Title page

Angst is een onafhankelijke voorspeller van ziekteactiviteit van vroege artritis patiënten op drie maanden nadat de patiënten zijn gestart met de behandeling van disease modifying anti-rheumatic drugs (DMARDs)

Anxiety is an independent predictor of disease activity at three months after initiating treatment with disease modifying anti-rheumatic drugs (DMARDs) in early arthritis patients

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Introduction

Rheumatoid arthritis (RA) is characterized by persistent synovitis, systematic inflammation and the presence of autoantibodies. RA occurs in about 1.0% of the adult population worldwide and is the most common inflammatory arthritis [1]. The main consequences of RA are pain, decreased quality of life, decreased functional ability and sick leave in short term and joint damage, disability, cardiovascular and other comorbidities in long term [1-3]. As no cure has been found to date, treatments for RA are focused on decreasing the negative consequences by preservation of function, prevention or control of joint damage and remission of disease activity [1,4]. Disease-modifying antirheumatic drugs (DMARDs), the key therapeutic agents of the treatment, are able to decrease the disease activity score (DAS), improve functional ability and prevent, slow down or arrest the progression of joint damage [1,5,6].

Although current treatments are effective in the majority of patients, large differences in treatment response on DAS are observed at the individual level. Depending on how remission is defined, only 10-50% of patients achieve remission after a treatment [1]. Part of these differences can be explained by demographic and clinical factors, such as sex, baseline DAS, age, rheumatoid factor (RF), anti-citrullinated protein autoantibodies (ACPA) and the type of treatment given. It is found that women experience more pain, resulting in higher DAS than men [7,8]. Apart from the baseline disease activity being an important predictor of disease activity [9]. Age also explains the variance of DAS, as higher age at presentation of RA leads to a higher DAS [10]. Furthermore, rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) are predictors of DAS. RF is the classical autoantibody in RA and ACPA are additional types of antibodies that are directed against citrullinated peptides. Almost all ACPA-positive patients are also positive for RF and 50-80% of individuals with RA have RF, ACPA or both [1]. It is found that seropositive patients have a higher disease activity than seronegative patients [11,12]. Finally, the choice of treatment strategy has impact on the DAS. Methotrexate (MTX) is the dominant DMARDs, but DMARDs are sometimes combined to increase the effectiveness. Studies showed that a combination of DMARDs is more effective than MTX monotherapy in early RA [13-16]. The treatment strategy therefore determines the clinical response of the patients.

However, taking the aforementioned known factors into consideration a large part of the variation in treatment response remains unclear. Part of this unexplained variance may be related to interpersonal differences, for instance genetics, sociodemographics or psychological factors. Psychosocial factors may influence the treatment response explaining part of the variation observed [17]. In accordance with the WHO definition of 'health', assessment of the course and outcome includes measures of physical, mental en social wellbeing [18]. Psychosocial factors take these domains into account and the relevant psychosocial factors are:

Social support

Social support is defined as the presence of others, or the resources provided by them, prior to, during and following a stressful event [19]. It is found that a lack of social support affect long-term functional disability and pain [20]. Zautra et al. (1994) suggest that interpersonal conflicts increase the inflammation and thereby the disease activity [21].

Locus of control

The locus of control is the patients' perception about his control of his health status. An "internal" locus of control means that a patient believes that he is responsible for his health, whereas someone with an "external" control believes that the practitioner is responsible for his health status. The last locus of control "chance" reflects a person who believes that his health is dependent on fate, luck and chances [22]. One study showed that an internal locus of control is significantly related to wellbeing and perceived functioning [23]. Internal locus of control stimulates positive health behaviors including seeking information, taking medication, making and keeping physician appointments. This results in a higher effectiveness of the treatment to decrease the disease activity [22].

Coping style

Coping is described as the purposeful efforts to manage or vitiate the negative impact of stress [24]. A stressor is any real or imagined event, condition, situation, or stimulus that instigates the onset of the human stress response process within an individual [25]. In this case patients could have experienced stress because of the negative consequences of rheumatoid arthritis. However, if a particular response is automatized or non-effortful, even if that response is adaptive, it is not considered to be a coping response [24]. Coping strategies could be categorized into active and

passive dimensions. Active strategies are defined as those strategies used by patients when they are attempting to control their pain or to function in spite of their pain, whereas passive coping involve strategies that relinquish control of the pain to others or allow other life areas to be adversely affected by pain [26]. Studies showed that passive coping is associated with worse outcomes on disease-specific measures of functioning [20,27].

