

The Impact of Personality Pathology on Treatment Outcome in Late-life Panic Disorder

Citation for published version (APA):

Gulpers, B., Voshaar, R. C. O., Kampman, M., Verhey, F., Van Alphen, S., & Hendriks, G.-J. (2020). The Impact of Personality Pathology on Treatment Outcome in Late-life Panic Disorder. *Journal of Psychiatric Practice*, 26(3), 164-174. <https://doi.org/10.1097/PRA.0000000000000472>

Document status and date:

Published: 01/05/2020

DOI:

[10.1097/PRA.0000000000000472](https://doi.org/10.1097/PRA.0000000000000472)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Research Article

The Impact of Personality Pathology on Treatment Outcome in Late-life Panic Disorder

Background: Comorbid personality disorders are assumed to negatively interfere with the treatment outcome of affective disorders. Data on late-life panic disorder remain unknown. We examined the association of personality pathology and treatment outcome related to age and treatment modality.

Methods: An observational study on the effectiveness of cognitive-behavioral therapy (CBT) for panic disorder with agoraphobia among patients 18 to 74 years of age and randomized controlled comparison of paroxetine and CBT in older patients (60 y of age or older) were performed. The diagnosis of panic disorder was confirmed by the Anxiety Disorder Interview Schedule-Revised (ADIS-IV) and personality features were assessed with the Personality Diagnostic Questionnaire. The impact of personality features on either agoraphobic cognitions (Agoraphobic Cognitions Questionnaire) or avoidance behavior (Mobility Inventory Avoidance Scale) was examined by multiple linear regression analyses adjusted for sex, level of education, duration of illness, comorbid psychopathology, and baseline severity. The interaction between personality and age was examined among those treated with CBT (n = 90); the interaction between personality and treatment modality was examined among the older subgroup (n = 34).

Results: Cluster B personality pathology (evaluated on the basis of either *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R)* or *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* criteria depending on the date of assessment) was negatively associated with outcomes of CBT in both younger and older adults with panic disorder and agoraphobia. Older adults with a higher number of features of any personality pathology or cluster A pathology had worse treatment outcomes when treated with paroxetine compared with CBT.

Conclusions: Cluster B pathology had a detrimental effect on CBT treatment outcome for panic disorder in both age groups. In late-life

panic disorder with comorbid personality pathology, CBT may be preferred over treatment with paroxetine.

(*Journal of Psychiatric Practice* 2020;26;164–174)

KEY WORDS: panic disorder, agoraphobia, personality disorders, elderly, treatment outcome

Research on late-life anxiety disorders is scarce despite high prevalence rates, and it is predominantly focussed on generalized anxiety disorder or mixed anxiety.¹ Hardly any empirical findings concerning panic disorder in later life are available, even though the 6-month prevalence in older patients is estimated to be between 1% and 2%.^{1,2}

GULPERS: MET ggz Maastricht, Regional Institute for Mental Health Care in Outpatients, and School for Mental Health and Neuroscience (MHeNS)/Alzheimer Centre Limburg and Department of Psychiatry and Psychology/MUMC, Maastricht University Medical Center, Maastricht, The Netherlands; OUDE VOSHAAR: Center for Psychiatry & Interdisciplinary Center of Psychopathology of Emotion regulation (ICPE), University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; KAMPMAN and HENDRIKS: Pro Persona Institute for Integrated Mental Health Care, Overwaal Centre of Expertise for Anxiety Disorders, OCD and PTSD, and Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, The Netherlands; VERHEY: School for Mental Health and Neuroscience (MHeNS)/Alzheimer Centre Limburg and Department of Psychiatry and Psychology/MUMC, Maastricht University Medical Center, Maastricht, The Netherlands; VAN ALPHEN: Department of Clinical & Life Span Psychology, Vrije Universiteit Brussel (VUB), Brussels, Belgium and Department of Old Age Psychiatry, Mondriaan Hospital, Heerlen-Maastricht, The Netherlands

Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

Please send correspondence to: Bernice Gulpers, MD, PhD, Parallelweg 45-47, Maastricht 6221BD, The Netherlands (e-mail: bgulpers.uop@gmail.com).

ACKNOWLEDGMENTS: The authors thank Dr Rob van den Brink, a senior researcher at the Rob Giel Research Institute of the University of Groningen, for performing the matching of older with younger patients.

The authors declare no conflicts of interest.

DOI: 10.1097/PRA.0000000000000472

Panic disorder is associated with a significantly lower quality of life and pervasive social and health consequences that seem to be similar to or even greater than those associated with major depression.^{3,4} In older adults with anxiety disorders, the effectiveness of cognitive-behavioral therapy (CBT) is generally lower than in younger adults with anxiety disorders,⁵ although this may not necessarily hold true for panic disorder.⁶

In clinical practice, treatment is often complicated by comorbid somatic and psychiatric conditions, which are often excluded when studying the effectiveness of CBT. Comorbid personality pathology is very prevalent in adults with panic disorder, with rates estimated to be between 40% and 65%.⁷ Most clinicians suppose that the presence of a personality disorder will have a negative impact on outcomes in the treatment of anxiety disorders due to several, underlying factors, such as poor adherence to the treatment regimen, problems in the therapeutic alliance, or poor motivation for treatment.⁸⁻¹⁰ Moreover, it has been suggested that panic disorder is often more severe when it occurs with comorbid personality pathology.¹¹ A recent systematic review found that personality pathology is associated with a negative treatment outcome for panic disorder in adults.¹² Data on the effect of personality disorders on treatment outcome in late-life panic disorder are unfortunately lacking.

