# Prediction of 6-yr symptom course trajectories of anxiety disorders by diagnostic, clinical and psychological variables

Philip Spinhoven (PhD) [a,*], Neeltje Batelaan (PhD) [b], Didi Rhebergen (PhD) [b], Anton van Balkom (PhD) [b], Robert Schoevers (PhD) [c], Brenda W. Penninx (PhD) [b]

[a] Institute of Psychology, Leiden University and Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands
[b] Department of Psychiatry/EMGO+ Institute, VU University Medical Center, Amsterdam, The Netherlands
[c] Department of Psychiatry, University Medical Center Groningen, Groningen, The Netherlands

## ARTICLE INFO

## ABSTRACT

This study aimed to identify course trajectories of anxiety disorder using a data-driven method and to determine the incremental predictive value of clinical and psychological variables over and above diagnostic categories. 703 patients with DSM-IV panic disorder with or without agoraphobia, agoraphobia, social phobia, or generalized anxiety disorder were selected from a prospective cohort study. Latent Growth Mixture Modeling was conducted, based on symptoms of anxiety and avoidance as assessed with the Life Chart Interview covering a 6-year time period. In 44% of the participants symptoms of anxiety and avoidance improved, in 24% remained stable, in 25% slightly increased, and in 7% severely increased. Identified course trajectories were predicted by baseline DSM-IV anxiety categories, clinical variables (i.e., severity and duration and level of disability) and psychological predictors (i.e., neuroticism, extraversion, anxiety sensitivity, worry, and rumination). Clinical variables better predicted unfavorable course trajectories than psychological predictors, over and above diagnostic categories.

© 2016 Elsevier Ltd. All rights reserved.

## 1. Introduction

Anxiety disorders are among the most prevalent and disabling mental health problems (Lepine, 2002). Results of epidemiological and clinical studies generally show that anxiety disorders are characterized by a 'chronic' or 'waxing and waning' clinical course with relatively low rates of recovery and a relatively high probability of recurrence (Bruce et al., 2005; Penninx et al., 2011; Scholten et al., 2013). Given this variable course, longitudinal studies with a long follow-up period are needed to examine different course trajectories of anxiety in more detail as well as patient characteristics that may predict which patient will show a favorable or less favorable course over time. Available studies indicate that type of anxiety disorder may predict prognosis, with a more favorable prognosis for

panic disorder without agoraphobia (Bruce et al., 2005; Hendriks, Spijker, Licht, Beekman, & Penninx, 2013; Scholten et al., 2013) and a less favorable prognosis for social phobia and panic disorder with agoraphobia (Hendriks et al., 2013) and to a lesser extent for generalized anxiety disorder (Bruce et al., 2005). Besides the main anxiety diagnosis, predictors of a less favorable course include disease characteristics such as severity and duration of anxiety and avoidance (Batelaan, Rhebergen, Spinhoven, van Balkom, & Penninx, 2014), level of disability (Batelaan et al., 2014), and multiple (anxiety) disorders (Bruce et al., 2005).

There is an absence of studies investigating whether psychological variables are also predictive of course of anxiety in already anxiety-disordered individuals, and whether these are useful in predicting course of anxiety over and above clinical and diagnostic characteristics. This is striking, as a large body of empirical studies indicates that psychological factors such as the personality traits of neuroticism and extraversion (for a review, see Kotov, Gamez, Schmidt, & Watson, 2010), pathological worry (for a review, see Olatunji, Wolitzky-Taylor, Sawchuk, & Ciesielski, 2010), rumination (for a review, see Olatunji, Naragon-Gainey, & Wolitzky-Taylor, 2013), and anxiety sensitivity (for a review, see Olatunji & Wolitzky-Taylor, 2009) are associated with presence of

* Corresponding author at: Leiden University, Institute of Psychology, Wassenaarseweg 52, 2333 AK Leiden, The Netherlands.
  *E-mail addresses:* spinhoven@fsw.leidenuniv.nl (P. Spinhoven),
n.batelaan@ggzingeest.nl (N. Batelaan), d.rhebergen@ggzingeest.nl (D. Rhebergen),
t.balkom@ggzingeest.nl (A. van Balkom), r.a.schoevers@umcg.nl (R. Schoevers),
b.penninx@ggzingeest.nl (B.W. Penninx).

anxiety disorders. As can be concluded on the basis of these reviews, most studies up to date are cross-sectional, precluding causal inferences, and longitudinal studies on predicting the persistence of anxiety disorders are rare. Available longitudinal studies mainly focused on the prediction of onset of anxiety suggesting that most of these psychological characteristics may be implicated in the onset of anxiety disorders (Kotov et al., 2010; Olatunji et al., 2010, 2013; Olatunji & Wolitzky-Taylor, 2009). Studies of psychological risk factors for the course of anxiety are needed to determine whether these risk factors for onset are also risk factors for persistence of anxiety. This is relevant from a scientific as well as a clinical point of view, as such characteristics may be amenable by specific interventions (e.g. focusing on anxiety sensitivity) and may therefore guide more personalized treatment approaches.

Most available longitudinal studies on anxiety disorders used a variable-centered approach examining the relative contribution that variables make in predicting future presence or absence of disorders based on DSM-categories. However, in clinical practice we are often interested in the possible existence of subgroups with different course trajectories as this allows to tailor treatment according to prognosis. Person-centered data-driven approaches such as growth mixture modeling provide a framework for post-hoc identification of multiple unobserved sub-populations, description of group differences in change and examination of indicators of group membership (Jung & Wickrama, 2008). Up till now, only a few studies have examined the course trajectories of anxiety and avoidance symptomatology and its indicators as identified by such data-driven methods. Most studies examined symptoms of depression and anxiety combined (Colman, Ploubidis, Wadsworth, Jones, & Croudace, 2007; Olino, Klein, Lewinsohn, Rohde, & Seeley, 2010) or examined different age groups in the general population (Broeren, Muris, Diamantopoulou, & Baker, 2013; Duchesne, Vitaro, Larose, & Tremblay, 2008; Feng, Shaw, & Silk, 2008; Morin et al., 2011).

