lab	-
Ultrasound Derived SDAI	28TJC; US 28SJC; Pt Global VAS; Pr Global VAS; CRP	5	28SJC + 28TJC + PtGA + PrGA + CRP	0–86	≤3.3	>3.3 to ≤11.0	>11.0 to ≤26	>26	Patient item, provider assessment, lab, imaging modality	-
Simplified RA MRI Score (SAMIS)	Synovitis (7 areas scored 0–2); Osteitis/bone edema (15 areas scored 0–1); Erosion (15 areas scored 0–10)	3	Subcomponents or total score (sum)	-	-	-	-	-	Imaging modality	-
Swiss Sonography in Arthritis and Rheumatism Score (SONAR)	Bilateral elbow and wrist; MCP2–5, PIP2–5; Knee; B mode (0–3) and PD (0–3) for each joint	22	Sum of individual scores (PD and B mode)	0–66 B-mode, 0–66 PD	-	-	-	-	Imaging modality	-
Ultrasound 6 Joint (Perricone)	Bilateral wrist; MCP2; Knee; synovial effusion (0–3); Synovial proliferation (0–3); PD (0–3)	6	Sum of individual scores	0–54	-	-	-	-	Imaging modality	-
Ultrasound 6 Joint (Rosa)	Bilateral wrist; MCP2; MCP3 (0–2)	6	Sum of individual scores	0–12	-	-	-	-	Imaging modality	-
Ultrasound 6 Joint (Kawashiri)	Bilateral wrist; MCP2; MCP3 (0–3)	6	Sum of individual scores	0–18	-	-	-	-	Imaging modality	-
Ultrasound 7 Joint (Backhaus)	Unilateral (dominant side) wrist; MCP2; MCP3; PIP2; PIP3; MTP2; MTP5; Synovitis PDUS (0–3); synovitis GSUS (0–3); tenosynovitis GSUS (0–1); tenosynovitis PDUS (0–3); erosion.	7	Sum of individual scores	S-GSUS 0–27, S-PDUS 0–39, TS-GSUS 0–7, TS-PDUS 0–21, E 0–14	-	-	-	-	Imaging modality	-
Ultrasound 8 Joint (Yoshimi)	Bilateral wrist; MCP2; MCP3; knees (0–3 PDUS)	8	Sum of individual scores	0–24	-	-	-	-	Imaging modality	-
Ultrasound 12 Joint (Naredo)	Bilateral elbow; wrist; MCP2; MCP3; knee, ankle (synovitis 0–3; PD 0–3)	12	Sum of individual scores, *alternative: sum of # joints	-	-	-	-	-	Imaging modality	-
Ultrasound 14 Joint (Dale)	Bilateral wrist; MCP2; MCP3; PIP2; PIP3; MTP; MTP5; GSUS 0–3; PDUS 0–3	14	-	-	-	-	-	-	Imaging modality	-
Ultrasound 20 Joint (Dougados)	Bilateral MCP1–5; MTP1–5	20	0–3 each joint for B-mode and PD	-	-	-	-	-	Imaging modality	-

(Continued)

Table 1. *(Cont'd)*

Measure†	Components	Items, no.	Formula	Range	Rem	Low DA	Moderate DA	High DA	Method of administration	MID, MCID
Ultrasound 28 Joint (Dougados)	Bilateral shoulders, elbows, wrists; MCPs; PIPs; knees	28	0–3 each joint for B-mode and PD	-	-	-	-	-	Imaging modality	-
Ultrasound 38 Joint (Dougados)	Bilateral shoulders, elbows, wrists; MCPs; PIPs; knees; bilateral MTPs	38	0–3 each joint for B-mode and PD	-	-	-	-	-	Imaging modality	-
Ultrasound 78 Joint (Hammer)	B-mode and PD: bilateral PIP1–5, MCP1–5, CMC1–5, wrist (radiocarpal, intercarpal, radioulnar), elbow (anterior, posterior), shoulder (GHu, AC), hip, knee, ankle, foot (talonavicular, subtalar, calcaneocuboid, cuneonavicular), TMT1–5, MTP1–5, First IP	78	0–3 each joint for B-mode and PD	B-Mode (0–234); PD (0–234)	-	-	-	-	Imaging modality	-
Ultrasound Score A, B (Aga)	Bilateral GSUS and PDUS of (A): MCP1; MCP2; PIP3; radiocarpal; elbow; MTP1; MTP2; TP tendon and ECU tendon. (B): A joints + MCP5; MTP5. Each location graded 0–3.	A 18; B 22	Sum of individual scores	A 0–54; B 0–66	-	-	-	-	Imaging modality	-

