

The Association Between Working Alliance and Clinical and Functional Outcome in a Cohort of 400 Patients With First-Episode Psychosis: A Cross-Sectional Study

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ABSTRACT

Objective: Working alliance between patients with a first-episode psychosis and their case manager is regarded as a key element in specialized early intervention services. The impact of this patient–case manager dyad on functional and clinical outcome is unknown. We aimed to investigate if a strong working alliance was associated with fewer clinical symptoms and better social functioning.

Method: In a cross-sectional design, patients with first-episode schizophrenia spectrum disorders (*ICD-10*, F20–29) were included after 18 months of treatment ($N = 400$). Baseline data were collected between June 2009 and December 2011. Symptoms were assessed using Scale for the Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS), Global Assessment of Functioning (GAF), Brief Assessment of Cognition in Schizophrenia (BACS), Working Alliance Inventory (WAI), and General Self-Efficacy (GSE). Linear regression analyses were adjusted for age, sex, cognition, and self-efficacy.

Results: Results revealed significant associations between working alliance and fewer negative ($\beta = -0.12$; 95% CI, -0.19 to -0.04) and disorganized symptoms ($\beta = -0.06$; 95% CI, -0.11 to -0.01), and between working alliance and better social functioning ($\beta = 1.45$; 95% CI, 0.55 to 2.36). General self-efficacy mediated the effect of working alliance, explaining 14%–18% of the variance in associated outcomes. Global level of cognitive functioning, compliance, and self-efficacy influenced clinical and functional outcome more strongly than working alliance.

Conclusions: Better working alliance was weakly associated with fewer negative and disorganized symptoms and better social functioning. A strong working alliance may be a prerequisite for adherence to the specialized early intervention services treatment, providing the basis for positive treatment outcome.

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The link between strong therapeutic alliance and successful treatment outcomes is well documented in the field of psychotherapy.^{1,2} *Working alliance* is understood as the dynamic process between client and therapist and their ability to work together in the interest of problem solving, hence increasing treatment outcome.^{1,3,4} Several studies have found evidence of a modest (effect size between 0.22 and 0.26), but consistent effect for working alliance on outcome, regardless of moderating variables such as type of therapy, time, intervention, or type of outcome measure used.^{1,2} Studies examining patients diagnosed within the schizophrenia spectrum disorder have found that working alliance between patients and their case manager or therapist is associated with reduced symptom severity levels, improved quality of life, better illness insight, and better adherence to medication and psychotherapy.^{5–11} Most studies in case-management settings focus on patients who have suffered from severe mental illness for many years.^{12–15} One study of patients with early psychosis examining the predictive value of symptoms, insight, and global functioning with regard to the strengths of alliance found only interpersonal factors, such as having friends and having leisure activities, to be possible predictors for therapeutic alliance.¹⁶

In specialized early intervention services for patients with a first episode of psychosis, the alliance between the patient and the case manager is regarded as a key element in the psychosocial treatment.^{17–21} Due to the psychoeducative and recovery-oriented content of the collaboration, the impact of working alliance on clinical and functional outcome might be mediated by improvement in the patients' compliance with the antipsychotic medication and their sense of self-efficacy. A recent study found working alliance to be a significant predictor of future medication adherence.⁹ Perceived self-efficacy is found to affect goal setting and goal attainment and form outcome expectancies.^{22,23} Consequently, we hypothesize that these variables might mediate the association between working alliance and better clinical and functional outcomes. With respect to cognition, we know it represents a complex set of functions necessary for being in a collaborative setting and might, together with age and sex, confound the impact of working alliance on clinical and functional outcome measures.

This study aims to examine the association between working alliance and clinical and functional outcome in a cohort of 400 first-episode psychosis patients. Our hypothesis is that a stronger working alliance will be associated with fewer psychotic, disorganized, and negative symptoms and better social functioning. Secondly, we aim to analyze if compliance and self-efficacy mediate

- Working alliance between patients with a first-episode psychosis and their case manager is regarded as a key element in specialized early intervention services.
- Patients with more severe negative symptoms and reduced social function are at higher risk for attaining poor working alliance.
- The Working Alliance Inventory (WAI) offers patients and clinicians a suitable tool for evaluating the quality of their working alliance.
- Regular assessment of working alliance together with clinical and functional outcome may provide a strategy to improve the working alliance.

the association and to explore the putative gender differences in clinical characteristics and predictors of outcome.

METHOD

This study was based on baseline data from the Danish OPUS II trial, a randomized clinical trial investigating the effect of 2 versus 5 years of specialized early intervention service for first-episode psychosis; the study design is described in detail elsewhere.²⁴

The Danish Ethics Committee assessed our protocol to be exempt from formal approval as it is a nonbiomedical trial (no. H-C-2009-035). All participants gave written informed consent.