To improve treatment for late-life panic disorder, it is important to identify predictors of treatment outcome, given that very few data on this question are available. Moreover, findings concerning predictors in adults cannot be generalized to older adults as, in general, the age of onset and the chronicity of symptoms will differ between older and younger patients and these factors may affect treatment outcome.¹³ To our knowledge, this is the first study to evaluate: (1) the impact of personality pathology on CBT outcome in younger versus older patients with panic disorder, and (2) the differential effect of personality pathology in treatment of late-life panic disorder with CBT or paroxetine.

METHODS

Patient Recruitment and Selection

This study was conducted on a consecutive series of patients with panic disorder with agoraphobia referred to a specialized outpatient anxiety clinic (Overwaal Centre of Expertise for Anxiety Disorders,

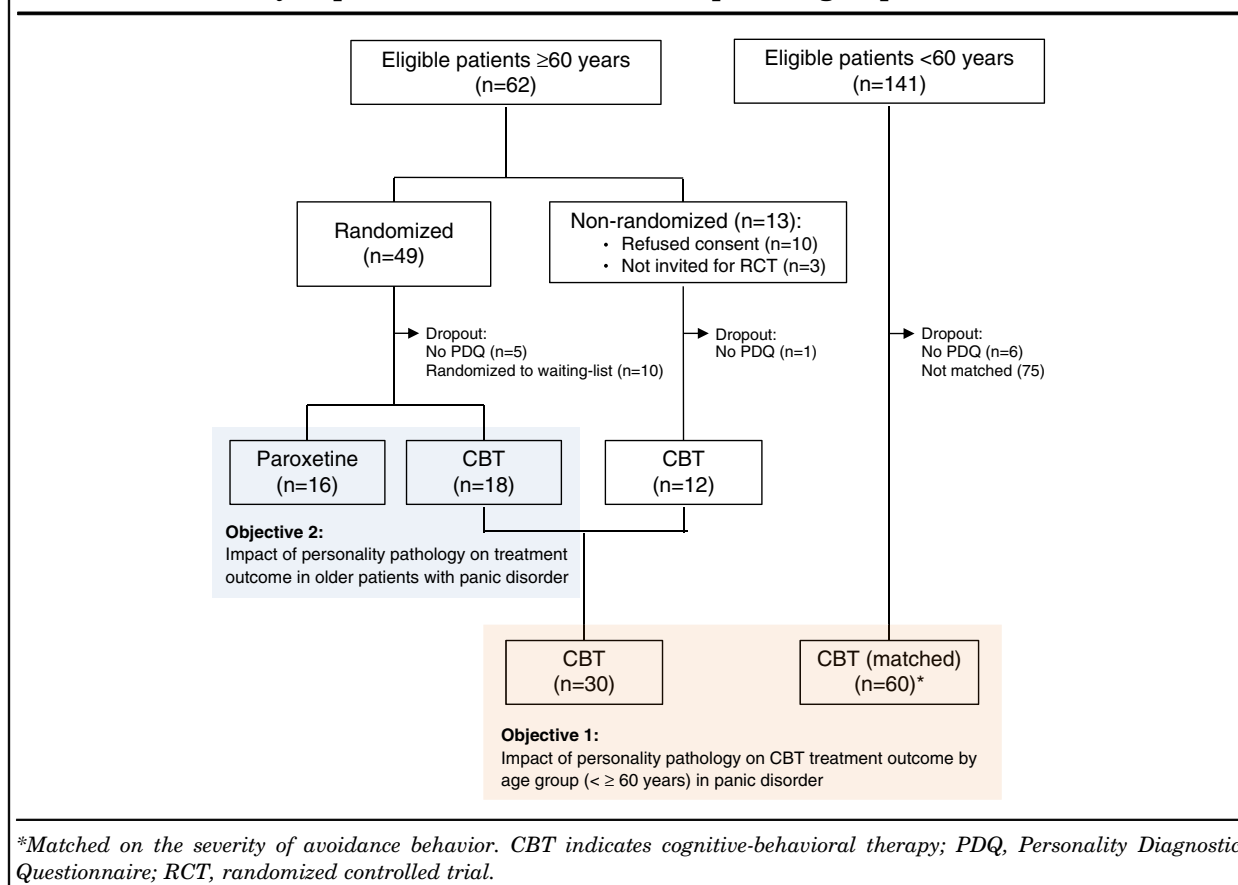
The Netherlands). Therefore, all patients were treated by the same team of professionals according to the same treatment protocols (in the case of CBT). For this study, we combined patients who had participated in 2 earlier studies.^{14,15} A previous study also combined these patients to address the effectiveness of CBT in older patients with panic disorder and compared the outcomes of older adults with younger patients.⁶ That study found that CBT appeared to be a feasible treatment option for older adults and that outcomes were similar and sometimes even superior to the outcomes in younger adults.⁶ The study presented here used data from those 2 earlier studies to specifically address whether personality features influence CBT treatment outcomes and whether the effect differs between older and younger adults. One study on consecutive treatment steps (Kampman et al¹⁴) was performed in 161 patients 18 through 65 years of age who had received CBT as their first treatment step. The other study (Hendriks et al¹⁵) was a randomized controlled trial evaluating CBT and paroxetine versus a waitlist control group in 49 patients 60 years of age or older. Older patients consented for the Hendriks and colleagues' trial who were not eligible for the study or who refused randomization were treated with their treatment of choice, which was without exception CBT, using the same protocol and measurements as those used for the patients participating in the 2 studies. All patients gave informed consent to participate in these studies.

