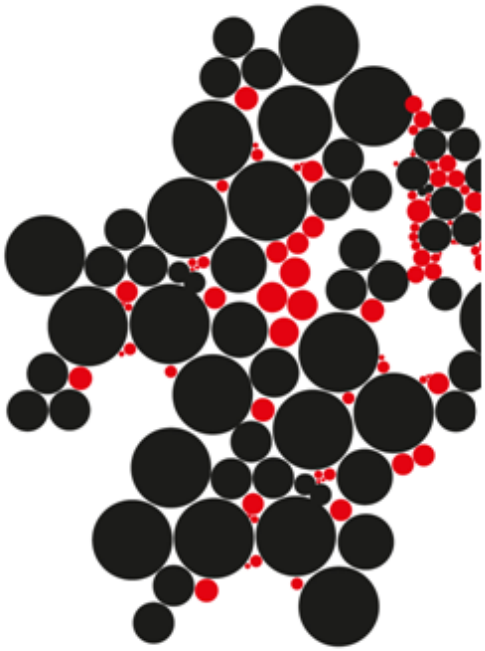

Predicting treatment outcome of a preventive and early intervention for sub-threshold and mild panic disorder

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CONTENT

ABSTRACT

Introduction: Each year, 2% to 3% of the adult population is affected by Panic Disorder (PD). The aim of this study is to investigate variables predicting post-treatment effect sizes of a preventive and early intervention in PD.

Method: Data concerning demographic information, initial symptom severity and personal variables were collected. A total of 166 participants suffering from panic symptoms followed the 'Don't Panic' course during 8 weeks. Pearson correlations were conducted to explore bivariate relationships between pre-treatment measurements and post-treatment effect sizes. Next, multiple linear regression analyses for all outcome measures with forced entry were completed to investigate the predictive value of the significant findings found in the bivariate analyses.

Results: Initial symptom severity proved to be predictive for treatment outcome of all corresponding outcome measures. Demographic variables were of little predictive value. The participants' expectations of treatment effectiveness explained little but significant additional variance for several outcome measures.

Discussion: Participants suffering from more severe pre-treatment symptoms seem to reach more improvement after the course. Additionally, participants with higher expectations of treatment effectiveness show significantly more improvement on several outcome measures after the course. Overall, the 'Don't Panic' course appeared to be suitable for a broad target population, since its efficacy was not clearly restricted by demographics.

SAMENVATTING

Inleiding: Elk jaar wordt 2% tot 3% van de volwassen populatie getroffen door een paniekstoornis. Het doel van dit onderzoek is het verkennen van variabelen die de behandelresultaten van een preventieve en vroege interventie voor paniekklachten voorspellen.

Methoden: Informatie over demografische kenmerken, de initiële ernst van de symptomen en persoonsgebonden kenmerken werd verzameld. In totaal hebben 166 deelnemers gedurende acht weken de cursus 'Geen paniek' gevolgd. Pearson correlaties werden berekend om de bivariate samenhang tussen de voor- en nametingen te exploreren. Vervolgens werden multiple lineaire regressieanalyses met forced entry uitgevoerd voor alle uitkomstmaten. Dit, om de voorspellende waarde te bepalen van de in de Pearson correlatie significant gebleken relaties.

Resultaten: De initiële ernst van de symptomen bleek voorspellend te zijn voor de behandeluitkomst van elke overeenkomstige uitkomstmaat. Demografische variabelen zijn van weinig voorspellende waarde. De verwachtingen van de deelnemers over de doeltreffendheid van de cursus bleek van weinig, maar significante voorspellende waarde voor sommige uitkomstmaten.

Discussie: Deelnemers met ernstigere symptomen aan het begin van de cursus lijken sterker verbeterd na afloop van de cursus. Deelnemers met hogere verwachtingen met betrekking tot de doeltreffendheid van de cursus zijn significant sterker verbeterd op verschillende uitkomstmaten na afloop van de cursus. Er kan geconcludeerd worden dat de cursus 'Geen paniek' geschikt is voor een breed publiek, aangezien de werkzaamheid van de cursus niet duidelijk afhangt van demografische kenmerken.

INTRODUCTION

Worldwide, anxiety disorders are the most common psychiatric disorders. Based on DSM-III-R criteria, a life time prevalence of 19,3% was found in a study by the Netherlands Mental Health Survey and Incidence Study (NEMESIS; Bijl, Ravelli & van Zessen, 1998). The most common anxiety disorders are simple phobia, social phobia and panic disorder (PD). Each year, 2% to 3% of the adult population is affected by PD (Bijl et al., 2007; Kessler et al., 1994; Eaton, Kessler, Wittchen & Magee, 1994). PD is a severe and persistent mental disorder, associated with a large burden of disease, extensive loss of productivity and considerable medical consumption. Smit et al. (2006) conducted a study to investigate the costs of nine common mental disorders. Using data derived from the NEMESIS among 5,504 adults of the Dutch population in 2003, the costs of health service uptake, patients' out-of-pocket costs, and production losses were calculated. They concluded that panic disorder was associated with the largest costs of all anxiety disorders in the study. Especially the costs of absence from work through illness were high. The economic costs were even comparable to those of some severe somatic disorders (e.g. heart disease, cancer).