Participants

At the time of assessment, all participants had been treated in specialized early intervention teams in the catchment areas of Copenhagen and Aarhus for at least 18 months. Participants were between 19–37 years of age with a diagnosis in the schizophrenia spectrum (*ICD-10* codes in the F2 category, which include schizotypal disorder [WHO 1992]).

The specialized early-intervention program consisted of 3 core elements: modified assertive community treatment,²⁵ family treatment,^{26–28} and social skills training.²⁹

The case-manager-to-patient ratio was 1:10. The working alliance between the patients and their case manager aimed to support the patients' recovery process and maintain their adherence to the specialized early intervention services. The initial assignments to a case manager in OPUS are usually random and most often based on pragmatic terms. Psychoeducation and a cognitive therapeutic approach were used in the treatment at various levels according to the patients' capabilities.

Measures and Procedures

Data collection. The participants were assessed before randomization by independent and trained professionals. Diagnoses were reassessed based on the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) version 2.1.³⁰

Working alliance. The Working Alliance Inventory (WAI) was designed to measure aspects of the alliance between patients and clinicians in all types of therapy.^{4,31,32} The WAI provides an overall global score of the strength and quality of the alliance. Furthermore, the WAI provides subscales for level of agreement between client and therapist on goals (goals subdomain), agreement on tasks (task subdomain), and the therapeutic bond (bond subdomain).^{3,33} In this study, we used the WAI-short form (12 items),³² a questionnaire rated by patients (WAI-c). Each subdomain consists of 4 items rated on a 7-point Likert scale. Higher scores on the WAI-c indicate better working alliance.

Clinical and demographic variables. Clinical outcome was assessed using the Scale for the Assessment of Positive Symptoms (SAPS)³⁴ and the Scale for the Assessment of Negative Symptoms (SANS).³⁵ The 2 scales are summarized into 3 dimensions: the psychotic, the disorganized, and the negative (all scored 0–5), with lower scores indicating lower symptom severity.³⁶ Social function was assessed using the Global Assessment of Functioning (GAF) split version (scores 0–100), higher score indicating better functioning.³⁷

The patients' compliance with antipsychotic medication was assessed by the interviewer and based on information given by the patients. Information regarding demographics and socioeconomic status was also collected.

Self-efficacy. General self-efficacy reflects a personal sense of competence to deal with a variety of stressful situations²³ and was assessed by the General Self-Efficacy scale (GSE).³⁸ The scale includes 10 questions. Patients rate each question on a 4-point Likert scale. Higher scores reflect greater levels of self-efficacy.

Global level of cognitive functioning. Global level of cognitive functioning was examined using the Brief Assessment of Cognition in Schizophrenia (BACS).^{39,40}

The "Tower of London" subtest raw scores, which were used to assess the patients' executive function, were truncated (4 standard deviations [SDs] below the raw score mean). Subsequently, all BACS subtest outcome raw scores were approximately normally distributed, and *z* scores were calculated for each subtest outcome variable based on the raw score mean and SD of the full sample. Higher subtest *z* scores indicate better performance. A composite score was calculated by averaging all of the subtest outcome *z* scores and then restandardized to ensure a mean of 0.00 and an SD of 1.00.

Data analysis. Gender comparisons were made with independent sample *t* tests for continuous outcome measures and Pearson χ^2 tests for categorical outcome measures.

Pearson correlations were calculated for global WAI-c scores to evaluate potential association with psychotic, negative, and disorganized dimensions and social functioning.

Bivariate correlations, Pearson, were used to examine associations between age and gender according to composite *z* scores of BACS outcomes.

Linear regression analyses were conducted for the psychotic, negative, and disorganized symptom dimensions and GAF scores as outcome variables and for WAI, GSE,

Table 1. Sociodemographic and Clinical Characteristics of 400 Patients With a First Episode of Psychotic Illness Treated for 19 Months in a Specialized Early Intervention Team^a