In the study described here, older patients are defined as being 60 years of age or older. To enable a valid comparison between younger and older patients who received CBT, we combined older patients from the 2 previous studies, that is, those randomized to CBT as well as those who refused or were not offered randomization as they participated in the observational study. All older patients were thus treated with CBT as the initial treatment step in our clinic (Study Objective 1). Furthermore, as the number of younger patients greatly exceeded the number of older patients, we included 2 younger patients for each older patient matched on the severity of avoidance behavior, as the frequency of panic attacks is dependent on the severity of avoidance behavior.¹⁵ Matching was performed by an independent researcher who was not related to the study and was blind to the study purpose (see the Acknowledgments section).

To enable a valid comparison between older patients receiving paroxetine and older patients receiving CBT (Study Objective 2), only participants

PERSONALITY AND TREATMENT OF PANIC DISORDER

FIGURE 1. Summary of patient recruitment and comparison groups.



from the randomized controlled trial by Hendriks et al¹⁵ were included. Figure 1 provides a summary of the patient flow and a comparison of the composition of the groups.

The clinical diagnosis of panic disorder with agoraphobia was verified by experienced, licensed clinical psychologists or psychiatrists using the Dutch version of the Anxiety Disorders Interview Schedule-Revised (ADIS-IV). Exclusion criteria were as follows: (1) severe somatic illnesses that could interfere with the therapy; (2) current use of an antidepressant; (3) current psychological treatment; and (4) the presence of a primary psychiatric diagnosis of a psychotic, bipolar, or substance use disorder or dementia. Any comorbid psychiatric disorder (eg, other anxiety disorders, depression) was allowed as long as the primary diagnosis was panic disorder with agoraphobia. Patients who were taking benzodiazepines at baseline were asked to use a fixed dosage for the duration of

the protocolized treatment period. The patients completed various questionnaires before treatment and after treatment completion (ie, after 14 wk) (see below).⁶

Treatment

The majority of the patients (n = 171) were treated with manual-based CBT, consisting of 14 weekly sessions of 50 minutes. Treatment followed the Craske and Barlow protocol^{16,17} and included: (1) psychoeducation about panic, anxiety, and avoidance behavior; (2) relaxation techniques (applied relaxation); (3) interoceptive exposure; (4) cognitive therapy; and (5) in vivo exposure. Therapists were psychologists (MSc level) who had received extensive training at the clinic and were highly experienced with the CBT protocol for panic disorder with agoraphobia. They were supervised weekly by certified supervisors of the Dutch Association

for Behavioral and Cognitive Therapy to ensure adequate application of the CBT techniques and adherence to the protocol. No age-specific adaptations were made for the older adults.⁶ According to the randomization in the Hendricks et al¹⁵ study, 17 older adults were treated with paroxetine according to a fixed-dose schedule. The paroxetine protocol started with a daily dose of 10 mg, which was gradually increased to 40 mg in week 4. During this period, these patients were seen for 30-minute weekly consultations to monitor for any adverse events and to encourage patients to adhere to the treatment protocol. Between weeks 5 and 14, all of the patients attended five 30-minute medical consultations, which occurred once every 2 weeks, during which their questions were addressed and information about the expected effects and side effects of the treatment was provided.¹⁵

Personality Assessment

Personality pathology according to criteria in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) was measured at baseline with the Dutch version of the Personality Diagnostic Questionnaire (PDQ).^{18,19} The PDQ is a self-report questionnaire. Validation studies have shown that the PDQ is a screening instrument with a high sensitivity and a moderate specificity.²⁰ Because patients were recruited between 1997 and 2005, 2 versions of the PDQ were used: the PDQ-R (133 items), which is based on the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised (DSM-III-R) criteria, and the PDQ-4+ (99 items), which is based on the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR) criteria. The Dutch translations of the PDQ-R and the PDQ-4+ have been cross-validated.^{18,19}

Differences between the 2 versions of the PDQ can be explained by: (1) the specific personality disorders of which the features are assessed, (2) whether 1 or more questions are asked to assess the presence of a specific feature, and (3) differences between the personality features and cutoff scores in the DSM-III-R and DSM-IV-TR. We made the following adaptations to guarantee the comparability of both measures.

First, we analyzed only those personality disorders for which the concepts are sufficiently validated and are therefore still used in DSM-5. Therefore, we excluded features related to passive-aggressive, depressive, masochistic, and sadistic personality disorders. Second,

some personality features were assessed with the aid of 2 subitems in the PDQ-R of which only 1 needed to be present, whereas in the PDQ-4+ these 2 subitems were combined into 1 overall item, either by leaving out 1 subitem [done for 5/133 (3.8%) features] or by rephrasing both items. Where possible, the 2 subitems were recalculated to represent the corresponding items in the PDS-4+.

When these adaptations are taken into account and the same numbering is administered for both versions, the total number of items for the current personality disorders are 96 and 94 for the PDQ-R and PDQ-4+, respectively. This final difference could be explained by differences between the DSM-III-R and the DSM-IV-TR and are considered minimal.

