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

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Depression and anxiety have been considered to influence disease activity and with great interest we read the recently published report by Michelsen *et al.*[1] In this large prospective multicentre observational study, depression and anxiety reduced the likelihood of joint-remission based on composite scores, in RA after 3 and 6 months. Differences were predominantly caused by subjective markers of disease activity rather than by CRP or ESR. 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 generalizability 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.[2] We studied patients included between 2010-2014 that fulfilled the 2010-criteria for RA (n=343) and selected patients that completed the SF-36 (n=293). RA-patients 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 DMARD was prescribed and in case of failure a biologic DMARD was allowed. [3] Outcome of joint-remission was 44-joint Disease Activity Score (DAS44 2.4) after 1-year.[4, 5] Similar as Michelsen *et al* we identified depression/anxiety by the SF-36 Mental Health subscale (MH 56) and SF-36 Mental Component Summary (MCS 38).

Baseline characteristics are shown in Table 1. The percentage of depressed/anxious RA-patients was 20% according to the SF-36MCS 38, and 23% according to the SF-36MH 56. Anxious/depressed patients were significantly younger and had a higher patient global (Table 1). Anxiety and depression was negatively associated with achieving DAS-remission after 1-year, analysed with logistic regression models corrected for age, gender and symptom duration (OR, 95%CI=0.21, 0.09-0.46 for MCS; 0.24, 0.11-0.51 for MH, p-values <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

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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's 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 RA-patients 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. Though the association between the mental state and DAS-components suggest that efforts to improve the psychological wellbeing 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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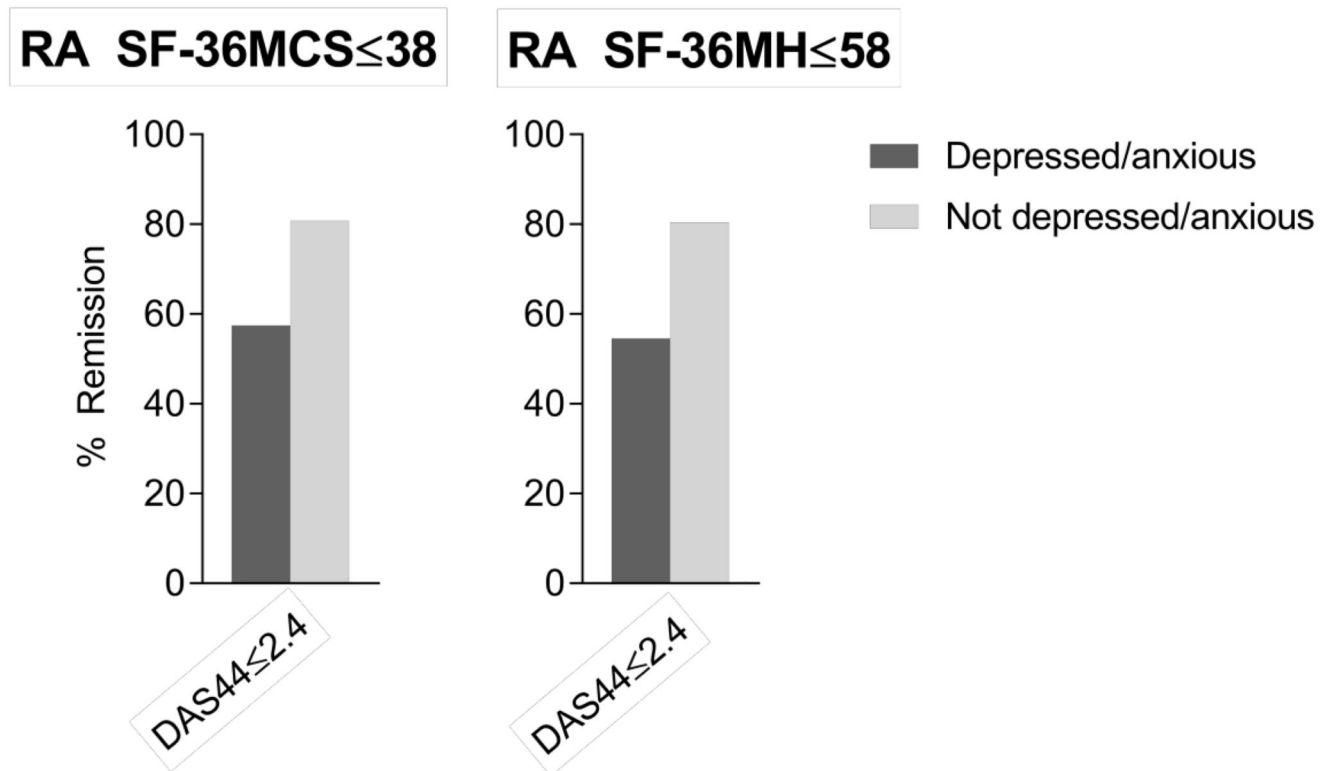


Figure 1. Percentages of rheumatoid arthritis patients in remission at 1-year (DAS44 ≤ 2.4) for RA patients that did or did not have depression/anxiety at the time of diagnosis.

DAS44, 44-joint Disease Activity Score; RA, rheumatoid arthritis; SF-36MCS, Medical Outcomes Survey Short Form-36 Mental Component Summary; SF-36MH, Medical Outcomes Survey Short Form-36 Mental Health subscale.

Table 1

Baseline characteristics for Rheumatoid Arthritis patients with versus without baseline depression/anxiety according to the MCS 38 or MH 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/h) 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 Visual Analogue Scale (VAS); ACPA, anti-citrullinated peptide antibody; 68-TJC, 68 tender joint counts; 66-SJC, 66 swollen joint counts; EGA, evaluator's global assessment by a 0-100 VAS; PGA, patient's global assessment by a 0-100 VAS; 44-joint Disease Activity Score; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; SD, standard deviation; IQR, Inter quartile range.