Depression

The World Health Organization described depression as a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration [28]. One study showed that the presence of depression is associated with the articular index and the degree of functional impairment [29]. In line with that, another study found that depressive symptoms were associated with negative health and functional outcomes [30]. Bishop et al. (1987) found a relationship between depression and increased RA activity [31].

Anxiety

Anxiety is defined in the Diagnostic and Statistical Manuel as a neurosis characterized by anxious over concern extending to panic and frequently associated with somatic symptoms [28]. Overman et al. (2012) found that psychological distress, including anxiety and depression, and disease activity were positively associated [32].

Fatigue

Fatigue is a common complaint among patients with RA and is a symptom of the disease. Unlike normal tiredness, fatigue is chronic state, typically not related to overexertion and poorly relieved by rest. It has an enduring subjective sensation of weakness, lack of energy, generalized tiredness or exhaustion [33]. Fatigue is strongly associated with severity of pain, disease activity, functional status and severity of inflammation [34-36].

These psychosocial factors could explain a part of the variance of treatment response and identifying these factors could help in further optimizing treatment of RA for the individual patient. The aim of this research is to identify factors that, in addition to known factors, predict the DAS in early arthritis patients with a high

likelihood of having RA three months after initiating DMARD therapy. Therefore, we set out to answer the following question:

Which factors predict, in addition to known factors, the Disease Activity Score (DAS) in early arthritis patients with a high likelihood of having RA three months after initiating treatment with disease modifying anti-rheumatic drugs (DMARDs)?

Methods

Patients

For this study data were used from a current clinical trial, Treatment in the Rotterdam Early Arthritis Cohort (tREACH), which is ongoing in eight rheumatology centers in the southwestern part of the Netherlands [37]. The tREACH is a cohort study with two years of follow-up, with assessment at baseline and every three months over two years. The aim of the tREACH study, a stratified single-blinded trail, is to evaluate different induction treatment strategies in early RA.

Patients were invited to participate if they are older than eighteen years, have arthritis in one or more joint(s) and symptom duration of less than one year. Respondents were stratified into three groups (low, intermediate and high) according to their likelihood of progressing persistent arthritis based on the prediction model of Visser [38]. The strata correspond to the probability of developing persistent arthritis, i.e. low: <30%, intermediate: 30-70% and high: >70% chance. In each stratum three treatment strategies were compared.

For this study patients were obtained from the high group and patients were randomized into one of the following initial treatment strategies:

(A) Combination therapy (methotrexate (MTX) + sulfasalazine + hydroxychloroquine) with glucocorticoids (GCs) intramuscularly;

(B) Combination therapy with an oral GC tapering scheme;

(C) Monotherapy (MTX) with oral GCs similar to B

One stratum was chosen in order to have a more homogeneous patient group with the same treatment strategies compared and same probability of developing persistent arthritis. If all strata were included, the patient group will be to divers because of the nine different treatment strategies. This stratum (high group) was

chosen because these patients had the highest probability of developing persistent arthritis. Results from other stratum will be less reliable as the chance that complaints disappear over time and no arthritis will be developed, is higher.

Assessment of demographic, psychosocial characteristics and disease activity
Baseline demographic and psychosocial characteristics were collected using questionnaires that were sent to the patients by post. In addition, patients visited a rheumatology center where their swollen joint counts, tender joint counts, general health and erythrocyte sedimentation rate were assessed in order to calculate the DAS. After three months the aforementioned components of the DAS were assessed in a rheumatology center again in order to calculate the DAS after three months.

Primary outcome
The disease activity score (DAS) measures the disease activity of RA. The score has a range of 0 to 10, where a higher score indicates a higher disease activity. A DAS lower than 2.4 indicates a low disease activity. An intermediate disease activity has a DAS between 2.4 and 3.7. A DAS of more than 3.7 defines a high disease activity. A patient is in remission if he/she has a DAS of less than 1.6 [39].