* Rem = remission; DA = disease activity; MID = minimum important difference; MCID = minimum clinically important difference; TJC = tender joint count; SJC = swollen joint count; Pt = patient; VAS = visual analog score; Pr = provider; GA = global assessment; RAI = Ritchie Articular Index; ESR = erythrocyte sedimentation rate; sqrt = square root; ln = natural logarithm; CRP = C-reactive protein level; mHAQ = modified Health Assessment Questionnaire; MSUS = musculoskeletal ultrasound; US = ultrasound; GS = gray scale; PD = power Doppler; HAQ = Health Assessment Questionnaire; EGF = epidermal growth factor; IL-6 = interleukin-6; MMP-1 = matrix metalloproteinase 1; SAA = serum amyloid A; TNFRI = tumor necrosis factor receptor type I; VCAM-1 = vascular cell adhesion molecule 1; VEGF-A = vascular endothelial growth factor A; PIP = proximal interphalangeal joint; MCP = metacarpophalangeal joint; MRI = magnetic resonance imaging; MDHAQ = Multidimensional HAQ; MTP = metatarsophalangeal joint; CMC = carpometacarpal joint; GHu = glenohumeral joint; AC = acromioclavicular joint; TMT = tarsometatarsal joint; TP: = tibialis posterior; ECU = extensor carpi ulnaris.
† Study references are listed in Supplementary Appendix 8, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract.

excluded if >80% of ratings were in the 1 to 3 range, following best practices (9). The voting process continued iteratively to a maximum of 3 voting cycles, with discussion of RA disease activity measures not fulfilling agreement held between voting cycles. Measures not achieving recommendation for inclusion or exclusion were deemed inconclusive. Measures deemed inconclusive remained on the list fulfilling the minimum standard.

The ACR Quality Measures Subcommittee reviewed these recommendations in parallel with the recommendations on functional status assessment, modifying as necessary based upon the goal of identifying preferred tools for regular use in most clinic settings, before voting. The ACR Quality of Care Committee and ACR Board of Directors reviewed and approved this article prior to publication.

RESULTS

Systematic literature review and identified disease activity measures. Our systematic literature review identified 5,199 articles (see Supplementary Appendix 3, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract). After screening titles, abstracts, and full texts, 104 articles met criteria for inclusion in the study. A review of the retrieved publications identified an additional 6 articles fulfilling eligibility criteria, resulting in a total of 110 included studies. There was 98.2% agreement between the reviewers for study inclusion.

Characteristics of the individual studies are provided in Supplementary Appendix 4, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract. The majority of studies had predominantly female participants, with a mean age in the 6th decade. Sample sizes, mean DAS28 score, location, design, and selection varied between studies.

Our search identified 47 RA disease activity measures. The components, number of items, scoring method, score range, disease activity category cutoffs, method of administration, and minimum important difference/minimum clinically important difference of each RA disease activity measure are