Assessment of Treatment Outcomes

The primary outcome measure was agoraphobic avoidance as measured with the Dutch version of the Mobility Inventory Avoidance scale (MI-A).^{21,22} The MI-A has 3 subscales: avoidance when alone (MI-AAL), avoidance when accompanied (MI-AAC), and frequency of panic attacks (MI-PF).⁶ We used the 2 MI-A scales as avoidance has been shown to be a better predictor of outcome than panic attack frequency. A higher level of avoidance behavior generally results in less frequent panic attacks.^{23,24}

The secondary outcome measure was severity of agoraphobic cognitions as assessed with the Dutch adaptation of the Agoraphobic Cognitions Questionnaire (ACQ).^{22,25}

Both instruments use 5-point Likert-scales for rating the individual items. The MI-A, the ACQ, and their Dutch adaptations are frequently used in outcome studies of panic disorder treatment and have good test-retest reliability, high internal consistencies, and reasonable concurrent validity.^{6,21,22,25}

Statistical Analysis

Differences between the comparison groups at baseline (younger vs. older patients and older patients treated with paroxetine vs. older patients treated with CBT) were compared using the χ^2 test for categorical variables and the independent-samples *t* test for dimensional variables. The duration of illness was skewed; therefore, in all analyses, the natural log-transformed was used.

The impact of personality pathology (as measured by number of personality features) on treatment outcome

was studied by multiple linear regression analyses with study outcome (either avoidance behavior based on MI-A or agoraphobic cognitions based on the ACQ) as the dependent variable. Both bivariate and multivariate analyses are presented. Because the patient groups were rather small, we include the covariates (age, sex, level of education, duration of illness, and comorbid psychopathology in addition to baseline severity of either avoidance behavior or agoraphobic cognitions) in step 1 using a stepwise procedure, where the independent variable of interest (number of personality features) is included.

To evaluate for a differential effect of personality pathology by age, we tested the interaction of age by number of personality features when examining the impact of personality pathology on CBT treatment outcome (Objective 1). To evaluate for a differential effect of personality pathology by treatment modality, we tested the interaction of treatment modality (paroxetine vs. CBT) by personality pathology. In the case of significant interaction terms, stratified results are presented.

All analyses were conducted using SPSS, version 22.0. *P*-value <0.05 was considered significant.

RESULTS

Objective 1: Impact of Personality Pathology on CBT Outcome for Panic Disorder Across the Lifespan

Baseline Comparisons

As shown in Table 1, sociodemographic characteristics did not differ between the 2 age groups. With respect to psychopathology, the group of older adults had a significantly longer duration of illness as expected, fewer agoraphobic cognitions, and a comorbid personality disorder less often than their younger counterparts. The lower frequencies of personality disorders in older adults were explained by fewer cluster B personality disorders. The number of features of any personality pathology and cluster B pathology were lower in older adults compared with younger adults, whereas features of cluster C pathology were higher in older adults compared with younger adults.

Impact of Personality Pathology on CBT Outcome

None of the personality dimensions (total number of personality features and number of features of the 3 clusters) significantly interacted with age in the

multivariate analyses on predicting CBT outcome with respect to avoidance behavior (lowest *P* = 0.345) and to agoraphobic cognitions (lowest *P* = 0.175). Therefore, Table 2 presents the results for the younger and older age groups combined.

For the whole sample, a higher number of cluster B personality features was associated with a worse treatment outcome for avoidance behavior after CBT (*B* = 0.03, *SE* = 0.01, *P* = 0.005), although the effect size was low (β = 0.17). No effect of cluster B pathology on the treatment outcome for agoraphobic cognitions was found (*B* = 0.02, *SE* = 0.01, *P* = 0.168). Cluster A or cluster C pathology was not associated with treatment outcome for either avoidance behavior or agoraphobic cognitions (Table 2).

Objective 2: The Impact of Personality Pathology on Treatment for Late-life Panic Disorder With Either CBT or Paroxetine

Baseline Comparisons

Table 3 shows that there were no significant differences between the older adults receiving CBT and those receiving paroxetine at baseline.

Differential Effect of Personality Pathology on Treatment Outcome With CBT or Paroxetine

The interaction term of personality pathology by treatment modality by time was significant for avoidance behavior in the adjusted analyses for the number of features of any personality pathology and cluster A pathology (*P* = 0.028 and <0.001, respectively). Stratified analyses showed that the interaction between treatment modality and number of features of overall personality pathology could be explained by the trend for an increased level of personality pathology to be associated with worsened treatment outcome in those treated with paroxetine (*B* = 0.02, *SE* = 0.01, *P* = 0.116), but to be associated with improved treatment outcome in those treated with CBT (*B* = -0.02, *SE* = 0.01, *P* = 0.257), although these stratified analyses did not reach statistical significance. Furthermore, a higher number of cluster A features was significantly associated with a worse treatment outcome in those treated with paroxetine (*B* = 0.08, *SE* = 0.03, *P* = 0.019), and a significantly better treatment outcome in those treated with CBT (*B* = -0.09, *SE* = 0.03, *P* = 0.017). The effect sizes were small to medium with β 's ranging from 0.22 to 0.49 (Table 4).