The score comprises four domains: swollen joint counts (SJC), Ritchie Articular Index (RAI), erythrocyte sedimentation rate (ESR) and General Health (GH) [46].
A trained research nurse conducted a physical examination and had the patient measure his general health status on a visual analog scale. SJC (44 joints) and RAI (53 joints) were computed. Blood tests were taken in order to determine the ESR (mm/hour) [37].

Psychosocial variables

Social support
Social support was measured by the Dutch questionnaire “Inventarisatielijst Sociale betrokkenheid” (Inventarization Social Involvement, ISB) [40]. Questions were asked about how many social contacts the patient had in the past half year. The rank of the sum score is between 5 and 20. A higher sum score indicates more social support. This scale has a Cronbach’s alpha of 0.89.

Locus of control

The locus of control is determined by the questionnaire Multidimensional Health Locus of Control (MHLC), with 18 questions about health and diseases [41]. The MHLC assesses 3 different locus of control: internal, external and chance. Each domain has a sum score ranging from 6 to 36. A higher score means that a patient's belief is stronger in that particular health locus of control. The Cronbach's alpha is 0.76 for the internal, 0.81 for the external and 0.70 for the chance locus of control.

Coping style

The questionnaire Coping of Rheumatic Stressors (CORS) was used to measure the coping style [42]. There are 8 questions about coping with pain and 10 questions about coping with limitations. The score of coping with pain has a range between 8 and 32 and coping with limitations between 10 and 40. A higher score indicates more frequent use of that coping strategy. Cronbach's alpha for coping with pain is 0.88, coping with limitations 0.93 and for the total scale 0.95.

Depression and anxiety

The Hospital Anxiety and Depression Scale (HADS) was used to measure depression and anxiety [43]. The scores of depression and anxiety range between 0 and 21, where a higher score means more anxiety or depression. The Cronbach's alpha for anxiety is 0.86 and for depression 0.85.

Fatigue

Fatigue was assessed using the Fatigue Assessment Scale (FAS) [44]. The score ranges from 10 to 50 (Cronbach's alpha= 0.87). A higher score indicates a higher level of fatigue.

Demographic and clinical characteristics

Blood tests were taken to measure the RF and ACPA and patients were asked about their age and sex in the questionnaire.

Statistical analysis

Characteristics of the study population were described using descriptive analyses with indicators such as the mean, standard deviation and median.

Univariate analysis

Pearson's correlations between the psychosocial factors (fatigue, coping style, social support, locus of control, depression and anxiety) and DAS at three months were computed to identify candidate predictors of DAS at three months after initiation of treatment. Predictors were selected using $p < 0.05$ as criteria of entering the predictor into the multivariate model.

Multivariate analysis

Thereafter, a multivariate linear regression was performed. The known factors (age, sex, treatment strategy, baseline DAS and RF/ACPA-positivity) were entered in the model first in order to explore the effect of the candidate predictors in addition to the known factors. Then the candidate predictors of the univariate analysis were added in the multivariate model. Subsequently, a backwards selection was performed until all variables reached significance of $p<0.05$, while known predictors age, sex, treatment strategy, baseline DAS and RF/ACPA-positivity were kept in the model regardless of level of significance. The backward method is preferable to the forward method, because of the suppressor effects. This occurs when a predictor has a significant effect only when another variable is held constant. The forward method exclude predictors with suppressor effect easier than backwards method. Meaning that the forward method runs a higher risk of making type II error, indicating that a predictor is excluded while in fact it does predict the outcome [45].

Further, the model is corrected for multicollinearity. Multicollinearity occurs when there is a strong correlation between two or more predictors in the regression model. This affects the βs and R of the model negatively, because of the increased standard errors and the little unique explaining variance. The variance inflation factor (VIF) and tolerance will be computed in order to determine multicollinearity. Myers (1990) suggests that a VIF value of 10 is worrying [46]. Related to the VIF is the tolerance (1/VIF) and a study showed that values below 0.2 are worthy of concern and values below 0.1 indicate serious problems [47]. If multicollinearity is found, then excluding the predictor from the model will be considered.

Separate multivariate analyses were performed in the same way for the DAS components: SJC, RAI, ESR and GH in order to explore the impacts of the predictors on the components of DAS. Before this, the element of DAS were squared or logged in order to normalize the distribution.

