

Original Article

Influence of the Structure of Mood in the Assessment of Rheumatoid Arthritis Through the Visual Analog Scale for Pain, HAQ and DAS28[☆]

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ABSTRACT

Objective: To analyze the effect of the structure of mood over the following assessment tools for rheumatoid arthritis: visual analog scale (VAS) for pain, HAQ and DAS28.

Patients and methods: We studied 86 patients with recent onset rheumatoid arthritis, of which 75.7% were female, with a mean age at disease onset of 55 years. All patients were administered the Spanish version of the PANAS questionnaire that evaluates the components of positive (PA) and negative mood (AN). Patients belonged to the registry of new-onset arthritis in our center, so clinical information was available for 282 patients visits. To determine the effect of PA and AN on each of the dependent variables we performed three multivariate linear regression models using generalized linear models through the Stata glm command 10.1.

Results: The mean score for PA and AN in our patients was similar to that described for the healthy Spanish population. The high scores on the subscale of AN were associated with worse scores in both the VAS for pain and the HAQ. By contrast, high scores on PA were associated with better outcomes of disease activity measured by DAS28.

Conclusion: The structure of mood may influence the tools we use for evaluating patients with rheumatoid arthritis, so it might be advisable to include the PANAS questionnaire as part of that assessment.

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Influencia de la estructura de los afectos en la evaluación de la artritis reumatoide mediante la escala visual analógica de dolor, el HAQ y el DAS28

RESUMEN

Objetivo: Analizar el efecto de la estructura del afecto en las siguientes herramientas de evaluación de la artritis reumatoide: escala visual analógica (EVA) de dolor, HAQ y DAS28.

Pacientes y métodos: Se estudiaron 86 pacientes con artritis reumatoide de reciente comienzo, de los que el 75,7% eran mujeres, con una mediana de edad al inicio de la enfermedad de 55 años. A todos los pacientes se les aplicó la versión adaptada a población española del cuestionario PANAS que evalúa las componentes de afecto positivo (AP) y negativo (AN). Los pacientes pertenecían al registro de artritis de reciente comienzo de nuestro centro por lo que se disponía de información clínica de los enfermos en 282 visitas. Para determinar el efecto de AP y AN en cada una de nuestras variables dependientes se estimaron 3 modelos de regresión lineal multivariable mediante modelos lineales generalizados usando el comando *glm* del programa Stata 10.1.

Resultados: El promedio de la puntuación de AP y AN en nuestros pacientes fue similar al descrito para la población española sana. Las puntuaciones elevadas en la subescala de AN se asociaron a peores puntuaciones, tanto en la EVA de dolor, como en el HAQ. Por el contrario, puntuaciones elevadas en AP se asociaron con una mejor evolución de la actividad de la enfermedad medida por el DAS28.

Palabras clave:

Artritis reumatoide

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Conclusión: La estructura del afecto puede influir en las herramientas que utilizamos para la evaluación de los pacientes con artritis reumatoide, por lo que podría ser recomendable incluir la realización del PANAS como parte de dicha evaluación.

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes deterioration of diarthrodial joints, leading to functional impairment, impaired quality of life, decreased life expectancy and social^{1–3} dependence. This generates a very elevated care cost.^{4,5} This bleak picture has improved in the last 10 years with the emergence of biological therapies but, above all, with the implementation of treatment strategies aimed at achieving targets based on composite indices for evaluating the activity of the disease.^{6,7} However, it has been recently proposed that these indices may be biased in the evaluation of patients.^{8,9} In some cases, personality factors related to the patients may also interfere. In this sense, RA is a clear example of a biopsychosocial model of disease. This model proposes that, in addition to the organic component, the emergence and subsequent evolution of diseases, especially chronic ones, are influenced by the environment in which the person lives, as well as the reality of every individual.^{10,11} Therefore, the tools used to assess the clinical activity of RA and its functional impact may be influenced by the psychological characteristics of the patients we serve.

