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The real-life effectiveness of psychosocial therapies on social autonomy in schizophrenia patients: results from a nationwide cohort study in France

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Abstract

The objectives of the present study were to describe the prescribing patterns for psychosocial therapies in routine clinical practice and to assess the impact of psychoeducation on symptoms and social autonomy of patients with schizophrenia. We used data from the nationwide French ESPASS observational cohort study including 5967 patients with schizophrenia, which provided data on exposure to psychosocial therapies from 4961 (83\%) participants. Patients who initiated psychosocial therapy within the first 3 months of study onset (n=143) were compared to patients not subject to psychosocial therapy throughout follow up (n=4268), using parametric tests. Symptom severity and social autonomy at 6 months from baseline were compared between patients undergoing psychoeducation (n=117)
and patients not subject to psychosocial therapy, matched (1:1) on propensity scores. Patients who initiated psychosocial therapy were significantly younger, more severely ill and used less often antipsychotic drugs than patients in the reference group. At 6 months, patients who initiated psychoeducation and their matched referents did not differ significantly in terms of symptom severity, but their level of improvement in social autonomy was significantly greater ($p=0.005$). In routine clinical practice, psychoeducation in addition to antipsychotic drugs provides some benefit among schizophrenia patients, particularly in terms of social autonomy.

**Keywords**
Psychotherapy; Psychoeducation; Clinical Effectiveness;

1. **Introduction**

Despite disagreement about recovery rates, remission in schizophrenia is now considered as an achievable objective of treatment. Remission encompasses both symptom remission and improvement of psychosocial aspects in patients’ lives (e.g., well-being, quality of life). This distinction is important, as impairment in psychosocial aspects may persist beyond symptom remission and despite efficacious antipsychotic drugs (Jorgensen et al., 2015; Roe et al., 2011). Psychosocial therapies may modify self-experience and improve metacognition in patients with schizophrenia (Lysaker, Buck, et al., 2011; Lysaker et al., 2010). Several types of psychosocial interventions have been developed to improve the specific cognitive or functional impairment features of schizophrenia (Kern et al., 2009; Medalia et al., 2009; Patterson et al., 2008; Roder et al., 2011): social skills training (Kopelowicz et al., 2006), cognitive remediation therapy (McGurk et al., 2007; Wykes et al., 2011), cognitive behavioral therapy (Jauhar et al., 2014; Jones et al., 2012; Morrison, 2009), psychoeducation (Lincoln et al., 2007), and family therapy (McWilliams et al., 2010), to name a few. These psychosocial therapies have demonstrated some benefit at cognitive and symptomatic levels for patients
with schizophrenia: metacognition (Kopelowicz et al., 2006; Lysaker, Erickson, et al., 2011), cognitive deficits (Wykes et al., 2011), thought disorders, or negative symptoms (Klingberg et al., 2011; Morrison, 2009), social autonomy (Cochet et al., 2006), prevention of relapse (Gumley et al., 2006). They might also improve patients’ well-being (Penn et al., 2004) or adherence to medication (Barkhof et al., 2012).

However, the benefit of psychosocial interventions has been nearly exclusively assessed through Randomized Clinical Trials (RCTs) (Jauhar et al., 2014; Lincoln et al., 2007; Pilling et al., 2002; Wykes et al., 2011; Xia et al., 2011). Although RCTs are the gold standard for measuring the efficacy of medical interventions as provided under ideal conditions, it is often difficult to extrapolate findings to routine clinical practice (Depp et al., 2007). RCTs of psychosocial therapies usually take place in specialized centers for treatment of schizophrenia, where healthcare providers are highly trained clinicians and where human and technical resources are more numerous. Therefore, little is known about patients who actually receive psychosocial therapies in real life. In addition, participants enrolled in RCTs are carefully selected and homogeneous (Jones et al., 2012; Stirman et al., 2003). The question of generalization from results of RCTs is of particular importance for psychoeducation which involve several types of programs and practices. Also, psychoeducation may be easier to implement across psychiatric teams, as opposed to cognitive-based therapies. In contrast to RCTs, observational studies provide the opportunity to explore those patients undergoing psychosocial therapies in routine clinical practice. They also provide the opportunity to measure the impact of psychosocial therapies in a more heterogeneous sample of patients, hence extending the scope for generalization of study results (Fleischhacker et al., 2009).