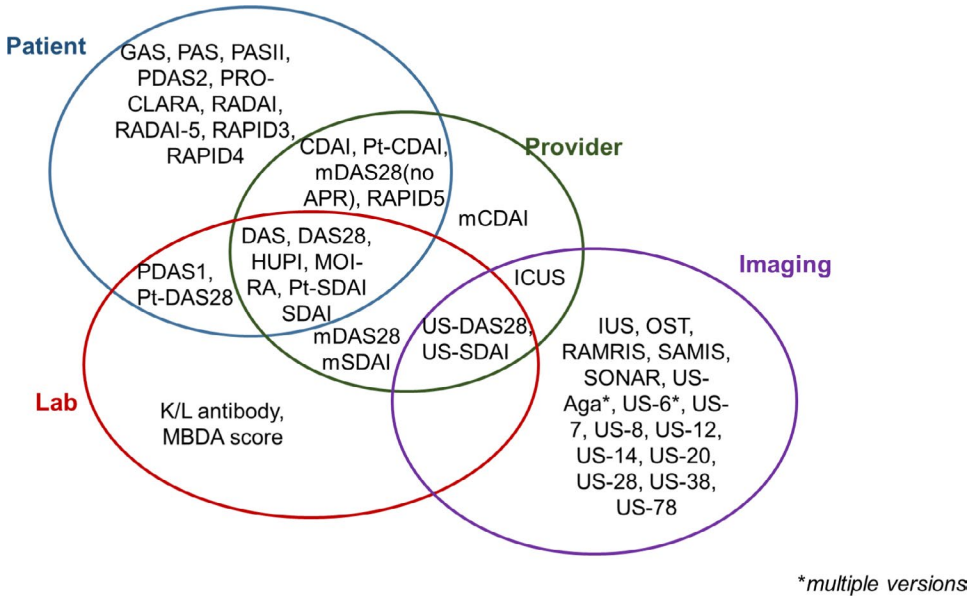

Figure 1. Venn diagram depicting the major domains of data (patient reported, provider assessment, laboratory, and imaging) included in rheumatoid arthritis (RA) disease activity measures, which are listed in the areas from which they are derived. GAS = Global Arthritis Score; PAS = Patient Activity Scale; PAS-II = Patient Activity Scale-II; PDAS2 = Patient Based Disease Activity Score 2; PRO-CLARA = Patient Reported Clinical Arthritis Activity; RADAI = RA Disease Activity Index; RADAI-5 = RA Disease Activity Index-5; RAPID3 = Routine Assessment of Patient Index Data 3; RAPID4 = Routine Assessment of Patient Index Data 4; CDAI = Clinical Disease Activity Index; Pt-CDAI = Patient Derived Clinical Disease Activity Index; mDAS28 = Modified Disease Activity Score in 28 joints; (no APR) = mDAS28 no acute-phase reactants; RAPID5 = Routine Assessment of Patient Index Data 5; mCDAI = Modified Clinical Disease Activity Index; DAS = Disease Activity Score; HUPI = Hospital Universitario La Princesa Index; MOI-RA = Mean Overall Index for RA; PDAS1 = Patient Based Disease Activity Score 1; Pt-DAS28 = Patient Derived DAS 28-Joint DAS; SDAI = Simplified Disease Activity Index; Pt-SDAI = Patient Derived SDAI; mSDAI = Modified SDAI; US-DAS28 = ultrasound-derived DAS28; US-SDAI = ultrasound-derived SDAI; ICUS = Individualized Composite Ultrasound Score; IUS = Individualized Ultrasound Score; OST = Optical Spectral Transmission; RAMRIS = RA Magnetic Resonance Imaging Scoring; SAMIS = Simplified RA Magnetic Resonance Imaging Score; SONAR = Swiss Sonography in Arthritis and Rheumatism Score; US-Aga = ultrasound sound score A & B proposed by Aga et al; US-6 = ultrasound 6 joint; US-7 = ultrasound 7 joint; US-8 = ultrasound 8 joint; US-12 = ultrasound 12 joint; US-14 = ultrasound 14 joint; US-20 = ultrasound 20 joint; US-28 = ultrasound 28 joint; US-38 = ultrasound 38 joint; US-78 = ultrasound 78 joint; K/L antibody = kappa/lambda hybrid antibody; MBDA score = Multibiomarker Disease Activity score.

Table 2. Level of evidence relevant to the psychometric properties of RA disease activity measures*

Measure†	Internal consistency	Reliability	Measurement error	Content validity	Structural validity	Hypotheses testing	Responsiveness
Clinical Disease Activity Index (CDAI)	+	++	+		++	+++	+++
Modified CDAI (Baker)						++	
Patient Derived CDAI		+	+			+	
Disease Activity Score (DAS)						++	
Disease Activity Score 28 Joints (DAS28)	++	++	++	- - -	++	+++	+++
Modified DAS28 (Baker)						++	
Modified DAS28 (Bentley)	?					++	++
Patient Derived DAS28		++	+			++	+
Ultrasound Derived DAS28		+				++	+
Global Arthritis Score (GAS)						++	++
Hospital Universitario La Princesa Index (HUPI)	?					++	++
Individualized Ultrasound Score							?
Individualized Composite Ultrasound Score							?
Kappa/Lambda Hybrid Antibody						+	
Mean Overall Index for RA (MOI-RA)						+	+
Multi-Biomarker Disease Activity Score (MBDA)		?		+++	+++	++	++
Optical Spectral Transmission (OST)						++	
Patient Activity Scale (PAS)						+	+
Patient Activity Scale-II (PAS-II)							
Patient Based Disease Activity Score (PDAS1)		+				+	
Patient Based Disease Activity Score (PDAS2)		+				+	
Patient Reported Clinical Arthritis Activity (PRO-CLARA)	+			?		++	+
Rheumatoid Arthritis Disease Activity Index (RADAI)		?	?			++	++
Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)	?				++	++	
Rheumatoid Arthritis MRI Scoring (RAMRIS)						- -	- -
Routine Assessment of Patient Index Data 3 (RAPID3)	?	?	?	+++		+++	+++
Routine Assessment of Patient Index Data 4 (RAPID4)				++		+	
Routine Assessment of Patient Index Data 5 (RAPID5)						++	++
Simplified Disease Activity Index (SDAI)	+	++	+			+++	+++
Modified SDAI (Baker)						++	
Patient Derived SDAI		+	+			++	
Ultrasound Derived SDAI		+				++	+
Simplified RA MRI Score (SAMIS)		+				?	
Swiss Sonography in Arthritis and Rheumatism (SONAR) Score		?	?			++	++
Ultrasound 6 Joint (Perricone)				+++		+	+
Ultrasound 6 Joint (Rosa)						+	
Ultrasound 6 Joint (Kawashiri)						?	
Ultrasound 7 Joint (Backhaus)		++		+++		++	++
Ultrasound 8 Joint (Yoshimi)				+++		++	
Ultrasound 12 Joint (Naredo)		+		+++		+	+
Ultrasound 14 Joint (Dale)						?	
Ultrasound 20 Joint (Dougados)	?	+					++
Ultrasound 28 Joint (Dougados)	?	+					++
Ultrasound 38 Joint (Dougados)	?	+					++
Ultrasound 78 Joint (Hammer)		?				?	?
Ultrasound Score A, B (Aga)				+++	+		+

