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## **Depression and anxiety associate with less remission after 1 year in rheumatoid arthritis**

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## Depression and anxiety associate with less remission after 1 year in rheumatoid arthritis

Depression and anxiety have been considered to influence disease activity, and with great interest we read the recently published report by Michelsen *et al.*<sup>1</sup> In this large, prospective, multicentre observational study, depression and anxiety reduced the likelihood of joint remission based on composite scores, in rheumatoid arthritis (RA) after 3 and 6 months. Differences were predominantly caused by subjective markers of disease activity rather than by C reactive protein or erythrocyte sedimentation rate. The study cannot prove causality; however, their findings imply that baseline depression/anxiety can impair the fulfilment of remission criteria during follow-up, influencing important treatment decisions.

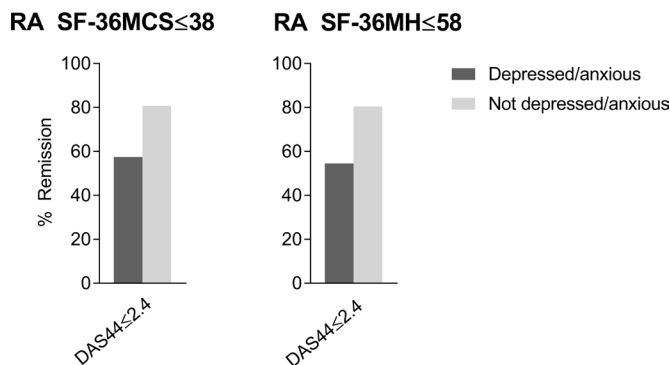
As replication is a keystone in research, we aimed to validate their findings in an independent cohort, the Leiden Early Arthritis Clinic (EAC), to assess generalisability of the results. The EAC is a population-based inception cohort of patients with newly diagnosed arthritis that started in 1993; from 2010 onwards patients completed the Short Form-36 (SF-36) at baseline.<sup>2</sup> We studied patients included between 2010 and 2014 who fulfilled the 2010 criteria for RA (n=343) and selected patients who completed the SF-36 (n=293). Patients with RA were treated according to the insight of the treating rheumatologist: standard therapy regimen consists of early initiation with methotrexate; in case of failure a second synthetic disease-modifying antirheumatic drug (DMARD) was prescribed and in case of failure a biologic DMARD was allowed.<sup>3</sup> Outcome of joint remission was 44-joint Disease Activity Score (DAS44  $\leq 2.4$ ) after 1 year.<sup>4,5</sup> Similar as Michelsen *et al* we identified depression/anxiety by the SF-36 mental health subscale (MH  $\leq 56$ ) and SF-36 mental component summary (MCS  $\leq 38$ ).

**Table 1** Baseline characteristics of patients with rheumatoid arthritis with versus without baseline depression/anxiety according to the MCS  $\leq 38$  or MH  $\leq 56$

	All patients (n=293)	Depressed/ anxious (n=81)	Not depressed/ anxious (n=212)	P value
Age, mean (SD)	57 (15)	54 (15)	58 (14)	0.02
Female, n (%)	193 (66)	58 (72)	135 (64)	0.20
Symptom duration in months, median (IQR)	3 (1–8)	3 (1–7)	3 (1–8)	0.72
Currently smoking, n (%)	65 (23)	25 (33)	40 (20)	0.08
ACPA-positive, n (%)	162 (55)	43 (53)	119 (56)	0.64
ESR (mm/hour), median (IQR)	28 (14–41)	28 (14–42)	28 (14–41)	0.85
CRP (mg/L), median (IQR)	10 (3–22)	7 (3–26)	10 (3–20)	0.76
EGA, mean (SD)	49 (20)	49 (24)	49 (19)	0.44
PGA, mean (SD)	45 (27)	54 (27)	42 (26)	0.001
Pain, mean (SD)	60 (25)	63 (24)	58 (25)	0.92
68-TJC, median (IQR)	10 (5–17)	11 (6–19)	10 (5–16)	0.18
66-SJC, median (IQR)	5 (2–11)	5 (2–10)	6 (2–11)	0.14
DAS44, mean (SD)	2.9 (0.8)	3.0 (0.8)	2.9 (0.8)	0.45

Pain measured by a 0–100 VAS.

68-TJC, 68 tender joint counts; 66-SJC, 66 swollen joint counts; ACPA, anticitrullinated peptide antibody; CRP, C reactive protein; DAS44, 44-joint Disease Activity Score; EGA, evaluator's global assessment by a 0–100 VAS; ESR, erythrocyte sedimentation rate; MCS, mental component summary; MH, mental health subscale; PGA, patient's global assessment by a 0–100 VAS; VAS, Visual Analogue Scale.



**Figure 1** Percentages of patients with RA in remission at 1 year (DAS44  $\leq 2.4$ ) who did or did not have depression/anxiety at the time of diagnosis.

DAS44, 44-joint Disease Activity Score; RA, rheumatoid arthritis; SF-36 MCS, Medical Outcomes Survey Short Form-36 mental component summary; SF-36 MH, Medical Outcomes Survey Short Form-36 mental health subscale.

Baseline characteristics are shown in [table 1](#). The percentage of depressed/anxious patients with RA was 20% according to the SF-36 MCS  $\leq 38$  and 23% according to the SF-36 MH  $\leq 56$ . Anxious/depressed patients were significantly younger and had a higher patient global assessment ([table 1](#)). Anxiety and depression were negatively associated with achieving DAS remission after 1 year, analysed with logistic regression models corrected for age, gender and symptom duration (OR, 0.21, 95% CI 0.09 to 0.46 for MCS; OR, 0.24, 95% CI 0.11 to 0.51 for MH;  $P < 0.001$ ; [figure 1](#)). Analyses with additional correction for baseline DAS showed similar results (MCS  $P < 0.001$ ; MH  $P = 0.001$ ). Further analyses on features of disease activity at year 1 showed that anxiety/depression was associated with more pain ( $\beta = 12.1$ ,  $P < 0.001$  for MCS;  $\beta = 11.1$ ,  $P = 0.03$  for MH) and a trend for a higher patient global assessment ( $\beta = 9.0$ ,  $P = 0.07$  for MCS).

Thus, our study on the association of baseline anxiety and depression with remission after 1 year validated the findings from Michelsen *et al*. We observed higher percentages of patients with RA in DAS remission, which could be caused by the longer duration of treatment (evaluation of remission at 1 year, instead of 3 and 6 months by Michelsen *et al*).

Concluding, baseline depression and anxiety are associated with a lower chance to achieve DAS remission, which was mostly reflected by associations with subjective features of disease activity. Also our study cannot prove causality, although the association between the mental state and DAS components suggests that efforts to improve the psychological well-being early in the disease course may prevent higher DAS scores later on. This could potentially prevent increased medical costs due to more intensified treatment strategies.

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