PERSONALITY AND TREATMENT OF PANIC DISORDER

TABLE 1. Baseline Characteristics of Patients Receiving CBT by Age Group

<i>Characteristics</i>	<i>Expression</i>	<i>Patients Receiving CBT</i>		<i>Statistics</i>
		<i>< 60 y (n = 60)</i>	<i>≥ 60 y (n = 30)</i>	
Sociodemographic				
Age (y)	Mean (SD)	35.9 (11.1)	67.2 (4.8)	$t = -14.7, df = 88, P < 0.001$
Female sex	n (%)	39 (65)	21 (70)	$\chi^2 = 0.2, df = 1, P = 0.635$
Level of education				
Low	n (%)	16 (27)	11 (37)	$\chi^2 = 1.6, df = 2, P = 0.452$
Medium	n (%)	22 (37)	12 (40)	
High	n (%)	21 (36)	7 (23)	
Psychopathology:				
Duration of illness panic disorder (yr)	Median (IQR)	4.1 (8.2)	6.0 (18.6)	$t = -0.7, df = 88, P = 0.060^*$
Avoidance behavior (MI)	Mean (SD)	2.4 (0.9)	2.5 (1.0)	$t = -0.4, df = 88, P = 0.669$
Agoraphobic cognitions (ACQ)	Mean (SD)	2.1 (0.6)	1.6 (0.5)	$t = 4.2, df = 88, P < 0.001$
Comorbid psychiatric disorder	n (%)	23 (38)	8 (27)	$\chi^2 = 1.2, df = 1, P = 0.272$
Personality pathology				
Personality disorder present	n (%)	44 (73)	17 (57)	$\chi^2 = 7.8, df = 1, P = 0.005$
Cluster A	n (%)	20 (33)	9 (30)	$\chi^2 = 0.1, df = 1, P = 0.750$
Cluster B	n (%)	24 (40)	3 (10)	$\chi^2 = 8.6, df = 1, P = 0.003$
Cluster C	n (%)	33 (55)	11 (37)	$\chi^2 = 2.7, df = 1, P = 0.101$
Total number of personality features	Mean (SD)	27.4 (10.1)	17.7 (11.7)	$t = 4.1, df = 88, P < 0.001$
Cluster A features	Mean (SD)	6.0 (3.8)	4.9 (3.7)	$t = 1.3, df = 88, P = 0.201$
Cluster B features	Mean (SD)	9.4 (3.9)	8.9 (3.6)	$t = 5.5, df = 88, P < 0.001$
Cluster C features	Mean (SD)	4.8 (3.6)	6.3 (4.7)	$t = 2.9, df = 88, P = 0.005$

*The Student *t* test is based on normal log-transformed values.

ACQ indicates Agoraphobic Cognitions Questionnaire; CBT, cognitive-behavioral therapy; IQR, interquartile range; MI, Mobility Inventory for Agoraphobia.

The interaction term of personality pathology by treatment modality by time was not significant for all personality dimensions related to treatment outcome on agoraphobic cognitions (Table 4).

DISCUSSION

Main Findings

The impact of personality pathology on CBT treatment outcome was independent of age. Only a higher number of cluster B personality features interfered negatively with the outcome of CBT in the whole sample, but only with respect to avoidance behavior and not for agoraphobic cognitions.

Among older adults, we found that the impact of the number of personality features differed

significantly between treatment modalities, which seemed to be driven by the presence of cluster A pathology. In the context of more cluster A personality features, treatment with paroxetine was associated with less improvement in avoidance behavior, whereas CBT was associated with more improvement in avoidance behavior.

Impact of Personality Pathology on CBT Outcome

To our knowledge, this is the first study to evaluate the impact of personality pathology on CBT treatment outcome that has included older patients with panic disorder. Although more than half of the older patients seeking treatment for panic disorder

PERSONALITY AND TREATMENT OF PANIC DISORDER

TABLE 2. Impact of Personality Pathology on Cognitive-Behavioral Therapy Outcome With Respect to Avoidance Behavior and Agoraphobic Cognitions

<i>Personality measure</i>	<i>Bivariate Analyses</i>			<i>Multivariate Analyses*</i>		
	<i>B (SE)</i>	β	<i>P</i>	<i>B (SE)</i>	β	<i>P</i>
<i>Avoidance behavior</i>						
Total number of personality features	0.02 (0.01)	0.29	0.009	0.01 (0.01)	0.12	0.056
Cluster A features	0.09 (0.03)	0.370	0.001	<0.01 (0.02)	0.02	0.823
Cluster B features	0.04 (0.02)	0.19	0.094	0.03 (0.01)	0.17	0.005
Cluster C features	0.04 (0.02)	0.21	0.066	<0.01 (<0.01)	<0.01	0.974
<i>Agoraphobic cognitions</i>						
Total number of personality features	0.02 (0.01)	0.40	<0.001	0.01 (0.01)	0.10	0.329
Cluster A features	0.04 (0.02)	0.26	0.019	0.01 (0.02)	0.04	0.716
Cluster B features	0.06 (0.02)	0.41	0.018	0.02 (0.01)	0.14	0.168
Cluster C features	0.04 (0.02)	0.30	0.007	0.01 (0.01)	0.04	0.710

*Adjusted for baseline severity of either avoidance behavior or agoraphobic cognitions, age, sex, level of education, duration of illness, and psychiatric comorbidity using a stepwise procedure.

suffered from clinically relevant personality pathology, the number of personality features was significantly lower in older patients compared with the younger patients. The number of cluster B personality features, which include features such as impulsiveness and self-harm that diminish with aging,^{26,27} especially had a lower frequency in the older compared with the younger patients.

Despite the small sample size and small to medium effect sizes in this study, our finding that personality pathology negatively interfered with treatment outcome in the whole sample is consistent with findings in younger adults, as summarized in several reviews.^{10,12,28} The studies summarized in these reviews differed with respect to the assessment of personality pathology (self-report questionnaires vs. semistructured interviews), adjustment for baseline anxiety severity (yes/no), treatment modality (elements of CBT, CBT, or pharmacotherapy), and duration of follow-up.^{10,12,28} These differences hamper the use of meta-regression techniques to quantitatively estimate the impact of personality pathology on treatment outcome.²⁹ A recent systematic review on the effect of comorbid personality pathology concluded that cluster A, B, and C personality pathology negatively interferes with the treatment outcome for panic disorder, even when the analysis is adjusted for baseline severity of the panic disorder.¹² Nonetheless, results with respect to cluster C pathology were less convincing, as cluster C

pathology was even associated with better treatment outcome in 3 studies.¹² In our study, we did not find any negative effect of cluster C personality features on treatment outcome after adjusting for baseline anxiety severity, while cluster B pathology had a negative influence on CBT treatment outcome independent of age. As we found no interaction with age, this effect could be considered to be of similar strength in younger and older patients. However, one could be critical of this conclusion, as cluster B personality pathology was significantly less prevalent in the older adults compared with the younger adults, which might have masked any differential effect by age. In contrast, it is known that older adults with similar severity of personality pathology meet fewer DSM criteria compared with younger adults.³⁰

