

Clinical disease activity assessments in rheumatoid arthritis

Over the years, the growing need to standardize methodologies in rheumatoid arthritis, to improve the clinical management and evaluation of the effectiveness of treatments, has led to the development of different assessment tools. Since there is no gold standard for measuring disease activity in rheumatoid arthritis, a variety of instruments, which include continuous measures of disease activity and patient-reported outcomes questionnaires, have been described and used for this purpose. Although they were originally developed to be used in clinical trials, some of these tools have been adopted in daily practice. Clear evidence from several studies has shown that treatment decisions driven by quantitative monitoring of the disease significantly improve patient outcomes. This review provides a comprehensive overview of assessment tools currently available in rheumatoid arthritis that are used in clinical trials and daily practice, highlighting their main features and limitations.

KEYWORDS: composite indices of disease activity ■ patient-reported outcome ■ rheumatoid arthritis ■ tight control ■ treat-to-target strategy

Over the last two decades, significant progress has been made in understanding the underlying pathophysiologic mechanism and treatment modalities in rheumatoid arthritis (RA). These aspects have ultimately led to the unassailable need for early diagnosis, initiation of intensive therapy and 'tight control' monitoring driven by regular measurements of disease activity [1-5]. These observations and systematic literature reviews [6,7] provided the basis for the formulation of the 'treat-to-target' (T2T) recommendations [1,8,9], which should be an essential part of the correct management of RA patients. A combination of T2T and tight control strategies has resulted in significantly improved outcomes in RA patients in comparison with more 'traditional' approaches [10,11].

The concept of disease activity is useful for characterizing the current degree of severity and the progression of the disease. Disease activity has to be differentiated from disease severity, which is a concept encompassing much broader aspects of the disease process and its consequences. Manifestations of disease activity are reversible and they represent the main target of symptomatic treatment. Disease activity may be assessed for the following purposes: to characterize the current status of the disease and to appreciate elements of the patient's suffering; to obtain a picture of the fluctuating disease course; to monitor the patient over time; to predict further outcome; and to make decisions with regard to the treatment. An appreciation of disease activity

helps the physician to decide whether or not to prescribe drugs or alternative treatments.

To standardize measures that assess disease activity, the ACR [12], the European League Against Rheumatism (EULAR) [13] and the WHO/International League Against Rheumatism [14] have proposed a core set of variables. The core set requires the inclusion of the following seven clinical end points in all RA clinical trials: swollen and tender joint counts (TJCs); physician's assessment of disease activity (PhGA); patient's assessment of disease activity (PtGA); patient's assessment of pain; patient's assessment of physical function; and levels of an acute-phase reactant (either the C-reactive protein [CRP] level or the erythrocyte sedimentation rate [ESR]).

In the early 1990s, the ACR committee used the core set to develop a single measure of improvement: the ACR preliminary criteria for improvement in RA (ACR20; Box 1) [12]. The ACR response criteria were developed to distinguish active treatment from placebo in RA randomized controlled clinical trials. The ACR20 response criteria was defined as at least 20% improvement in both tender and swollen joint counts (SJC) and at least 20% improvement in three of the other core set measures listed in Box 1 [12]. The ACR20 became the primary outcome response criteria used by the US FDA to evaluate new treatments in RA. However, the ACR20 criteria are focused on the improvement of individual patients, rather than on the mean

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Box 1. ACR improvement criteria for use in rheumatoid arthritis.

- Tender joint count
- Swollen joint count
- Acute-phase reactant (ESR or CRP)
- Patient assessment of pain
- Patient global assessment of disease activity (PtGA)
- Physician global assessment of disease activity (PhGA)
- Physical disability (HAQ)

A patient is classified as improved if there is at least 20% improvement in five out of seven core set variables (the first two are required).

CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; PhGA: Physician's assessment of disease activity; PtGA: Patient's assessment of disease activity.

Data taken from [12].

improvement of patients treated. The main advantage of this approach is that the outcome is clearly expressed as a dichotomized response (e.g., yes/no or success/failure), despite the lack of power of the measure. Other ways to define response using core set measures have been proposed. These include the number of ACR core set measures improved by at least 20% (nACR) and an average of three variables; the percentage improvement in TJC; the percentage improvement in SJC; and the median percentage improvement in the other five core set measures (ACRn). ACRn and nACR have been evaluated in clinical trials and have been shown to be more sensitive to change than the ACR20 criteria. The assessment of inflammatory activity in RA, using disease-activity indices, has emerged as the most promising way to judge the success of therapies in clinical care and trials. Indeed, authorities and payers in many countries have accepted the use of these tools for allocating new expensive biological therapies to RA patients. The development and implementation of simplified joint assessments that require an evaluation of 28 joints has facilitated the adoption of these composite scores by rheumatologists and in routine clinical practice, to provide a continuous measure of disease activity.

Composite indices recommended for assessment of RA in daily clinical practice

In routine clinical practice, achievement of tight control monitoring has two prerequisites. First, a validated quantitative assessment is needed to facilitate continual monitoring of disease activity over time. Second, assessments need to be quick and easy to perform in routine clinical practice and adaptable to multiple formats. Composite indices are frequently used in clinical trials, as well as in daily practice, as they are useful to evaluate the response to treatment or

to make a decision to start or change treatment. To be accepted as an Outcome Measures in Rheumatology Clinical Trials (OMERACT)-endorsed outcome measure, the measure must have passed through the OMERACT filter that has three component criteria: truth, responsiveness and feasibility. Each component criterion represents a question to be answered about the measure, in each of its intended settings. Truth determines whether the outcome measures what is intended. This includes face and content validity as well as criterion and construct validity. Responsiveness is the ability to discriminate between situations of interest. Feasibility assesses whether the measure can be applied easily given constraints of time, money and interpretation. Composite indices producing a single score have an advantage over the interpretation of individual components of disease activity as they provide clinically meaningful and reliable estimates of disease activity with interpretation of multiple data points simultaneously. Moreover, composite indices are more responsive to change than single items, less susceptible to selection bias related to the reporting of a single measurement and more flexible for deriving other end points. Depending on what is considered appropriate, composite indices allow defining in advance whether to use the absolute change in the measure, the percentage of patients below a cutoff point, time-to-reach that cutoff point or the number of visits below a cutoff point. In addition, composite indices are recommended by many insurers and regulators to justify escalation of RA therapy [1-5,10,11]. A variety of established validated composite disease activity indices are available and have been recommended for use in clinical trials, they include continuous measures of disease activity and patient-reported outcome (PRO) measures of disease activity [15]. Although they were originally developed for use in RA clinical trials, some of these tools have been adopted for use in daily clinical practice.