We previously reported on the 2-year course trajectories of anxiety and avoidance symptoms in adults with DSM-defined anxiety disorders. This study identified a class with enduring minimal symptoms and a moderately severe and severe chronic class of which the symptoms tended to improve during the 2-year follow-up (Batelaan et al., 2014). Remarkably, no course trajectory showed worsening of symptoms over time. Given the presumed course of anxiety disorders with relatively low rates of recovery and a relatively high probability of recurrence, a much longer follow-up period may be necessary to observe more unfavorable course trajectories after a period of symptom stabilization or even symptom improvement. Moreover, although short-term course trajectories were predicted by severity and duration of anxiety and level of disability on top of DSM-categories, short-term trajectories may be more easy to predict and it remains to be established whether the same variables are also predictive of long-term course trajectories. Finally, the role of psychological variables in predicting course trajectories was not examined in this or other previous studies. As we now have longitudinal data on a 6-year follow-up period, we are able to study possibly more diverging course trajectories of anxiety during a longer follow-up period into more detail while also studying the predictive validity of psychological variables for persistence of anxiety in addition to diagnostic and clinical variables.

In conclusion, the aim of the present study was two-fold: (a) to identify clinically relevant 6-year course trajectories of persons with an anxiety disorder and their relation with diagnostic categories; and (b) to examine whether psychological (i.e., neuroticism, extraversion, anxiety sensitivity, worry and rumination) and clinical (i.e. severity, duration, and functioning) variables are predictive of course trajectories, also after taking diagnostic categories into account.

## 2. Material and methods

### 2.1. Study sample

The Netherlands Study of Depression and Anxiety (NESDA) is designed to investigate the course and consequences of the most common depressive and anxiety disorders. It is a multi-site naturalistic cohort study of adults (18–65 years) recruited from the general population, general practices, and mental health organizations. The method of recruitment was extensively described elsewhere (Penninx et al., 2008). The study protocol was approved by the Ethical Review Board of all participating institutes and written informed consent was obtained from all respondents. For the present analysis, we selected 1101 respondents from the NESDA baseline assessment (T0) with a 1-month recency diagnosis of Panic Disorder with Agoraphobia (PD+), Panic Disorder without Agoraphobia (PD-), Agoraphobia (Ag), Social Phobia (SP), or Generalized Anxiety Disorder (GAD). Of these, 907 (82.2%) were reassessed after two years (T2), 826 (75.0%) after four years (T4) and 754 (68.5%) after six year of follow-up (T6). Non-response at T6 was inversely associated with years of education ($p < 0.001$) and positively with severity of anxiety ($p < 0.001$), avoidance ($p < 0.001$), and depression ($p < 0.001$) and level of neuroticism ($p < 0.01$) at baseline. The size of the differences, however, was small (Cohen's d larger than 0.2 but smaller then 0.5). Non-response was not associated with gender, age, presence of a particular anxiety disorder, anxiety sensitivity, worry and rumination. The present study sample consisted of the 713 respondents who completed the Life Chart Interview (LCI) at T2, T4 and T6. Of these 66.5% were female, the mean age was 42.0 years (SD 12.2), the mean number of years of education was 11.9 years (SD 3.2), and 65.1% had a partner. With regard to baseline one-month recency psychiatric status, 49.8% had SP, 30.3% PD+, 14.7% PD-, 14.0% Ag, and 34.9% GAD. Of the participants 64.8% had one, 26.6% had two, and 8.6% had three anxiety disorders.

### 2.2. Measurements

#### 2.2.1. Type of anxiety disorder

One-month recency anxiety disorders (PD+, PD-, Ag, SP, GAD) at T0 and 6-month recency anxiety disorders at T2, T4 and T6 were established using the Composite Interview Diagnostic Instrument (CIDI) version 2.1, according to DSM-IV criteria. The CIDI is a structured interview with acceptable reliability and validity (Andrews & Peters, 1998; Wittchen, 1994). It was administered at baseline and the two-, four- and 6-year follow-up assessments (T0, T2, T4 and T6) by more than 40 research assistants, including psychologists, nurses, or residents in psychiatry. Research assistants received one week of training by the fieldwork coordinator, and were certified to conduct assessments following approval of audiotapes of at least two complete interviews. Question wording and probing behavior of interviewers were constantly monitored by checking a random selection of about 10% of all taped interviews. In addition, a continuous monitoring system of interviewer variances and interviewer-specific item-nonresponse was maintained through computer analyses in SPSS software.

#### 2.2.2. Course of anxiety and avoidance symptoms

Data on presence of anxiety and avoidance symptoms were derived from the Life Chart Interview (LCI; Lyketsos, Nestadt, Cwi, Heithoff, & Eaton, 1994). The LCI was assessed by a trained interviewer at T0, T2, T4 and T6. Similar instruments show a good test-retest reliability for time periods varying from months (Keller et al., 1983; Keller et al., 1987) to 5 years (Freedman, Thornton, Camburn, Alwin, & Young-Demarco, 1988) suggesting that recall of symptoms is accurate for the three time spans of 2 years as used in the present study. Because self-generated personal, and affec-