The high prevalence, early onset, large burden of disease and considerable economic costs to society emphasizes the public health importance of prevention of anxiety disorders. A substantial proportion of the population suffers from subthreshold and mild PD and is at risk of developing chronic PD (Batelaan, De Graaf, Van Balkom, Vollebergh & Beekman, 2007; Norton, Cox & Malan, 1992; Reed & Wittchen, 1998). Subthreshold PD can be defined as the presence of some of the symptoms of PD, but not meeting the DSM-IV diagnostic criteria. Batelaan et al. (2007) concluded that subthreshold PD seems clinically relevant and occupies an intermediate position

between no panic and panic disorder with regard to for example the number of symptoms, comorbidity, economic costs, and almost every scale of functioning.

So far, only research into variables predicting treatment outcome of matured panic disorder treatment has been conducted. It is important to know which baseline variables are correlated to treatment outcome as this can be used to identify patients that are most likely to benefit from an intervention, and contrary, patients that are less likely to benefit from or even be harmed by the intervention. Increasing demand over the past three decades, among both 'suppliers' and 'consumers', for more cost-effective and accessible treatments for common mental health also calls for more research into predictors of outcome.

Kampman, Keijsers, Hoogduin and Hendriks (2008) investigated the predictive value of five variables for cognitive behavioural treatment (CBT) outcome in a large sample of PD patients. They found that only initial symptom severity proved to be highly predictive of all outcome measures. Ramnerö and Öst (2004) predicted outcome of pre-treatment characteristics for patients with a primary diagnosis of panic disorder with agoraphobia. They concluded that agoraphobic severity was a significant negative predictor of behavioral treatment outcome. Sharp and Power (1999) found that frequency of panic attacks, general anxiety, agoraphobic avoidance and level of depression all showed some influence on treatment outcome of PD. Keijsers, Hoogduin and Schaap (1994) found a significant association between moderate initial treatment motivation and poor treatment outcome. However, others failed to find a relationship between treatment motivation and treatment outcome (De Beurs, 1993; Ramnerö & Öst, 2004). Futhermore, Keijsers et al. (1994), O'Rourke et al. (1996) and McCrusker et al. (2000) found that sociodemographic variables have the weakest relationship with treatment outcome. It can be

concluded that, besides the predictive value of initial symptom severity, no consistent results have been found.

The psychiatric community has shifted away from acute treatment to a focus on early intervention over the last years (Altamura, Buoli, Camuri & Dell'osso, 2010). Several studies found that early interventions of anxiety disorders can be successful (Dadds, Spence, Holland, Barrett & Laurens, 1997; Schmidt et al,. 2007; Seligman, Schulman, DeRubeis & Hollon, 1999; Meulenbeek at al., 2010). As the interest in preventive and early interventions grows, the question which variables predict the outcome of these early interventions rises. To date, no studies have examined variables predicting treatment outcome of preventive and early interventions in PD. Therefore, the overall aim of this study is to investigate which variables are correlated to and predictive of the treatment outcome of a preventive and early intervention in PD.

METHOD

Study design

The data derived in a study by Meulenbeek et al. (2010) to investigate the effects of the 'Don't Panic' course, were also used in this study. The study was designed as a pragmatic, multi-site, randomized controlled trial. The measurements were taken pre-treatment and after three months as a posttest measurement. In terms of patient recruitment and the manner in which intake, offering the intervention, and monitoring outcomes are conducted, this study was designed to imitate the Dutch health care system as naturally as possible to amplify external validity. Via the internet and through media announcements participants were recruited from the general