Continuous measures of disease activity

In order to measure disease activity several, continuous composite scores have been developed, such as the Disease Activity Score (DAS) [16], DAS in 28 joints (DAS28) [17], the Clinical Disease Activity Index (CDAI) [18], the Simplified Disease Activity Index (SDAI) [19,20], the Chronic Arthritis Systemic Index (CASI) [21,22] and the Mean Overall Index for RA (MOI-RA) [23]. All of the abovementioned indices include

a 28-SJC and -TJC (except for the original DAS and CASI, which employ the Ritchie Articular Index (RAI), a graded assessment of 26 joint regions to evaluate tenderness and a 44-joint count to assess swelling). Acute-phase reactants are integrated into DAS (ESR), DAS28 (ESR), SDAI (CRP), CASI and MOI-RA (ESR), but not into CDAI. The inability to obtain ESR tests or to obtain them in a timely fashion to be used for clinical decision making were the rationale for the development of CDAI. All of these composite disease activity indices include a formal swollen and TJC performed by a physician.

The DAS44 is a composite disease activity index including the RAI (ranging from 0 to 78), SJC among 44 joints (SJC44), ESR and general health status (GH; 0–100 visual analog scale [VAS]). The DAS44 is computed by the following equation:

$$\text{DAS44} = 0.53938 \times \sqrt{\text{RAI}} + 0.0675 \times (\text{SJC44}) + 0.330 \ln(\text{ESR}) + 0.00722 \times \text{GH}$$

The DAS44 can range from 0.23 to 9.87, and the values are normally distributed. High disease activity is defined as a DAS44 of >3.7, moderate activity is defined as a DAS44 between 2.4 and 3.7, low activity is defined as a DAS44 between ≤ 2.4 and ≥ 1.6 and remission is defined as a DAS44 <1.6. Despite the usefulness and importance of the DAS in the evaluation of disease activity being well accepted, its implementation in daily practice remains a challenge. The RAI may be subjective and complicated, it includes a 0–3 graded evaluation of the severity of the tenderness of joint groups, where the highest value that counts is the highest value within each group. Recently, Koevoets *et al.* used data from the BeSt trial to evaluate three DAS alternatives, not including the RAI, and to compare the use of PtGA versus GH status in DAS, DAS alternatives and DAS28 [24]. DAS alternatives were derived as follows: the DAS 0–1 was calculated by the substitution of RAI greater than 0 with '1', while the RAI '0' score remained as '0', resulting in a maximum TJC of 26. The DASTJC53 was calculated according to a dichotomized response (0 = no and 1 = yes) of the 53 joints of RAI. The DASTJC44 was calculated with a TJC in the same 44 joints that are assessed for swelling in the DAS. All DAS variations, as well as the original DAS and DAS28, were calculated with VAS–PtGA and VAS–GH. The authors demonstrated that scoring the presence or absence of tenderness in individual joints to calculate a disease activity

score performs just as well as scoring a graded tenderness score in joint groups. In daily practice or clinical studies, using a DAS alternative may be much easier than using the original DAS with RAI. The score based on the assessment of tenderness in the same 44 joints assessed for swelling may be more practical. For reasons of convenience, a reduced original DAS was proposed by Prevo *et al.* [25]. The DAS28 includes evaluation of SJC among 28 joints (SJC28), TJC among the same 28 joints (TJC28), ESR and GH status (0–100 VAS), is computed by the following equation:

$$\text{DAS28} = 0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{GH}$$

DAS28 can range from 0.49 to 9.07, and the values are normally distributed. High disease activity is defined as a DAS28 >5.1, moderate activity as a DAS28 >3.2 and ≤ 5.1 , low activity as a DAS28 ≤ 3.2 and >2.6, and remission as a DAS28 less than 2.6. By comparing the DAS28 from one patient on two different time points, it is possible to define improvement or response. A change of 1.2 (i.e., two-times the measures error) of the DAS28 in an individual patient is considered a significant change. The use of DAS28 is officially recommended by EULAR for evaluating disease activity and the improvement in disease activity in clinical trials and also in daily clinical practice [26]. The EULAR response criteria are defined as reported in TABLE 1. DAS and the DAS28 are not interchangeable. DAS cannot be computed from the DAS28, while DAS28 can be computed from the DAS ($[1.072 \times \text{DAS}] + 0.938$). DAS28 values can be higher than DAS values in the same patient. The substitution of CRP (mg/l) with ESR for the DAS and DAS28 indices has been evaluated [27]. Although recent authors reported high levels of agreement between the DAS28–CRP and DAS28–ESR [28,29], two large cohort studies from Japan have highlighted the tendency

Table 1. The European League Against Rheumatism response criteria.

Present DAS28	DAS28 improvement		
	>1.2	>0.6 & ≤1.2	≤0.6
≤3.2	Good response	Moderate response	No response
>3.2 and ≤5.1	Moderate response	Moderate response	No response
>5.1	Moderate response	No response	No response

Both the thresholds for high and low disease activity and remission, and the abovementioned improvement criteria, should allow the interpretation of DAS28 scores. DAS28: Disease Activity Score in 28 joints.