* Grading scale: +++ or - - - = strong (consistent findings in multiple studies of good methodologic quality OR in one study of excellent methodologic quality); ++ or - - = moderate (consistent findings in multiple studies of fair methodologic quality OR in one study of good methodologic quality); + or - = limited (one study of fair methodologic quality); ± = conflicting (conflicting findings); ? = unknown (studies only of poor methodologic quality). RA = rheumatoid arthritis; MRI = magnetic resonance imaging.
† Study references are listed in Supplementary Appendix 8, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract.

listed in Table 1. A Venn diagram illustrating the components (e.g., patient reported, provider assessment, laboratory values, and imaging modalities) of the identified RA disease activity measures is shown in Figure 1.

Properties of RA disease activity measures. The individual performance of RA disease activity measures in each study is provided in Supplementary Appendix 5 available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract. The study quality assessment using the COSMIN checklist with 4-point scale is provided in Supplementary Appendix 6, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract. Based on both the measure performance and study quality, an overall level of evidence was generated for each psychometric property for each RA disease activity measure (Table 2). This process was completed in duplicate with 96.6% agreement between raters in assessing the overall level of evidence for RA disease activity measures.

Hypothesis testing (testing hypotheses regarding relationships to other instruments measuring similar constructs, i.e., content validity) was the most frequently assessed psychometric property. Reliability and responsiveness were also frequently assessed for RA disease activity measures. The CDAI, DAS28, Multibiomarker Disease Activity (MBDA) score, RAPID3, and SDAI were the most frequently studied RA disease activity measures. Although negative content validity was reported for the DAS28, it should be noted this was based on one study of excellent quality that showed underestimation of radiographic progression in the feet, i.e., joints not included in the 28-joint count (10).

Properties of RA disease activity measures from before the current search period were collected from the prior review (3) and from hand searches for measures not previously included (see Supplementary Appendix 7, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract). A full reference list of all articles identified and abstracted in the systematic literature review, as well as searches for earlier time periods, is shown in Supplementary Appendix 8, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract.

Feasibility of RA disease activity measures. Feasibility scoring of the RA disease activity measures is shown in Table 3. Twenty-five measures were scored to be feasible for regular use in most clinics. Of these measures, 11 (44%) received a score of 4 (++++), 6 (25%) a score of 3 (+++), 5 (20%) a score of 2 (++), and 3 (12%) a score of 1 (+).

Recommended RA disease activity measures. Eleven measures fulfilled the minimum standard defined for RA disease activity measures for regular use (Table 4). Four measures (the CDAI, DAS28 using the erythrocyte sedimentation rate or C-reactive protein level [DAS28-ESR/CRP], RAPID3, and SDAI) were part of the prior ACR RA disease activity measure recommendations (2). Of the 7 measures not listed in the original recommendations, the Disease Activity Score (DAS) was a predecessor to the DAS28, the patient-derived DAS28 was derived from the DAS28, and the Routine Assessment of Patient Index Data 5 (RAPID5) was related to the RAPID3. The remaining measures were the Hospital Universitario La Princesa Index (HUPI), MBDA score, Rheumatoid Arthritis Disease Activity Index (RADAI), and RADAI-5. Of the 36 measures not fulfilling the minimum standard, 27 (75%) did not categorize into disease activity states, 28 (78%) did not have adequate psychometrics, and 22 (61%) were not scored as feasible for regular use (Table 4).

Results of the modified Delphi voting process are shown in Table 5. Four measures achieved consensus for preferred use: the CDAI, DAS28, RAPID3, and SDAI. The CDAI (mean score 8.8) and SDAI (mean score 7.6) achieved consensus during the first round of voting, the RAPID3 (mean score 7.6) during the second round of voting, and the DAS28 (mean score 7.6) during the third round of voting. The remaining 7 RA disease activity measures (mean score range 2.6–5.6) did not achieve consensus after the third round of voting and were deemed "inconclusive" for preferred use.