In our study, personality pathology did not have any influence on the outcome with respect to agoraphobic cognitions. As agoraphobic cognitions decline with treatment, this finding might suggest that patients can differentiate between maladaptive cognitions as a result of personality pathology not targeted by CBT and specific agoraphobic cognitions targeted by CBT.

Personality and Treatment Modality in Later Life

In older patients, the number of features of overall personality pathology significantly interfered with

PERSONALITY AND TREATMENT OF PANIC DISORDER

TABLE 3. Baseline Characteristics of Older Patients Randomised to Either Paroxetine or CBT

<i>Characteristics</i>	<i>Expression</i>	<i>Randomized Older Patients</i>		<i>Statistics</i>
		<i>Paroxetine (n = 16)</i>	<i>CBT (n = 18)</i>	
Sociodemographic				
Age (y)	Mean (SD)	69.0 (4.4)	69.1 (5.0)	$t = -0.1, df = 32, P = 0.946$
Female sex	n (%)	10 (63)	10 (56)	$\chi^2 = 0.2, df = 1, P = 0.681$
Level of education				
Low	n (%)	6 (38)	5 (28)	
Medium	n (%)	6 (38)	8 (44)	$\chi^2 = 0.4, df = 2, P = 0.831$
High	n (%)	4 (25)	5 (28)	
Psychopathology				
Duration of illness panic disorder (y)	Median (IQR)	6.0 (17.5)	6.5 (21.4)	$t = -0.2, df = 32, P = 0.866^*$
Avoidance behavior (MI)	Mean (SD)	2.4 (0.7)	2.4 (1.0)	$t = 0.1, df = 32, P = 0.937$
Agoraphobic cognitions (ACQ)	Mean (SD)	1.7 (0.4)	1.6 (0.5)	$t = 0.6, df = 32, P = 0.586$
Comorbid psychiatric disorder	n (%)	7 (44)	3 (17)	$\chi^2 = 3.0, df = 1, P = 0.084$
Personality pathology				
Personality disorder present	n (%)	10 (63)	8 (44)	$\chi^2 = 1.1, df = 1, P = 0.292$
Cluster A	n (%)	5 (31)	5 (28)	$\chi^2 = 0.5, df = 1, P = 0.824$
Cluster B	n (%)	1 (6)	2 (11)	$\chi^2 = 0.2, df = 1, P = 0.618$
Cluster C	n (%)	8 (50)	7 (39)	$\chi^2 = 0.4, df = 1, P = 0.424$
Total number of personality features	Mean (SD)	19.8 (12.5)	17.9 (12.0)	$t = 0.4, df = 32, P = 0.662$
Cluster A features	Mean (SD)	5.4 (4.4)	5.0 (4.0)	$t = 0.3, df = 32, P = 0.783$
Cluster B features	Mean (SD)	5.7 (6.0)	5.1 (3.6)	$t = 0.4, df = 32, P = 0.698$
Cluster C features	Mean (SD)	6.7 (3.6)	6.2 (4.8)	$t = 0.3, df = 32, P = 0.733$

*The Student *t* test is based on normal log-transformed values.

ACQ indicates Agoraphobic Cognitions Questionnaire; CBT, cognitive-behavioral therapy; IQR, interquartile range; MI, Mobility Inventory for Agoraphobia.

treatment modality with respect to avoidance behavior. This effect was driven by cluster A pathology. When more cluster A personality features were present in a patient, response to CBT was better and response to paroxetine was worse. To date, the impact of personality pathology on pharmacotherapy for panic disorder has only been evaluated in younger adults. Two reviews concerning benzodiazepines and antidepressants in the treatment of panic disorder showed a negative response in both short-term and long-term treatment outcome in the presence of personality pathology.^{9,12}

As the effectiveness of pharmacotherapy decreases in the presence of personality pathology, CBT should be considered the first choice for older patients suffering from panic disorder and comorbid personality pathology. Effectiveness of CBT for late-life anxiety disorders

has been demonstrated in several meta-analyses, although the studies included in these analyses were restricted either to a generalized anxiety disorder or to mixed anxiety disorders in which only some of the patients suffered from panic disorder.^{5,31}

Strengths and Limitations

To our knowledge, this is the first study that has focused on the effect of comorbid personality pathology on treatment outcomes in late-life panic disorder, with a direct comparison between younger and older adults receiving CBT treatment and between 2 different treatment modalities in a group of older adults.