The present study aimed to (1) describe the real-life prescribing patterns for psychosocial therapies among patients with schizophrenia, and (2) assess the impact of psychosocial therapies on schizophrenia symptoms and social autonomy in routine clinical practice, with a
focus on psychoeducation. Based on previous data published on psychoeducation (Xia et al., 2011), we hypothesized that the improvement of schizophrenia symptoms and social autonomy would be higher in patients receiving psychoeducation.

2. Materials and Methods

Data were drawn from the “Enquête Sur les Prescriptions antipsychotiques et sur l’Autonomisation et la Socialisation des patients Schizophrènes” (ESPASS) cohort, a non-interventional, observational prospective cohort study including schizophrenia patients at the time of antipsychotic medication initiation or of a change in antipsychotic medication (Leguay et al., 2010; Limosin et al., 2008; Nordon et al., 2014).

After complete description of the study to the patients, verbal consent was obtained for all patients included. The study design was approved by the French National Order of Physicians (“Ordre National des Médecins”) and the French commission on data computerization and personal freedoms (“Commission Nationale d’Informatique et des Libertés”).

2.1. Study participants

Between January 2005 and April 2006, 985 psychiatrists – 649 working in public settings and 336 working in private settings throughout France – included 5967 schizophrenia patients consecutively, on the following inclusion criteria: (a) age ≥18 years, (b) diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders criteria, fourth edition (American Psychiatric Association., 2000), (c) need for antipsychotic medication initiation or a change in antipsychotic medication in the normal course of care as decided by the psychiatrist, and (d) consent to participate. The investigators (psychiatrists) included their own patients when appropriate and all medical decisions were left at their discretion in order to adhere to real-life conditions and to maximize the scope for generalizing the results.
For the present study, we restricted the original ESPASS population to patients with available data on psychosocial therapy prescription at baseline and during follow-up. In addition, we excluded patients who had already received psychosocial therapy at baseline or who initiated the psychological intervention after the 3-month visit.

2.2. Measures

Data was collected by the psychiatrists during the visit corresponding to recruitment (baseline) and in follow-up visits at 1 month, 3 months and 6 months.

2.2.1. Intervention and outcome measures

The intervention of interest was the initiation of any psychosocial therapy. Patients who initiated psychosocial therapy within the first 3 months from study onset were identified as belonging to the “intervention group”. Patients who did not initiate any psychosocial therapy were identified as being in the “no-intervention group”.

Real-life prescribing patterns for psychosocial therapies among patients with schizophrenia were described for any type of psychosocial therapy (initiation, yes/no). The effectiveness of psychoeducation 3 to 5 months after its initiation was measured as the evolution of symptom severity and social autonomy at 6 months, in patients initiating psychoeducation.

The severity of symptoms was measured at baseline and each follow-up visit, using two clinician-completed questionnaires: the Clinical Global Impression-Severity scale (CGI-S) (Guy, 1976) and the Investigator’s Assessment Questionnaire (IAQ) (Tandon et al., 2005). The CGI-S uses a 7-point Likert-type single-item scale – a higher score indicating greater severity of illness – that measures the global severity of disorders affecting the central nervous system. It has been validated in multiple languages, settings and diseases, in particular schizophrenia where it was found to be correlated with the PANSS and BPRS scales (Leucht et al., 2006) and sensitive enough to identify patients in remission (Pinna et al., 2015). This scale is widely used in observational effectiveness studies (Grimaldi-Bensouda et
al., 2012; Haro et al., 2005) because it can be completed rather quickly, therefore not interfering with routine clinical practice. The IAQ is a 10-item questionnaire that measures not only the severity of positive, negative, mood and cognitive symptoms, but also up to 6 types of antipsychotic drug-related adverse events. The questionnaire was developed and validated in patients with schizophrenia across 6 different countries. It showed a good internal consistency (Cronbach’s alpha=0.87) and was found to be highly correlated to the CGI-I scale (Tandon et al., 2005). Each item is rated on a 5-point Likert-type scale, a higher score indicating greater severity of symptoms. The “IAQ-4” was derived by including only the items related to the severity of positive, negative, mood and cognitive symptoms. In addition, the items related to negative symptoms and positive symptoms were divided into sub-scores (IAQ-neg and IAQ-pos, respectively).