Sociodemographic Characteristic	Men (n = 192) ^b	Women (n = 208) ^c	<i>P</i>	Total (N = 400) ^d
Age, mean (SD), y	26.2 (4.2)	25.0 (4.3)	.003	25.56 (4.3)
Brought up with both parents at age 12	101 (52.6)	108 (51.9)	.49	209 (52.3)
Having an intimate relationship	41 (21.4)	99 (47.6)	<.001	140 (35.0)
Being a parent	14 (7.3)	16 (7.7)	.57	30 (7.5)
Completed high school or more	66 (34.4)	93 (44.7)	.04	159 (39.8)
Employed	29 (15.1)	27 (13.0)	.54	56 (14.0)
Living conditions			<.001	
Living independently	140 (72.9)	173 (83.2)		313 (78.3)
Living with parents	32 (16.7)	22 (10.6)		54 (13.5)
Living in supervised setting	16 (8.3)	10 (4.8)		26 (6.5)
Homeless	4 (2.1)	3 (1.4)		7 (1.8)
Clinical conditions				
DUP (median duration of untreated psychosis in wk) ^e	52	56	.51	52
Diagnosis (<i>ICD-10</i>)			.48	
Schizophrenia (F20)	146 (76.0)	152 (73.1)		298 (74.5)
Schizotypal disorder (F21)	39 (20.3)	45 (21.6)		84 (21.0)
Delusional disorder (F22)	3 (1.6)	7 (3.4)		10 (2.5)
Brief psychosis (F23)	1 (0.5)	1 (0.5)		2 (0.5)
Schizoaffective disorder (F25)	3 (1.6)	1 (0.5)		4 (1.0)
Unspecified nonorganic psychosis	0 (0.0)	2 (1.0)		2 (0.5)
Psychopathology, mean (SD)				
Psychotic dimension (0–5)	1.8 (1.1)	2.0 (1.3)	.10	1.9 (1.2)
Negative dimension (0–5)	2.0 (0.9)	1.76 (1.0)	.001	1.9 (1.0)
Disorganized dimension (0–5)	0.6 (0.7)	0.4 (0.5)	.01	0.53 (0.6)
Comorbidity				
Diagnosis of substance abuse	55 (28.6)	38 (18.3)	.01	93 (23.3)
Social functioning				
GAF function (1–100), mean (SD)	47.4 (11.3)	50.4 (12.2)	.01	49.0 (11.9)

^aValues are numbers (percentages) unless stated otherwise. Variables in bold reflect statistically significant differences between women and men.

^bRange from 189 to 192.

^cRange from 204 to 208.

^dRange from 393 to 400.

^eDUP was assessed for patients not diagnosed with schizotypal disorder. Mann-Whitney *U* tests were used for nonparametric outcome measures (DUP).

Abbreviations: DUP = duration of untreated psychosis, GAF = Global Assessment of Functioning.

compliance, and global level of cognitive function as predictor variables. All linear regression analyses were adjusted for age and sex, and then additionally for global level of cognitive function (BACS composite *z* scores). In case of justification by the correlation analyses, the linear regression analyses were additionally adjusted for compliance and self-efficacy. This approach allowed us to examine if changes occurred in the regression coefficient for the association between working alliance and outcome, indicating a possible mediating effect of compliance and self-efficacy, as these factors were a priori assumed to be on the causal pathway from working alliance to outcome of treatment. We considered a difference of >10% of the regression coefficient between 2 models as an indicator for mediation.

To be able to generalize our results to other studies in first-episode psychosis using the diagnostic criteria of *ICD-10*, *DSM-IV*, and *DSM-5* for a schizophrenia spectrum psychosis, we conducted the analyses of outcomes both with and without patients with schizotypal disorder.

All significance tests were 2-tailed at the 5% level of significance.

Data analysis was carried out using SPSS Version 19.0 for Windows (IBM Corp Released 2010. Armonk, New York: IBM Corp).

RESULTS

Sample

A total of 468 patients were evaluated to participate in the trial. The nonparticipation rate was 15% (*n* = 68), due to geography (*n* = 17), no longer meeting the inclusion criteria (*n* = 20), declining to participate (*n* = 23), impossible to contact (*n* = 5), deceased (*n* = 2), or unknown (*n* = 1). A total of 400 patients (85%) signed up for participation in the OPUS II trial.

Gender differences in sociodemographic and clinical characteristics of participants are listed in Table 1. Compared to men, women were significantly more likely to be involved in an intimate relationship (48% vs 21%, *P* < .001) and to be living independently (83% vs 73%, *P* < .001). Women were significantly more likely than men to have completed high school (64% vs 34%, *P* = .04), and women had a significantly higher GAF score than men (mean [SD] = 50.4 [12.23] vs 47.4 [11.27], *P* = .01). Men had significantly worse negative symptoms (mean [SD] = 2.0 [0.92] vs 1.8 [0.96], *P* = .001) and disorganized symptoms (mean [SD] = 0.6 [0.66] vs 0.4 [0.52], *P* = .01) compared to women. Significantly more men than women had an additional diagnosis of substance abuse (28.6% vs 18.3%, *P* = .01).

Table 2. Gender Differences of Treatment Affiliations of 400 Patients Treated for 19 Months in a Specialized Early Intervention Team^a

OPUS Treatment	Men (n = 192) ^b	Women (n = 208) ^c	P	Total (N = 400) ^d
Months treated at inclusion in the study, mean (SD)	19.3 (2.6)	19.1 (2.4)	.47	19.2 (2.5)
Relatives involved in treatment ^e	155 (80.7)	174 (83.7)	.50	329 (82.3)
Patients with relatives involved in multifamily groups	21 (11.1)	49 (24.0)	.009	70 (17.8)
Patients involved in social skills training groups	73 (38.2)	70 (34.0)	.54	143 (36.0)
Patients involved in psychoeducational groups	67 (35.0)	70 (33.8)	.13	137 (34.4)
Patients involved in group cognitive-behavioral therapy	11 (5.8)	23 (11.3)	.14	34 (8.6)
Patients involved in any recovery-orientated group	101 (52.9)	118 (57.0)	.41	219 (55.0)
Antipsychotic medication ^f	169 (88)	178 (86)	.46	347 (87)
Compliance (75%–100% of full prescribed dosages of antipsychotic medication taken last wk)	154 (87)	158 (89)	.87	312 (90)

^aValues are numbers (percentages) unless stated otherwise. Variables in bold reflect statistically significant differences between women and men.