for DAS28-CRP to underestimate DAS28-ESR and they recommended an adjustment factor based on regressing DAS28-ESR on DAS28-CRP (i.e., $\text{DAS28-ESR} = 1.01 \times \text{DAS28-CRP} + 0.590$) [30,31]. The implementation of this adjustment factor to the data set led to a larger percentage of patients being classified with a worse response state using DAS28 (CRP: 2.9% classified as better and 12.9% classified as worse, compared with the unadjusted results of 12.7 and 4.9%, respectively). Other approaches can be considered. For example, an adjustment factor could be based on regressing $\ln(\text{ESR})$ on $\ln(\text{CRP} + 1)$, which is the essential difference between the two DAS28 definitions, and using this adjustment in the DAS28-ESR formula. After applying this adjustment, a more equitable division resulted, with 4.5% in an improved state and 8.6% in a worse state. However, the generalizability of the transformation may be an issue. Inoue *et al.* suggested new threshold values corresponding to remission, low disease activity and high disease activity that were 2.3, 2.7 and 4.1, respectively [30]. Landewé *et al.* found that the DAS remission criterion of the original version is more conservative than the DAS28 remission criterion [32]. This discrepancy was accounted for by the features of DAS28, which assigns a higher value to the perception of pain by the patient compared with other variables, the type of assessment of disease activity and the exclusion of ankles and feet from the evaluation. However, at the time of presentation, 60% of patients with early RA had forefoot involvement, while after 2 years, the prevalence decreased to 36% and then stabilized [33]. Moreover, patients with a disease in remission, according to the DAS28, may have relatively large numbers of 'residual joint counts', especially swollen joints [34,35]. Synovitis of the metatarsophalangeal (MTP) joints is believed to be the main cause of foot pain in early RA and is usually accompanied by joint swelling. Furthermore, the small joints of the foot erode more quickly and this erosion affects a greater number of joints compared with the joints of the hands [36,37]. According to a recent report, nearly 40% of patients with disease in remission, according to the DAS28, had forefoot involvement (pain and/or swelling in at least one MTP joint) [38]. This aspect suggests that DAS28 remission criterion for RA neglects patients with active forefoot involvement, and that the DAS28 cutoff point of 2.6 for RA remission has insufficient construct validity and should, therefore, be used with

caution in clinical practice and trials. However, in daily practice, assessment of MTP joint synovitis is cumbersome [39]. Therefore, an alternative simple test to include foot involvement may be of added value to assess disease activity at an early stage, whereupon treatment decisions could be made. The squeeze test of forefeet, which examines bilateral compression pain across the MTP joints, may be such a test (FIGURE 1) [40,41]. Recently, de Jong *et al.* added the squeeze test of forefeet in order to optimize use of the DAS28 in early RA [42]. The authors showed, that compared with the DAS28, the DAS28 squeeze test improved disease-state categorization in patients with RA according to the 2010 ACR/EULAR criteria [43]. Moreover, the addition of the squeeze test elicited correct reclassification of DAS28 remission assessments that were classed as nonremission assessments according to the Boolean criteria [44]. In the development process, the DAS28 squeeze test was constructed using a linear regression model with the DAS as the dependent variable and the DAS28 and squeeze test as the independent variables. The model was then validated by predicting the DAS based on the new formula. Its mathematical formula is the following: $\text{DAS28-squeeze} = 0.64 \times \text{DAS28} + 0.23 \times \text{squeeze test}$. The squeeze test was coded as follows: 0 = test is negative on both forefeet; 1 = test is positive on one side; and 2 = test is positive on both forefeet. The authors set DAS28 squeeze test thresholds for remission and moderate-to-high disease activity at <1.6 and ≥ 2.4 , respectively, in accordance with DAS (dependent variable) thresholds. The DAS28 squeeze test model had an explained variance of 97.5% [42].

The SDAI and CDAI both use a 28-joint count to enumerate swollen and tender joints. The SDAI was published in 2003 to provide a simpler tool than the DAS. The SDAI is obtained by the algebraic sum of the following five factors: 28TJC + 28SJC + CRP level + overall disease activity on a 0–10 VAS completed by the patient (PtGA) + overall disease activity on a 0–10 VAS completed by the physician (PhGA). For the final score no calculator is needed; the values can range from 0 to 86. High disease activity is defined as a SDAI >26 , moderate activity as a SDAI >11 and ≤ 26 , low activity as a SDAI ≤ 11 and >3.3 , and remission as a SDAI ≤ 3.3 (Box 2). A change in the SDAI of 22 or more was found to represent major improvement, while a change of 10–22 suggested moderate improvement. A change in the SDAI of 10 is very close to the value of 9, which is associated with a change

of 0.6 in the DAS28, indicative of a moderate clinical improvement [45].

The CDAI omits the CRP level and is based on the simple summation of the 28SJC, 28TJC, PtGA and PhGA [18]. CDAI values can range from 0 to 76. High disease activity is defined as a CDAI >22, moderate activity as a CDAI >10 and ≤22, low activity as a CDAI ≤10 and >2.8, and remission as a CDAI ≤2.8. Validity of CDAI was determined by studying its correlational validity (refers to the comparison with other measures of disease activity), discriminant validity (in this setting it relates to the correlation of changes in the scale with changes in other measures of disease activity) and construct validity (considers correlations with important outcomes of the disease, such as radiological progression) by various statistical methods [18,46]. CDAI have proved to be of greatest value in clinical practice rather than in research, where acute-phase reactants are nearly always available. The greater advantage of CDAI is its potential to be employed in the evaluation of patients with RA, and that does not require the use of calculators. Therefore, it can essentially be used everywhere and at anytime for disease activity assessment in RA patients. Moreover, CDAI cutoff values for remission are more stringent compared with DAS28; CDAI allows for lesser residual disease activity since DAS28 <2.4 allows up to eight tender/SJC while CDAI <2.8 only allows less than two tender/SJC [34,46]. In Box 3 different formulas that have been developed and validated for DAS, DAS28, SDAI, CDAI and CASI are reported.

Recently, a new set of remission criteria has been presented by ACR and EULAR. The Boolean-based definition requires four criteria (PtGA [on a 0–10 scale], 28SJC, 28TJC and CRP [mg/dl]) to be ≤1. A remission definition for clinical practice was also proposed, eliminating the CRP level (Box 4) [44]. Although new ACR/EULAR criteria do not include an evaluation of ankles and forefeet to define a remission, an assessment of these joints is highly recommended.

All the abovementioned indices, used to assess disease activity in RA, have some shortcomings. DAS includes four variables and it requires complex calculations, such as square root and logarithm. Furthermore, DAS, SDAI and CDAI do not include patient functional status, such as the Health Assessment Questionnaire (HAQ), which is the best predictor of most severe long-term outcomes of RA [47,48]. These considerations led us to develop a disease activity index based on four core set components of the



Figure 1. The squeeze test of forefeet.