As part of the individual psychological characteristics, the structure of affect consists of 2 dimensions or dominant factors commonly labeled as positive affect (PA) and negative affect (NA). This division between positive and negative affective states is manifested from early childhood, and can already be seen, as positive emotions correlate with increased activity of the left hemisphere, while the right is more affected by negative ones.¹² Therefore, PA and NA are considered personal provisions of emotionality with little variability over time, influenced by genetics and, in part, by the individuals first experiences.¹³ Elevated levels of PA are associated with high energy, focus and dedication of the individual, while low levels are characterized by sadness and lethargy; on the other hand, high levels of NA reflect a variety of moods including anger, guilt, fear and nervousness, while low NA is a state of calm and serenity.¹⁴ Clark and Watson developed in 1988 the PANAS questionnaire to adequately weigh PA and NA.¹⁴ Subsequently, the results obtained with its application to patients and healthy controls were used to establish their tripartite model of anxiety-depression.¹⁵ In this model, scores of NA and PA, along with distress in response to environmental stimuli, lead the authors to properly classify cases of anxiety, depression or mixed cases.

With respect to RA patients, previous studies have shown that there is an association between higher pain scores and higher levels of NA.^{16,17} Therefore, the objective of this study was to investigate the influence of NA and PA in two of the most widely used measurement instruments in clinical practice employed to assess RA: the DAS28 activity index and the HAQ questionnaire to assess functional capacity.

Patients and Methods

Registration of patients with recent onset arthritis at the Hospital Universitario de La Princesa includes patients referred from primary care who have had one or more swollen joints for at least 4 weeks and a maximum of one year. The only exclusion criterion is that along the course of their follow up, patients are diagnosed microcrystalline arthritis, septic arthritis or viral infections, spondyloarthropathies or connective tissue diseases.

The study protocol provides for four follow-up visits in a period of 2 years: baseline, at 6 months, one year and two. At each visit, we collect demographic data (gender, educational level and marital status), clinical data (date of onset of illness, 28 tender joint count [TJC28] and swollen [SJC28], global assessment of disease by the physician [GADP] and by the patient [GADPa] and assessment of pain on a visual analog scale (VAS) from 0 to 100 mm) and laboratory data (erythrocyte sedimentation rate [ESR, measured by the Westergren method], C-reactive protein [CRP, nephelometry], rheumatoid factor [FR; nephelometry], levels of anti-CCP antibody [AAPCC; determined by ELISA: Immunoscans CCPlus®, Euro-Diagnostica, Arnhem, Netherlands]) and hematology and blood biochemistry. Functional capacity is estimated by a HAQ questionnaire validated in Spanish population¹⁸ and DAS28 with ESR is calculated every visit as described previously: $0.56 * \sqrt{(TJC28)} + 0.28 * \sqrt{(SJC28)} + 0.70 * \ln(ESR) + 0.014 * (GADP)$.¹⁹

For the present study we analyzed the clinical data of 282 visits (86 first visits, 52 visits after 6 months follow-up, 71 visits at one year and 73 visits at two years), performed between September 2001 and November 2009, with 86 patients having RA according to the American College of Rheumatology (ACR) criteria of 1987.²⁰ 75.7% of patients were women, with a median age at disease onset of 54.6 years (interquartile range: 44.3–68.6). As shown in Table 1, the characteristics of this group are similar to those of other cohorts in our environment. In these patients the evaluation of PA and NA was performed by applying, on one occasion, the PANAS (Positive and Negative Affect Scale) as adapted to the Spanish population, which scores for both PA and for NA, ranging from 10 to 50 points.²¹

Both the record of recent onset arthritis and the study described in this paper have been approved by the Ethics Committee of the Clinical Health Research Institute of the Hospital Universitario de La Princesa. Patients signed informed consent at the time of inclusion into the registry and another specifically made for performing the PANAS scale.

Statistical analysis was performed using Stata 10.1® software for Windows (StataCorp LP, College Station, TX, USA). We calculated the median and interquartile range (RI) for continuous variables and non-Gaussian distribution and the median and standard deviation for those with normal distribution. To evaluate differences

Table 1
Demographic Characteristics of Patients an Disease at Baseline.

Female gender, n (%)	65 (75.6)
Marital status n (%)	
Married	54 (62.8)
Separated	7 (8.1)
Single	16 (18.6)
Widowed	9 (10.5)
Schooling, n (%)	
None	9 (10.5)
Primary	29 (33.7)
High school	24 (27.9)
Superior	24 (27.9)
Age at onset of disease, median (RI)	54.2 (44.4–68.2)
Months of progression since first visit, median (RI)	5.4 (3.3–7.9)
Positive rheumatoid factor, n (%)	38 (44.2)
Positive AAPCC, n (%)	39 (45.4)
VAS pain, median (RI)	50 (17–65)
HAQ, median (RI)	0.875 (0.375–1.5)
DAS28, median (RI)	4.3 (3.1–5.6)

AAPCC, anti cyclic citrullinated peptide antibodies.