^bRange from 189 to 192.

^cRange from 204 to 208.

^dRange from 393 to 400.

^eAt least 1 relative involved at 1 time in the treatment.

^fThe proportion of participants in treatment with antipsychotic medication at the time of the interview.

Participants had received on average 19 months of OPUS treatment at the time of inclusion (SD = 2.50) without gender differences ($P = .47$). Treatment-related characteristics of the study population are listed in Table 2.

Table 3 shows means and SDs for scores of working alliance, self-efficacy, and cognitive function. Gender differences and group total are shown, and key findings are summarized below.

Working Alliance

Of the 400 participants, 383 (95.8%) completed the full WAI-c. Patients who did not complete a full WAI-c ($n = 17$) were similar to the participants who completed it, concerning age, gender, diagnosis, clinical and functional status, and compliance with antipsychotic medication (all P values $> .18$; data not shown).

The mean global WAI-c score was 66.7 (SD = 11.5). Scores of the study population were distributed in the following quartiles: (23–60), (61–68), (69–75), and (76–84). No significant gender differences were found on the WAI-c global scores ($P = .37$) or on the scores of the 3 subdomains: task ($P = .36$), bond ($P = .74$), and goal ($P = .22$).

Global Level of Cognitive Function

A total of 386 of the participants (97%) completed a full BACS test. The results of the assessment revealed significant differences between men and women according to raw scores of semantic fluency (men: mean [SD] = 22.51 [6.5], women: mean [SD] = 25.3 [9.0], $P = .001$) and letter fluency “F” (men: mean [SD] = 11.73 [5.2], women: mean [SD] = 13.00 [5.2], $P = .02$). The test “symbol coding,” which reflects the patients’ processing speed, also showed gender difference favoring women (men: mean [SD] = 51.79 [11.7], women: mean [SD] = 54.99 [13.2], $P = .01$). A mild-to-moderate association between age and processing speed was found for women ($r = 0.17$, $P = .01$) for whom higher age was associated with better performance.

Self-Efficacy

There were 391 participants (98%) who completed the GSE. Men had significantly better scores on self-efficacy than women (mean [SD] = 25.4 [6.8] vs mean [SD] = 23.2 [6.6], $P = .007$).

Table 4 shows a significant but mild association between working alliance and negative and disorganized symptoms ($r = -0.20$, $P < .01$ and $r = -0.14$, $P = .01$, respectively), and social function ($r = 0.20$, $P < .01$). The correlations between working alliance and positive symptoms and compliance with antipsychotic medication were not significant. Mild-to-moderate and significant Pearson correlations were found between cognitive function and outcome, ranging from $r = -0.22$, $P < .01$ (positive symptoms) to $r = -0.38$, $P < .01$ (negative symptoms), and $r = 0.41$, $P < .01$ (social function). All associations between the different outcome variables and predictors are shown in Table 4.

Linear regression analyses were used to assess the associations between working alliance and clinical and functional outcome. We adjusted for covariates in different models; all were adjusted for age and sex, 1 additionally was adjusted for cognitive status, and 1 finally for self-efficacy. There was no significant association between WAI and compliance with antipsychotic medications, and consequently, we did not enter compliance as a mediator, allowing us to withdraw it as a covariate in the regression analyses. Adjustment for substance use disorders and level of education showed that these were not confounders (data not shown). Finally, we adjusted all analyzed models for WAI in a separate model, which did not alter any of the regression analyses, indicating that working alliance is not a confounder of the other observed associations (data not shown). All models and the proportion of variance explained by each model (R^2) are shown in Table 5.

Results of the linear regressions revealed an overall trend of a significant association between working alliance and negative and disorganized symptoms, as well as social

Table 3. Gender Differences and Scores of Working Alliance, Cognitive Function, and Self-Efficacy in a Cohort of 400 Patients With a First-Episode Psychosis After 19 Months of Treatment^a