According to de Jong *et al.*, the squeeze test is performed by placing the thumb just below the first metatarsophalangeal joint (to prevent direct compression of this joint) and placing the index finger over the fifth metatarsophalangeal joint [42]. The metatarsal joints are then compressed bilaterally using a force equal to a handshake.

ACR response criteria for RA (termed CASI). The CASI includes the RAI, patient assessment of pain VAS, HAQ and ESR [21,22]. The RAI ranges from 0 to 78, the HAQ ranges from 0 to 3, the VAS pain ranges from 0 to 100 and the ESR ranges from 0 to 100. The final score

Box 2. Comparison of the Simplified Disease Activity Index Criteria and the Clinical Disease Activity Index Criteria.

SDAI

- Tender joint count of 28 joints
- Swollen joint count of 28 joints
- C-reactive protein
- Patient global assessment of disease activity on visual analogue scale (0–10)
- Physician global assessment of disease activity on visual analogue scale (0–10)
- SDAI is the numerical sum of the above components (range 0–86)
- Categories:
 - Remission ≤3.3
 - Low disease activity >3.3 and <20
 - Moderate disease activity >20 and ≤40
 - High disease activity >40

CDAI

- Tender joint count of 28 joints
- Swollen joint count of 28 joints
- Patient global assessment of disease activity on visual analogue scale (0–10)
- Physician global assessment of disease activity on visual analogue scale (0–10)
- CDAI is the numerical sum of the above components (range 0–76)
- Categories:
 - Remission ≤2.8
 - Low disease activity >2.8 and ≤10
 - Moderate disease activity >10 and ≤22
 - High disease activity >22

CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index.

Box 3. Different formulas that have been developed and validated for Disease Activity Score, Disease Activity Score-28, Simplified Disease Activity Index and Clinical Disease Activity Index.

- DAS44-ESR (four variables) = $0.54 \times \sqrt{(\text{RAI})} + 0.065 \times (\text{SJC44}) + 0.33 \times \ln(\text{ESR}) + 0.0072 \times \text{GH}$
- DAS44-ESR (three variables) = $0.54 \times \sqrt{(\text{RAI})} + 0.065 \times (\text{SJC44}) + 0.33 \times \ln(\text{ESR}) + 0.22$
- DAS44-CRP (four variables) = $0.54 \times \sqrt{(\text{RAI})} + 0.065 \times \text{SJC44} + 0.17 \times \ln(\text{CRP} + 1) + 0.0072 \times \text{GH} + 0.45$
- DAS44-CRP (three variables) = $0.54 \times \sqrt{(\text{RAI})} + 0.065 \times \text{SJC44} + 0.17 \times \ln(\text{CRP} + 1) + 0.65$
- High disease activity >3.7, low disease activity <2.4 and remission <1.6
- DAS28-ESR (four variables) = $(0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{GH}) \times 1.08 + 0.16$
- DAS28-ESR (three variables) = $(0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.70 \times \ln(\text{ESR})) \times 1.08 + 0.16$
- DAS28-CRP (four variables) = $(0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.36 \times \ln(\text{CRP} + 1)) \times 1.10 + 1.15$
- DAS28-CRP (three variables) = $(0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.36 \times \ln(\text{CRP} + 1)) \times 1.10 + 1.15$
- DAS28-squeeze = $0.64 \times \text{DAS28} + 0.23 \times \text{squeeze test}$
- High disease activity >5.1, low disease activity <3.2 and remission <2.6
- DAS28 = $(1.072 \times \text{DAS}) + 0.938$
- SDAI = $\text{TJC28} + \text{SJC28} + \text{PtGA (0-10)} + \text{PhGA (0-10)} + \text{CRP (mg/dl)}$
- CDAI = $\text{TJC28} + \text{SJC28} + \text{PtGA (0-10)} + \text{PhGA (0-10)}$
- CASI = $13 \times \text{HAQ} + 0.21 \times \text{ESR} + 0.08 \times \text{VAS pain (0-10)} + 0.07692 \times \text{RAI}$

CASI: Chronic Arthritis Systemic Index; CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAS: Disease Activity Score; DAS28: Disease Activity Score in 28 joints; DAS44: Disease Activity Score in 44 joints; ESR: Erythrocyte sedimentation rate in mm/h; GH: General health or patient's global assessment of disease activity on a 100-mm VAS; HAQ: Health assessment questionnaire; PhGA: Physician's assessment of disease activity; PtGA: Patient's assessment of disease activity; RAI: Ritchie Articular Index; SDAI: Simplified Disease Activity Index; SJC: Swollen joints count; TJC: Tender joint count; VAS: Visual analog scale.

of CASI ranges from 0 to 74. For this index, an optimal point of 24.6 comes close to maximizing both sensitivity and specificity. With this cutoff point, sensitivity and specificity are 90.9 and 71.1%, respectively. Additional categories of disease activity have not been established. The following formula is used to calculate CASI:

$$\text{CASI} = 13 \times \text{HAQ} + 0.21 \times \text{ESR} + 0.08 \times \text{pain VAS} + 0.07692 \times \text{RAI}$$

No training is required to interpret the scores. The calculation for the CASI requires the use of a calculator or computer, which may make the measure difficult to use at the point of care. The CASI was designed using a factorial analysis of 29 available variables with the intent to design a RA measure of both disease activity and severity for use by practicing rheumatologists [21,22]. Validation studies were mainly performed on measures no longer in general use. The use of the RAI increases the time required to perform joint counts compared with standard joint counts as grading of tenderness is required. In addition, inclusion of ESR may render the usage of CASI difficult in clinics that do not have laboratory values available at the time a patient is examined. The inclusion of the original HAQ increases the time required of the patient to complete the measure compared with measures using shorter versions of the HAQ or alternative quality of life measures, and may not provide sufficient additional information to justify the increase in time spent. The HAQ is a

