Symptom severity, quality of sleep, and treatment adherence among patients suffering from schizophrenia and depression

Peggy Bosch[1,2,3], Janina Waberg[1,2], Maurits van den Noort[3,4], Heike Staudte[2], Sabina Lim[3], Jos Egger[1,5,6,7]

[1]Centre for Cognition, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, 6500 GL Nijmegen, the Netherlands.
[2]Psychiatric Research Institute, LVR-Klinik Bedburg-Hau, 47511 Bedburg-Hau, Germany.
[3]Research Group of Pain and Neuroscience, Kyung Hee University, Seoul 130-701, South Korea.
[4]Brussels Institute for Applied Linguistics, Vrije Universiteit Brussel, 1050 Brussels, Belgium.
[5]Behavioural Science Institute, Radboud University Nijmegen, 6500 GL Nijmegen, the Netherlands.
[6]Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute for Psychiatry, 5803 AC Venray, the Netherlands.
[7]Pompe Institute for Forensic Psychiatry, PRO Persona, 6503 CK Nijmegen, the Netherlands.

Dr. Peggy Bosch received her PhD from the Radboud University, Nijmegen in the Netherlands and works as a clinical psychologist for the LVR-Klinik Bedburg-Hau in Germany. She is especially interested in schizophrenia, depression and sleep disorders.

ABSTRACT

Aim: Treatment non-adherence is a common problem in patients suffering from schizophrenia and depression. This study investigated the possible relationships between symptom severity, quality of sleep, and treatment adherence. **Methods:** Thirty outpatients with schizophrenia and 58 outpatients with depression were enrolled in this study. The beck depression Inventory-II, the positive and negative syndrome scale, and the pittsburgh sleep quality index were used to assess symptom severity and quality of sleep, and sleep log data were used to measure treatment adherence. **Results:** The preliminary results showed no significant relationship between symptom severity and treatment adherence or between quality of sleep and treatment adherence in patients with depression. However, a significant positive relationship was found between negative symptoms and treatment adherence and a significant negative relationship between quality of sleep and treatment adherence in patients with schizophrenia. **Conclusion:** The present exploratory study revealed a positive relationship between symptom severity and treatment adherence and a negative relationship between quality of sleep and treatment adherence in patients with schizophrenia, but no significant relationships in patients with depression were found. Future studies are needed in order to gain a better understanding of possible risk factors related to treatment non-adherence.

Key words: Depression; quality of sleep; schizophrenia; symptom severity; treatment adherence

INTRODUCTION

Dropout is a serious problem in treating patients because treatment can only be effective if delivered adequately and completely.[1] To date, very little is known about possible risk factors that might predict patient dropout.[2] Findings by Herman et al.[3] indicate that early treatment dropout is an essential factor in determining treatment success and failure because in case of dropout, patients receive little or nothing of the intervention involved and, therefore, cannot

Corresponding Author: Dr. Peggy Bosch, Centre for Cognition, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Postbus 9104, Montessorilaan 3, 6500 GL Nijmegen, the Netherlands. E-mail: P.bosch@donders.ru.nl

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benefit from therapy. "Adherence to treatment" refers to the extent to which a patient's behavior conforms to the advice of health professionals.[4] Although dropout and adherence to treatment are related issues, there are also important distinctions between these two concepts.[5]

Clinical psychologists have reported that, unfortunately, non-compliance with homework as part of cognitive-behavioral therapy is a common phenomenon in clinical practice.[6] This is problematic because research has shown that homework compliance is positively associated with reduced symptom severity.[7]

Treatment non-adherence is a common problem in patients suffering from depression or schizophrenia.[8] In cases of schizophrenia, poor adherence to medication and psychosocial treatment are prevalent and increase the probability of relapse and re-hospitalization.[9] In their review of 39 studies published in English since 1980 and specifically examining risk factors for medication non-adherence, Lacro *et al.*[10] pointed out that in those studies, the mean rate of non-adherence to medication for patients with schizophrenia was 41%. Moreover, in their systematic review of 103 studies on adherence to treatment by patients with psychosis, Nosé *et al.*[11] reported a mean rate of failure to keep scheduled follow-up appointments of 24% in patients with psychoses. Rates of treatment dropout are reported less often; the figures for this range from 20% to 56% in patients with schizophrenia.[12-14] In patients with depression, the severity of the disorder has been associated with treatment dropout in some studies,[15] but not in all.[16] Agreeing with Last *et al.*[15] Leserman[17] indicated that patients with depression were less likely to adhere to a treatment program than patients without depression and experienced worse outcomes in health.

