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Supplementary Material

Article Title: A Comprehensive Model of Predictors of Recurrence or Persistence in Individuals With Panic Disorder: Results From a National 3-Year Prospective Study

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SUPPLEMENTARY MATERIAL

Supplementary Table 1. Risk factors reported by prior studies of increased recurrence or persistence risk in individuals with panic disorder.

<i>Factors</i>	<i>Overall</i>	<i>Recurrence</i>	<i>Persistence</i>
Specific symptoms of panic disorder		Ehlers et al., (1995) ; Liu et al., (2015)	
Panic disorder severity	Heldt et al., (2010)		Batelaan et al., (2009) ; Faravelli et al., (1987) ; Noyes et al., (1989) ; Toni et al., (2000)
Other associated features			
Duration of illness			Katschnig et al., (1995) ; Noyes et al., (1993) ; Pollack et al., (1992)
Frequency of panic attacks			Batelaan et al., (2010) ; Ehlers et al., (1995)
Phobic avoidance		Katschnig et al., (1995)	
Early age at onset		Ramsawh et al., (2011)	Segui et al., (1999) ; Warshaw et al., (1997)
Greater number of panic attacks		Ehlers et al., (1995)	Aronson et al., (1987)
Insomnia			Aronson et al., (1987)
Psychiatric comorbidity			
Greater number of comorbidities		Ehlers et al., (1995)	Brown et al., (1995) ; Cowley et al., (1996)
Major depressive disorder	Bruce et al., (2005) ; Roy-Byrne et al., (1994)	Nay et al., (2013)	Albus et al., (1993) ; Benitez et al., (2009) ; Coryell et al., (1988) ; Cowley et al., (1996) ; Francis et al., (2007) ; Reich et al., (1988)
Dysthymic disorder		Liu et al., (2015)	Heldt et al., (2006)

Alcohol and other substance use disorders		Liu et al., (2015) ; Nay et al., (2013)	Batelaan et al., (2009)
Anxiety disorders			Batelaan et al., (2009) ; Benitez et al., (2009) ; Faravelli et al., (1987)
Agoraphobia	Bruce et al., (2005) ; Roy-Byrne et al., (1994)	Weisberg et al., (2002)	Andersch et al., (2003) ; Batelaan et al., (2009) ; Carpinello et al., (2002) ; Cowley et al., (1996) ; Faravelli et al., (1987) ; Francis et al., (2007) ; Warshaw et al., (1997)
Generalized anxiety disorder	Nay et al., (2013)	Mavissakalian et al., (2004) ; Rodriguez et al., (2005)	Heldt et al., (2006)
Social anxiety disorder			Heldt et al., (2006) ; Nay et al., (2013) ; Warshaw et al., (1997)
Personality disorders	Roy-Byrne et al., (1994) ; Svanborg et al., (2008)	Pollack et al., (1992)	Faravelli et al., (1987) : O'Rourke et al., (1996)
Histrionic			Cowley et al., (1996) ; Reich et al., (1988)
Antisocial			Reich et al., (1988)
Schizotypal			Cowley et al., (1996)
Borderline		Ansell et al., (2011)	
Paranoid			Faravelli et al., (1987)
Family history of psychiatric disorders			Faravelli et al., (1987)
Childhood trauma		Liu et al., (2015)	
Stressful life events	Heldt et al., (2010) ; Roy-Byrne et al., (1986)	Nay et al., (2013)	Aronson et al., (1987) ; Batelaan et al., (2009) ; Faravelli et al., (1987) ; Moitra et al., (2011)
Functional impairment		Mavissakalian et al., (2004) ; Rodriguez et al., (2005)	

Low physical health			Benitez et al., (2009) ; Bringager et al., (2008) ; Warshaw et al., (1997)
Sociodemographic characteristics			
Younger age		Liu et al., (2015) ; Nay et al., (2013)	Francis et al., (2007)
Female sex		Liu et al., (2015) ; Nay et al., (2013) ; Yonkers et al., (2003)	Maier et al., (1988)
Being divorced or separated or widowed			Wade et al., (1993)
Poverty and low socioeconomic			Warshaw et al., (1997)
Low education			Aronson et al., (1987) ; Faravelli et al., (1987)
African-American			Sibrava et al., (2013)
Treatment-seeking behavior		Liu et al., (2015)	Aronson et al., (1987)