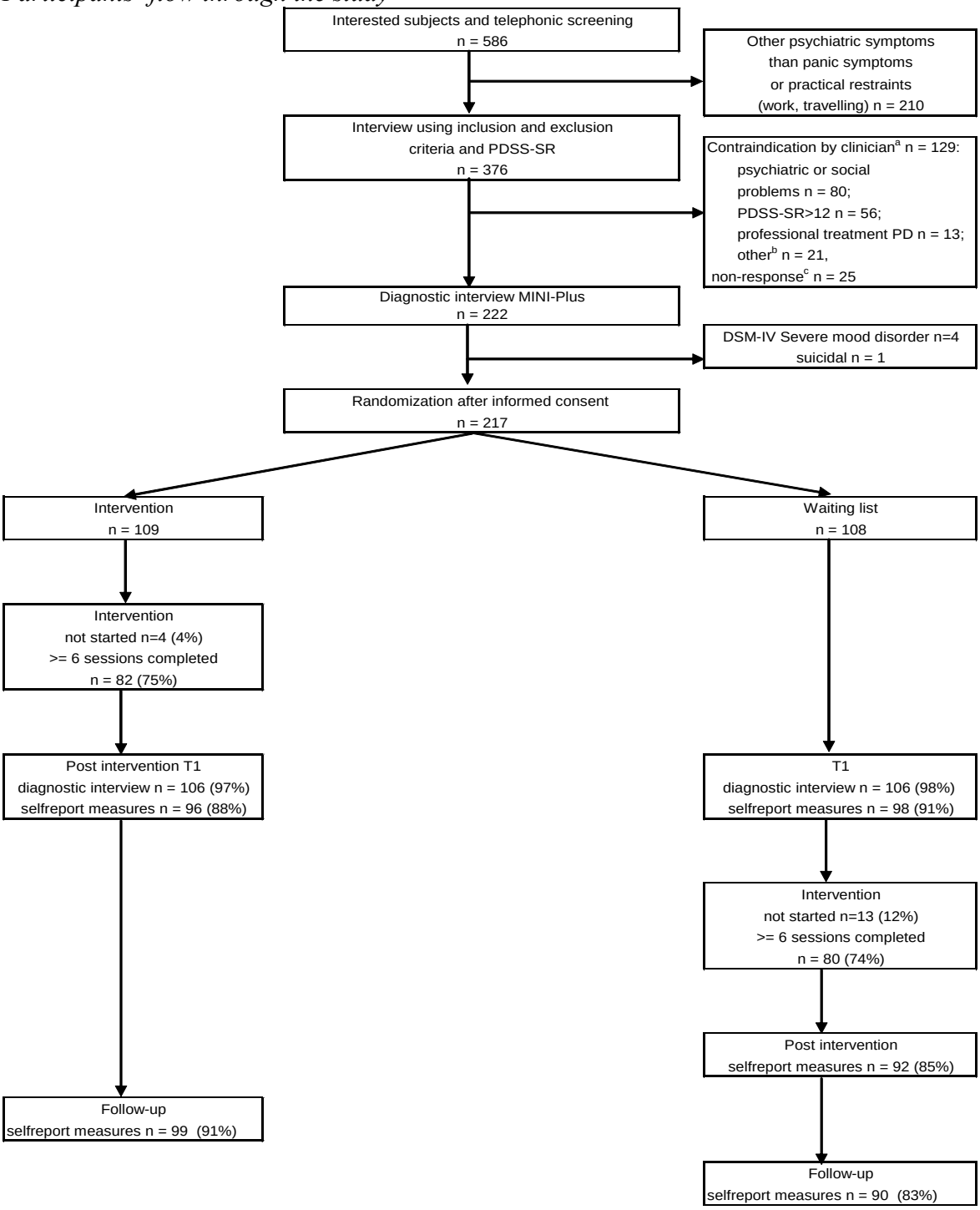
population. Standard procedures utilized by the Community Mental Health Centers were used for screening. First, the people who showed interest in the course and the study were given more information. An initial screening by telephone was used to determine the presence of panic symptoms. Secondly, an experienced psychologist from a Community Health Centre conducted an interview with potential participants. The purpose of this interview was to check the exclusion criteria. Also, trained interviewers from the Trimbos Institute (Netherlands Institute of Mental Health and Addiction) interviewed the potential participants using the Mini International Neuropsychiatric Interview-Plus (MINI-Plus) (Sheehan et al., 1998). This interview was done to measure the PD status according to the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), the presence of current co-morbid agoraphobia, and also to exclude the presence of current severe major depressive disorder.

Study sample

The present study combined the data from both the experimental and the control group. Since the control group attended the course only four months after the experimental group, it can be seen as a comparable treatment and this also provides a higher power in the analysis. **Figure 1** provides an overview of the participants' flow through the study. The participants, recruited from the general adult population in the Netherlands, were eligible when over 18 years and presenting with subthreshold or mild PD. Having symptoms of PD falling below the cut-off of 13 on the Panic Disorder Severity Scale-Self Report (PDSS-SR) was the inclusion criterion.

Figure 1

Participants' flow through the study



Note. PDSS-SR = Panic Disorder Severity Scale-Self Report; PD = Panic Disorder; MINI-Plus = Mini-International Neuropsychiatric Interview-Plus.

[a] Participants can have more than one contraindication.

[b] Including: somatic problems (n=11).

[c] Including: practical restraints.

Exclusion criteria were current psychological treatment for PD-related complaints, having more severe PD, other current severe psychiatric symptoms or social problems and suicidal intention warranting treatment or likely to interfere with participation in the group course. As well was illness requiring immediate medical attention and the inability to function both in a group and independently. If someone met one of the exclusion criteria, they were advised to seek regular treatment. Participants using medication agreed on not to change the medication during the study period. Finally, a written informed consent was obtained after a thorough explanation of the study procedure. An independent medical ethics committee (METIGG) approved the trial protocol.