Schizophrenia and depression are both seemingly dropout-prone disorders,[18,19] but which specific factors can be related to the non-adherence to treatment in patients with either condition is arguable. An association between less severe psychiatric symptoms and better treatment adherence was found,[20] and both the severity of the disease and the patient's attitude towards the prescribed medication were found to be related to adherence in patients with schizophrenia.[21] In this case, the severity was found to correlate negatively with treatment adherence while the patient's attitude towards the prescribed medication was found to correlate positively with treatment adherence.

Also, a role for quality of sleep in treatment adherence

of patients with schizophrenia or depression has been suggested.[22,23] Phillips and colleagues,[23] for instance, considered adherence to treatment to be a factor that correlated with sleep disturbance and depression. Their results showed that women with greater sleep disturbances also had a higher level of depressive symptoms and poor adherence to their medication regimen. According to these findings,[23] not only the severity of the disorder but also suffering from sleep disturbances might be related to treatment non-adherence in patients with schizophrenia or depression. A possible role for quality of sleep in treatment adherence is further supported by the fact that both schizophrenia and depression are co-morbid with sleep disturbances.[24,25]

However, to date, not much research has been conducted on the specific factors that can be related to the non-adherence to treatment in patients with schizophrenia or depression. As a result, more research is needed on the possible factors suggested in the literature, symptom severity and quality of sleep, as being related to treatment non-adherence. The aim of the present study was, therefore, to investigate the possible relationships between symptom severities, quality of sleep, and treatment adherence further. Thereby, noting that treatment non-adherence limits the improvements in independent living, employment, and quality of life to a large degree in patients with schizophrenia or depression is important.[26] First, patients with a more severe depression were hypothesized to have worse treatment adherence than patients with a less severe depression. Secondly, patients with schizophrenia who show more positive and negative symptoms were hypothesized to have worse treatment adherence than patients with schizophrenia who show fewer positive and negative symptoms. A final hypothesis was that patients who have a poor quality of sleep have worse treatment adherence than patients who have a good quality of sleep.

METHODS

Setting and participants

The participants in this study consisted of 17 female and 13 male adult patients with schizophrenia with an average age of 41 (SD = 8.80) and 40 female and 18 male adult patients with depression with an average age of 45 (SD = 12.14). All participants were outpatients of the LVR-Klinik Bedburg-Hau in Germany and were diagnosed by their psychiatrist according to the 10th revision of the International Classification of Diseases and Related Health Problems (ICD-10).[27] Note that in Germany, the ICD-10[27] is used instead of the Diagnostic and Statistical Manual

of Mental Disorders, fifth edition (DSM-V).[28] The inclusion criterion for all participants was that they be between 18 and 65 years of age, and the exclusion criteria for the patients with schizophrenia or depression were substance abuse, epilepsy, and other neurological disorders. Finally, all patients took part voluntarily without any inducement and signed the informed consent form.

Material

BDI-II

The Beck Depression Inventory-II (BDI-II)[29] was used to assess depression severity. The BDI-II is a 21-item self-report inventory, and each item is rated on a 4-point scale (i.e. from 0 to 3). Thus, an individual's scoring range would lie between 0 and 63. The higher the total scores on the BDI-II, the more severe the depressive symptoms of the patients are.

PANSS

In addition, the Positive and Negative Syndrome Scale (PANSS)[30] was used to measure the symptom severity of the patients with schizophrenia. The PANSS has to be filled in by a psychiatrist. It consists of three subscales: the positive scale, the negative scale and the general psychopathology scale. The scoring range for an individual is between 7 and 49 for the positive scale, 7 and 49 for the negative scale, and 16 and 112 for the general psychopathology scale; as a result, the total scores on the PANSS are between 30 and 210. The higher the total scores on the PANSS are, the more severe the positive and negative symptoms of the individuals with schizophrenia are.