Predictor Variable	n	Mean (SD)	P	N = 400 ^b Mean (SD)
WAI-c				
Bond subdomain				
Male	181	22.7 (4.2)	.74	22.79 (4.5)
Female	202	22.9 (4.7)		
Task subdomain				
Male	181	21.4 (4.1)	.36	21.64 (4.3)
Female	202	21.8 (4.5)		
Goal subdomain				
Male	181	22.0 (3.9)	.22	22.22 (3.9)
Female	202	22.5 (4.0)		
WAI-c total				
Male	181	66.1 (10.8)	.37	66.66 (11.5)
Female	202	67.2 (12.0)		
BACS				
Verbal memory				
Male	186	45.0 (11.2)	.15	45.84 (10.7)
Female	200	46.6 (10.2)		
Digit sequencing total				
Male	186	18.3 (4.8)	.54	18.18 (4.9)
Female	200	18.0 (5.0)		
Token motor total				
Male	186	58.4 (15.9)	.13	59.67 (16.3)
Female	200	60.9 (16.5)		
Semantic fluency				
Male	186	22.5 (6.5)	.001	23.94 (8.0)
Female	200	25.3 (9.0)		
Letter fluency "F"				
Male	186	11.7 (5.2)	.02	12.38 (5.3)
Female	200	13.0 (5.2)		
Letter fluency "S"				
Male	186	12.9 (5.0)	.10	13.40 (5.3)
Female	200	13.8 (5.5)		
Symbol coding				
Male	186	51.8 (11.7)	.01	53.45 (12.6)
Female	200	55.0 (13.2)		
Tower of London				
Male	186	17.7 (3.7)	.75	17.59 (3.4)
Female	200	17.5 (3.2)		
GSE				
Total score				
Male	186	25.4 (6.8)	.007	24.40 (6.7)
Female	205	23.2 (6.6)		

^aAll numbers (WAI-c, BACS, and GSE) reflect cases with total answers in all subdomains. Variables in bold reflect statistically significant differences between women and men.

^bRange from 383 to 391.

Abbreviations: BACS = Brief Assessment of Cognition in Schizophrenia, GSE = General Self-Efficacy scale, WAI-c = Working Alliance Inventory-client version.

functioning. The associations were strongest when adjusted for only age and sex; for example, the associations between working alliance and the negative symptoms ($\beta = -0.17$; $P < .001$, 95% CI, -0.25 to -0.08). In the fully adjusted model, we found significant, though weak, associations between working alliance and negative symptoms ($\beta = -0.12$; $P < .001$, 95% CI, -0.19 to -0.04); likewise, for the association between working alliance and social functioning ($\beta = 1.45$; $P < .001$, 95% CI, 0.55 to 2.36). Linear regression analyses were conducted for GSE and compliance, and for global level of cognitive function as predictor variables, as well. These analyses revealed that especially GSE and cognitive function were associated more robustly with outcome variables than

WAI. The fully adjusted association between working alliance and psychotic symptoms is, however, not significant in the expected direction ($\beta = -0.07$; 95% CI, -0.17 to 0.04).

The comparison of the change (Δ) in the regression coefficient (β) between models 2 and 3 was made in order to establish whether self-efficacy mediated the association between the main predictors and clinical and functional outcomes. Self-efficacy seemed to mediate some of the association between working alliance and negative symptoms and social function as it accounted for 14.3% and 17.6% of the changes in β association (Table 5).

In order to generalize our results to other studies of working alliance in a first-episode sample, we conducted a subgroup analysis of the full data set without the participants with a diagnosis of schizotypal disorder, which revealed no substantial differences (data not shown).

DISCUSSION

This study examined the association between working alliance and outcome in a cohort of patients suffering from first-episode psychosis. We found significant associations between working alliance and negative and disorganized symptoms, as well as social functioning; better scores of working alliance were associated with less severe negative and disorganized symptoms and better social functioning. Although data support our hypotheses, the associations were weak. The association between alliance and symptoms corresponds with other studies carried out in a case-manager setting that found some relationship between strength of client-rated alliance and psychiatric symptoms.^{13,15} However, 1 study found only the consequences of the negative symptoms, such as lack of friendship and fewer leisure activities, to be a predictor of therapeutic alliance.¹⁶ The association between working alliance and psychotic symptoms in our study was not significant, and the level of psychotic symptoms seemed to be associated with the patients' compliance with antipsychotic medication.

Our design is limited by a single assessment, and it is not possible to ascertain causality or determine the direction of the association between working alliance and outcome. It may be that less severe negative symptoms and better social function are factors facilitating a positive assessment of working alliance after 18 months in treatment. Or, a strong working alliance may optimize the patients' adherence to and benefit from the treatment in general. Poor adherence to treatment has been linked to poor outcome in a first-episode psychosis population.⁴¹

Self-Efficacy and Global Level of Cognitive Function

Our results indicate that self-efficacy may mediate the association between working alliance and outcome when used as a confounder variable. This means that intrapersonal factors, such as the patients' belief in their capacity to manage future stressful situations, may be an important factor in order to benefit from the collaboration with their case manager. In line with a previous study finding that self-efficacy may be related to coping responses,⁴² self-efficacy

Table 4. Univariate Correlation Matrix of Continuous Outcome Variables Among 400 Patients Treated for 19 Months in a Specialized Early Intervention Team^a

Outcome Variable	WAI-c	Psychotic Dimension	Negative Dimension	Disorganized Dimension	GAF	GSE	Compliance	BACS
WAI-c		-0.09	-0.20**	-0.14**	0.20**	0.10*	0.09	0.08
Psychotic dimension ^b			0.31**	0.24**	-0.32**	-0.22**	-0.24**	-0.22**
Negative dimension ^c				0.28**	-0.61**	-0.24**	-0.10*	-0.38**
Disorganized dimension ^d					-0.20**	-0.05	-0.15**	-0.07
GAF						0.31**	0.16**	0.41**
GSE							0.06	0.06
Compliance								-0.04
BACS ^e								

^aValues are Pearson *r* correlation coefficients; numbers in bold reflect a significant correlation.