All statistical analyses were performed with the statistical package STATA (12.0 SE) using $p < 0.05$ as level of statistical significance.

Results

Patients

A total of 693 patients were approached to participate in tREACH and of those, 515 patients (74%) were included in the tREACH [13]. A total of 281 (55%) patients were included in the high probability stratum at baseline and 264 patients (94%) had a DAS assessment after three months.

Descriptive analysis

Patient characteristics are shown in table 1. The group consisted of 190 (68%) women and the mean age was 53.2 years. While 162 (57.7%) patients were RF positive, 170 (60.5%) were ACPA positive. Mean (SD) DAS at baseline was 3.4 (1.0). The mean (SD) of DAS decreased to 2.0 (1.0) after three months ($t=22.14$; $p<0.001$).
Characteristics of candidate predictors for DAS at three months are shown in table 2.

Predictors for DAS at three months

Univariate analysis showed that fatigue, coping with pain and limitations, anxiety, depression and internal locus of control were significantly associated with DAS at three months [table 3]. All factors were positively associated with the DAS, except for internal locus of control. Meaning that a higher fatigue score, more passive coping style, higher depression and anxiety scores and less internal locus of control are correlated with a higher DAS.

The multivariate analysis started with the known factors and the candidate predictors. After backwards selection, but forcing the known factors into the model, anxiety was identified as an independent predictor for DAS ($\beta=0.18$; $p=0.002$), while coping with pain reached borderline significance ($\beta=0.11$; $p=0.07$) [table 4]. For our model the VIF values are all well below 10 and the tolerance statistics all well above 0.2; therefore, we can safely conclude that there is no collinearity within our data [table 4].

Predictors for the components of the DAS

Univariate linear regression on the components of the DAS at three months showed a significant influence of fatigue (r=0.19; p=0.02), anxiety (r=0.25; p=0.001), depression (r=0.15; p=0.04), coping with limitations (r=0.17; p=0.02) and coping with pain (r=0.25; p=0.001) on logged RAI.

Furthermore, coping with pain (r=0.24; p<0.001), coping with limitations (r=0.24; p<0.001) and external locus of control (r=0.14; p=0.027) had a significant influence on logged ESR at three months.

Also, fatigue (r=0.27; p<0.001), anxiety (r =0.30; p<0.001), depression (r =0.30; p<0.001), coping with pain (r=0.14; p=0.033) and internal locus of control (r =-0.20; p=0.001) was found to be associated with square root of GH at three months.

Finally, fatigue (r=0.16; p=0.01), anxiety (r=0.14; p=0.02), depression (r=0.15; p=0.02), coping with limitations (r=0.18; p=0.004) and coping with pain (r=0.20; p=0.001) were associated with square root of SJC at three months.

To identify independent predictors for the components of the DAS at three months, models were generated for each of the components and backwards selection was performed in the same fashion as for the DAS. Passive coping with pain was associated with higher levels of logged ESR (β =0.15; p=0.02), while anxiety (β=0.24; p<0.001) and internal locus of control (β =-0.14; p=0.02) were related to square root of GH. Furthermore, anxiety had a significant influence on the logged RAI (β =0.14; p=0.05).

Explained variance of the multivariate models (R^2)

The known factors age, sex, baseline DAS, treatment strategy, RF and ACPA explained a total of 27.1% of the variance in DAS of which the contribution of the baseline DAS was the largest. The multivariate model with known factors and anxiety explained 30.6% of the variance, while the multivariate model containing known factors, anxiety and coping with pain explained 31.6%. Thus, anxiety explained an additional 3.5% of the observed difference in DAS and anxiety and coping with pain 4.5% [figure 1].

Discussion and conclusion

This study suggests that especially anxiety is independent predictors of disease activity in early arthritis patients three months after the initiation of DMARD therapy. We found that anxiety additionally explains 3.5% more of the variance in treatment responses, while anxiety and coping with pain explains 4.5% more of the variance. Considering the individual components of the DAS, we found that anxiety was associated with GH and RAI, more subjective components of the DAS, but not with ESR and SJC, the more objective components. On the other hand, passive coping with pain was found to be associated with higher levels of ESR.