PSQI

The Pittsburgh Sleep Quality Index (PSQI)[31] was used to measure the subjective quality of sleep of the patients with schizophrenia or depression. The PSQI is a self-report inventory and measures sleep quality and patterns of sleep. It has seven separate domains: (1) "subjective sleep quality"; (2) "sleep latency"; (3) "sleep duration"; (4) "habitual sleep efficiency"; (5) "sleep disturbances"; (6) "use of sleep medication"; and (7) "daytime dysfunction over the last month". Individuals score all items on a Likert scale, ranging from 0 to 3. As a result, the total scores on the PSQI are between 0 and 21, and the higher the total PSQI score is, the poorer the quality of sleep is. In daily clinical practice, often a cut-off score of 5[31] is used, meaning that participants who score below 5 have a good quality of sleep and participants who score above 5 have a poor quality of sleep. In the present study, the total PSQI scores were used for further analyses.

Sleep log

As part of the treatment adherence measurements for the schizophrenic and depressive patients,[32] the participants were asked to complete a sleep log for two weeks. It consisted of the following six sleep variables: (1) "total sleep time"; (2) "how many minutes awake during the night"; (3) "how many minutes awake before falling asleep"; (4) "how relaxing was your sleep"; (5) "did you feel exhausted"; (6) "how was your average performance level today". The sleep log was to be completed every morning just after awakening and every evening just before falling asleep.[33] Completing the sleep log took approximately 10 min a day, 140 min in total.

Procedure

Every participant in the group of patients with depression was asked to complete the BDI-II and the PSQI. The PANSS was completed by the patient's psychiatrist in the group of patients with schizophrenia, and these patients were also asked to complete the PSQI. All participants were asked to keep a sleep log and return it to their clinical psychologist at the end of the two weeks. At the end of the study, a debriefing was offered to all participants, in which they were individually informed of their test results. The study was approved by the local ethics committee (Ärztekammer Nordrhein, number: 2008331); moreover, the clinical trial has officially been registered under number NTR3132 at the Dutch Trial Register (see also http://www.trialregister.nl/trialreg/admin/rctview.asp? TC = 3132). Finally, the study was performed in accordance with the Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/).

Design and statistics

An experimental design was used in which the first categorical dependent variable was called "Absolute Treatment Adherence"; it was measured by using the returned sleep logs (i.e. if the patient returned the sleep log, the patient was considered as being treatment adherent vs. if the patient did not return the sleep log, the patient was considered as not being treatment adherent). The second continuous dependent variable was called "Degree of Treatment Adherence" because it consisted of the total number of days the participants had completed the sleep log, with 0 day meaning a very low degree of treatment adherence and 14 days meaning a very high degree of treatment adherence. In other words, "Absolute Treatment Adherence" showed whether a patient returned the sleep log or not while "Degree of Treatment Adherence" showed to what degree the patient was treatment adherent. Note that in the present study, a very narrow definition of the word "treatment" was used (e.g. completing and returning a sleep log) and did not include any pharmacological

Table 1: The number of adherent and non-adherent patients with depression and their mean scores and standard deviations on the BDI-II and the PSQII

Adherence	Instrument	Number	Mean	SD
Non-adherent	BDI-II	21	20.81	12.21
	PSQI	21	9.05	4.28
Adherent	BDI-II	37	19.24	11.28
	PSQI	37	9.51	4.17
Total	BDI-II	58	19.81	11.54
	PSQI	58	9.34	4.18

All $P > 0.05$; PSQI: pittsburgh sleep quality index; BDI-II: beck depression inventory-II

Table 2: The number of adherent and non-adherent patients with schizophrenia and their mean scores and standard deviations on the PANSS and the PSQI