mixed variable reflecting both disease activity and damage in late disease and, therefore, its inclusion in composite activity indices should be considered with caution. However, the presence of a HAQ score provides a picture of the severity of the disease considering that, in predicting prognosis, the functional disability is the most powerful determinant of all outcomes in RA. To develop a continuous composite index of disease activity for RA, based on the seven ACR core data set of disease activity measures, Mäkinen *et al.* developed the MOI-RA [23]. The MOI-RA is the mean of standardized values of TJCs and SJCs (28, 42 or 66/68 joint counts), physical function (HAQ 0–3), patients' and physicians' assessments of global health status, and patients' assessment of pain (VAS 0–100 mm) and ESR (1–100). All of the seven components are normalized (0–100) and the mean of standardized values can be calculated. The range of MOI-RA is 0–100 where higher values indicate poorer outcomes [23]. The MOI-RA index was designed for simplicity and feasibility, while incorporating patient physical function (HAQ). The components of MOI-RA include all the important measures of disease activity from both the physicians' and patients' perspectives. Furthermore, MOI-RA has some advantages compared with previous indices; various joint counts can be used with comparable outcome and the imputation stability is high, enabling the use of incomplete data. Disadvantages of the MOI-RA in clinical practice are the need for a blood sample, the time needed to perform

joint counts and a complicated mathematical calculation of the composite score. In addition, cutoffs for categories of disease activity have not been established.

PRO measures of disease activity

Most of the RA patients managed by rheumatologists experience chronic symptoms and, therefore, patient opinion is a crucial component for the treatment-efficacy assessment. Recently, PROs have been included for the evaluation of disease and response to therapy in RA clinical trials. The escalating importance of PROs is proved by the US FDA's issuance of Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims in December 2009 [101] and by the Outcome Measures in Rheumatology OMERACT [49,50]. However, PROs are considered to be subjective and less reliable than objective criteria by clinicians. Besides the ability to discriminate between responders and nonresponders, self-reporting instruments are very easy to administer, have no cost, are noninvasive and they pass the OMERACT quality filter (truth, discrimination and feasibility) [51]. These self-report questionnaires provide scores based on three patient-reported variables: physical function, pain intensity and overall assessment of the disease. Thus, they allow a quantitative assessment of disease activity based on patient-reported data, without requiring routine joint counts. Self-report questionnaires are designed to monitor patients in everyday clinical practice but they cannot replace clinical examination. These composite indices include the RA Disease Activity Index (RADAI) [52] and the newly adapted RADAI-5 [53], the Routine Assessment of Patient Index Data (RAPID) [54], the Patients Activity Scale (PAS) or PAS II [55], the validated Rheumatoid Arthritis Impact of Disease (RAID) questionnaire [56] and the Patient-Reported Outcome CLinical ARthritis Activity (PRO-CLARA) questionnaire [57,58].

The RADAI is a five-item questionnaire related to: the patient's global disease activity over the last 6 months; the patient's disease activity in terms of current swollen and tender joints; arthritis pain; the duration of morning stiffness; and tender joints to be rated according a joint list [52]. The first three items are all rated on an anchored numerical rating scale (NRS) from 0 to 10, where higher scores indicate greater disease activity. The scores for the last two items range from 0 to 6 and 0 to 48,

respectively, but can be transformed on to the same scale that ranges from 0 to 10. If all items are answered, the scores can be added and then divided by the number of items to provide a single index of patient-assessed disease activity. The RADAI has been shown to be feasible and valid in the assessment of disease activity in a large cross-sectional sample of RA patients [59]. Rintelen *et al.* recently published a five-item questionnaire, the RADAI-5, which is a modification of the RADAI and omits the patient self-assessed TJC in comparison with its original version [53]. The rationale for the development of the RADAI-5 was to provide an instrument to physicians, especially those who are not familiar with joint assessment such as nonrheumatologists, to assess RA activity in daily routine care. The RADAI-5 was shown to be capable of measuring RA activity accurately when compared with the DAS28 and the CDAI. Since the RADAI-5 is calculated by the addition of five integral numbers ranging from 0 to 10 on a NRS, followed by a division by five. Derived from this observation, the following thresholds were proposed for patient categorization: 0.0–1.4 for a remission-like state; 1.6–3.0 for mild disease activity; 3.2–5.4 for moderate disease activity; and 5.6–10.0 for high disease activity [60,61].

The RAPID scores include combinations of physical function, pain, PtGA and self-reported TJC and SJC. Physical function is evaluated by

Box 4. ACR/European League Against Rheumatism definitions of remission in rheumatoid arthritis clinical trials.

- Boolean-based definition
 - At any time point, patient must satisfy all of the following:
 - Tender joint count $\leq 1^{\dagger}$
 - Swollen joint count $\leq 1^{\dagger}$
 - C-reactive protein ≤ 1 mg/dl
 - Patient global assessment ≤ 1 (on a 0–10 scale)[‡]
- Index-based definition
 - At any time point, patient must have a SDAI $\leq 3.3^{\S}$
- Boolean-based suggestion for clinical practice
 - At any time point, patient must satisfy all of the following:
 - Tender joint count $\leq 1^{\dagger}$
 - Swollen joint count $\leq 1^{\dagger}$
 - Patient global assessment ≤ 1 (on a 0–10 scale)[‡]
- Index-based suggestion for clinical practice
 - At any time point, patient must have a CDAI $\leq 2.8^{\S}$

[†]For tender and swollen joint counts, a 28-joint count may miss active joints, especially in the feet and ankles and, therefore, it is preferable to include feet and ankles when evaluating remission.

[‡]The following wording and response categories should be used for global assessment: 'Considering all of the ways your arthritis has affected you, how do you feel your arthritis is today?' The response can range from 'asymptomatic' to 'severe symptoms'.

[§]SDAI is defined as the simple sum of the tender joint count in 28 joints, swollen joint count in 28 joints, patient global assessment (on a 0–10 scale), physician global assessment (on a 0–10 scale) and C-reactive protein (mg/dl). CDAI is the same as the SDAI minus C-reactive protein.

CDAI: Clinical Disease Activity Index; SDAI: Simplified disease activity index. Data taken from [44].

Please try to answer each question, even if you do not think it is related to you at this time. **There are no right or wrong answers.** Please answer exactly as you think or feel. Thank you.