Sample size

A total of 217 participants were selected to participate in the study. Completers are seen as the participants who attended at least six out of eight sessions. For several reasons, 66 participants did not complete the course (e.g. personal reasons, practical reasons, and dissatisfaction with the course). This leaves data of 166 completers on which statistical tests were done. **Table 1** provides an overview of patient characteristics for the total group, the completers and the non-completers. Measures are done with data from the completers only to examine the prediction of treatment effects, because as regards content, completers finished the course. In the total group of participants, 71% is female. The mean age was 42 (S.D. 12.4), ranging from 20-75 years and most participants were married or living with a partner (78%) and were employed (70%). There are no visible large demographic differences between the completers and the non-completers.

Table 1
Pre-treatment patient characteristics for the total group, the completers and the non-completers.

	Total group (*N*=217)	Completers (*n*=166)	Non-Completers (*n*=51)
Female, N (%)	154 (71)	119 (71.70)	35 (68.60)
Mean age, Years (S.D.)	42 (12.40)	43 (12.20)	39.82 (12.80)
Age, Range	20-75	20-75	20-74
Married/living with partner, N (%)	169 (78)	130 (78.30)	39 (76.50)
Employed (paid), N (%)	151 (70)	112 (67.50)	39 (76.50)
Years of education, mean (S.D.)	14.04 (3.26)	14.25 (3.30)	13.37 (3.10)
PDSS-SR, mean (S.D.) (range: 0-28)	7.18 (3.23)	7.03 (3.10)	7.69 (3.65)
BDI-II, mean (S.D.) (range: 0-63)	12.46 (7.64)	12.24 (7.83)	13.20 (7.02)
HADS-Anx, mean (S.D.) (range: 0-21)	9.54 (3.83)	9.51 (3.72)	9.6 (4.20)
MI, mean (S.D.) (range: 1-5)	1.96 (0.66)	1.97 (0.67)	1.92 (0.61)
PAI-1, mean (S.D.) (range: 0-100)	32.12 (18.55)	31.92 (18.06)	32.75 (20.23)
PAI-2, mean (S.D.) (range: 0-100)	24.84 (16.25)	24.51 (15.29)	25.90 (19.20)
PAI-3, mean (S.D.) (range: 0-100)	54.52 (18.39)	54.53 (18.65)	54.47 (17.67)
Mastery, mean (S.D.) (range: 5-25)	17.07 (3.23)	17.14 (3.20)	16.84 (3.35)
Subtype generalized social phobia, N (%)	36 (16.60)	26 (15.70)	10 (19.60)
Generalized anxiety disorder, N (%)	43 (19.80)	29 (17.50)	14 (27.50)
Number of symptoms, mean (S.D.) (range: 0-13)	8.50 (2.10)	8.46 (2.01)	8.65 (2.39)
TCQ, mean (S.D.) (range 1-49)	37.48 (5.57)	37.61 (5.28)	36.95 (6.43)

Notes: PDSS-SR = Panic Disorder Severity Scale-Self Report; BDI-II = Beck Depression Inventory-second edition; HADS-Anx = Hospital Anxiety and Depression Scale, subscale Anxiety; MI = Mobility Inventory; PAI-1 = Panic Appraisal Inventory, subscale anticipation; PAI-2 = Panic Appraisal Inventory, subscale consequences; PAI-3 = Panic Appraisal Inventory, subscale coping; Mastery = Mastery-scale; Number of symptoms = number of symptoms during a panic attack; TCQ= Treatment Credibility Questionnaire.

Intervention

The 'Don't Panic' course is based on cognitive behavioral principles. It is an early intervention for panic symptoms and makes use of interventions that appeared effective in treatment of matured PD (Bakker, 2001; Margraf, Barlow, Clark & Telch, 1993; Van Balkom, Nauta & Bakker, 1995; Van Balkom et al., 1997; Landon & Barlow, 2004). The intervention was found effective in a randomized control trial. For a detailed overview of the treatment effects of the 'Don't Panic' course we refer to Meulenbeek et al. (2010). Groups of six to twelve participants came together for eight weekly sessions of two hours. The psychologist and prevention worker offering the course used a course manual. The participants used an accompanying workbook (Meulenbeek, Herzmanatus, Smit, Willemse & Van der Zanden, 2005). The intervention was

extensively pilot-tested before entering the clinical stage and includes (a) a psycho-educational element, (b) life-style changes, (c) stress management, (d) relaxation training, (e) cognitive restructuring, (f) interoceptive exposure, (g) exposure 'in vivo', and (h) techniques aimed at relapse prevention.

Predictive variables

In the present study, several possible predictive variables were selected for investigation. The selection of these variables was based on literature research as well as the research conducted by Meulenbeek et al. (2010). The variables were divided into three categories: (1) demographic variables, (2) initial symptom severity and (3) personal variables.