Supplementary Table 2. Confirmatory factor analysis model of the structure “Respiratory-Cardiac-Vestibular” underlying the 10 disaggregated DSM-IV criteria for Panic Disorder in individuals with a past year DSM-IV diagnosis of Panic Disorder (N=775) in Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

CFI	0.991			
TLI	0.988			
RMSEA	0.029			
	Panic disorder liability	Respiratory	Cardiac	Vestibular
Shortness of breath	0.58****	0.58****		
Feeling of choking	0.57****	0.50****		
Palpitations	0.54****		0.59****	
Chest pain or discomfort	0.81****		-0.38	
Sweating	0.26***			0.68****
Feeling dizzy	0.35****			0.38***
Nausea or abdominal distress	0.23***			0.40****
Paresthesias	0.59****			0.32***
Chills or heat sensations	0.35****			0.62****
Trembling or shaking	0.39****			0.22*
Factor correlation				
Panic disorder liability	1.00			
Respiratory	0.00	1.00		
Cardiac	0.00	0.00	1.00	
Vestibular	0.00	0.00	0.00	1.00

Abbreviations: CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation.

**** p<.001; *** p<.005; ** p<.01; * p<.05.

Supplementary Table 3. Comparison of baseline indicators of panic disorder severity, psychiatric comorbidity, quality of life, sociodemographic characteristics and treatment-seeking behavior at Wave 1 in individuals with a past-year DSM-IV diagnosis of panic disorder (n=775) according to the 3-year occurrence of recurrence or persistence.

	Persistence vs Recurrence
	OR [95%CI] / Wald F ^c
Severity of panic disorder	
Palpitations	0.3 [0.1-1.6]
Sweating	1.2 [0.5-3.0]
Trembling or shaking	1.9 [0.7-4.7]
Sensations of shortness of breath	1.9 [0.6-6.4]
Feelings of choking	1.4 [0.8-2.6]
Chest pain or discomfort	1.4 [0.7-3.0]
Nausea or abdominal distress	1.4 [0.7-2.7]
Feeling dizzy	1.1 [0.4-2.9]
Chills or heat sensations	1.1 [0.5-2.3]
Paresthesias	1.1 [0.5-2.1]
Derealization or depersonalization	0.6 [0.3-1.5]
Fear of losing control or going crazy	1.5 [0.7-3.1]
Fear of dying	1.5 [0.8-3.0]
Number of lifetime panic attacks	16.9****
Duration of illness	3.9
Age at onset of panic disorder	3.0
First degree relatives' history of psychiatric disorders	1.3 [0.5-3.3]
Psychiatric comorbidity^a	
Any Axis I or II disorder	0.5 [0.2-1.4]
Any Axis I disorder	1.2 [0.5-2.9]

Any Axis II disorder	0.7 [0.4-1.3]
MDE	0.9 [0.4-1.7]
Dysthymia	1.2 [0.4-3.6]
Mania/hypomania	1.6 [0.8-3.2]
GAD	1.2 [0.7-2.3]
Social anxiety disorder	0.7 [0.3-1.4]
Specific phobia	0.7 [0.4-1.4]
Agoraphobia	1.0 [0.5-2.0]
Alcohol use disorder	1.1 [0.5-2.5]
Drug use disorder	0.4 [0.1-1.2]
Nicotine dependence	1.1 [0.6-2.2]
Histrionic PD	0.8 [0.2-2.5]
Schizoid PD	0.9 [0.4-2.0]
Paranoid PD	1.0 [0.4-2.1]
OCPD	0.9 [0.4-2.0]
Dependent PD	1.1 [0.3-4.2]
Avoidant PD	1.0 [0.4-2.3]
Antisocial PD	1.2 [0.4-3.0]
Quality of life	
Mental component score (MCS)	
≥50	0.8 [0.4-1.8]
<50	
Physical component score (PCS)	
≥50	1.3 [0.7-2.4]
<50	
Sociodemographic characteristics	
Sex	
Men	
Women	1.4 [0.7-2.7]
Race/Ethnicity	
White	
Non-White	0.9 [0.4-1.8]

Marital Status	
Married or as if married	
Not married	1.0 [0.5-2.1]
Age	0.1
Poverty (household income<\$20,000)	1.1 [0.6-2.2]
Number of past year stressful life events	
≤3	
>3	1.3 [0.7-2.8]
Education	
College or higher	1.1 [0.6-2.2]
High school graduate or less	
Seeking treatment for panic symptoms	1.7 [0.6-4.8]

- ^aAxis I disorders were past year diagnoses while Axis II disorders were assessed on a lifetime basis. Abbreviations: MDE, major depressive episode; GAD, generalized anxiety disorder; SE, standard error; PD, personality disorder; OCPD, obsessive-compulsive personality disorder; NA, not applicable.
- ^c Crude ORs/Wald F (d.f.=1) indicate measures of association for binary/continuous variables and were estimated using logistic regression models; ORs and Wald F tests in bold are statistically significant with alpha set *a priori* fixed at 0.05.
- **** two-sided p-value (p) <.001; *** p<.005; ** p<.01; * p<.05.