The level of social autonomy was assessed at baseline and each follow-up visit, using the Social Autonomy Scale (SAS), a clinician-completed questionnaire developed and validated in French (Leguay et al., 1998; Leguay et al., 2010). In patients with schizophrenia, it showed both good internal consistency (Cronbach’s alpha=0.91) and good sensitivity to change. The SAS contains 17 items regrouped in 5 dimensions (“personal care”, “monitoring of everyday life”, “financial control”, “relationships with the environment”, and “affective life and social relatedness”). Each item scored on a 7-point Likert-type scale and the global score was standardized, ranging from 0 to 100, a higher score indicating a lower level of autonomy.

2.2.2. Confounding variables

Other data collected at baseline included patients’ characteristics (socio-demographics and Body Mass Index – BMI), illness characteristics (age at onset, duration of psychiatric care, schizophrenia subtype, severity of symptoms and level of autonomy) and characteristics of the healthcare setting and medical management: type of setting (full-time hospitalization or day-time hospitalization/outpatient care), characteristics of the psychiatrist (age, gender), the main
antipsychotic drug prescribed before and after baseline, and other psychotropic drugs prescribed. Antipsychotic drugs were categorized into first-generation antipsychotics (FGA) or second-generation antipsychotics (SGA).

2.3. Statistical Analyses
Analyses were performed with R 3.0.2 (R Development Core Team., 2008) “epicalc”, “psy” and “matchIt” packages. All comparative tests were two-sided with a type-1 error $\alpha=0.05$. Multiple imputations were performed on baseline data using the Markov Chain Monte Carlo (MCMC) method, to generate 5 imputed datasets. No imputation was made for exposure (initiation of psychological therapy between baseline and 3 months) or outcome (symptom severity and autonomy at 6 months). Patients with missing data on exposure were excluded from the analyses and were compared to patients included in the analyses, to detect any selection bias.

Firstly, real-life prescribing patterns of psychosocial therapies were explored by comparing patients from the “intervention group” to patients from the “no-intervention group”, using parametric tests where appropriate (Chi$^2$ or Fischer’s exact tests or Student’s t-tests), regarding characteristics of patients, illness, healthcare setting and medical management.

Secondly, to assess the effectiveness of psychoeducation on the severity of schizophrenia symptoms and on the level of autonomy, while taking into account the potential effect of an indication bias, we matched each patient from the “intervention group” to one patient from the “no-intervention group” on propensity score (PS). Briefly, the PS corresponds to the probability of being prescribed an intervention (vs. not), given a set of observed covariates. In our analyses, the propensity for initiating psychosocial therapy was computed using the imputed datasets, as a function of baseline variables (patient characteristics, illness characteristics, and healthcare setting characteristics), using a multivariate logistic regression model. The nearest-neighbor approach was used with the acceptable difference in the
matching procedure defined \textit{a priori} using a conservative calliper (logit=0.2 Standard Deviations – SD – determining the width of the propensity score interval). Those patients matched to one patient from the “intervention group” constituted a “reference group” of equal size. Next, the mean scores on the CGI-S, IAQ-4, IAQ-neg, IAQ-pos and SAS scales were computed in the “intervention group” and the “reference group” at baseline, 1, 3, and 6 months, using Student’s paired t-tests. At baseline and as a result of propensity score matching, the mean scores were expected to be similar. The primary end-point measure for effectiveness was the difference in mean scores between paired groups at 6 months.

Finally, should a difference be found between the two groups regarding CGI-S, IAQ-4 or SAS, the evolution overtime of this difference was explored through mixed linear multivariate modelling using a random intercept for the patient (the repeated observations being clustered within a patient), and where the dependent variables (changes in CGI-S, IAQ-4 and SAS from baseline to each time point) were explained by the intervention (psychoeducation yes/no), baseline values, time (1-, 3- or 6-month follow-up), and the “group x time” interaction. Testing the interaction term parameter returned a statistically significant result at the 0.05 level.

3. Results

3.1. Study population

Out of 5967 patients included in the ESPASS cohort, 1006 (16.9%) had information missing on prescription of psychosocial therapy, 504 (8.4%) patients were already receiving psychosocial therapy at baseline, 46 (0.8%) patients initiated psychosocial therapy after the period of interest (after 3 months) thus leaving 4411 (73.9%) patients available for the analyses (Figure 1). Table 1 provides the characteristics of the 4411 patients included in the analyses and 1006 patients excluded as a result of missing data on exposure. The patients excluded were not comparable to the patients included: they were younger, more often
isolated, more often hospitalized at baseline and had shorter illness duration (51% had a duration of psychiatric care inferior to 1 year).