The ACR Quality Measures Subcommittee approved the previously mentioned recommendations with a single modification, which was the additional recommendation of PAS-II. This recommendation was based upon PAS-II feasibility, current use, strength of its inclusion in prior ACR recommendations that included evidence not captured in this current work, and alignment with the concurrent functional status assessment project (2).

DISCUSSION

Patient outcomes in RA, including physical function, quality of life, and achieving remission/low disease activity, have improved as a result of treatment advances, including the early initiation of treatment, treating to target, and novel therapeutics (11,12). Critical to adhering to a treat-to-target approach is the regular integration of disease activity measurement as part of routine care, a practice included in ACR RA treatment guidelines (1) and selected as a quality measure by the Centers for Medicare and Medicaid Services (Quality ID #177: Rheumatoid Arthritis: Periodic Assessment of Disease Activity). In this study, we have updated the initial ACR 2012 recommendations for RA disease activity measures (2) through an updated systematic literature review, RA disease activity measure performance assessment, study quality assessment, level of evidence synthesis, and a modified Delphi voting process. Five preferred RA disease activity measures for regular clinical use were selected: the CDAI, DAS28-ESR/CRP, PAS-II, RAPID3,

Table 3. Feasibility of RA disease activity measures*

Measure†	Items, no.	Time	Provider joint count	Lab testing required	Advanced imaging	Feasibility‡
Clinical Disease Activity Index (CDAI)	3	2–5 mins	Yes	No	No	+++
Modified CDAI (Baker)	2	5 mins	Yes	No	No	+++
Patient Derived CDAI	4	5 mins	No	No	No	++++
Disease Activity Score (DAS)	4	10 mins	Yes	Yes	No	+
Disease Activity Score 28 Joints (DAS28-ESR/CRP)	3 or 4	5 mins + lab	Yes	Yes	No	++
Modified DAS28 (Baker)	3	5 mins + lab	Yes	Yes	No	++
Modified DAS28 (no acute-phase reactants, Bentley)	6	5 mins	Yes	No	No	+++
Patient Derived DAS28	4	5 mins + lab	No	Yes	No	+++
Ultrasound Derived DAS28	4	N/R	No	Yes	Yes	-
Global Arthritis Score (GAS)	3	5 mins	No	No	No	++++
Hospital Universitario La Princesa Index (HUPI)	4	5 mins + lab	Yes	Yes	No	++
Individualized Ultrasound Score	Up to 7 or 12	N/R	No	No	Yes	-
Individualized Composite Ultrasound Score	Up to 7 or 12	N/R	No	No	Yes	-
Kappa/Lambda Hybrid Antibody	1	Not commercially available	No	Yes	No	-
Mean Overall Index for RA (MOI-RA)	7	10–20 mins + lab	Yes	Yes	No	+
Multi-Biomarker Disease Activity Score (MBDA, VECTRA)	12	Days	No	Yes	No	+
Optical Spectral Transmission (OST)	22	Not commercially available	No	No	Yes	-
Patient Activity Scale (PAS)	3	5 mins	No	No	No	++++
Patient Activity Scale-II (PAS-II)	3	2 mins	No	No	No	++++
Patient Based Disease Activity Score (PDAS1)	4	5–10 mins + lab	No	Yes	No	+++
Patient Based Disease Activity Score (PDAS2)	4	5–10 mins	No	No	No	++++
Patient Reported Clinical Arthritis Activity (PRO-CLARA)	3	5 mins	No	No	No	++++
Rheumatoid Arthritis Disease Activity Index (RADAI)	5	5 mins	No	No	No	++++
Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)	5	30 sec to 2 mins	No	No	No	++++
Rheumatoid Arthritis MRI Scoring (RAMRIS)	3	N/R	No	No	Yes	-
Routine Assessment of Patient Index Data 3 (RAPID3)	3	30 sec to 2 mins	No	No	No	++++
Routine Assessment of Patient Index Data 4 (RAPID4)	4	5–10 mins	No	No	No	++++
Routine Assessment of Patient Index Data 5 (RAPID5)	5	5–10 mins	No	No	No	++++
Simplified Disease Activity Index (SDAI)	5	2–5 mins + lab	Yes	Yes	No	++
Modified SDAI (Baker)	3	5 mins + lab	Yes	Yes	No	++
Patient Derived SDAI	5	5 mins + lab	No	Yes	No	+++
Ultrasound Derived SDAI	5	N/R	No	Yes	Yes	-
Simplified RA MRI Score (SAMIS)	3	N/R	No	No	Yes	-
Swiss Sonography in Arthritis and Rheumatism (SONAR) Score	22	20–30 mins	No	No	Yes	-
Ultrasound 6 Joint (Perricone)	6	14 mins	No	No	Yes	-
Ultrasound 6 Joint (Rosa)	6	5–12 mins	No	No	Yes	-
Ultrasound 6 Joint (Kawashiri)	6	N/R	No	No	Yes	-
Ultrasound 7 Joint (Backhaus)	7	10–20 mins	No	No	Yes	-
Ultrasound 8 Joint (Yoshimi)	8	N/R	No	No	Yes	-
Ultrasound 12 Joint (Naredo)	12	20–25	No	No	Yes	-
Ultrasound 14 Joint (Dale)	14	N/R	No	No	Yes	-
Ultrasound 20 Joint (Dougados)	20	N/R	No	No	Yes	-
Ultrasound 28 Joint (Dougados)	28	N/R	No	No	Yes	-
Ultrasound 38 Joint (Dougados)	38	N/R	No	No	Yes	-
Ultrasound 78 Joint (Hammer)	78	N/R	No	No	Yes	-
Ultrasound Score A, B (Aga)	A =18, B = 22	N/R	No	No	Yes	-