Adherence	Instrument	Number	Mean	SD
Non-adherent	PANSS-total	16	67.81	19.56
	PANSS-negative	16	16.81*	6.76
	PANSS-positive	16	14.13	7.37
	PANSS-psychopathology	16	36.88	11.62
	PSQI	16	6.31	3.32
Adherent	PANSS-total	14	81.86	26.74
	PANSS-negative	14	23.43*	10.42
	PANSS-positive	14	20.71	26.44
	PANSS-psychopathology	14	44.86	14.36
	PSQI	14	8.57	4.50
Total	PANSS-total	30	74.37	23.86
	PANSS-negative	30	19.90*	9.14
	PANSS-positive	30	17.20	18.78
	PANSS-psychopathology	30	40.60	13.37
	PSQI	30	7.37	4.01

*$P < 0.05$; PANSS: positive and negative syndrome scale

Table 3: Results of the multiple regression analysis for variables predicting degree of treatment adherence

Predictor	B	SEB	β
Constant	8.95	2.48	-
BDI-II	-0.03	0.07	-0.05
PSQI	0.13	0.21	0.08

$R^2 = 0.01$; B: unstandardized multiple regression coefficient; SEB: standard error of multiple regression coefficient; β: standardized multiple regression coefficient

Table 4: Results of the multiple regression analysis for variables predicting degree of treatment adherence

Predictor	B	SEB	β
Constant	-2.14	4.13	-
PANSS-positive	0.08	0.07	0.21
PANSS-negative	0.21	0.25	0.29
PANSS-psychopathology	0.01	0.32	0.02
PANSS-total	-0.02	0.22	-0.06
PSQI	0.65	0.31	0.39*

$R^2 = 0.27$ *$P < 0.05$; B: unstandardized multiple regression coefficient; SEB: standard error of multiple regression coefficient; β: standardized multiple regression coefficient

interventions; neither did we use the sleep variables recorded in the sleep log to predict adherence. The scores on the BDI-II, the PANSS, and the PSQI served as "predictor" variables.

With SPSS version 22.0[34] a discriminant function analysis[35] was conducted with "Absolute Treatment Adherence" as a categorical dependent variable and the scores on the BDI-II and PSQI as predictor variables for the group of patients with depression. For the group of patients with schizophrenia, a discriminant function analysis was performed with "Absolute Treatment Adherence" as a categorical dependent variable and the scores on the PANSS and PSQI as predictor variables. Furthermore, two multiple regression analyses[36] were conducted with one analysis containing "Degree of Treatment Adherence" as the dependent variable and the score on the BDI-II, as well as the score on the PSQI, as independent variables for the group of patients with depression. In the second analysis, "Degree of Treatment Adherence" was used as the dependent variable, and the score on the PANSS, as well as the score on the PSQI, were used as independent variables for the group of patients with schizophrenia.

RESULTS

Absolute treatment adherence in the depression group

For the group of patients with depression, a discriminant function analysis was conducted in order to identify patients who were adherent to treatment *vs.* those who were not; this was done using the patient's scores on the BDI-II and the PSQI as predictors. The discriminant function analysis explained 100% of the variance, canonical $R^2 = 0.01$ (Note that this does not mean that the discriminant function accounts for 100% of the variance in the response variable; rather, this means that it is the only discriminant function extracted for the analysis).[37] The discriminant function analysis did not significantly differentiate the patients who were treatment-adherent from the ones who were not [Λ = 0.99, χ^2 (2) = 0.43, $P > 0.05$]. Table 1 summarizes the descriptive statistics of the group of patients with depression.

Absolute treatment adherence in the schizophrenia group

In addition, a discriminant function analysis was conducted for the group of patients with schizophrenia. The discriminant model was used to identify patients who were adherent to treatment versus those who were not treatment-adherent by using the patient's scores on the PANSS (also divided into positive symptoms, negative symptoms, and general psychopathology) and on the PSQI as predictors. The discriminant function analysis explained 100% of the variance, canonical $R^2 = 0.26$. The discriminant function analysis did not significantly differentiate the patients who were treatment-adherent from the ones who were not [Λ = 0.74, χ^2 (5) = 7.67, $P > 0.05$]. The correlations between outcomes and the discriminant function revealed that the score on the PANSS-negative loaded highly onto the function ($r = 0.67$), followed by the score on the PSQI ($r = 0.50$). Table 2 summarizes the descriptive statistics of the group of patients

with schizophrenia.