Please check (✓) the **one** best answer for your abilities at this time:

Over the last week, were you able to:	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
– Close your hand completely?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Accept a hand shake?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Do up buttons?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Open jars that have been previously opened?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Reach up and take down a 2-kg object from above your head?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Stand up?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Walk on a flat ground?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Climb up five steps or stairs?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Get into and out of a car?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Wash and dry your body?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4
– Are you still able to work at home or/and on your job?	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4

Please place a check (✓) in the appropriate spot to indicate the amount of pain you are having today in each of the joint areas listed below:

Left	None	Mild	Moderate	Severe	Right	None	Mild	Moderate	Severe
Hand	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Hand	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Wrist	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Wrist	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Elbow	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Elbow	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Shoulder	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Shoulder	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Hip	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Hip	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Knee	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Knee	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Ankle	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Ankle	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Foot	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	Foot	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3

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ROAD	<input type="checkbox"/>	1=0.2	2=0.4	3=0.6	4=0.8	5=1.0	6=1.3	7=1.5	8=1.7	9=1.9	10=2.1	11=2.3	12=2.5
SELF-TJC	<input type="checkbox"/>	13=2.7	14=2.9	15=3.1	16=3.3	17=3.5	18=3.8	19=4.0	20=4.2	21=4.4	22=4.6	23=4.8	24=5.0
		25=5.2	26=5.4	27=5.6	28=5.8	29=6.0	30=6.3	31=6.5	32=6.7	33=6.9	34=7.1	35=7.3	36=7.5
		37=7.7	38=7.9	39=8.1	40=8.3	41=8.5	42=8.8	43=9.0	44=9.2	45=9.4	46=9.6	47=9.8	48=10

Please place a check (✓) in the appropriate numerical scale to indicate how you would describe your general health:

Very well 0 1 2 3 4 5 6 7 8 9 10 **Very poorly**

Figure 2. Patient-Reported Outcome Clinical ARthritis Activity (PRO-CLARA) index.

ROAD: Recent-Onset Arthritis Disability; SELF-TJC: Self-tender joint count.

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the Multidimensional HAQ, while pain and global estimate are assessed according to VAS, both scored on a 0–10 scale. The self-reported TJC is evaluated according the joint list of

RADAI, which includes eight joints or joint groups, scored 0, 1, 2 or 3, a 0–48 scale (recoded to 0–10). There are five RAPID score versions. The RAPID3 includes physical function, pain

and patient global estimate evaluation. RAPID3 is mathematically identical to the PAS, but has a raw score of 0–30 and an adjusted score of 0–10 [55]. The score for physical function is converted from 0–3 to 0–10 by multiplying by 3.33, using a template from the Multidimensional HAQ. The three 0–10 scores for physical function, pain VAS and global VAS were added together for a raw score of 0–30, which was divided by 3 to give an adjusted 0–10 score for comparison with other RAPID indices. Proposed severity (rather than activity) categories for RAPID3 are: >4 = high; 2.01–4.00 = moderate; 1.01–2.00 = low; and ≤1 = near-remission, on an adjusted 0–10 scale. On an unadjusted 0–30 scale, the severity categories are defined as: >12 = high; 6.1–12.0 = moderate; 3.1–6.0 = low; and ≤3 = near-remission [15,54]. RAPID4 adds to RAPID3 and the RADAI self-reported joint count. A 66 TJC is converted to a 0–10 scale using simple division by 6.6. The raw RAPID 4-joints count score is 0–40, and is the sum of four 0–10 scores for physical function, pain VAS, global VAS and TJC. The raw RAPID 4-joints count score is divided by 4 to give an adjusted

0–10 score. RAPID5 adds a physician global estimate (0–10) to RAPID4. The rationale for RAPID5 was to include both the measure that most rheumatologists indicate as the most valuable to assess patients with RA (joint count) and the measure with the highest relative efficiency in clinical trials. Therefore, RAPID5 is the most comprehensive RAPID index. The RAPID5 raw score is 0–50 and is divided by 5 to give an adjusted 0–10 score.

The PAS and PAS II contain only patient-derived data and include a patient assessment of pain on a 10-cm VAS, a PtGA on a 10-cm VAS and HAQ for the PAS or the HAQ-II for the PAS II [55]. The PAS is analogous to the PAS II and RAPID3.

Recently, the EULAR has proposed and validated a new patient-reported composite index, termed RAID [56,62]. The RAID includes seven domains (pain, function, fatigue, physical and psychological wellbeing, sleep disturbance and coping). Each domain is evaluated using a single question answered by a 0–10 NRS have the following weightings: pain 21%, functional disability 16%, fatigue 15%, sleep problems