* RA = rheumatoid arthritis; Lab = laboratory; mins = minutes; N/R = not reported; sec = seconds; MRI = magnetic resonance imaging.
† Study references are listed in Supplementary Appendix 8, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract.
‡ Feasibility was assessed by the number of items, time to complete, and the need for provider joint counts, laboratory testing, and advanced imaging. Feasibility was graded - to ++++ with + to ++++ meeting minimum feasibility for regular use. Scoring was as follows: measures started with a score of ++++; any measure not commercially available or requiring advanced imaging was graded -; requiring a provider joint count reduced feasibility by +; requiring a laboratory test reduced feasibility by +; number of items and time to completion were considered and score was reduced by + if not feasibile in a routine clinic visit or by ++ if not feasible on the same day as the clinic visit.

Table 4. RA disease activity measures assessment of minimum standard for regular use*

Measure†	Numeric	Categorizes 3–4 states	Feasible‡	Adequate psychometrics§	Meet minimum standard
Fulfilled minimum standard					
Clinical Disease Activity Index (CDAI)	+	+	+	+	+
Disease Activity Score (DAS)	+	+	+	+	+
Disease Activity Score 28 Joints (DAS28-ESR/CRP)	+	+	+	+	+
Patient Derived DAS28	+	+	+	+	+
Hospital Universitario La Princesa Index (HUPI)	+	+	+	+	+
Multi-Biomarker Disease Activity Score (MBDA score, VECTRA DA)	+	+	+	+	+
Rheumatoid Arthritis Disease Activity Index (RADAI)	+	+	+	+	+
Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)	+	+	+	+	+
Routine Assessment of Patient Index Data 3 (RAPID3)	+	+	+	+	+
Routine Assessment of Patient Index Data 5 (RAPID5)	+	+	+	+	+
Simplified Disease Activity Index (SDAI)	+	+	+	+	+
Did not fulfill minimum standard					
Modified CDAI (Baker)	+	-	+	-	-
Patient Derived CDAI	+	+	+	-	-
Modified DAS28 (Baker)	+	-	+	-	-
Modified DAS28 (Bentley)	+	-	+	+	-
Ultrasound Derived DAS28	+	+	-	+	-
Global Arthritis Score (GAS)	+	-	+	+	-
Individualized Ultrasound Score	+	-	-	-	-
Individualized Composite Ultrasound Score	+	-	-	-	-
Kappa/Lambda Hybrid Antibody	+	-	-	-	-
Mean Overall Index for RA (MOI-RA)	+	-	+	-	-
Optical Spectral Transmission (OST)	+	-	-	-	-
Patient Activity Scale (PAS)	+	+	+	-	-
Patient Activity Scale-II (PAS-II)	+	+	+	-	-
Patient Based Disease Activity Score (PDAS1)	+	+	+	-	-
Patient Based Disease Activity Score (PDAS2)	+	+	+	-	-
Patient Reported Clinical Arthritis Activity (PRO-CLARA)	+	-	+	+	-
Rheumatoid Arthritis MRI Scoring (RAMRIS)	+	-	-	-	-
Routine Assessment of Patient Index Data 4 (RAPID4)	+	+	+	-	-
Modified SDAI (Baker)	+	-	+	-	-
Patient Derived SDAI	+	+	+	-	-
Ultrasound Derived SDAI	+	+	-	+	-
Simplified RA MRI Score (SAMIS)	+	-	-	-	-
Swiss Sonography in Arthritis and Rheumatism (SONAR) Score	+	-	-	+	-
Ultrasound 6 Joint (Perricone)	+	-	-	-	-
Ultrasound 6 Joint (Rosa)	+	-	-	-	-
Ultrasound 6 Joint (Kawashiri)	+	-	-	-	-
Ultrasound 7 Joint (Backhaus)	+	-	-	+	-
Ultrasound 8 Joint (Yoshimi)	+	-	-	+	-
Ultrasound 12 Joint (Naredo)	+	-	-	-	-
Ultrasound 14 Joint (Dale)	+	-	-	-	-
Ultrasound 20 Joint (Dougados)	+	-	-	-	-
Ultrasound 28 Joint (Dougados)	+	-	-	-	-
Ultrasound 38 Joint (Dougados)	+	-	-	-	-
Ultrasound 78 Joint (Hammer)	+	-	-	-	-
Ultrasound Score A, B (Aga)	+	-	-	-	-