^bGlobal item scores of hallucinations and delusions.

^cGlobal item scores of affective flattening, alogia, avolition, and anhedonia.

^dGlobal item scores of bizarre behavior, formal thought disorder, and single item score of inappropriate affect.

^eComposite *z* score.

*Correlations are significant at the .05 level (2-tailed).

**Correlations are significant at the .01 level (2-tailed).

Abbreviations: BACS = Brief Assessment of Cognition in Schizophrenia, GAF = Global Assessment of Functioning, GSE = General Self-Efficacy scale, WAI-c = Working Alliance Inventory–client version.

Table 5. Linear Regression Analyses of the Association Between Working Alliance and Outcome Variables in a Cohort of 400 Patients Treated for 19 Months in a Specialized Early Intervention Team^a

Predictor	Outcome Variable	Model 1: Association Between Predictor and Outcome Variable Controlled for Age and Sex as Confounder	Model 2: Association Between WAI-c and Outcome Variable Controlled for Age, Sex, and Cognitive Status as Confounder	Model 3: Association Between WAI-c and Outcome Variable Controlled for Age, Sex, and Cognitive Status as Confounder and General Self-Efficacy as a Mediator	Percentage Decrease (%) in Regression Coefficient (β) After Adjusted for Self-Efficacy as Mediator
		β (CI) R ²	β (CI) R ²	β (CI) R ²	Δ
WAI-c ^b	Psychotic dimension	-0.11 (-0.22 to 0.00) 3%	-0.09 (-0.20 to 0.01) 7%	-0.07 (-0.17 to 0.04) 10%	22.2%
	Negative dimension	-0.17 (-0.25 to -0.08)** 6%	-0.14 (-0.21 to -0.06)** 19%	-0.12 (-0.19 to -0.04)** 23%	14.3%
	Disorganized dimension	-0.07 (-0.12 to -0.02)* 3%	-0.06 (-0.11 to -0.01)* 3%	-0.06 (-0.11 to -0.01)* 2%	0%
	GAF, function	2.06 (1.04 to 3.08)** 5%	1.76 (0.81 to 2.71)** 20%	1.45 (0.55 to 2.36)** 28%	17.6%
GSE ^b	Psychotic dimension	-0.36 (-0.54 to -0.18)** 5%	0%
	Negative dimension	-0.36 (-0.50 to -0.23)** 9%	
	Disorganized dimension	-0.06 (-0.14 to 0.31) 1%	
	GAF, function	5.85 (4.17 to 7.53)** 12%	
Compl	Psychotic dimension	-0.22 (-0.32 to -0.13)** 6%	
	Negative dimension	-0.07 (-0.15 to 0.00) 3%	
	Disorganized dimension	-0.07 (-0.12 to -0.03)** 3%	
	GAF, function	1.45 (0.52 to 2.38)** 3%	
Cog	Psychotic dimension	-0.28 (-0.40 to -0.16)** 6%	
	Negative dimension	-0.35 (-0.44 to -0.26)** 16%	
	Disorganized dimension	-0.04 (-0.10 to 0.02) 2%	
	GAF, function	4.73 (3.64 to 5.82)** 17%	

^aVariables in bold reflect significant association between predictor and outcome variables. Numbers are unstandardized regression coefficients (95% confidence interval), adjusted *R*² for model success; Δ = (-β model 1) - (-β model 2)/(-β model 1). For simplicity, Models 2 and 3 do not present data for Cog and GSE as predictors. Compliance is not included in Models 2 and 3.

^bRegression coefficients reflect 10-point increase in WAI-c and GSE scores, respectively.

**P* < .05.

***P* < .001.

Abbreviations: Cog = cognitive status assessed with Brief Assessment of Cognition in Schizophrenia, Compl = compliance with antipsychotic medication, GAF = Global Assessment of Functioning, GSE = General Self-Efficacy scale, WAI-c = Working Alliance Inventory–client version.

is considered to be a mediator due to the recovery-oriented impact of patient–case-manager collaboration.

Cognition represents a complex set of functions necessary for being in a collaborative setting. We consider level of cognitive function to be a confounder or moderator variable influencing the strengths of the association between working alliance and outcome. Theoretically, it has been

suggested that basic cognitive functions are a prerequisite for developing self-efficacy,^{43,44} so that the 2 factors may be interdependent.

