Predictors of outcome in outpatients with anxiety disorders: The Leiden routine outcome monitoring study

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ABSTRACT

Little is known about the predictors of outcome in anxiety disorders in naturalistic outpatient settings. We analyzed 2-year follow-up data collected through Routine Outcome Monitoring (ROM) in a naturalistic sample of 917 outpatients in psychiatric specialty care in order to identify factors predicting outcome. We included patients with panic disorder with or without agoraphobia, agoraphobia without panic, social phobia, or generalized anxiety disorder. Main findings from Cox regression analyses demonstrated that several socio-demographic variables (having a non-Dutch ethnicity [HR = 0.71)], not having a daily occupation [HR = 0.76]) and clinical factors (having a diagnosis of agoraphobia [HR = 0.67], high affective lability [HR = 0.80] and behavior problems [HR = 0.84]) decreased chances of response (defined as 50% reduction of anxiety severity) over the period of two years. Living with family had a protective predictive value [HR = 1.41]. These results may imply that factors that could be thought to limit societal participation, are associated with elevated risk of poor outcome. A comprehensive ROM screening process at intake may aid clinicians in the identification of patients at risk of chronicity.

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1. Introduction

Anxiety disorders are highly prevalent (Wittchen et al., 2011) and are associated with marked functional impairment, high disease burden, substantial costs (Gustavsson et al., 2010), and a chronic course (Angst and Vollrath, 1991; Baldwin et al., 2010; Penninx et al., 2011). The manifesto for a European anxiety disorders network (Baldwin et al., 2010) states that, although psychological and pharmacological treatment have been proven effective in (randomized) clinical trials (RCT), for a substantial number of patients in clinical practice they do not translate into good outcome. Therefore, studies on predictors of response in naturalistic settings need to be conducted (Baldwin et al., 2010; Rothwell, 2005).

Previous studies have focused on various socio-demographic predictors of outcome of anxiety disorders. Different studies failed to demonstrate an association with gender (Tyrer et al., 2004; Yonkers et al., 2003; Serretti et al., 2009). Older age was associated with longer time to remission in treated as well as untreated panic disorder with or without agoraphobia (PD/A), agoraphobia without panic (AP), social phobia (SP), generalized anxiety disorder (GAD) and/or depression (MDD) (Penninx et al., 2011). Conversely, older age was associated with lower severity at one-year follow-up and a steeper decline in anxiety over time in subjects with PD/A and GAD but not in SP (Ramsawh et al., 2009). Others found no predictive value of age (Chavira et al., 2009; Van Ameringen et al., 2004; Beutel et al., 2011; Beard et al., 2010; Serretti et al., 2009). Additional socio-demographic factors that have been linked to poor outcome in anxiety disorders are: lower education-level (Ramsawh et al., 2009), and being unemployed and having low socio-economic status in PD/A (Roy-Byrne et al., 2003). Finally, although no association with ethnicity has been established, results do render further research necessary (Serretti et al., 2009).

Besides socio-demographic characteristics, several clinical factors have been studied in relation to outcome in anxiety disorders. First of all, in a sample diagnosed with GAD, SP and/or PD/A, patients with SP were least likely to have recovered at 12-year follow-up (Bruce et al., 2005). PD patients without agoraphobia were most likely to recover (Bruce et al., 2005; Roy-Byrne et al., 2003). In SP comorbid PD/A predicted poor outcome (Beard et al., 2010). In a

sample of inpatients diagnosed with PD/A, AP, SP, GAD, post-traumatic stress disorder (PTSD), obsessive compulsive disorder (OCD) and/or specific phobia (SPP), poor outcome was predicted by comorbid eating disorders and having multiple anxiety disorders (Beutel et al., 2011). The presence of comorbid MDD or alcohol abuse or dependence was associated with worse 12-year outcome in PD/A, SP and GAD (Bruce et al., 2005), although other studies showed no association with MDD (Roy-Byrne et al., 2003; Serretti et al., 2009; Beutel et al., 2011). Comorbid personality disorders or maladaptive personality traits have repeatedly been associated with poor outcome (Beutel et al., 2011; Ansell et al., 2011; Telch et al., 2011). Finally, early age of onset of the anxiety disorder predicted remission in treated as well as untreated PD/A, AP, SP, GAD and/or MDD (Penninx et al., 2011) and in SP in a Sertraline RCT (Van Ameringen et al., 2004). Although in PD/A, SP and GAD, early onset did not predict recovery while it did predict relapse in PD/A (Ramsawh et al., 2011).

However, generalizability of research findings to patients seen in everyday clinical practice is often limited (Hoertel et al., 2012). This lack of generalizability could result from the use of strict in— and exclusion criteria (Tyrer et al., 2004; Chavira et al., 2009; Roy-Byrne et al., 2003; Roy-Byrne et al., 2006; Van Ameringen et al., 2004), the focus on a single treatment modality (Telch et al., 2011; Van Ameringen et al., 2004; Serretti et al., 2009) and the focus on a narrowly defined patient group (Beutel et al., 2011; Chavira et al., 2009; Roy-Byrne et al., 2003; Roy-Byrne et al., 2006; Telch et al., 2011; Beard et al., 2010; Van Ameringen et al., 2004). Also, in observational cohort studies, high selectiveness may result from patients' motivation to participate in long-term follow-up studies stretching over a decade (Yonkers et al., 2003; Bruce et al., 2005; Ramsawh et al., 2009; Ramsawh et al., 2011; Beard et al., 2010).