* RA = rheumatoid arthritis; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein level; MRI = magnetic resonance imaging.
† Study references are listed in Supplementary Appendix 8, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24042/abstract.
‡ Measures deemed feasible if feasibility scoring was ≥1 as shown in Table 3.
§ Measures were considered to have adequate psychometrics if the level of evidence suggested at least moderate positive results in the Consensus-Based Standards for the Selection of Health Measurement Instruments (COSMIN) area of hypothesis testing plus had ≥1 of the following: level of evidence suggesting at least moderate positive results in another COSMIN area, level of evidence suggesting at least limited positive results in ≥2 COSMIN areas (one of which must be responsiveness), or a defined minimum important difference/minimum clinically important difference.

and SDAI. Seven additional RA disease activity measures that met a minimum standard for regular use were identified: the DAS, patient-derived DAS28, HUPI, MBDA score, RADAI, RADAI-5, and RAPID5. Preferred measures represent those with the most support for their performance and feasibility as assessed by the working group, while those fulfilling the minimum standard have adequate performance and feasibility for regular use. Clinicians can utilize these recommendations when selecting an RA disease

Table 5. Summary of 3-round Delphi method with recommendations for rheumatoid arthritis disease activity measures*

Measure	Round 1		Round 2†		Round 3		Final recommendation‡
	Mean	Rating 1–3/4–6/7–9‡	Mean	No. 1–3/4–6/7–9‡	Mean	Rating 1–3/4–6/7–9‡	
Clinical Disease Activity Index (CDAI)	8.8	0/0/10	N/A	N/A	N/A	N/A	Recommended
Simplified Disease Activity Index (SDAI)	7.6	0/1/9	N/A	N/A	N/A	N/A	Recommended
Routine Assessment of Patient Index Data 3 (RAPID3)	7.4	0/3/7	7.6	0/1/7	N/A	N/A	Recommended
28-Joint Disease Activity Score (DAS28)	7.6	0/2/8	7.1	0/2/6	7.6	1/0/9	Recommended
Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5)	6.1	4/2/4	5.3	2/4/2	5.6§	2/4/3§	Inconclusive
Disease Activity Score (DAS)	5.0	3/4/3	3.8	5/2/1	4.2	4/5/1	Inconclusive
Patient Derived-DAS28	4.9	4/2/4	4.5	2/6/0	4.2	4/6/0	Inconclusive
Rheumatoid Arthritis Disease Activity Index (RADAI)	5.1	4/3/3	4.2	5/2/1	4.4	4/5/1	Inconclusive
Routine Assessment of Patient Index Data 5 (RAPID5)	5.2	4/1/5	4.5	2/5/1	3.8§	5/3/1§	Inconclusive
Multibiomarker Disease Activity (MBDA) score	4.2	7/1/2	3.5	5/2/1	3.2§	7/1/1§	Inconclusive
Hospital Universitario La Princesa Index (HUPI)	4.0	6/1/3	3.5	5/3/0	2.6	8/2/0	Inconclusive

* N/A = not applicable; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.
† Eight voters participated in round 2 voting.
‡ Ratings were on a 1–9 Likert scale, where 1–3 = not recommended, 4–6 = sometimes recommended, 7–9 = essential to have, and >80% agreement is required for recommendation.
§ There was one missing vote for this score.

activity measure for integration into their care for RA patients, and any of the 11 measures shown in Table 4 that meet the minimum standard reasonably satisfy quality measures for assessing RA disease activity.

The purpose of these recommendations was to assist clinicians in the care of RA patients by identifying RA disease activity measures and evaluating their performance and feasibility for regular use. These recommendations are not meant to dictate the specific RA disease activity measure a clinician utilizes. The working group recognizes that feasibility varies based on practice and provider. Furthermore, providers may have experience with and be comfortable with specific RA disease activity measures. Therefore, we aimed to identify not only preferred RA disease activity measures, but also RA disease activity measures that met a minimum standard by categorizing into disease activity states, possessing adequate psychometric properties, and being feasible for regular clinical use. For providers adopting an RA disease activity measure or aiming to integrate disease activity measurement into care through a standardized fashion (i.e., integration into the electronic health record), we recommend selecting a preferred RA disease activity measure (CDAI, DAS28-ESR/CRP, PAS-II, RAPID3, or SDAI).