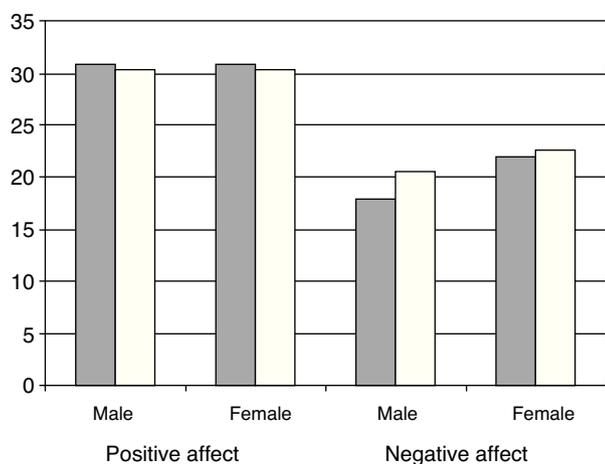


Fig. 1. The positive and negative affect score of recent onset arthritis patients is similar to the Spanish general population. The gray columns correspond to patients with arthritis and white to healthy population. The healthy Spanish population data shown in the chart are that described by Sandin et al.²²

between groups we used the “*U*” test of Mann and Whitney for continuous independent variables. For qualitative variables we used the chi-square test. We considered $P < .05$ as statistically significant.

To estimate the effect of PA and NA on DAS28, HAQ and pain, we performed a multivariable linear regression for each, where to get the best fit, and the model initially included all sociodemographic and clinical variables available, and later we phased out the variables with worse *P* values one by one repeating it in every step of the model, until all remaining variables in the model had a $P < .15$. This was considered for each dependent variable (pain, HAQ and DAS28) the best possible model and we were forced to include PA and NA variables to estimate the effect on these dependent variables.

Results

Rating Positive Affect and Negative Affect in Patients With Recent-Onset Rheumatoid Arthritis

In our population the PA median was 29 (RI: 25–37) and the NA median 20 (16–24). As shown in Fig. 1, these scores were similar to those obtained by Sandin et al.²² for the Spanish population. In our population, women had a higher NA score than men (Table 2,

Table 2
Positive and Negative Affect Scores in Patients With Early Onset Rheumatoid Arthritis According to Different Sociodemographic Variables.

	PA	<i>P</i>	NA	<i>P</i>
<i>Gender</i>				
Male	28 (25–37)	.96	17 (15–20)	.02
Female	30.5 (25–37.50)		20 (16–27)	
<i>Marital status</i>				
Single	31 (25.5–36)	.18	19 (14–27)	.36
Married	31 (26–38)		20 (15–23)	
Separated	25 (12–30)		24 (20–33)	
Widowed	26 (21–36)		21 (18–27)	
<i>Schooling</i>				
None	27 (21–28)	.03	18 (14–21)	.62
Primary	27 (24–34)		20 (16–26)	
Secondary	33 (26–43)		20.5 (15.5–28)	
Superior	35 (27.5–39)		19 (16–22)	
<i>Age at disease onset</i>				
–	$r = -0.21$.05	$r = -0.24$.03

NA, negative affect; *P*, significance levels; PA, positive affect; *r*, correlation coefficient.

$P = .02$), whereas no significant differences in the PA scores between the two genres were seen. In addition, there was a significant trend to increased PA scores related to the level of education, while this factor did not affect the NA score (Fig. 2 and Table 2, $P = .03$ for AP). Moreover, with increasing age, both genders had lower scores (Fig. 2 and Table 2, $P = .05$ for PA, $P = .03$ for NA).

Influence of Emotions on Pain Perception

The most influential factor in the assessment of pain perceived by patients with RA in our population was the activity of the disease, so that for every point gained on the DAS28, pain assessment increased 12.5 ± 1.2 points ($P < .001$, Table 3, left column). We also calculated the influence of education level, marital status and, possibly, female gender on pain (Table 3, left column). Adjusting for these variables, we found that those patients with the highest NA score tended to score higher on the visual analog pain scale. However, the psychological components encompassed by the PA level seemed not to influence the patient expressed pain intensity (Table 3, left column).