Variables predicting degree of treatment adherence in the depression group

For the group of patients with depression, a multiple regression analysis with "Degree of Treatment Adherence" as the dependent variable and the scores on the BDI-II and the PSQI as predictors was conducted. Note that the adherent depression group had a mean of 13.44 days (SD = 2.02 days). Table 3 shows the results of the multiple regression analysis using the enter method for predicting "Degree of Treatment Adherence". The scores on the BDI-II and the PSQI were insignificant predictors.

Variables predicting degree of treatment adherence in the schizophrenia group

For the group of patients with schizophrenia, a multiple regression analysis was conducted with "Degree of Treatment Adherence" as the dependent variable and the scores on the PANSS-total (also split into PANSS-positive, PANSS-negative, and PANSS-general psychopathology) and on the PSQI as predictors. Note that the adherent schizophrenia group had a mean of 12.82 days (SD = 2.43 days). Table 4 shows the results of the multiple regression analysis using the enter method for predicting "Degree of Treatment Adherence". The scores on the PANSS-total, PANSS-positive, PANSS-negative, and PANSS-general psychopathology were insignificant predictors while the score on the PSQI was a significant predictor. Moreover, the score on the PANSS-negative and the score on the PSQI correlated significantly with "Degree of Treatment Adherence" (PANSS-negative: $r = 0.31$, $P < 0.05$; PSQI: $r = 0.39$, $P < 0.05$).

DISCUSSION

The general results of our study showed that for the group of patients with depression, in contrast to our hypotheses, symptom severity and quality of sleep did not significantly predict whether a patient would be adherent to treatment or not; the severity of depression and the quality of sleep did not differ significantly between treatment adherent and non-adherent patients. For the group of patients with schizophrenia, in line with our hypotheses, a relationship was found between symptom severity and treatment adherence, as well as between quality of sleep and treatment adherence; however, the directions of those relationships were contrary to our expectations. Experiencing more severe negative symptoms was found to be significantly related to better treatment adherence. Moreover, quality of sleep did serve as a significant predictor of treatment

adherence; however, in general, the patients with schizophrenia who reported a worse quality of sleep were more treatment-adherent than those who reported a better quality of sleep and not vice versa.

The surprising findings that no relationships were found between quality of sleep and treatment adherence and between symptom severity and treatment adherence in the depression group are opposed to the findings by Ong *et al.*[2] who investigated the risk factors associated with dropping out of group cognitive-behavior therapy for insomnia and found that short sleep duration and elevated symptoms of depression at baseline could be especially associated with an increased risk of early therapy dropout. Also, in their study, Phillips *et al.*[23] reported that women with greater sleep disturbances had a higher level of depressive symptoms and poor adherence to their medication regimen. Noticeably, research that targets adherence to medication dominates research that targets adherence to treatment. Possibly, different risk factors may be related to these two forms of adherence, which might make a direct comparison between studies that target adherence to medication and studies that target adherence to treatment difficult. This suggestion remains to be verified. Overall, to date, only a few studies have been conducted on treatment non-adherence by patients with depression and its predictors,[38] so further research is warranted.

Nevertheless, in the group of patients with schizophrenia in the present study, symptom severity and quality of sleep may be related to better treatment adherence. Steger *et al.*[39] reported similar findings. The researchers assessed medication adherence in a sample of 216 patients with a first episode of psychosis; the assessments were done at program entry and three and six months later. They found an association between early resolution of negative symptoms and poor adherence. Patients whose positive symptoms had been resolved after three months of treatment did not show a change in adherence behavior compared to those whose symptoms persisted. On the contrary, early resolution of negative symptoms was significantly associated with less medication adherence compared to the patients whose negative symptoms persisted. Unfortunately, patients whose negative symptoms had been resolved but who were non-adherent experienced a worsening of both positive and negative symptoms at six month. Steger *et al.*[39] concluded that patients who experience a rapid reduction of negative symptoms must be closely followed, as they are at high risk for non-adherence. As a possible

explanation for these findings, the researchers stated that patients might associate reduction of negative symptoms with a return to normal functioning and, therefore, might decide that they no longer need medication. This assumption is supported by the finding of Quach et al.[40] whose study indicated that a high level of functioning after one year of treatment was associated with non-adherence at year two.

