



## Empirical evidence of the effect of personality pathology on the outcome of panic disorder

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### ABSTRACT

**Background:** Treatment resistant disorders are a significant clinical problem. Impediments to good outcome need to be identified and addressed. Personality pathology has been hypothesized to be one such factor in panic disorder. There is no consensus as to the effects of personality pathology on the outcome of panic disorder. This study examined empirical evidence. The hypothesis was that personality pathology would cause poorer outcome of panic disorder.

**Methods:** A literature search was conducted that winnowed 2627 articles down to 27 based on 1) longitudinal design; 2) validated measures of personality; 3) validated outcome measures; and 4) the presence of effect size or data to calculate effect size. All effect sizes were translated into odds ratios (ORs) for ease of comparison.

**Results:** An overall median OR of 2.7 was found, indicating personality pathology negatively affected outcome. This finding persisted even when adjusted for baseline severity of illness. The effects were found for both clinical outcomes (OR = 2.7) and for social adjustment (OR = 2.9). There was a tendency for more dropouts in the personality pathology group. More highly structured drug therapy regimens and highly structured psychotherapy seemed to partially mitigate this outcome.

**Conclusion:** The negative effect of personality pathology was confirmed in well-designed longitudinal studies. This was not related to initial clinical severity. Clinical implications are that patients with personality pathology require the therapist to stick more closely to treatment protocols and to mitigate the tendency of these patients to drop out of treatment.

Panic disorder is a disorder of high prevalence that may affect as much as four percent of the population on a lifetime basis (Grant et al., 2006). In one study, as many as 50% of panic patients had a chronic course and notable disability as measured by the World Health Organization Disability Assessment Schedule II (WHODAS-II) (Hendriks et al., 2016). There is evidence that panic patients have a poorer quality of life and are at greater risk of work disability (Katerndahl and Realini, 1997). Unfortunately, as many as 50% of those treated with standard protocols fail to respond (Bandelow et al., 2008). To move forward, our field needs to improve its recognition and treatment of those who do not do as well with our current approaches. We need to understand the variables involved in an inadequate response and see if there are clues as to how we can improve our treatment in the presence of these variables. This report will examine one such variable for panic disorder—personality pathology—to determine if the empirical literature provides clues as to how we can improve our care.

Personality pathology has been reported to be associated with poor

outcome for many syndrome disorders (Reich and Green, 1991; Reich and Vasile, 1993). In depression, there is fairly strong evidence of personality pathology comorbidity causing poorer outcome (Newton-Howes et al., 2014a, 2014b). In the treatment of panic disorder, there is no consensus on how personality pathology is associated with outcome. Some findings find no effect of personality pathology (Dreessen et al., 1994) while others indicate a significant effect (Black et al., 1994a; Reich, 1988; Ansell et al., 2011a). Perhaps because the issue remains unresolved, some recent reviews on the treatment of panic disorder do not even mention the issue (Freire et al., 2016; Bandelow et al., 2015). If personality pathology is a prognostic factor in panic disorder it would be more relevant if it occurred frequently. A meta-analysis of 30 years of panic research indicates a comorbidity of approximately 50 per cent (Friborg et al., 2013), a high frequency.

How personality pathology affects outcome has not been determined by empirical studies. One possibility is that personality pathology affects the focus of the therapist. One study of treatment of

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panic noted the more on track therapist comments the better the outcome (Keefe et al., 2018). Another indicated that therapists adherence to the treatment plan was affected by a patient personality variable (aggression) (Boswell et al., 2013). It is possible that personality pathology would affect the focus on treatment and therefore the outcome.

In an attempt to clarify this issue, this systematic review examines empirical evidence of well-designed longitudinal and treatment studies of panic disorder with an aim to provide direction for clinicians and researchers.

## 1. Methods

The literature from 1980 until August 1, 2018 was searched using the PubMed, PsychInfo, and Index Medicus online databases. The key words used were: panic disorder, personality disorders, anxiety disorder, clinical course, predictors of treatment outcome, relapse and remission. While individual searches were conducted for the first three terms, additional searches were conducted for panic disorder, personality disorders, and anxiety disorder in combination with the remaining key phrases.

Initial searches resulted in a total of 2627 articles of possible relevance. These articles were run through a preliminary check of title and abstract to determine their relevance for further evaluation. This process yielded 562 articles.

The resulting 562 articles were then examined to identify those that met the following four criteria: 1) Panic disorder was diagnosed by a standardized method accepted in the literature as having validity: an example would be the Structured Clinical Interview for the DSM-IV Disorders (SCID); 2) Personality pathology was measured by a standardized, validated measure of personality: this could be a DSM measure, such as the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID II), or a Big Five personality measurement instrument using the Big Five personality factors, such as the NEO-PI, or another instrument that appeared to meet the validity requirements; 3) The study was longitudinal: for example, the study had beginning and ending measures separated by a period of time; and 4) The study contained well described outcome measures. This screening resulted in a total of 43 publications.