Previous research has shown that the factors sex, baseline DAS, treatment strategy, age, sex, RF and ACPA influence the DAS [7-16]. We included those factors in the model. In accordance with previous findings, we found that sex, baseline DAS and treatment strategy were associated with DAS [table 3]. A relationship between RF or ACPA positivity and DAS was not confirmed in this study. It remains a possibility that such an association was not observed in our population because seropositivity was one of the scoring criteria to get classified in the high probability group used for our analysis.

We also observed an association between passive coping with pain and higher levels of ESR. As ESR is a biomarker for inflammation, it is possible that higher levels of ESR indicate higher disease activity, which may increase the patients' need to make use of a passive coping style. However, the observed relation remained after correcting for baseline disease activity, making a reversed association of coping style influencing the ESR more plausible. In line with our observation, one study showed that positive (active) coping is associated with lower levels of C-reactive protein, which is another biomarker for inflammation [48]. These findings could be a starting point for further research into this subject.

This study has several strengths and weaknesses. Strong point of this study includes the fact all patients were selected with the same selection criteria and treatment strategies were randomly divided. Most studies that evaluated risk factors or prognostic factors make use of a prospective cohort design, which almost always suffers from confounding by severity, as treatment is not controlled for. Most studies

that control treatment (randomized controlled trials) do not include multiple sources of data collection such as questionnaires on psychosocial variables. tREACH on the other hand includes the strong parts of both designs enabling us to observe risk factors other than clinical observations and also allows for controlling the treatment [37].

Our research has certain limitations. The disadvantage of a randomized controlled trial to study risk factors is often that the sample size is based on finding a treatment effect rather than allowing the study of multiple risk factors. We had the advantage of including 3 different initiation therapies resulting in a sample of just below 300 participants. But this relatively small sample could have leaded us to incorrectly dismiss predictors that were associated with DAS. Another issue is that psychological factors were measured by self-reported questionnaires, introducing a potential for information bias. Patients might have had a tendency to respond in a way they thought the researchers would expect from them. However, as this study was not the primary goal of the tREACH we expect the relationship we observed not to be biased in a specific direction.

Another point is the small effect sizes (beta's) of the independent predictors in the multivariate model. The research period of three months could be the cause. Even within this short period a significant, though small, effect is found. This indicates that anxiety is important in the determination of the effectiveness of treatments. Anxiety might have a larger impact over a longer period and further research on this subject is needed to explore the effect of this factor. Further, a research with a longer period could also detect possible predictors that were not found in our research. It is possible that psychosocial characteristics were not developed in the first three months or a longer period of time may be needed to affect the DAS. The tREACH data could be used for further research, because multiple questionnaires will be obtained prospectively and repeatedly for the following two years.

The univariate analysis showed that coping with pain was associated with DAS, while coping with pain reached borderline significance in the multivariate analysis (β=0.11; p=0.07) [table 4]. This suggests that coping with pain is an important candidate predictor. The borderline significance could be caused by the aforementioned weaknesses of this study and further research is needed to confirm this finding.

Based on our findings we would recommend physicians to take into account anxiety and passive coping style when prescribing the first medication. Talking with the patient about fears and barriers with respect to disease and medical treatment from the first visit onwards may impact the DAS later on. In medical terms this may lead to less (expensive) steps needed to enter a state of low disease activity or remission. For the patients this may increase trust in the doctor leading to more satisfaction in medical care and better quality of life.

In conclusion, our results suggest that anxiety is an independent predictor of disease activity in early arthritis patients three months after initiation of disease modifying anti-rheumatic drugs therapy. Coping with pain might also be an important predictor. Physicians should address these characteristics when initiating treatment to increase the (cost-) effectiveness of treatment.