To collect *demographic information* about the participants, self-report questionnaires were used, including questions concerning age, gender, marital status, education and occupation. Although Sharp & Power (1999) found that demographic variables had little predictive value, they are often included as control variables in research into predictors.

In several studies *initial symptom severity* proved to be significantly predictive of treatment outcome. Ramnerö and Öst (2004) found initial severity of avoidance behaviour to be negatively predictive of treatment outcome. These results are consistent with a study by Sharp and Power (1999), who also found a significant predictive value of initial severity of avoidance behaviour, as well as a significant predictive value of initial anxiety level and panic frequency. In regard to a possible negative or even possible positive effect of comorbid anxiety or depressive disorders, inconsistent findings have been reported. Finally, parts of the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness (TiC-P; Hakkaart-Van Roijen, Van Straten & Donker, 2002) were used to collect data about the economic costs.

To measure *personal variables* the Treatment Credibility Questionnaire (TCQ; Meyer et al., 2002) and the Dutch version of the Mastery-scale (Pearlin & Schooler, 1978) were used. Keijsers et al. (1994) reported a significant association between moderate initial treatment motivation and poor treatment outcome. However, more recent studies (e.g. Kampman, Keijsers & Hoogduin, 2008; Ramnerö & Öst, 2004) failed to find such relationship. The Mastery-scale was included to asses perceived control.

Measurements

All instruments used are frequently applied in international studies and are well validated. Most of the self-report questionnaires could be completed at home and were used for all moments of measurement. Therapy outcome was assessed for severity of panic symptoms, anxiety symptoms, symptoms of agoraphobia, depressive symptoms and cognitive aspects of panic disorder. Additionally, several variables to measure personal variables and treatment credibility were included.

To measure *demographic variables*, questions about gender, age, living situation, education and occupation were added to the self-report questionnaires.

To assess the *severity of panic symptoms* the Dutch adaptation of the Panic Disorder Severity Scale - Self Report (PDSS-SR; Shear et al., 2001; Van der Meer & Burgerhout, 2004) was used. The PDSS-SR contains seven items that assess the severity of seven dimensions of panic disorder and associated symptoms: (1) frequency of panic attacks, (2) distress during panic attacks, (3) anticipatory anxiety (worry about future panic attacks), (4) agoraphobic fear and avoidance, (5) interoceptive fear and avoidance (i.e., apprehension and avoidance of bodily

sensations), (6) impairment of or interference in work functioning and (7) impairment of or interference in social functioning. A higher score indicates more severe panic symptoms.

To indicate the possible presence of *anxiety symptoms* the subscale for anxiety of the Dutch version of the Hospital Anxiety and Depression Scale (HADS) was used (Zigmond & Sniath, 1983; Spinhoven et al., 1997). A higher score means a higher state of anxiety.

To measure *symptoms of agoraphobia* the Dutch adaptation of the Mobility Inventory (MI; Chambless, Caputo, Jasin, Gracely & Williams, 1985; De Beurs, 1993) was used. A higher score indicates more avoidance.

To assess *depressive symptoms*, the Dutch version of the Beck Depression Inventory, second edition (BDI-II; Beck, Steer & Brown, 1996; Van der Does, 2002) was used. The 21-item self-report questionnaire assesses the severity of depressive symptoms in the past week. A higher score indicates a higher level of depression.

The Dutch version of the Panic Appraisal Inventory (PAI; Telch, Brouillard, Telch, Agras & Taylor, 1989; De Beurs, Smit & Comijs, 2005) was used as a *cognitive measure for panic disorder*. The inventory measures cognitive aspects of panic disorder such as perceived likelihood of panic occurrence (PAI-anticipation), perceived negative consequences of panic occurrence (PAI-consequences) and perceived self-efficacy in coping with panic (PAI-coping). Each of the three subscales contains 15 items and a higher score means a more negative cognitive state.

The Mini International Neuropsychiatric Interview-Plus (MINI-Plus; Van Vliet, Leroy & Megen, 2000), a structured diagnostic interview that systematically identifies DSM-IV and ICD-10 diagnoses, was used to measure the presence of a *subtype generalized social phobia*, the *number of symptoms* and the presence of a *generalized anxiety disorder*.

To evaluate *economic costs*, a cost-effective analysis was done using parts of the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness (TiC-P; Hakkaart-Van Roijen et al., 2002). This economic evaluation included measurements of the following costs: direct medical costs (costs of health-care use), direct non-medical costs (costs patients make to obtain health-care, like travelling-expenses and parking fee) and the indirect non-medical costs (production loss caused by the disease) were assessed (Cuijpers & Smit; 2008). The 'total costs' are the sum of all costs, and are expressed as monthly per capita costs in Euro's (€) of the reference year 2003.