Supplementary Table 4. Bifactor model of the structure “Distress-Fear-Externalizing” underlying past-year Axis I disorders and antisocial personality disorder in individuals with a past-year DSM-IV diagnosis of Panic Disorder (N=775) in Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

CFI	0.990			
TLI	0.986			
RMSEA	0.033			
Disorder	General psychopathology factor	Externalizing	Fear	Distress
MDE	0.50****			0.71****
Dysthymia	0.31*			0.58****
GAD	0.52****			0.27***
Social Anxiety Disorder	0.59****		0.57****	
Specific phobia	0.45****		0.45****	
Agoraphobia	0.23***		0.92****	
Alcohol use disorder	0.14	0.67****		
Drug use disorder	0.36***	0.77****		
Nicotine dependence	0.37****	0.50****		
Antisocial PD	0.36****	0.66****		
Factor loading of the factor Internalizing			-0.11	0.71****
Factor correlation				
General psychopathology factor	1.00			
Externalizing	0.00	1.00		
Fear	0.00	0.00	1.00	
Distress	0.00	0.00	0.00	1.00

Abbreviations: CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation; MDE, major depressive episode; GAD, generalized anxiety disorder; PD, personality disorder.

**** p<.001; *** p<.005; ** p<.01; * p<.05.

Supplementary Table 5. Bifactor model of the structure “Internalizing-Externalizing” underlying past-year Axis I disorders and lifetime Axis II disorders in individuals with a past year DSM-IV diagnosis of Panic Disorder (N=775) in Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

CFI	0.987		
TLI	0.983		
RMSEA	0.023		
Disorder	General psychopathology factor	Internalizing	Externalizing
MDE	0.65****	-0.14	
Dysthymia	0.45****	-0.28	
GAD	0.48****	0.15*	
Social Anxiety Disorder	0.53****	0.68****	
Specific phobia	0.35****	0.47****	
Agoraphobia	0.23**	0.77****	
Mania/Hypomania	0.71****	-0.04	
Avoidant PD	0.69****	0.39****	
Dependent PD	0.78****	0.35***	
OCPD	0.52****	0.22*	
Paranoid PD	0.63****	0.29***	
Schizoid PD	0.56****	-0.06	
Histrionic PD	0.62****	-0.09	
Antisocial PD	0.48****		0.51****
Alcohol use disorder	0.14		0.71****
Drug use disorder	0.41****		0.77****
Nicotine dependence	0.36****		0.49****
Factor correlation			
General psychopathology factor	1.00		
Internalizing	0.00	1.00	
Externalizing	0.00	0.00	1.00

Abbreviations: CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation; MDE, major depressive episode; GAD, generalized anxiety disorder; PD, personality disorder; OCPD, obsessive-compulsive personality disorder
**** p<.001; *** p<.005; ** p<.01; * p<.05.