Influence of Affect on the Perception of Disability

With regard to disability, disease activity and pain perception by the patient were the variables that most influenced the HAQ score (Table 3, middle column). In addition, we observed a tendency to higher HAQ scores in female patients and probably to educational levels and marital status on the perception of disability (Table 3, middle column). After adjusting for these variables, we observed that patients with higher NA scores refer greater disability (Table 3, middle column). Although, as shown in Fig. 3, this effect was less clear in the visits in which the patient was in remission and became more evident with increased disease activity.

Influence of Affect on Disease Activity Estimated by DAS28

As previously described by our group,²³ the DAS28 value was higher in women, almost one point higher than in men, and in older patients (Table 3, right column). Logically, we detected an improvement in activity along the track following treatment (Table 3, right column). After adjusting the model for these variables, patients with high PA scores tended to have lower levels of activity, according to the DAS28 (Table 3, right column). However, this effect seems to be clearer once treatment was established in follow-up visits at 6, 12, and 24 months after the initial visit, as shown by the slopes of the regression lines in Fig. 4.

Discussion

The current model proposes a close relationship between the presence of chronic illness with biological, psychological and social aspects throughout the process. However, the personal disposition of the emotion scale assessed by the PANAS does not seem to be intensely affected by the occurrence or persistence of the disease. Thus, our data show that the development of the clinical phase of the disease is not incident on the basic psychological factors detected by the PANAS scale, since the average score of our populations' positive or negative emotions is similar to that obtained in other studies with healthy Spanish population.^{22,24} Rated in reverse, our data indicate that the structure of affect does not affect the risk of developing RA. However, the main finding of this study is that the structure of affect has an important influence on the assessment of the disease by the patient using three of the most frequently found tools in daily clinical practice to assess RA.

With respect to the assessment of pain by the patient, as expected, our data show that the activity of the disease is the

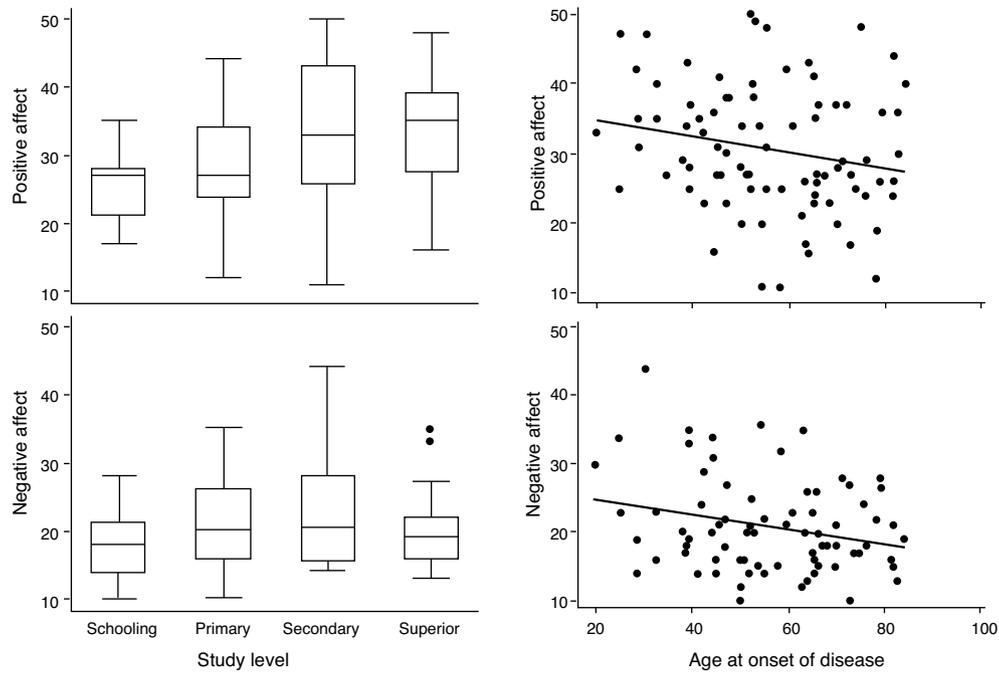


Fig. 2. Effect of educational level (left) and age (right) on the PANAS score. The data of positive and negative affect in the case of educational level are shown as box plots where the line inside the box represents the median, and the lower and upper edges of the boxes represent the 25th and 75th percentiles, respectively, and upper and lower lines outside the boxes represent the 5 and 95 percentiles, respectively. The circles represent outliers. In the case of age, the point cloud represents the estimated regression line with the lfit command of Stata 10.1.