However, opposing findings have also been reported in the treatment adherence literature on patients with schizophrenia. A study by Tattan and Creed[41] regarding negative symptoms of schizophrenia and compliance with medication, for instance, found that patients with schizophrenia who had a poor medication compliance experienced a significantly greater severity of negative symptoms. Especially avolition, apathy, and alogia were related to poor compliance. The researchers presumed that patients who suffered from avolition and apathy would lack the motivation to regularly go to a satellite clinic. They also suggested that these patients might question the beneficial effects that the medication given at such clinics had had on their positive symptoms and might have instead focused on the limited effect that the medication had had on the negative symptoms from which they still suffer. Another point considered was that patients with alogia could possibly lack insight into their illness and, therefore, might not understand the importance of taking medication regularly. In sum, hitherto, as for depression, not much research has been conducted on the relationship between symptom severity and treatment adherence in patients with schizophrenia, and the results are conflicting.[39-41] Clearly, negative symptoms can be related to adherence, but further research is needed to gain a better understanding of this relationship.

An interesting new finding of our study is the fact that poor quality of sleep significantly predicted better treatment adherence in the group of patients with schizophrenia. This finding contradicts the finding in the study by Ong et al.[2] who reported that insomnia might be a risk factor for poor treatment adherence. To the authors' knowledge, this study was among the first to investigate a possible relationship between quality of sleep and treatment adherence in patients with schizophrenia; therefore, comparing this group of patients to another that has sleep disorders such as obstructive sleep apnoea and insomnia might be difficult. Possibly, the patients with a worse subjective quality of sleep were more treatment adherent because they could benefit from completing the sleep log and, hence, register their own sleeping patterns for a period of two weeks. Patients without sleeping problems might not understand the therapeutic use of registering their sleeping patterns and, therefore, might be more likely to not complete the sleep log.

In sum, treatment adherence appears to be a complex phenomenon and can only partly be associated with symptom severity and quality of sleep in patients with schizophrenia and patients with depression. Some studies indicate, for instance, that a weak therapeutic alliance and low insight might be related to poor adherence in patients with schizophrenia.[42] Another study by Spiekermann et al.[43] stated that patients with schizophrenia who had stronger cognitive impairments showed lower adherence behavior compared to those without cognitive impairments.

The present study has several limitations that should be discussed in order to correctly interpret its results. One limitation of our study is the fact that all data were derived from self-report inventories, which have their strengths and weaknesses.[44] However, the disadvantages, for instance, self-report measures being potentially biased by social desirability,[45] might have negatively affected the reliability of the results. Moreover, future studies might vary in their means to measure treatment adherence. For instance, attendance at a psycho-education group for patients with schizophrenia[46] could be additionally used to measure treatment adherence. Another limitation of our study is that a mixed sample of subjects, e.g., outpatients with schizophrenia and outpatients with depression, was used. Although we have presented our treatment-adherence results for the depression group and the schizophrenia group separately, having a larger sample of one patient group in order to investigate the possible relationships between symptom severity, quality of sleep, and treatment adherence would have been better because the main reasons related to non-adherence in patients with schizophrenia and those with depression may differ significantly. This is an important issue for future research. Finally, the exploratory nature of the analyses, as well as the cross-sectional study design,[47,48] used in the present study should be mentioned as further limitations, making it impossible to generalisze the results.

In conclusion, the current exploratory study revealed a significant positive relationship between symptom severity and treatment adherence, as well as a significant negative relationship between quality of sleep and treatment adherence in patients with schizophrenia, but no significant relationships between symptom

severity, quality of sleep, and treatment adherence were found in patients with depression. However, more research is needed to identify possible risk factors that can be related to treatment non-adherence to, in a second step, determine strategies to improve treatment adherence. Treatment non-adherence might be reduced, and at best prevented, if specific predictors can be related to the adherence behavior of psychiatric patients. Furthermore, identifying the characteristics of clinical patients who drop out of treatment could lead to improvements in the care these patients receive.

Conflicts of interest
There are no conflicts of interest.

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