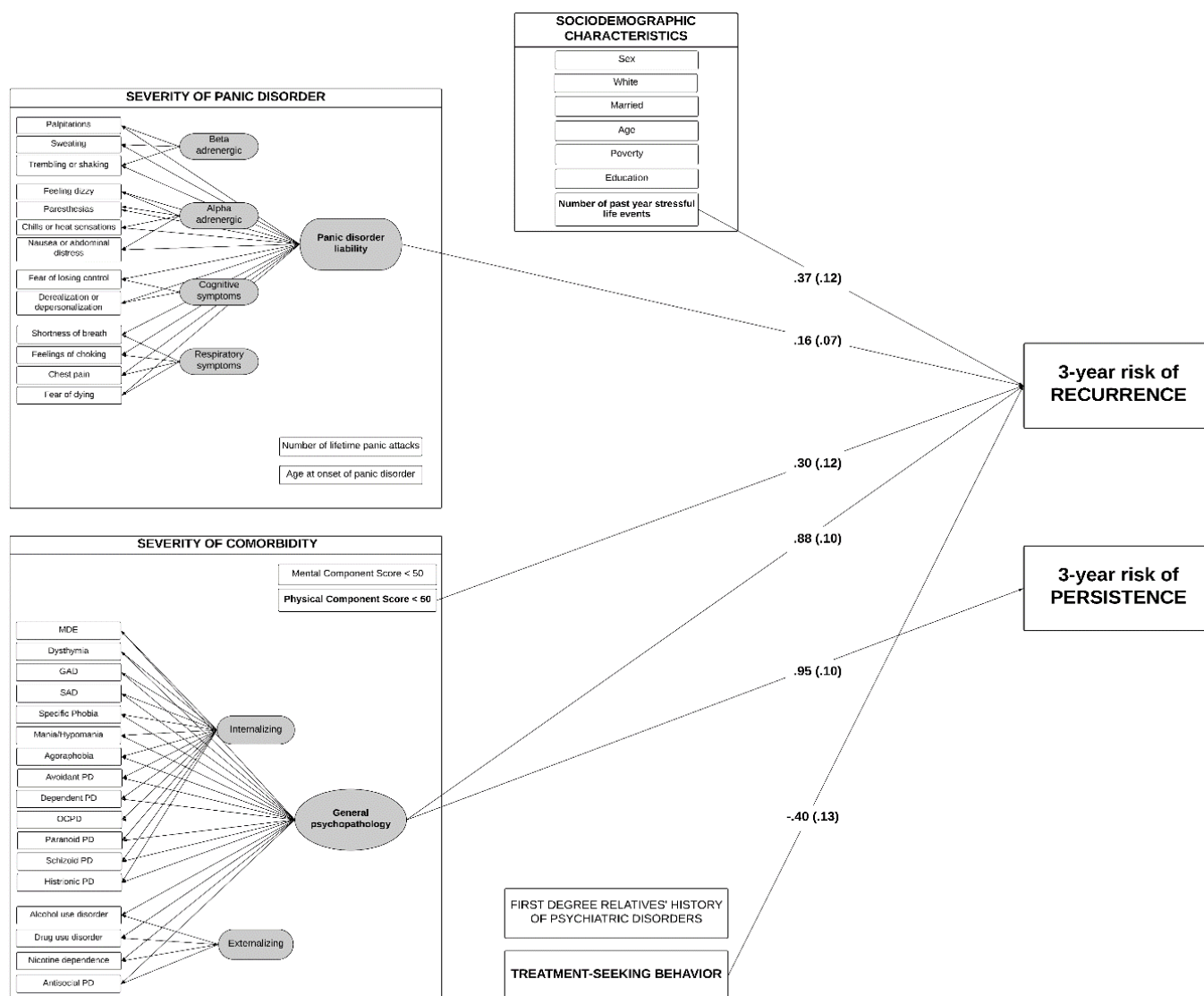
Supplementary Table 6. Confirmatory factor analysis model of the structure “Beta adrenergic-Alpha adrenergic-Cognitive-Respiratory” underlying the 13 disaggregated DSM-IV criteria for Panic Disorder in individuals with a past year DSM-IV diagnosis of Panic Disorder (N=775) in Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

CFI	0.982				
TLI	0.977				
RMSEA	0.031				
	Panic disorder liability	Beta-adrenergic	Alpha-adrenergic	Cognitive	Respiratory
Palpitations	0.45****	0.63****			
Trembling or shaking	0.46****	0.13			
Sweating	0.45****	0.19			
Feeling dizzy	0.40****		0.65****		
Paresthesias	0.65****		0.29***		
Chills or heat sensations	0.46****		0.43****		
Nausea or abdominal distress	0.36****		0.24*		
Derealization or depersonalization	0.43****			0.64****	
Fear of losing control	0.51****			0.25*	
Shortness of breath	0.58****				0.58****
Feeling of choking	0.47****				0.61****
Chest pain or discomfort	0.61****				0.33***
Fear of dying	0.45****				-0.01
Factor correlation					
Panic disorder liability	1.00				
Beta adrenergic	0.00	1.00			
Alpha adrenergic	0.00	0.00	1.00		
Cognitive	0.00	0.00	0.00	1.00	
Respiratory	0.00	0.00	0.00	0.00	1.00

Abbreviations: CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation.