Table 1. Clinical and demographic characteristics

(N=281 unless indicated otherwise)

Age, mean (SD)	53.2 (14.2)		
Sex	Men, n (%)	91 (32%)	
	Women, n (%)	190 (68%)	
Treatment strategies	A[1], n (%)	91 (32%)	
	B[2], n (%)	93 (33%)	
	C[3], n (%)	97 (35%)	
RF/ACPA positivity	Positive, n (%)	194 (69%)	
	Negative, n (%)	87 (31%)	
DAS T0 [0-10], mean (SD)	3.4 (1.0)	**DAS T3 [0-10],** mean (SD) [n]	2.0 (1.0) [264]
RAI T0 [0-78], mean (SD)	7.8 (6.1)	**RAI T3 [0-78],** mean (SD)	3.2 (4.4)
GH T0 [0-100], mean (SD)	52.1 (22.4)	**GH T0 [0-100],** mean (SD) [n]	32.6 (22.4) [264]
BSE T0 [0-150], mean (SD)	29.7 (21.1)	**BSE T0 [0-150],** mean (SD) [n]	16.7 (14.5) [267]
SJC T0 [0-44], mean (SD)	8.7 (6.5)	**SJC [0-44],** mean (SD)	2.5 (3.7)

***** T0 = baseline

***** T3 = after three months

[..-,,]= theoretical range

Treatment strategies:

1. Combination therapy (methotrexate (MTX) + sulfasalazine + hydroxychloroquine) with glucocorticoids (GCs) intramuscularly
2. Combination therapy with an oral GC tapering scheme
3. MTX with oral GCs similar to B

Table 2. Characteristics of psychosocial variables

Variables (Theoretical range)	N	Mean (SD)	Questionnaire	Cronbach's alpha
Fatigue (10-50)	256	22.2 (7.0)	FAS	0.87
Coping with pain (8-32)	262	15.5 (5.2)	CORS	0.88
Coping with limitations (10-40)	263	22.9 (7.4)	CORS	0.93
Depression (0-21)	263	4.6 (3.4)	HADS	0.85
Anxiety (0-21)	263	5.8 (3.7)	HADS	0.86
Locus of control				
Internal (6-36)	259	20.7 (4.6)	MHLC	0.76
External (6-36)	259	20.4 (4.2)	MHLC	0.81
Chance (6-36)	258	19.3 (5.5)	MHLC	0.70
Social support (5-20)	260	16.6 (3.6)	ISB	0.89

Table 3. Univariate analysis of potential predictors on DAS at three months

	Univariate (Pearson's correlation)	
	r	p
Known factors		
Age	0.07	0.24
Sex (male)	**-0.15**	0.01
DAS (baseline)	**0.46**	<0.001
RF/ACPA positivity	-0.07	0.24
Treatment		
Strategy A	ref	ref
Strategy B	-0.11	0.09
Strategy C	**0.18**	0.003
Psychosocial factors		
Fatigue (FAS)	**0.26**	<0.001
Coping with pain (CORS)	**0.31**	<0.001
Coping with limitations (CORS)	**0.21**	0.001
Depression (HADS)	**0.28**	<0.001
Anxiety (HADS)	**0.28**	<0.001
Social support (ISB)	-0.02	0.78
Locus of control (MHLC)		
Internal	**-0.14**	0.03
External	0.07	0.27
Chance	-0.05	0.40

