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Research Letter

Evaluation of Disease Burden by (Separate) Patient-reported, Clinical, and Laboratory Factor Scores in Patients With Established Rheumatoid Arthritis: A Factor Analysis Replication

To the Editor:

Rheumatoid arthritis (RA) can cause significant burden to patients. Some of these aspects are directly related to disease activity and are manageable with antirheumatic drugs, whereas others require nonpharmacological interventions. An evaluation of specific needs to better tailor treatment decisions would improve patient care. When exploring the evolution of RA burden in the 2-year Care in early RA (CareRA) trial, 3 factor scores (patient-reported factor [PRF], clinical factor [CF], and laboratory factor [LF] scores) were obtained by exploratory factor analysis (EFA).[1] EFA uncovers the fact that multiple observed variables have similar response patterns because they are all associated with latent (ie, not directly observable) variables. We further studied these factor scores with a 3-fold aim: (1) to reproduce the factors in another study context; (2) to extend the validity of these factors in a population with established RA; and (3) to compare them to the 3 factors and their individual components as originally extracted in CareRA (Figure 1).

The TapERA (Tapering Etanercept in RA; EU Clinical Trials Register, https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-004631-22/BE; EudraCT number 2012-004631-22) trial collected data from patients with established RA in sustained remission (≥ 6 months) who were treated with etanercept (ETN) 50 mg weekly (≥ 1 yr) between 2012 and 2014 and randomized to evaluate the possibility of tapering to ETN 50 mg every 2 weeks. Patients also completed the Flare Assessment in RA (FLARE-RA) questionnaire.[2] The trial received ethical committee approval (EC number: S54805) and all patients gave written informed consent.

Sixty-six patients with a mean disease duration of 14.80 (SD 9.03) years and mean age of 55.21 (SD 12.87) years were included in this analysis. Of these, 96% (63/66) were RF- and/or ACPA-positive, 77% (51/66) had erosions, and 68% (45/66) were female. Components of disease activity scores (clinical variables with swollen/tender joint counts, physician and patient global health assessments, and laboratory variables with C-reactive protein or erythrocyte sedimentation rate), pain and fatigue (question 2 and 8 from the FLARE-RA questionnaire, respectively), as well as Health Assessment Questionnaire (HAQ) scores, were recorded at every visit (n = 5). Detailed information on the trial was published previously.[3,4,5]

The same analysis method was used as in the CareRA trial. Three hundred seventy-nine patients with early RA (< 1 yr) with a mean disease duration of 14.14 (SD 31.00) days and mean age of 53.91 (SD 12.98) years were included. Of these, 77% (292/379) were RF- and/or ACPA-positive, 26% (97/379) had erosions, and 69% (262/379) were female. Missingness on all previously mentioned variables was handled with multiple imputation (n = 100). Pain and fatigue were rescaled from their original Likert scale of 1–6, to 0–100 to resemble how CareRA

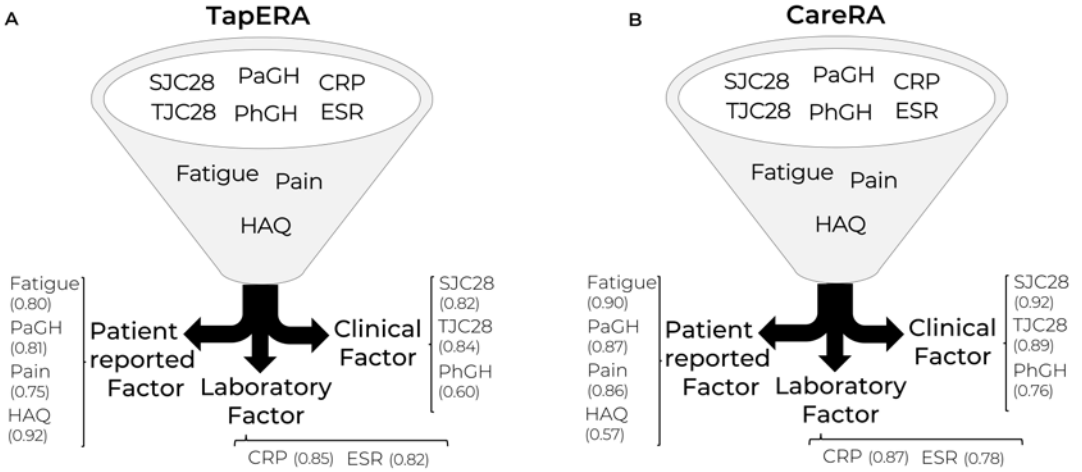

Figure 1. Results from the EFA* in (A) TapERA (replication dataset) and (B) CareRA (original dataset) trials. Presented between brackets are the factor loadings (correlation between the observed score and the latent factor) of the different variables representing each of the 3 factors that were identified behind the concept of RA disease burden, ordered according to original results in CareRA. Each variable was related strongly only to 1 factor, cross-loadings, which is when the same variable loads on > 1 factor; these were negligible (< 0.3) and are not presented. * EFA uncovers the fact that multiple observed variables have similar patterns of responses because they are all associated with a latent—not directly observable—factor or concept. CareRA: Care in early Rheumatoid Arthritis; CRP: C-reactive protein; EFA: exploratory factor analysis; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; PaGH: patient global health assessment; PhGH: physician global health assessment; SJC28: swollen joint count in 28 joints; TapERA: Tapering Etanercept in Rheumatoid Arthritis; TJC28: tender joint count in 28 joints.

variables were recorded. Next, timepoint clustering was removed with multiple outputation 1000 times, and each of the 100,000 datasets was analyzed by EFA. The analyses were combined after reordering the factors by maximizing factor congruence.[6] Factors were compared using Tucker congruence coefficient (TCC), a measure of factor similarity, and deemed equal when > 0.95.[7]

Figure 1 provides the results of the EFAs from CareRA and TapERA. The factor structure of the 3 factors and their components remained the same in both datasets. The factor loadings, which indicate how strongly a variable relates to its factor (correlation between the observed score and latent score) were also comparable. However, the HAQ did have a stronger factor loading in TapERA (0.92 vs 0.57). TCC indicated equivalence of all factors (TCCs were 0.972, 0.971 and 0.980 for the PRF, CF, and LF, respectively).

The latent factor structure for disease burden originally found in CareRA was successfully reproduced in the TapERA dataset, underlining the robustness of the PRF, CF, and LF scores. Further, this replication happened in a smaller sample (which tends to be more unstable) and in a different patient group, providing further evidence that the PRF is an important concept on its own. This replication study indicates a greater validity and reliability compared to the original CareRA findings[1] and suggests a broader generalizability of these results. Deviations in factor loadings could be attributed to several differences. For example, physical function measured by the HAQ had a stronger factor loading in TapERA than CareRA (0.92 vs 0.57), possibly due to the different stages in the disease of early (CareRA) vs established (TapERA) RA. Other possibilities for deviations in factor loadings can be attributed to variables measured differently in the trials (pain and fatigue were extracted from the FLARE-RA questionnaire in TapERA as opposed to a standalone question), the smaller sample size in TapERA, or simply random noise. We conclude that the patient's unmet needs in terms of pain, fatigue, functionality, and overall well-being deserve more specific attention, in both early and established RA. Obtaining patient-related, clinical, and laboratory factor scores could facilitate this process and evaluating them separately could improve our steering of both pharmacological and nonpharmacological treatments. This analysis further supports the idea of a dual-target approach in the management of RA.[8]

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The authors declare no conflicts of interest relevant to this article.

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