Finally, some additional *personal variables* were assessed. The Treatment Credibility Questionnaire (TCQ; Meyer et al., 2002) was used to assess patients' treatment credibility. Also, the Dutch version of the Mastery-scale (Pearlin & Schooler, 1978) was used to assess locus of control.

Statistical analyses

All analyses were accomplished for completers only (defined as participants attending at least six out of eight sessions). Cohen's *d* (Cohen, 1962) effect sizes were calculated for each of the post-treatment measurements as outcome measures. In all analyses the post-treatment effect size on the PDSS-SR is described as primary outcome measure, since the effects on the PD symptoms is the primary target of the course. Pearson correlations were used to examine any association between pre-treatment measures and post-treatment effect sizes. Multiple linear regression analyses with forced entry were done for the significant correlations ($P<.05$) found in the bivariate analyses. Because of the exploratory nature of this study, variables that showed a marginally significant ($P<.2$) relationship with any of the outcome effect sizes were included in

additional multiple regression analyses. All analyses were done with SPSS 18.0 using a two-sided significance level at p=0.05.

RESULTS

Table 2 presents an overview of the Pearson correlations between pre-treatment variables and post-treatment effect sizes. As primary outcome measure the PDSS-SR effect size was used. Significant correlations were found with both age and PDSS-SR intake score. More significant correlations are found with the HADS-Anx outcome measure: marital status, educational level, PDSS-SR, BDI-II, HADS-Anx, PAI-1, number of symptoms and the TCQ. Significant correlations found with the BDI-II effect size are pre-treatment measures on BDI-II, HADS-Anx, PAI-1, PAI-2, subtype generalized social phobia, the number of symptoms and the TiC-P. Significant correlations with the effect size of MI are pre-treatment scores on BDI-II, HADS-Anx, MI, PAI-1, PAI-2, generalized anxiety disorder and number of symptoms. The effect size of PAI-1 was significantly correlated with pre-treatment scores on PDSS-SR, BDI-II, HADS-Anx, MI, PAI-1, PAI-2, the number of symptoms and the TCQ. Significant correlations with the effect size of PAI-2 are found with pre-treatment scores on PAI-1, PAI-2 and the TCQ. Finally, a significant correlation was found between the effect size of PAI-3 and the pretreatment scores on PAI-3.

Table 2

Pearson correlation between pre-treatment measurements and post-treatment effect size

	Effect size PDSS-SR		Effect size HADS		Effect size BDI-II		Effect size MI		Effect size PAI-1		Effect size PAI-2		Effect size PAI-3	
	ρ	P	ρ	P	ρ	P	ρ	P	ρ	P	ρ	P	ρ	P
Demographic Variables														
Gender	-.043	.583	.024	.763	.087	.264	.059	.452	-.060	.443	-.030	.697	.079	.309
Age	**-.154**	.047	.018	.816	-.047	.545	.032	.682	-.078	.316	-.128	.100	.100	.202
Marital status	-.068	.387	**-.154**	.048	-.033	.669	-.002	.976	-.062	.429	-.051	.510	.053	.501
Years of education	.117	.134	-.024	.763	-.066	.400	-.121	.120	.019	.808	-.027	.725	.028	.718
Educational level	.132	.090	**-.156**	.045	-.072	.360	-.132	.090	-.003	.972	-.034	.660	.021	.791
Degree of Severity at intake														
PDSS-SR intake	**.576**	.000	**.180**	.021	.134	.088	.134	.087	**.206**	.008	.052	.509	-.020	.798
BDI-II intake	.082	.296	**.161**	.038	**.439**	.000	**.240**	.002	**.173**	.026	.046	.557	.066	.396
HADS-Anx intake	.115	.139	**.524**	.000	**.239**	.002	**.193**	.013	**.193**	.013	.109	.161	-.025	.744
MI intake	.031	.688	.146	.060	.114	.145	**.521**	.000	**.159**	.041	.077	.325	.015	.849
PAI-1 intake	.121	.122	**.229**	.003	**.346**	.000	**.310**	.000	**.494**	.000	**.169**	.029	.081	.298
PAI-2 intake	.083	.286	.125	.109	**.229**	.003	**.219**	.005	**.227**	.003	**.514**	.000	.021	.790
PAI-3 intake	-.073	.349	.004	.963	.065	.402	.061	.438	.000	1.000	-.004	.961	**.331**	.000
Subtype generalized social phobia	.061	.439	.078	.326	**.175**	.026	.071	.371	.012	.882	-.044	.580	.101	.201
Generalized anxiety disorder	.046	.557	.038	.633	.008	.918	**.163**	.037	-.009	.908	-.108	.169	-.020	.795
Number of symptoms	.093	.235	**.327**	.000	**.281**	.000	**.175**	.025	**.214**	.006	.128	.102	.005	.947
TiC-P	-.131	.094	-.071	.361	**-.212**	.006	-.058	.457	-.096	.218	-.094	.227	-.084	.283
Personal variables														
TCQ	.047	.548	**.158**	.042	.049	.535	.130	.096	**.188**	.015	**.160**	.039	.108	.167
Mastery intake	.091	.245	-.019	.812	-.058	.456	.006	.938	.047	.548	-.017	.831	.056	.471