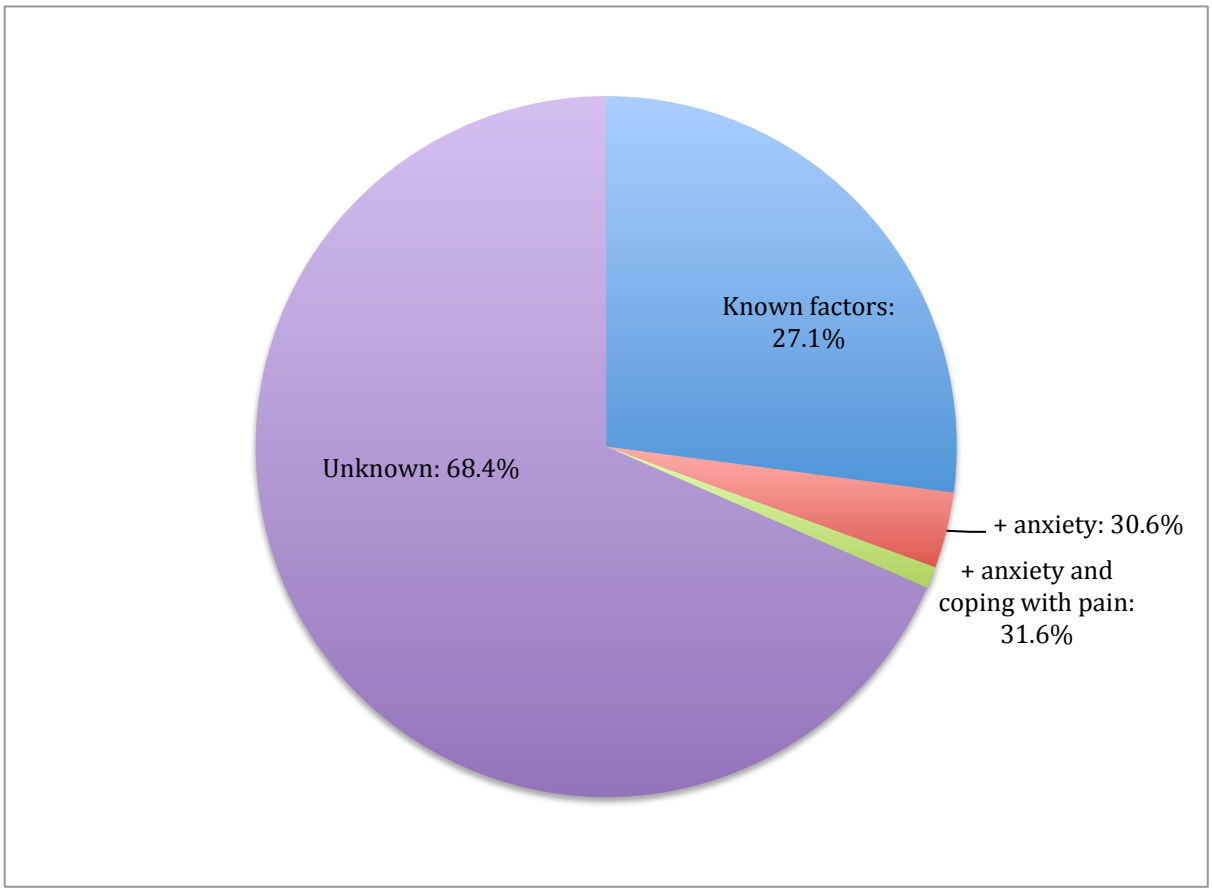
Bold = significant ($p<0.05$)

Table 4. Multivariate linear regression analysis of potential predictors on DAS at three months

	Multivariate (Known factors)			**Multivariate (Known factors + candidate predictors)**					**Multivariate (After backward method)**	
	R^2=0.26 N=264 F14.89			R^2=0.32 N=239 F=8.68					R^2=0.32 N=248 F=13.79	
Known factors	**β**	**p**		**β**	**p**	**Tole-rance**	**VIF**		**β**	**p**
Age	0.03	0.56		0.09	0.14	0.86	1.16		0.07	0.22
Sex (male)	**-0.15**	0.01		-0.10	0.11	0.86	1.17		-0.09	0.10
DAS (baseline)	**0.44**	<0.001		**0.38**	<0.001	0.78	1.28		**0.37**	<0.001
RF/ACPA positivity	-0.03	0.56		-0.04	0.46	0.97	1.03		-0.04	0.45
Treatment										
Strategy A	Ref	Ref		Ref	Ref	Ref	Ref		Ref	Ref
Strategy B	-0.07	0.30		-0.05	0.46	0.69	1.45		-0.04	0.54
Strategy C	0.12	0.06		**0.14**	0.03	0.71	1.40		**0.14**	0.02
Psychosocial factors										
Fatigue (10-50)				0.01	0.94	0.58	1.72			
Coping with pain (8-32)				0.15	0.10	0.39	2.57		0.11	0.07
Coping with limitations (10-40)				-0.07	0.44	0.43	2.34			
Depression (0-21)				-0.04	0.62	0.49	2.06			
Anxiety (0-21)				**0.19**	**0.01**	0.57	1.75		**0.18**	0.002
Locus of control										
Internal (6-36)				-0.03	0.64	0.89	1.12			

Bold = significant (p<0.05)

Figure 1. Explained variance (R^2) of anxiety and coping with pain in addition to known factors on DAS at three months (N=248)



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