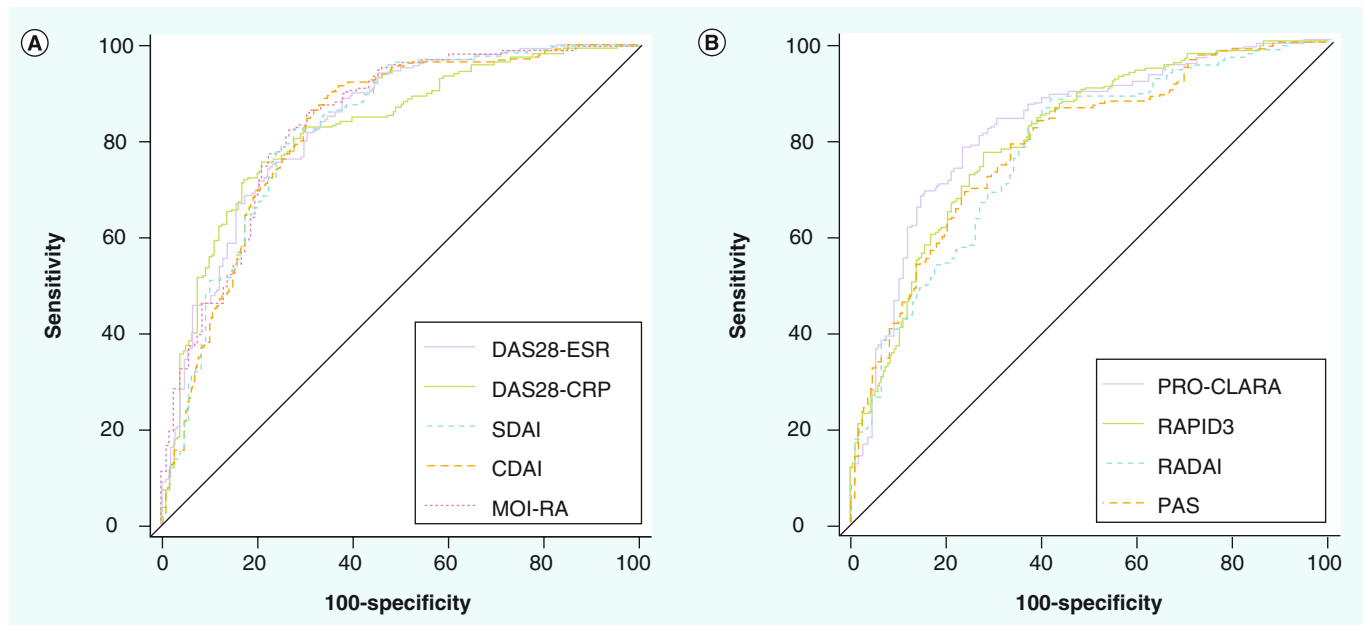


Figure 3. Receiver operating characteristic curves of most common continuous measures of disease activity and patient-reported outcomes questionnaires used in rheumatoid arthritis.

Receiver operating characteristic curves illustrating the relationship between sensitivity and complement of specificity (100-specificity) in rheumatoid arthritis for (A) the self-report questionnaires and (B) traditional composite disease activity indices using changes in global disease activity as an external indicator. The area under the receiver operating characteristic curve can be interpreted as the probability of correctly identifying the improved patients from those not improved. Lines that run diagonally across the graphs will have an area of 0.5; this represents an instrument that has no discriminating capacity.

CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAS28: Disease Activity Score in 28 joints; ESR: Erythrocyte sedimentation rate; MOI-RA: Mean Overall Index for Rheumatoid Arthritis; PAS: Patients Activity Scale; PRO-CLARA: Patient-Reported Outcome CLinical ARthritis Activity; RADAI: Rheumatoid Arthritis Disease Activity Index; RAPID3; Routine Assessment of Patient Index Data 3; SDAI: Simplified Disease Activity Index.

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12%, emotional wellbeing 12%, physical wellbeing 12% and coping 12%. The score has a range from 0 to 10 (where 10 indicates worst health status). Dougados *et al.* have shown that a change of at least three points (absolute) or 50% (relative) in the RAID score should be used to define a minimal clinically important improvement and that a maximal value of two defines an acceptable status [63].

Previously, we have analyzed the performance of a self-report questionnaire for assessing RA activity, termed PRO-CLARA [57,58]. The PRO-CLARA is a short and easy-to-complete self-administered index, without formal joint counts, combining three items on patients' physical function (as measured by Recent-Onset Arthritis Disability [ROAD] questionnaire), self-administered TJC and PtGA into a single measure of disease activity (FIGURE 2). The ROAD questionnaire, developed and validated in Italy [64–67], comprises 12 items that capture a combination of common symptoms related to a patient's level of functional ability and includes important questions concerning fine movements of the upper extremity, activities of the lower extremity and activities that involve both upper and lower extremities. The ROAD has 12 items assessing three reported patient-relevant dimensions: upper extremity function, lower extremity function and activities of daily living/work. These items represent a combination of symptoms that are common, frequently recurring and of general importance to RA patients. For each item, patients are asked to rate the level of difficulty over the past week on a five-point scale that ranges from 0 (without any difficulty) to 4 (unable to do). The ROAD ranges from 0 to 48. In order to express these scores in a more clinically meaningful format, a simple mathematical normalization procedure was then performed so that all the scores could be expressed in the range 0–10, with 0 representing better status and 10 representing poorer status. The ROAD can be scored in 15–20 s. The self-administered TJC was evaluated according to joint list of the RADAI. The RADAI joint mannequin list queries pain 'today' in 16 joints or joint groups including left and right shoulders, elbows, wrists, fingers, hips, knees, ankles and toes [52,53]. The self-administered TJC weighted the degree of tenderness of each joint on the following scale: 0 = none; 1 = mild; 2 = moderate; and 3 = severe. The self-administered TJC is scored as 0–48; the raw 0–48 score may be recoded to 0–10 using a scoring template. The PtGA is scored as 0–10 on NRS with the following question:

“How would you describe your general health today? (0 = very well to 10 = very poorly)”. The total score of the PRO-CLARA was calculated by summing the scores of the three individual measures and dividing this value by three, and ranges from 0 to 10.

Conclusion & future perspective

Although there is currently no ideal measure of disease activity, based on available evidence and expert opinion, we believe that we have identified composite indices and questionnaires, endorsed by EULAR and ACR, which are currently the most reliable, valid, feasible and acceptable measures of disease activity in RA [68–70]. Incorporation of these validated RA-disease activity measures into a practice's workflow will facilitate adherence to the guidelines for the treatment of RA [1] and provide the necessary tools for treating to target.

Clear evidence from several studies has shown that treatment decisions driven by quantitative monitoring are significantly better than subjective monitoring for improving patient outcomes [1–3,5–9]. Therefore, by incorporating quantitative assessment tools in the current management strategy of the clinical approach, rheumatologists could vastly improve the outcomes of patients with RA.

In this discussion, we have provided an overview of different measures and validated assessment tools for use in routine clinical practice, including those assessing clinical efficacy and patient-centered benefits. Clinical composite measures, such as DAS28, CDAI and SDAI, or questionnaires, such as RAPID3, RAID and PRO-CLARA, allow the physician to easily and quickly quantify disease activity levels and patient responses to therapy. These outcome measures can help to identify issues that the patient is facing and can also help to form a more comprehensive understanding of the patient's progress.

A systematic literature analysis of studies comparing the psychometric properties of the composite disease activity indices does not allow a ranking in terms of their metrological properties [71]. The self-reported questionnaire showed comparable internal and external responsiveness in comparison with continuous measures of disease activity (FIGURE 3) [57].