Gender Differences

Significant gender differences in favor of women are comparable with other study findings showing that women

have fewer negative and disorganized symptoms, better social functioning, higher levels of education, and a lower prevalence of comorbid diagnoses of substance abuse, as well as a higher probability of being in an intimate relationship.^{17,20,45–47} Consistent with previous studies, we did not find an association between gender and strength of the working alliance.^{12,14} Concerning cognition, women performed better than men on verbal memory and semantic and letter fluency. Men, on the other hand, assessed themselves higher on the scale of self-efficacy than did women.

Limitation

Participants in this study all signed up for the OPUS II trial and indirectly signed up for the opportunity to extend their treatment in OPUS. We have no knowledge of the working alliance for the patients who were approached but did not participate in the trial; this introduces a risk of selection bias. Another limitation is the cross-sectional design of the study and the inability to ascertain the direction of the associations.

CONCLUSIONS

Our results indicate that working alliance between patient and case manager is not the only keystone in the OPUS treatment. However, a strong working alliance may be a prerequisite for achieving and maintaining treatment adherence, thus providing the basis for fully utilizing intrapersonal factors such as self-efficacy and cognition in order to achieve better clinical and functional outcome. Our findings also suggest that patients with more severe negative symptoms and reduced social function are at higher risk for attaining poor working alliance. Consequently, the case manager must provide more concrete support and help in order to assist these patients to attain the full advantages of the working alliance.

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REFERENCES

- Horvath AO, Symonds BD. Relation between working alliance and outcome in psychotherapy: a meta-analysis. *J Couns Psychol*. 1991;38(2):139–149.
- Martin DJ, Garske JP, Davis MK. Relation of the therapeutic alliance with outcome and other variables: a meta-analytic review. *J Consult Clin Psychol*. 2000;68(3):438–450.
- Bordin ES. The generalizability of the psychoanalytic concept of the working alliance. *Psychother Theory Res Pract*. 1979;16(3):252–260.
- Horvath AO, Greenberg LS. Development and validation of the Working Alliance Inventory. *J Couns Psychol*. 1989;36(2):223–233.
- Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophr Bull*. 1997;23(4):637–651.
- Frank AF, Gunderson JG. The role of the therapeutic alliance in the treatment of schizophrenia: relationship to course and outcome. *Arch Gen Psychiatry*. 1990;47(3):228–236.
- Svensson B, Hansson L. Relationships among patient and therapist ratings of therapeutic alliance and patient assessments of therapeutic process: a study of cognitive therapy with long-term mentally ill patients. *J Nerv Ment Dis*. 1999;187(9):579–585.
- Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry*. 2002;63(10):892–909.
- Montreuil TC, Cassidy CM, Rabinovitch M, et al. Case manager- and patient-rated alliance as a predictor of medication adherence in first-episode psychosis. *J Clin Psychopharmacol*. 2012;32(4):465–469.
- Misdrachi D, Petit M, Blanc O, et al. The influence of therapeutic alliance and insight on medication adherence in schizophrenia. *Nord J Psychiatry*. 2012;66(1):49–54.
- Howeggo IM, Yellowlees P, Owen C, et al. The therapeutic alliance: the key to effective patient outcome? a descriptive review of the evidence in community mental health case management. *Aust N Z J Psychiatry*. 2003;37(2):169–183.
- Klinkenberg WD, Calsyn RJ, Morse GA. The helping alliance in case management for homeless persons with severe mental illness. *Community Ment Health J*. 1998;34(6):569–578.
- Calsyn RJ, Klinkenberg WD, Morse GA, et al. Predictors of the working alliance in assertive community treatment. *Community Ment Health J*. 2006;42(2):161–175.
- Calsyn RJ, Morse GA, Allen G. Predicting the helping alliance with people with a psychiatric disability. *Psychiatr Rehabil J*. 1999;22(3):283–287.
- Cunningham J, Calsyn RJ, Burger GK, et al. Client outcomes and the working alliance in the client-case manager relationship: a causal analysis. *Care Manag J*; 2007;8(3):106–112.
- Bourdeau G, Thérout L, Lecomte T. Predictors of therapeutic alliance in early psychosis. *Early Interv Psychiatry*. 2009;3(4):300–303.
- Petersen L, Jeppesen P, Thorup A, et al. A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ*. 2005;331(7517):602–605.
- Bertolote J, McGorry P. Early intervention and recovery for young people with early psychosis: consensus statement. *Br J Psychiatry suppl*. 2005;187(48):s116–s119.
- McGorry PD, Edwards J, Mihalopoulos C, et al. EPPIC: an evolving system of early detection and optimal management. *Schizophr Bull*. 1996;22(2):305–326.
- Craig TK, Garety P, Power P, et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ*. 2004;329(7474):1067.
- Marshall M, Lockwood A, Lewis S, et al. Essential elements of an early intervention service for psychosis: the opinions of expert clinicians. *BMC Psychiatry*. 2004;4:17.
- Bandura A, Locke EA. Negative self-efficacy and goal effects revisited. *J Appl Psychol*. 2003;88(1):87–99.
- Bandura A. On the functional properties of perceived self-efficacy revisited. *J Manage*. 2012;38(1):9–44.
- Melau M, Bertelsen M, Jeppesen P, et al. A randomised clinical trial of the effect of five-years versus two-years specialised assertive intervention for first episode psychosis—the Opus II Trial. *Schizophr Res*. 2010;117(2–3):526.
- Stein LI, Santos AB. *Assertive Community Treatment of Persons With Severe Mental Illness*. New York, NY; London, UK: W W Norton & Company; 1998.
- McFarlane WR, Dixon L, Lukens E, et al. Family psychoeducation and schizophrenia: a review of the literature. *J Marital Fam Ther*. 2003;29(2):223–245.
- Anderson CM, Reiss D, Hogarty GE. *Schizophrenia and the Family: A Practitioner's Guide to Psychoeducation and Management*. New York, NY: The Guilford Press; 1986.
- McFarlane WR, Lukens E, Link B, et al. Multiple-family groups and psychoeducation in the treatment of schizophrenia. *Arch Gen Psychiatry*. 1995;52(8):679–687.
- Lieberman RP, Mueser KT, Wallace CJ. Social skills training for schizophrenic individuals at risk for relapse. *Am J Psychiatry*. 1986;143(4):523–526.
- Wing JK, Babor T, Brugha T, et al. Schedules for Clinical Assessment in Neuropsychiatry. SCAN: Schedules for Clinical Assessment in