The remaining 43 articles were reviewed by one of the authors (JR) in consultation with the study statistician (KD) to determine those that included effect sizes, or had data that could be used to calculate an effect size, and whose effect sizes could be converted to a common effect size for comparison. This process resulted in 27 articles (See Table 1).

We examined the resulting reports to see if there was sufficient data supplied to allow us to perform a meta-analysis. The study statistician

**Table 1**  
Process of selection of articles for review.

Initial search terms: panic disorder, personality disorders, anxiety disorder, clinical course, predictors of treatment outcome, relapse, and remission. Possible relevant articles identified.
↓
2627 articles
Checked for relevance by examining title and abstract.
↓
562 articles
Articles screened for: 1) Panic disorder standardized diagnosis (62 articles eliminated); 2) Personality pathology standardized measure (203 articles eliminated); 3) The study was longitudinal (150 articles eliminated); and 4) Well described outcome measures (55 articles eliminated).
↓
43 articles
Articles screened for presence of effect size or data that could calculate an effect size.
In two, the personality measures could not be used to assess longitudinal outcome; in twelve, an effect measure could not be found or calculated.
↓
27 articles

(KD) determined that there was not, so we decided to compare effect sizes.

As the most common measure of effect was the odds ratio, it was decided to convert the other effect sizes, such as R or R squared, Cohen's d, eta squared or AUC, to that metric (Borenstein et al., 2009; Ruscio, 2008). If the article provided means and standard deviations for significant findings, we calculated Cohen's d, which we then used to calculate an equivalent odds ratio (OR). If the article provided the raw numbers that allowed us to directly calculate an OR, we performed that calculation. (In one instance, when performing that OR calculation, there was a cell with a value of 0. In that case, we added 1 to each cell to allow an odds ratio calculation.) When calculating the OR we used unadjusted numbers except in the case where the article had performed calculations adjusting for baseline symptom severity. The resulting ORs were then compared for different categories using median values.

An estimate of the quality of the studies was performed using the method of Jadad et al. (1996)

In order to get some idea of how personality pathology varied in the different studies we calculated the average prevalence of DSM personality clusters A, B and C where the data was available.

## 2. Results

After screening, we were left with 27 studies that met our criteria for inclusion in the study. Of the 45 comparisons in the 27 studies, all but 3 indicated that the presence of personality pathology resulted in poorer outcome. The overall median odds ratio was 2.7. This median odds ratio did not change when we restricted studies to those that adjusted for the initial level of symptom severity between personality and non-personality disordered groups (OR = 2.7), although, when examining studies that did not adjust for baseline severity, the median OR was a bit higher at 3.1. When we restricted the findings to clinical outcomes (measures such as Hamilton Anxiety, panic frequency or clinical global improvement), the median odds ratio was 2.7. When using the Social Adjustment Scale as an outcome, the median odds ratio was 2.9. Findings for outcomes with fewer data points, and therefore somewhat less reliability, the direction is the same; for personality cluster A, median odds ratio was 16.7; the median odds ratio for personality cluster B was 2.9; the median odds ratio for personality cluster C was 1.7; and for dropouts, the median odds ratio was 21.2. The overall study results can be found in Table 2 while the summary of findings can be found in Table 3.

Examining the quality of the studies by the method of Jadad et al. (1996) yielded an overall rating of 2.2 (sd = 1.3). This would place the studies in the quality range average to good. The quality of the drug studies was higher but not significantly different from the psychotherapy studies (Drug mean = 2.5, sd = 1.0; Psychotherapy mean = 1.7, sd = 1.4).

We were able to get prevalence data on the DSM personality disorder clusters from thirteen studies. The mean (Standard deviation) for the three clusters was; A 10% (6.0); B 15.5% (7.1); and C 34.5% (10.5). In nine of these studies the general prevalence was C greater than B which was greater than A. The other studies only varied minimally from this. There was no significant difference between the groups using psychotherapy and those using medications on these variables.

The total number of subjects in all studies was 2152. The number of subjects in the three studies that indicated personality predicted a positive outcome was 170. It should be noted that, in each of these three studies, the positive outcome only occurred in a subgroup. In each of these studies, one type of personality pathology was associated with a positive outcome while a second type of personality pathology was associated with a negative outcome. The number of subjects where their personality predicted only negative findings was 1982.

We also examined whether the type of intervention affected the findings. We separated the groups, where possible, into drug treatment only, psychotherapy treatment only, and no specific treatment. Drug

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