**** p <.001; *** p<.005; ** p<.01; * p<.05.

Supplementary Figure 1. Structural equation model of the 3-year risk of recurrence or persistence in a general population sample of adults with a past-year DSM-IV diagnosis of panic disorder (n=775), including the bifactor models of the structures “Internalizing-Externalizing” and “Beta adrenergic-Alpha adrenergic-Cognitive-Respiratory” underlying comorbid psychiatric disorders and panic disorder symptoms, respectively.^a

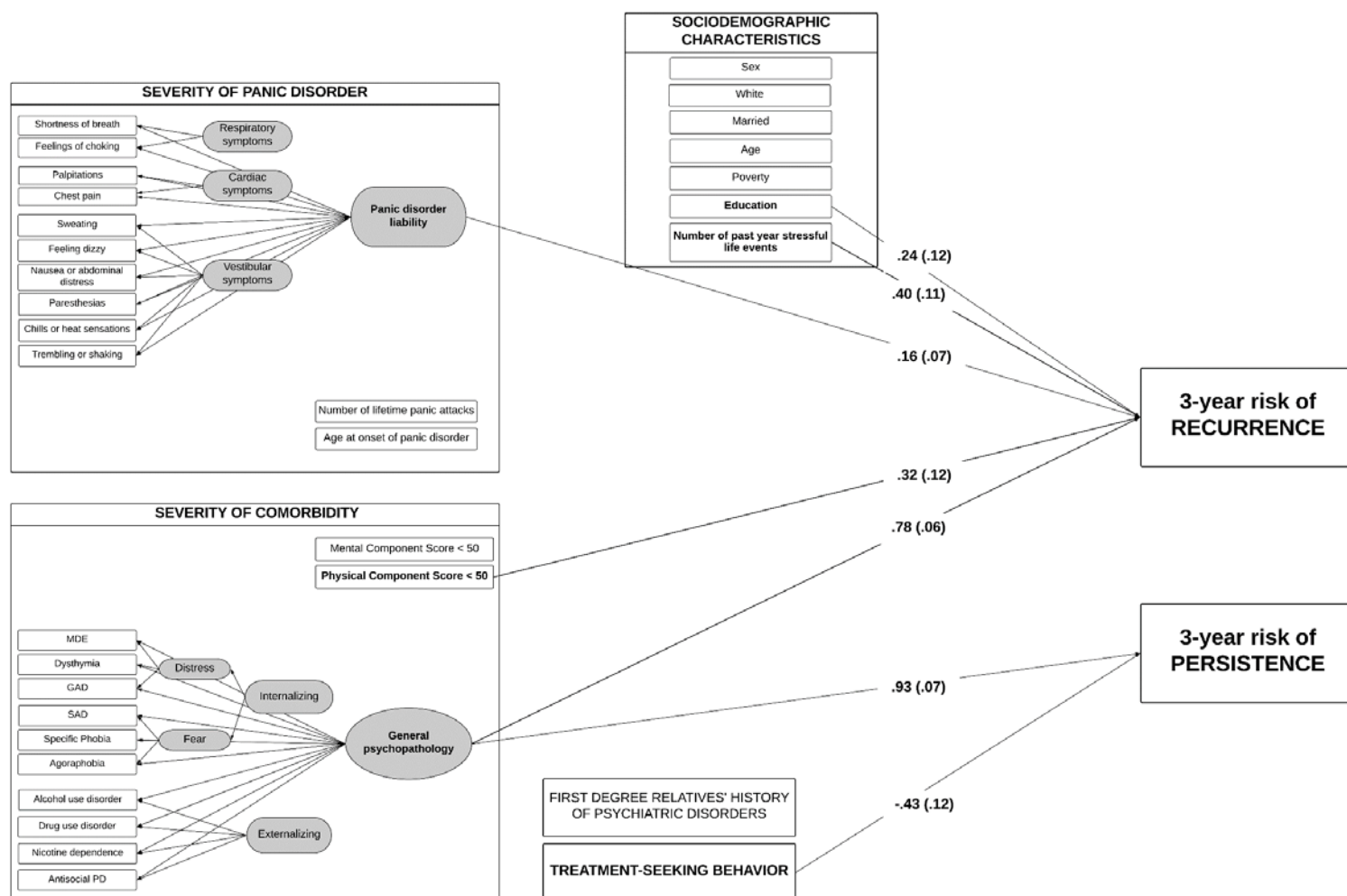


^a Ellipses are used to denote latent constructs, rectangles are used to denote the observed variables. Regression coefficients shown are standardized. Values in brackets indicate their standard errors. Only significant effects (two-sided $p < .05$) are represented in the model.