Therefore, the present study aimed at establishing predictors of outcome in a large naturalistic cohort of outpatients suffering from anxiety disorders with a follow-up of up to 2 years. We used a broad range of 6 patient characteristics that have been gathered as part of standard clinical procedure as potential predictors, avoiding the previously discussed limitations to generalizability. Although in the Diagnostic and Statistical Manual of Mental Disorders fourth edition-text revision (DSM-IV-TR), the category of anxiety disorders comprises PD/A, AP, SP, GAD, PTSD, SPP, OCD and acute stress disorder; marked differences exist with regard to etiology, expression and clinical course between PD/A, AP, SP and GAD on the one hand, and PTSD, SPP, OCD and acute stress disorder on the other (Friedman et al., 2011; Stein et al., 2010; Lebeau et al., 2010). Therefore, following a common approach (Penninx et al., 2011; Bruce et al., 2005; Ramsawh et al., 2009; Ramsawh et al., 2011), this study focused primarily on predictors of outcome in patients diagnosed with PD/A, AP, SP and/or GAD.

2. Method

2.1. Routine outcome monitoring

As part of routine practice at the facilities involved in this study, all patients were administered an extensive battery of self-report and observer-rated measures at intake and at follow-up, every 3—4 months of treatment. This procedure is known as Routine Outcome Monitoring (ROM) and it continues for as long as the patient is being treated. Therefore the total number of assessments per patient varies as it depends on the duration of treatment. A more extensive description can be found in De Beurs et al. (de Beurs et al., 2011). Both generic and disorder-specific questionnaires were administered by formally trained psychiatric nurses and through computerized self-report, supervised by trained psychiatric nurses. This computerized administration prevents missing data within

questionnaires as item-completion is necessary for progression to the next item (de Beurs et al., 2011). Inter-rater reliability in a small sample of research nurses on several questionnaires has been tested and was within acceptable range (Cohen's $\kappa = 0.55-0.73$) (de Beurs et al., 2011). The primary goal of this data-collection is to inform both clinicians and patients. An estimated average of 80% of all patients is assessed at intake (van Noorden et al., 2012; Zitman, 2012). Data were anonymized and their use in scientific research was approved by the Ethical Review Board at the Leiden University Medical Centre (LUMC).

2.2. Patients and procedure

Subjects were outpatients referred to Rivierduinen, a regional mental healthcare provider, or the psychiatry department of the LUMC between March 2004 and November 2009. To allow two years of follow-up for all patients, follow-up data were collected until the end of November 2011. Inclusion criteria held that patients must be aged between 18 and 65, have adequate command of the Dutch language and meet DSM-IV-TR diagnostic criteria for one or more of the following disorders: PD/A, AP, SP or GAD. The patient population from which we drew our sample contained patients diagnosed with mood- and somatoform- as well as anxiety disorders, therefore, a risk of overdiagnosing has been suggested when using a semi-structured interview in a clinical sample (Zimmerman and Chelminski, 2003). Also, our dataset did not include clinical diagnoses (i.e. diagnoses made by treating psychiatrist). We therefore filtered out patients who did meet the criteria for anxiety diagnosis but were unlikely to have been treated for anxiety, by setting a criterion of moderate to severe baseline anxiety scores. Moderate to severe baseline severity was defined as ≥ 10.38 on the Brief Anxiety Scale (BAS) (Tyrer et al., 1984), equaling the average BAS score in a group of general practice patients diagnosed with anxiety disorders (Tyrer et al., 1984), and ≥ 6 on the Brief Symptom Inventory-12 item version (BSI-12), with scores <6 signifying no to mild anxiety (Roy-Byrne et al., 2010). All patients received standard outpatient care, consisting of psychotherapy, pharmacotherapy or combination therapy, based on a stepped care model and in concordance with Dutch evidence-based treatment guidelines (van Fenema et al., 2012). Absence of follow-up assessments and missing data (resulting from the incidental failure to administer complete questionnaires), served as exclusion criteria.

3. Measures

3.1. Predictors of 2-year outcome

Besides patients' age and gender, a wide range of demographic variables was ascertained. Marital status was categorized as 'married or cohabiting' versus 'being unmarried and living without a partner.' Dutch ethnicity was assumed when both the patient and the patient's parents were born in the Netherlands (excluding former Dutch colonies). Education was divided into three levels, 'low education' (no education, primary school until approximately 10th grade), 'medium education' (ranging from 11th grade through high school and community college) and 'high education' (college undergraduate/graduate and higher). Patients were asked about their daily routine, patients who were employed full-time or part-time, were taking care of children or were receiving education, were classified as 'having a daily occupation'. Patients who were unemployed, retired or on sick leave (without having any care giving responsibilities or receiving education), were classified as 'having no daily occupation'. Living situation was categorized as 'living independently with a partner and/or children', 'living independently alone,' and 'living with family.'