variable that most affects the score on the visual analog pain scale. Moreover, sociodemographic factors such as the gender^{25,26} or level of schooling^{27,28} are also related to the level of sensitivity to pain. Although in our study there was a tendency to confirm these associations with sociodemographic variables, the second variable most associated with increased pain perception was the NA score. The negative affect represents a state of subjective distress that

includes unpleasant aversive states such as nervousness, fear or disgust,²² so logically, it leads these patients to a more intense perception of the pain experience. In this sense, our data are similar to that previously reported both in general health and in patients with RA.^{16,17}

Moreover, even when adjusting for the level of disease activity and perceived pain in our patients with early arthritis, high NA

Table 3
Multivariate Analysis of the Effect of Positive and Negative Affects on Pain, Disability and Disease Activity Evaluations in Early Onset Rheumatoid Arthritis Patients.

	Pain		HAQ		DAS28	
	Coef. $\beta \pm SE$	P	Coef. $\beta \pm SE$	P	Coef. $\beta \pm SE$	P
<i>Marital status</i>						
Married	Reference	–	–	–	–	–
Separated	–7 \pm 4.6	.128	–0.21 \pm 0.11	.056	0.3 \pm 0.28	ns
Single	–0.5 \pm 3.6	ns	0.14 \pm 0.07	.051	–0.41 \pm 0.19	.031
Widowed	–10.8 \pm 3.9	.006	–0.04 \pm 0.11	ns	0.06 \pm 0.28	ns
<i>Schooling</i>						
None	Reference	–	–	–	Reference	–
Primary	–9.5 \pm 3.9	.015	0.08 \pm 0.09	ns	–0.02 \pm 0.25	ns
Secondary	–7.8 \pm 4.4	.076	0.07 \pm 0.1	ns	0.54 \pm 0.29	.060
Superior	–10.4 \pm 4.1	.011	0.16 \pm 0.1	.117	0.41 \pm 0.28	.146
<i>Gender</i>						
Male	Reference	–	Reference	–	Reference	–
Female	5.1 \pm 8.8	.073	0.18 \pm 0.07	.012	0.92 \pm 0.18	<.001
<i>DAS28</i>	11.3 \pm 0.9	<.001	0.23 \pm 0.03	<.001	ni	ni
<i>Pain (VAS 0–100)</i>	ni	ni	0.008 \pm 0.002	<.001	–	–
<i>Negative affect (10–50)</i>	0.52 \pm 0.2	.008	0.011 \pm 0.005	.022	–	–
<i>Positive affect (10–50)</i>	–	–	–	–	–0.025 \pm 0.009	.005
<i>Age (years)</i>	–	–	0.008 \pm 0.002	.127	0.022 \pm 0.006	<.001
<i>Visit</i>						
Baseline	ni	ni	ni	ni	Reference	–
6 months					–1.24 \pm 0.19	<.001
12 months					–1.22 \pm 0.20	<.001
24 months					–1.57 \pm 0.21	<.001

For this analysis we took into account data from 261 visits in which all data were available. Coef., coefficient; SE, standard error; ns, non significant con $P > .15$; ni, not included; VAS, visual analog scale.

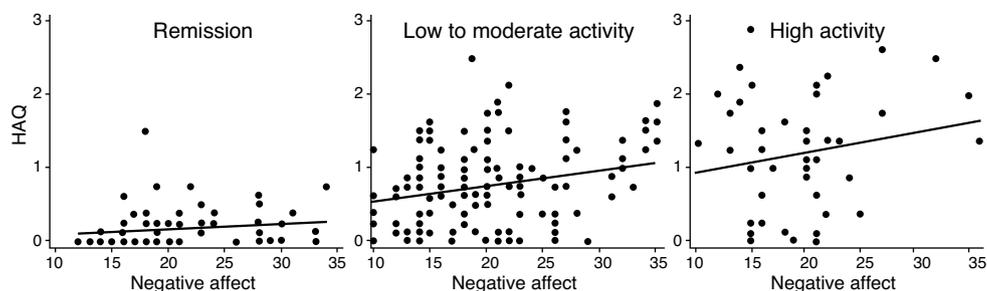


Fig. 3. Effect of negative affect on the assessment of disability measured by HAQ. Data are shown as a point cloud with the estimated regression line calculated using the `lfit` Stata 10.1 command for 3 subgroups of activity levels (remission, mild-moderate activity and high activity).