Axis I disorders were past year diagnoses while Axis II disorders were assessed on a lifetime basis.

Abbreviations: MDE, major depressive episode; GAD, generalized anxiety disorder; SAD, social anxiety disorder; PD, personality disorder; OCPD, obsessive-compulsive personality disorder.

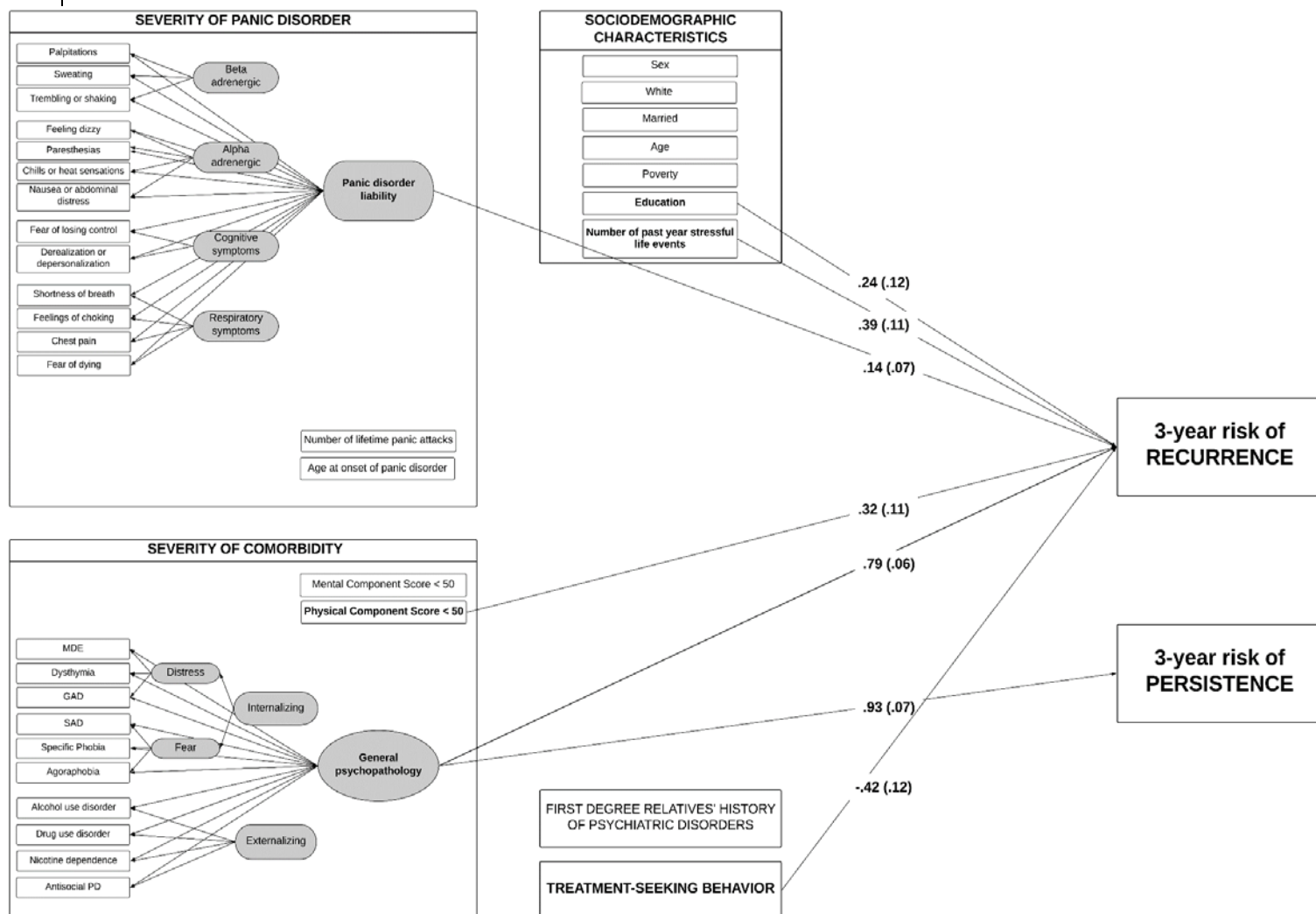
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