In addition to not precluding the use of other RA disease activity measures, these recommendations importantly do not provide recommendations on disease activity measures in special circumstances. An example might include the use of musculoskeletal ultrasound or magnetic resonance imaging in a patient with a difficult or equivocal joint examination who is being considered for treatment escalation or withdrawal. There are certainly specific circumstances or patient populations where alternative disease activity assessments may be clinically indicated. Additionally, there are certain RA subpopulations where the validity of RA disease activity measures may vary. Disease activity scores including patient-reported measures are higher in patients with comorbid fibromyalgia (13), and disease activity scores including inflammatory markers are higher in obese patients (14). Providing recommendations for disease activity assessment in these specific situations or patient populations was beyond the scope of these recommendations and are left to the judgement of the treating clinician.

The preferred RA disease activity measures are largely unchanged from those previously recommended (2), with the difference being that the PAS was not recommended for preferred use in these updated recommendations. Both the PAS and PAS-II were infrequently studied since the time of the prior recommendations and subsequently did not satisfy the requirement of having demonstrated adequate psychometrics during this period. It is important to note that the PAS and PAS-II differ from the RAPID3 only by the functional status component of each composite measure. The PAS-II contains the Health Assessment Questionnaire II (HAQ-II) (15), while PAS contains the HAQ (16) and RAPID3 contains the Multidimensional Health Assessment Questionnaire (MDHAQ) (17). Assessment and recommendation of functional status measures in RA has been conducted in parallel, with recommendations for the use of Patient-Reported Outcomes Measurement Information System Physical Function 10, MDHAQ, and HAQ-II. Given the overlap between PAS-II and RAPID3 as well as the results from the parallel functional status assessment project, the Quality Measures Subcommittee additionally recom-

mended the PAS-II as a preferred measure. The consistency in the selection of preferred disease activity measures between the prior and current recommendations provides further support for these measures.

There are limitations to this effort. We conducted a systematic literature review from the time of the prior review. Therefore, generation of overall level of evidence from measure performance and study quality assessment was only able to be completed for studies since the initial review. Properties assessed early in measure development may not have been routinely re-assessed in later literature. Although not included into level of evidence, we synthesized data from the prior literature review as well as additional searches from before our current search period and provided these to working group members to inform the selection process. In contrast to the parallel functional status assessment recommendations, which were limited to patient-reported measures, we assessed RA disease activity measures with several different components: patient reported, provider assessment, laboratory, and imaging. The broad nature of these components makes selecting adequate measure performance and study quality assessment tools challenging. We selected the COSMIN checklist with 4-point scoring system to adapt for our study because it was designed to facilitate selection of health instruments in systematic reviews (18) and could be applied to both the RA disease activity and functional status assessment projects. While COSMIN was designed primarily for patient reported outcomes measures, it has been adapted beyond health-related patient-reported instruments (19,20). An updated COSMIN tool was developed after study inception that penalizes studies less for having smaller sample sizes and not reporting handling of missing data, which may affect the level of evidence grading (21). Finally, because there are no validated feasibility scoring systems for RA disease activity measures, we developed a scoring system to be used for this effort. Feasibility is inherently subjective based on varying viewpoints of different providers and practice types; therefore, we focused our feasibility scoring on identifying measures that could be regularly used by the majority of providers and practice types. As adoption of, and training in, the advanced imaging modalities continues to increase, the feasibility will need to be re-assessed in future efforts (22). While advanced imaging modalities were all deemed not feasible for regular use, all measures solely based on advanced imaging also did not fulfill the minimum standard by the absence of categorizing into 3 to 4 disease activity states.

There are several strengths to this effort. The working group was composed of content experts and practicing rheumatologists. The process and preliminary results were presented at the 2017 ACR Annual Scientific Meeting and underwent public comment. A systematic literature review with duplicate screening of articles for inclusion and standardized data abstraction was performed. Study quality was assessed using a standardized approach with a widely accepted tool and combined with the performance of RA disease activity measures to generate an overall level of evidence. A modified Delphi process was used to obtain final recommendations and incorporated the prior literature search as well as additional hand searches over the period before the current literature review.

In conclusion, we updated prior ACR recommendations for RA disease activity measures, providing recommendations for both measures that meet a minimum standard for regular use and preferred measures for regular use, specificially the CDAI, DAS28-ESR/CRP, PAS-II, RAPID3, and SDAI. These recommendations can assist clinicians with adhering to a treat-to-target approach for the management of RA but should not be interpreted as dictating the "proper" measure to be used in individual circumstances or clinical practices. As additional measures are developed and performance of measures is further characterized, these recommendations should again be evaluated.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Michaud had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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