In properly interpreting the results presented here, several limitations need to be considered. First, to

PERSONALITY AND TREATMENT OF PANIC DISORDER

TABLE 4. Impact of Personality Pathology on Treatment Outcome in Older Patients (N = 34), Stratified by Treatment Modality

<i>Personality Measure</i>	<i>Whole Sample Personality Pathology by Treatment by Time</i>	<i>Paroxetine</i>			<i>CBT</i>		
	<i>P</i>	<i>B (SE)</i>	<i>β</i>	<i>P</i>	<i>B (SE)</i>	<i>β</i>	<i>P</i>
Bivariate regression analyses <i>Avoidance behavior</i>							
Total number of personality features	0.181	0.03 (0.01)	0.58	0.036	< -0.01 (0.02)	-0.01	0.967
Cluster A features	0.117	0.09 (0.04)	0.31	0.034	-0.02 (0.06)	-0.10	0.712
Cluster B features	0.425	0.05 (0.03)	0.46	0.117	< -0.01 (0.06)	-0.01	0.974
Cluster C features	0.162	0.12 (0.05)	0.60	0.029	0.01 (0.05)	0.07	0.788
Multivariate regression analyses <i>Avoidance behavior*</i>							
Total number of personality features	0.028	0.02 (0.01)	0.32	0.116	-0.02 (0.01)	-0.22	0.257
Cluster A features	< 0.001	0.08 (0.03)	0.49	0.019	-0.09 (0.03)	-0.44	0.017
Cluster B features	0.282	0.03 (0.02)	0.23	0.263	0.04 (0.04)	0.16	0.422
Cluster C features	0.183	0.07 (0.04)	0.33	0.117	< 0.01 (0.03)	-0.02	0.917
Bivariate regression analyses <i>Agoraphobic cognitions</i>							
Total number of personality features	0.076	< -0.01 (0.01)	-0.15	0.615	0.02 (0.01)	0.49	0.052
Cluster A features	0.318	-0.02 (0.02)	-0.25	0.417	0.02 (0.03)	0.17	0.532
Cluster B features	0.060	-0.01 (0.02)	-0.21	0.483	0.05 (0.03)	0.44	0.088
Cluster C features	0.283	0.01 (0.03)	0.09	0.766	0.05 (0.02)	0.56	0.023
Multivariate regression analyses <i>Agoraphobic cognitions*</i>							
Total number of personality features	0.178	< -0.01 (0.01)	-0.03	0.885	< 0.01 (0.01)	0.02	0.906
Cluster A features	0.983	-0.01 (0.02)	-0.06	0.785	-0.02 (0.02)	-0.16	0.318
Cluster B features	0.125	< 0.01 (0.01)	-0.01	0.980	< 0.01 (0.02)	0.03	0.888
Cluster C features	0.206	-0.01 (0.02)	-0.08	0.714	0.01 (0.01)	0.17	0.338

Personality pathology was measured by number of features.

**Adjusted for baseline severity of either avoidance behavior or agoraphobic cognitions, age, sex, level of education, psychiatric comorbidity, and duration of illness using a stepwise procedure.*

CBT indicates cognitive-behavioral therapy.

answer our research questions, we combined data from 2 earlier studies conducted in 2 different populations selected on the basis of age. Recruitment procedures in the 2 studies used the same inclusion and exclusion criteria, and both studies employed exactly the same CBT protocol delivered by the same

therapists. Nonetheless, we cannot exclude that different referral rates may have led to a systematic bias. Since late-life panic disorders are frequently not recognized and subsequently left untreated, the relatively small sample size of older adults might point to referral bias. Second, we recruited our population at a

specialized outpatient anxiety clinic. Older adults are less inclined to seek help for psychiatric problems. This might have led to a subgroup of older patients with more severe panic disorder and/or highly motivated patients. Third, the results have been presented without a Bonferroni correction. As data on the effect of personality disorders on treatment outcome in late-life panic disorder are lacking and therefore specific hypotheses in this older age group are absent, a Bonferroni correction was not applied to avoid type II errors. This strategy, however, could lead to type I errors. Finally, 2 different versions of the PDQ were used in our research sample. For the results presented here, we analyzed data only on those personality disorders that were captured by both versions and are still included in DSM-5.³² Personality pathology was analyzed dimensionally using the number of features, in line with more recent views on personality pathology as dimensional disorders.^{33,34}

CONCLUSIONS

Cluster B pathology had a negative influence on CBT treatment outcomes in both younger and older adults with panic disorder and agoraphobia. Despite this negative influence, it is important not to exclude patients with comorbid personality pathology from CBT, as improvement with CBT is still to be expected, albeit not as great as in patients without comorbid personality pathology.¹⁰ In late-life panic disorder with comorbid personality pathology, CBT may be recommended over antidepressants. Future research should take psychiatric comorbidity into account and, with respect to personality pathology, should especially address long-term effects on treatment outcome which may be particularly affected.³⁵