Notes: Marital status: 0 = married/living together, 1 = single, divorced, widowed, other. PDSS-SR = Panic Disorder Severity Scale-Self Report; BDI-II = Beck Depression Inventory-second edition; HADS-Anx = Hospital Anxiety and Depression Scale, subscale Anxiety; MI = Mobility Inventory; PAI-1 = Panic Appraisal Inventory, subscale anticipation; PAI-2 = Panic Appraisal Inventory, subscale consequences; PAI-3 = Panic Appraisal Inventory, subscale coping; Number of symptoms = number of symptoms during a panic attack; TiC-P = Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness; TCQ = Treatment Credibility Questionnaire; Mastery = Mastery-scale.

Note: The PAI-3 scale has been converted: a lower score indicates better coping with panic.

Bold: Correlation is significant at the 0.05 level (2.tailed).

All significant correlations were used to conduct multiple linear regression analyses with forced entry for each of the outcome measures. The results are shown in **Table 3**. The multiple linear regression analyses for the primary outcome measure PDSS-SR showed a significant predictive value for the pre-treatment score on PDSS-SR. Pre-treatment scores that are significantly predictive for HADS outcome measures are pre-treatment scores on the HADS-Anx and the TCQ. Post-treatment BDI-II outcome was significantly predicted by pre-treatment scores on BDI-II and number of symptoms. The only measure significantly predicting post-treatment MI outcome is pre-treatment MI. More significant predictive values are found for PAI-1: MI, PAI-1 and the TCQ. Significant predictive values for PAI-2 are found in pre-treatment scores on PAI-2 and TCQ. The significant predictive value for PAI-3 is pre-treatment scores on PAI-3. Initial symptom severity is significantly predictive for each corresponding outcome measure. Treatment credibility is significantly predictive for post-treatment effect sizes of HADS-Anx, PAI-1 and PAI-2. Another notable fact is that the total amount of explained variance is relatively similar for each of the outcome measures.

Additionally, regression analyses with marginally significant values up to a $P<.2$ level found in the Pearson correlations were done. The results showed little difference with Table 2. Two additional significant predictive values are found: PAI-2 post-treatment is then additionally significantly predicted by generalized anxiety disorder (B=-.351, SE B=.165, β=.094) and PAI-3 is then additionally significantly predicted by the TCQ (B=.029, SE B=.013, β=.161). Because of the little difference between using only significant correlations and both significant correlations and tendencies, this table was not displayed.

Table 3

Multiple linear regression analyses of pre-treatment factors associated with post-treatment effect sizes

	PDSS-SR				HADS				BDI				MI				PAI-1				PAI-2				PAI-3			
	B	SE *B*	β	R^2	*B*	SE *B*	β	R^2	*B*	SE *B*	β	R^2	*B*	SE *B*	β	R^2	*B*	SE *B*	β	R^2	*B*	SE *B*	β	R^2	*B*	SE *B*	β	R^2
Demographic variables				**.024**				**.052**				-				-				-				-				-
Age	-.009	.006	-.097		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-	
Marital status	-	-	-		-.251	.148	-.111		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-	
Years of education	-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-	
Educational level	-	-	-		-.021	.045	-.033		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-	
Degree of severity				**.341**				**.326**				**.262**				**.272**				**.283**				**.274**				**.110**
PDSS-SR	.210	.024	.566*		-.006	.023	-.019		-	-	-		-	-	-		.013	.019	.053		-	-	-		-	-	-	
HADS-Anx	-	-	-		.147	.022	.583*		-.026	.020	-.122		.000	.015	-.005		-.011	.019	-.052		-	-	-		-	-	-	
BDI-II	-	-	-		-.013	.010	-.109		.037	.010	.367*		.004	.007	.052		-.007	.009	-.074		-	-	-		-	-	-	
MI	-	-	-		-	-	-						.458	.079	.498*		-.239	.096	-.206*		-	-	-		-	-	-	
PAI-1	-	-	-		-.003	.004	-.059		.003	.004	.072		.000	.003	-.024		.027	.004	.629*		-.007	.004	-.135		-	-	-	
PAI-2	-	-	-		-	-	-		.000	.004	-.019		-.000	.003	-.015		.001	.004	.025		.035	.005	.584*		-	-	-	
PAI-3	-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		.017	.004	.331*	
Generalized anxiety disorder	-	-	-		-	-	-		-	-	-		.087	.117	.054		-	-	-		-	-	-		-	-	-	
Number of symptoms	-	-	-		.038	.036	.082		.070	.033	.177*		.012	.025	.038		.006	.030	.016		-	-	-		-	-	-	
Subtype generalized social phobia	-	-	-		-	-	-		.248	.154	.115		-	-	-		-	-	-		-	-	-		-	-	-	
TiC-P	-	-	-		-	-	-		.000	.000	.133		-	-	-		-	-	-		-	-	-		-	-	-	
Personal variables				-				**.352**				**.262**				-				**.306**				**.306**				-
TCQ	-	-	-		.029	.012	.166*		.005	.011	.030		-	-	-		.023	.010	.154*		.032	.012	.181*		-	-	-	
Mastery	-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-	