- Neuropsychiatry. *Arch Gen Psychiatry*. 1990;47(6):589–593.
31. Horvath AO, Greenberg LS. *The Working Alliance: Theory, Research, and Practice*. New York, NY: Wiley; 1994.
 32. Tracey TJ, Kokotovic AM. Factor structure of the Working Alliance Inventory. *Psychol Assess*. 1989;1(3):207–210.
 33. Bordin ES. *Theory and Research on the Working Alliance: New Directions. The Working Alliance: Theory, Research, and Practice*. New York, NY: Wiley; 1994:13–37.
 34. Andreasen NC, Olsen S. Negative v positive schizophrenia: definition and validation. *Arch Gen Psychiatry*. 1982;39(7):789–794.
 35. Andreasen NC. Negative symptoms in schizophrenia: definition and reliability. *Arch Gen Psychiatry*. 1982;39(7):784–788.
 36. Arndt S, Andreasen NC, Flaum M, et al. A longitudinal study of symptom dimensions in schizophrenia: prediction and patterns of change. *Arch Gen Psychiatry*. 1995;52(5):352–360.
 37. Endicott J, Spitzer RL, Fleiss JL, et al. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976;33(6):766–771.
 38. Luszczynska A, Scholz U, Schwarzer R. The General Self-Efficacy Scale: multicultural validation studies. *J Psychol*. 2005;139(5):439–457.
 39. Keefe RSE, Goldberg TE, Harvey PD, et al. The Brief Assessment of Cognition in Schizophrenia: reliability, sensitivity, and comparison with a standard neurocognitive battery. *Schizophr Res*. 2004;68(2–3):283–297.
 40. Keefe RSE, Harvey PD, Goldberg TE, et al. Norms and standardization of the Brief Assessment of Cognition in Schizophrenia (BACS). *Schizophr Res*. 2008;102(1–3):108–115.
 41. Malla A, Payne J. First-episode psychosis: psychopathology, quality of life, and functional outcome. *Schizophr Bull*. 2005;31(3):650–671.
 42. Ventura J, Nuechterlein KH, Subotnik KL, et al. Self-efficacy and neurocognition may be related to coping responses in recent-onset schizophrenia. *Schizophr Res*. 2004;69(2–3):343–352.
 43. Bandura A, Caprara GV, Barbaranelli C, et al. Role of affective self-regulatory efficacy in diverse spheres of psychosocial functioning. *Child Dev*. 2003;74(3):769–782.
 44. Bandura A. Regulation of cognitive-processes through perceived self-efficacy. *Dev Psychol*. 1989;25(5):729–735.
 45. Thorup A, Petersen L, Jeppesen P, et al. Gender differences in young adults with first-episode schizophrenia spectrum disorders at baseline in the Danish OPUS study. *J Nerv Ment Dis*. 2007;195(5):396–405.
 46. Thorup A, Petersen L, Jeppesen P, et al. The opus trial: gender differences in a sample of 547 first-episode psychotic patients. *Schizophr Bull*. 2005;31(2):505.
 47. Koester A, Lajer M, Lindhardt A, et al. The Danish national schizophrenia project: response to clinical treatment according to gender in first episode psychosis. *Eur Psychiatry*. 2008;23:S124–S125.