REFERENCES

1. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:593–602.
2. Grant BF. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood, and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Mol Psychiatry*. 2009;14:1051–1066.
3. Markowitz JS, Weissman MM, Ouellette R, et al. Quality of life in panic disorder. *Arch Gen Psychiatry*. 1989;46:984–992.
4. Schuurmans J, Van Balkom A. Late-life anxiety disorders: a review. *Curr Psychiatry Rep*. 2011;13:267–273.
5. Gould RL, Coulson MC, Howard RJ. Efficacy of cognitive behavioral therapy for anxiety disorders in older people: a meta-analysis and meta-regression of randomized controlled trials. *J Am Geriatr Soc*. 2012;60:218–229.
6. Hendriks GJ, Kampman M, Keijsers GP, et al. Cognitive-behavioral therapy for panic disorder with agoraphobia in older people: a comparison with younger patients. *Depress Anxiety*. 2014;31:669–677.
7. Marshall JR. Comorbidity and its effect on panic disorder. *Bull Menninger Clin*. 1996;60(suppl A):A39–A53.
8. Padesky CA. Schema-focused CT: comments and questions. *International Cognitive Therapy Newsletter*; 1988;4:5–7.
9. Slaap BR, den Boer JA. The prediction of nonresponse to pharmacotherapy in panic disorder: a review. *Depress Anxiety*. 2001;14:112–122.
10. Reich J. The effect of Axis II disorders on the outcome of treatment of anxiety and unipolar depressive disorders: a review. *J Pers Disord*. 2003;17:387–405.
11. Dreesen L, Arntz A, Lutjels C, et al. Personality disorders do not influence the results of cognitive-behaviour therapies for anxiety disorders. *Compr Psychiatry*. 1994;35:265–274.
12. Reich J, Schatzberg A, Delucchi K. Empirical evidence of the effect of personality pathology on the outcome of panic disorder. *J Psychiatr Res*. 2018;107:42–47.
13. Hendriks GJ, Keijsers GP, Kampman M, et al. Predictors of outcome of pharmacological and psychological treatment of late-life panic disorder with agoraphobia. *Int J Geriatr Psychiatry*. 2012;27:146–150.
14. Kampman M, Keijsers GPJ, Hoogduin CAL, et al. Outcome prediction of cognitive behavior therapy for panic disorder: initial symptom severity is predictive for treatment outcome; comorbid anxiety or depressive disorder, cluster C personality disorders and initial motivation are not. *Behav Cogn Psychother*. 2008;36:99–112.
15. Hendriks GJ, Keijsers GP, Kampman M, et al. A randomized controlled study of paroxetine and cognitive-behavioural therapy for late-life panic disorder. *Acta Psychiatr Scand*. 2010;122:11–19.
16. Craske MG, Barlow DH. Panic disorders and agoraphobia. In: Barlow DH, editor. *Clinical Handbook of Psychological Disorders*. New York, NY: Guilford; 1993:1–47.
17. Craske MG, Meadows E, Barlow DH. *Therapist Guide for the Mastery of Your Anxiety and Panic II and Agoraphobia Supplement*. Albany, NY: Graywind Publications; 1994.
18. Ouwensloot door G, Brink Wvd, Diekstra en RFW. *Diagnostiek van persoonlijkheidsstoornissen. Een evaluatie van Nederlandstalig instrumentarium* [Diagnosis of personality disorders. An evaluation of Dutch instruments]. *Tijdschr Psychiatr*. 1994;36:558–570.
19. Dingemans PMAJ, Sno HN. *Meetinstrumenten bij persoonlijkheidsstoornissen* [Measuring instruments for personality disorders]. *Tijdschr Psychiatr*. 2004;46:705–709.
20. Wilberg T, Dammen T, Friis S. Comparing Personality Diagnostic Questionnaire-4+ with longitudinal, expert, all data (LEAD) standard diagnoses in a sample with a high prevalence of axis I and axis II disorders. *Compr Psychiatry*. 2000;41:295–302.
21. Chambless DL, Caputo GC, Jasin SE, et al. The Mobility Inventory for Agoraphobia. *Behav Res Ther*. 1985;23:35–44.
22. De Beurs E. *The Assessment and Treatment of Panic Disorder and Agoraphobia*. Amsterdam, The Netherlands: Thesis Publishers; 1993.
23. Baçoğlu M, Marks IM, Swinson RP, et al. Pre-treatment predictors of treatment outcome in panic disorder and

PERSONALITY AND TREATMENT OF PANIC DISORDER

- agoraphobia treated with alprazolam and exposure. *J Affect Disord.* 1994;30:123–132.
24. de Beurs E, Lange A, van Dyck R, et al. Respiratory training prior to exposure in vivo in the treatment of panic disorder with agoraphobia: efficacy and predictors of outcome. *Aust N Z J Psychiatry.* 1995;29:104–113.
 25. Chambless DL, Caputo GC, Bright P, et al. Assessment of fear of fear in agoraphobics: the Body Sensations Questionnaire and the Agoraphobic Cognitions Questionnaire. *J Consult Clin Psychol.* 1984;52:1090–1097.
 26. Stevenson J, Meares R, Comerford A. Diminished impulsivity in older patients with borderline personality disorder. *Am J Psychiatry.* 2003;160:165–166.
 27. Zanarini MC, Laudate CS, Frankenburg FR, et al. Predictors of self-mutilation in patients with borderline personality disorder: a 10-year follow-up study. *J Psychiatr Res.* 2011;45:823–828.
 28. Mennin DS, Heimberg RG. The impact of comorbid mood and personality disorder in the cognitive-behavioral treatment of panic disorder. *Clin Psychol Rev.* 2000;20:339–357.
 29. Porter E, Chambless DL. A systematic review of predictors and moderators of improvement in cognitive-behavioral therapy for panic disorder and agoraphobia. *Clin Psychol Rev.* 2015;42:179–192.
 30. Balsis S, Gleason MEJ, Woods CM, et al. An item response theory analysis of DSM-IV personality disorder criteria across younger and older age groups. *Psychol Aging.* 2007;22:171–185.
 31. Hendriks GJ, Oude Voshaar RC, Keijsers GP, et al. Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis. *Acta Psychiatr Scand.* 2008;117:403–411.
 32. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition. Arlington, VA: APA; 2013.
 33. Widiger TA, Simonsen E. Alternative dimensional models of personality disorder: finding a common ground. *J Pers Disord.* 2005;19:110–130.
 34. Clark LA. Assessment and diagnosis of personality disorder: perennial issues and an emerging reconceptualization. *Annu Rev Psychol.* 2007;58:227–257.
 35. Newton-Howes G, Mulder R, Ellis PM, et al. Predictive utility of personality disorder in depression: comparison of outcomes and taxonomic approach. *J Pers Disord.* 2018;32:513–526.