In our clinical practice, we have found the PRO-CLARA assessment tool to be useful for quantitatively monitoring the patient's response to therapy and validly assessing disease activity in RA patients. This fast and simple tool,

supplemented with a close patient–nurse relationship, has allowed us to determine whether our patients are responding adequately to therapy. The information obtained by the nurse can give additional insight to the rheumatologist, who may see the patient on a less-frequent basis. Such data can now be easily and reliably recorded with advances in information and communication technologies, which enables a fundamental redesign of healthcare processes based on the use and integration of electronic communication at all levels. Many opportunities

exist for use of web/internet-based diaries. Tele-monitoring can improve the medical care, quality of life and prognosis of patients with RA, and can support a transition from institution-centric to patient-centric applications. Electronic pain assessment has been incorporated in an internet-based clinical trial for osteoarthritis of the knee [72] and has potential benefits for pain assessment in telemedicine interventions, such as self-regulation training for chronic pain [73]. Experiences of web-based platforms are now operational at our rheumatology center for remote

Executive summary

Assessment of disease activity in rheumatoid arthritis

- A variety of established validated composite disease activity indices are available and have been recommended for use in clinical trials and in daily practice and include continuous measures of disease activity and patient-reported outcomes.

Most common continuous measures of disease activity

- Disease Activity Score in 44 joints includes evaluation of the Ritchie Articular Index (0–78), swollen joint counts (SJC) among 44 joints (SJC44), erythrocyte sedimentation rate (ESR) and general health status (0–100 visual analog scale [VAS]). The final score can range from 0.23 to 9.87. High disease activity is defined as >3.7 , moderate activity as 2.4–3.7, low activity as ≤ 2.4 and ≥ 1.6 , and remission as <1.6 .
- Disease Activity Score in 28 joints includes evaluation of SJC among 28 joints (SJC28), tender joint counts (TJC) among 28 joints (TJC28), ESR and general health status (0–100 VAS). The total score can range from 0.49 to 9.07. High disease activity is defined as >5.1 , moderate activity as >3.2 and ≤ 5.1 , low activity as ≤ 3.2 and >2.6 , and remission as <2.6 .
- Simplified Disease Activity Index is obtained by the algebraic sum of five factors: TJC28, SJC28, C-reactive protein level, overall disease activity (0–10 VAS) completed by the patient (patient's assessment of disease activity [PtGA]) and overall disease activity (0–10 VAS) completed by the physician (physician's assessment of disease activity [PhGA]). The values can range from 0 to 86. High disease activity is defined as >26 , moderate activity as >11 and ≤ 26 , low activity as a Simplified Disease Activity Index ≤ 11 and >3.3 , and remission as a Simplified Disease Activity Index ≤ 3.3 .
- Clinical Disease Activity Index omits the C-reactive protein level and is based on the simple summation of the SJC28, PtGA and PhGA for estimating disease activity. The values can range from 0 to 76. High disease activity is defined as Clinical Disease Activity Index >22 , moderate activity as >10 and ≤ 22 , low activity as ≤ 10 and >2.8 , and remission as Clinical Disease Activity Index ≤ 2.8 .
- Chronic Arthritis Systemic Index includes the Ritchie Articular Index, patient assessment of pain VAS, Health Assessment Questionnaire (HAQ) and ESR. The level of disease activity can be interpreted as Chronic Arthritis Systemic Index remission of 24.65 corresponding to a Disease Activity Score of 3.32. Additional categories of disease activity have not been established.
- Mean Overall Index for Rheumatoid Arthritis is the mean of standardized values of TJC and SJC (28, 42 or 66/68 joint counts), physical function (HAQ 0–3), PhGA, PtGA and ESR. The range of Mean Overall Index for Rheumatoid Arthritis is 0–100; higher values indicate poorer outcomes.

Patient-reported outcomes measures of disease activity

- The Rheumatoid Arthritis Disease Activity Index (RADAI) is a five-item questionnaire related to: patient's global disease activity over the last 6 months; patient's disease activity in terms of current swollen and tender joints; arthritis pain; duration of morning stiffness; and tender joints to be rated according to a joint list.
- The RADAI5 omits the patient self-assessed TJC of the original RADAI and is calculated by addition of five integral numbers from 0 to 10 on a numerical rating scale, followed by a division of five. The disease activity thresholds for patient categorization are the following: 0.0–1.4 for a remission-like state; 1.6–3.0 for mild disease activity; 3.2–5.4 for moderate; and 5.6–10.0 for high disease activity.
- The RAPID scores include combinations of 2–5 items from the following list: the Multidimensional Health Assessment Questionnaire, a pain VAS, PtGA on a 10-cm VAS, PhGA on a 10-cm VAS, SJC and the RADAI self-reported TJC.
- The Patients Activity Scale (PAS) and PAS II contain patient-derived data and include a patient assessment of pain on a 10-cm VAS, a PtGA on a 10-cm VAS and a HAQ for the PAS or the HAQ-II for the PAS II.
- Rheumatoid Arthritis Impact of Disease includes seven domains (pain, function, fatigue, physical and psychological wellbeing, sleep disturbance and coping). Each domain is evaluated using a single question answered using a 0–10 numerical rating scale. The score ranges from 0 to 10.
- Patient-Reported Outcome CLinical ARthritis Activity is a short and easy-to-complete self-administered index, without formal joint counts, combining three items (patient's physical function measured by Recent-Onset Arthritis Disability questionnaire, self-administered TJC and PtGA) into a single measure. The Recent-Onset Arthritis Disability questionnaire has 12 items assessing the physical ability of upper and lower extremities and the ability to perform daily living/work activities.

telemonitoring of patients with RA [102]. Such applications bridge clinical and nonclinical sectors and include both individual and population health-oriented tools.

Nevertheless, clinical evaluation by a physician remain crucial. Completion of a questionnaire helps the patient prepare for the visit and improves doctor–patient communication. On the other hand, patient self-reporting questionnaires must be complemented by careful completion of a formal joint count or any other measure by a treating physician. Patient self-reporting questionnaires may provide a useful cost-effective method to implement T2T in patients with RA as well as other rheumatic diseases. A self-reporting questionnaire does not

replace a joint count, but is complementary to a careful joint examination including a formal joint count.

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No writing assistance was utilized in the production of this manuscript.

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▪ of interest

▪▪ of considerable interest

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