* =significant at a level of <.05

Notes: Marital status: 0 = married/living together, 1 = single, divorced, widowed, other. PDSS-SR = Panic Disorder Severity Scale-Self Report; BDI-II = Beck Depression Inventory-second edition; HADS-Anx = Hospital Anxiety and Depression Scale, subscale Anxiety; MI = Mobility Inventory; PAI-1 = Panic Appraisal Inventory, subscale anticipation; PAI-2 = Panic Appraisal Inventory, subscale consequences; PAI-3 = Panic Appraisal Inventory, subscale coping; Number of symptoms = number of symptoms during a panic attack; TiC-P = Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness; TCQ = Treatment Credibility Questionnaire; Mastery = Mastery-scale.

Note: The PAI-3 scale has been converted: a lower score indicates better coping with panic.

DISCUSSION

Main findings

The aim of this study was to investigate the predictive variables of treatment outcome of a preventive and early intervention for panic symptoms, the 'Don't Panic' course (Meulenbeek, 2010). No demographic variables were found to be predictive for any of the treatment outcome effect sizes. Initial symptom severity seems to be highly predictive for each corresponding treatment outcome effect size. Participants' expectations of treatment effectiveness appear to be predictive for several treatment outcome effect sizes.

Comparison to prior work

No significant predictive values of demographic variables were found for any of the post-treatment effect sizes. These findings are in line with the results reported by Sharp & Power (1999). Such findings show the wide clinical utility of the intervention, in that its efficacy is not allegedly restricted by demographics, such as age or gender.

Pre-treatment initial symptom severity seems to be highly predictive of symptom severity effect sizes at the end of the course for each corresponding outcome measures. The amount of additional explained variance ranged from 11% to 32%. Participants suffering from more severe symptoms before the course, turned out to be more improved after the course. This is statistically logical: higher symptom severity leaves more space for improvement. Since one of the inclusion criteria was a PDSS-SR-score below the cut-off score of 13, there might have been participants with a low score on the PDSS-SR. Since there is little space to improve, for these participants the

course was just preventive. In this respect, the predictive value of pre-treatment initial symptom severity is no surprise.

The participants' expectations of treatment effectiveness (TCQ) also proved to be predictive for several treatment outcome measures. Higher expectations predicted higher treatment outcome effect sizes on the presence of anxiety states (HADS-Anx), perceived likelihood of panic occurrence (PAI-anticipation) and perceived negative consequences of panic occurrence (PAI-consequences). The amount of additional explained variance ranged from 0% to 3,2% for the different outcome measures. These percentages are not very high, but they are significant. Future participants with poor expectations of treatment effectiveness might benefit from more treatment information to enhance treatment credibility. For example, more information about the effectiveness of the course can be given during the interview with the psychologist from the Community Health Centre. When participants' expectations remain very low, they might need to look for a treatment in which they have more faith. Keijsers et al. (1994) found a significant association between moderate initial treatment motivation and poor treatment outcome. Participants who had lower expectations of the course may have had a lower treatment motivation. However, whether participants' expectations of treatment effectiveness and treatment motivation are two different concepts is unclear. More research into treatment motivation and treatment expectations in preventive and early interventions in PD is needed to obtain a clear picture of these two concepts.

Limitations

There are several limitations the present study had to cope with. First, the decision was made to use the data of the completers only. No statements can be made about the people in the target

population who did not sign up for the course or those who didn't finish the course for whatever reasons. On some aspects, completers may differ from non-completers. Second, the results may be biased if participants in the study differed from people in the target population that did not participate in the course. Third, some of the instruments differ from the instrumentation used in other studies (e.g. TCQ). This makes it more difficult to compare the results to prior research. Finally, motivation may be an important concept that was not measured.

Future research

This study was the first to examine predictive variables for a preventive and early intervention in subthreshold PD. More research is needed to confirm the results before general conclusions can be drawn. Furthermore, motivation seems to be an important concept in predicting treatment outcome. Finally, future research into preventive and early interventions should include motivation as a pre-treatment measurement.

Conclusion

In conclusion, only initial symptom severity appears to be a consistent significant predictor of treatment outcome effect sizes. Because other variables are not, the 'Don't Panic' course appears to be suitable for a broad target population.

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