scores were also associated with higher scores of the HAQ. However, this effect was less important in patients in remission and detected more clearly than in patients with moderate and high activity. Because patients with higher scores tend to have higher NA somatic¹⁴ complaints, it seems logical to have a greater sense of disability when their disease is not well controlled. Previous studies indicate that psychosocial factors can explain up to 9% of disability when assessed with the HAQ, almost radiological progression could explain as much as 11%, with the disease activity which is involved in up to 51% of the HAQ.²⁹ In our study, the NA score, as a psychological endpoint, achieved very manifest significance. It is possible that in a larger sociodemographic population sample, factors such as gender, educational level and marital status would have attained greater significance, but our data seem to derive its clinical relevance less than that of psychological parameters.

Finally, with respect to the assessment of disease activity in DAS28, we describe here for the first time that patients with higher PA scores showed a better evolution of disease activity. This effect was more pronounced in the follow-up visits at baseline where practically no effect was observed on the PA score. A possible explanation for our finding is that patients with high scores on PA are more optimistic when assessing clinical response to treatment and that two of the parameters included in the DAS28 depend on the patient's subjectivity. Thus, neuroimaging studies have shown that positive affect is associated with high levels of left prefrontal activation, effective modulation of activation in the amygdala and rapid recovery in response to negative and stressful events.³⁰ Another possibility is that patients with high PA scores on treatment performed better than those with low scores on this subscale of the PANAS. Although the impression is that adherence to treatment

can significantly influence psychological characteristics, there are no studies to confirm this suspicion and the greater is the influence of other factors such as comfort of medication or educational³¹ level that have been well demonstrated.

Possible limitations of the study include the small number of patients in which the study was conducted and no healthy population control. In the latter case, this gap was filled with a comparison with previously published data by Sandin et al. in a Spanish²² population, although the age in that group was lower than that in our patients. Regarding the limited number of cases studied, we think it could prevent some variables from reaching statistical significance in the multivariate models, but the effect of PA and NA on the pain, disability and disease activity variables is solid, as has been detected even in this sample. Clearly, further studies would be needed to validate these findings in other populations and confirm the influence that the affect structure seems to have on the tools we use routinely to evaluate patients with RA.

In conclusion, our data indicate that the affective structure of our patients may have an impact on the results obtained after the application of the tools to evaluate our patients with RA. It is very likely that rheumatologists unconsciously evaluate these conditions. This aspect is relevant because today we make important decisions, such as starting biological therapy, according to the DAS28 score, so it is probably better to objectify parameters in our patients, such as the PA and NA scales, taking into account that they are easy to fill out in a questionnaire and have a high reproducibility over time.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Confidentiality of Data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and /or subjects mentioned in the article. The author for correspondence is in possession of this document.

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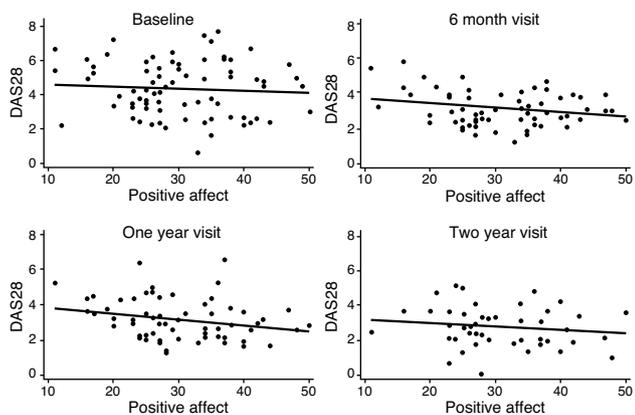


Fig. 4. Effect of positive affect on the assessment of disease activity by DAS28. Data are shown as a point cloud with the estimated regression line of the 4 study visits calculated with the `lfit` command in Stata 10.1.

Conflict of Interest

The authors have no conflict of interest to declare.

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