3.2. Prescribing patterns of psychosocial therapy

Among the 4961 patients with data available on psychotherapy, 4268 (86.0%) patients were not subject to any type of psychotherapy over the whole study course, as opposed to 504 (10.2%) patients who underwent psychosocial therapy at the time of study onset, 143 (2.9%) patients who initiated psychosocial therapy between baseline and 3 months and 46 (0.9%) patients who initiated psychosocial therapy after month 3.

Psychosocial therapy initiated between baseline and 3 months consisted in psychoeducation for 117 patients (81.8%), social skills training for 34 (23.8%), cognitive remediation therapy for 19 (13.3%) and CBT for 21 (14.7%). Regarding the intensity of the therapy, it consisted in ≥10 sessions over 6 months for 14 patients (out of 19) receiving cognitive remediation therapy and 26 patients (out of 34) receiving social skills training.

Compared to the 4268 patients with no psychosocial therapy, the 143 patients from the “intervention group” were younger, less frequently employed, more severely ill, more frequently antipsychotic drug-naïve (first-episode schizophrenia patients) and less autonomous (Tables 2a and 2b). The two groups also differed in terms of medical management at baseline: patients who initiated psychosocial therapy were more frequently hospitalized or not taking anti-psychotic drugs (APDs) at study baseline and were less often on antidepressant drugs. Apart from the first-episode schizophrenia patients (APD-naïve patients), the proportion of patients without any APDs at study entry was 32% (40 out of 125) among patients who initiated psychosocial therapy compared to 15.5% (613 out of 3944) among the patients who did not (p<.0.01), suggesting that compliance problems may have been more frequent in patients who initiated psychosocial therapy. Compared to the
psychiatrists who did not prescribe any psychosocial therapy (n=859), the psychiatrists who did (n=33) were more often working in specialized hospitals and were younger (p<.001).

3.3. Effectiveness of psychological therapies

Table 3 displays the differences in symptom severity and social autonomy at baseline and 6 months, between patients who initiated psychoeducation (n=117) and their matched “referent” (n=117) who did not initiate any psychosocial therapy. At baseline, symptom severity and level of social autonomy were strictly comparable in the two groups, as a result of PS matching. At 6 months, the symptoms severity was comparable in the two groups, as measured by the CGI-S (p-value=0.22) and the IAQ-4 scales (p-value=0.80). The mean social autonomy score was significantly higher in the “reference group”, indicating a lower level of autonomy (p-value=0.005).

Figure 2 displays the evolution in clinical symptoms (CGI-S, IAQ-4 scores) and in social autonomy (SAS score) throughout the study period in the two groups. Regarding the evolution of the SAS scores overtime, the mixed linear multivariate model revealed a non-significant group x time interaction (βInteraction=-0.42; 95%CI=[-1.12; 0.28]; p-value=0.24), meaning that the rapidity of improvement was not significantly different between patients from the intervention group and their matched controls.

4. Discussion

The prescribing patterns for psychosocial therapies and the real-life impact of psychoeducation were evaluated in an observational cohort of 4961 schizophrenia patients from across France.

4.1. Who are prescribed psychological therapies in routine practice?

In routine practice, psychosocial therapies were prescribed to young and rather severely ill patients, more often during a hospitalization. Among patients who were not antipsychotic drug-naïve, we evidenced that psychosocial therapies were prescribed more often to patients
not taking antipsychotic drugs at study entry, thus possibly to less compliant patients. Adherence to medication is known to be affected in schizophrenia patients (Lacro et al., 2002; Lieberman et al., 2005), in particular as a result of neurocognitive impairment (Boyer et al., 2012). In these patients, psychosocial therapy may have been prescribed to foster adherence to medication.

The infrequency of psychosocial therapy prescriptions in routine practice can be noted: only 504 (8.4%) patients were receiving psychosocial therapy at baseline. This result could reflect insufficient healthcare resources, or barriers to translating innovation into practice. However, the data used were collected nearly ten years ago in France, and their generalizability in time and space is limited. Today, staff specialized in psychosocial therapies for schizophrenia patients may be more numerous, and awareness of their usefulness may have improved.

4.2. Is psychoeducation effective in routine clinical practice?

Regarding the effectiveness of psychoeducation on symptoms severity, as measured by the CGI-S and the IAQ-4 scales, we did not evidence any significant benefit compared to standards of care, 3 to 5 months after the initiation of this therapy. This result is in line with findings from a recent systematic literature review of RCTs (Xia et al., 2011) suggesting that global state improvement based on the CGI-S was not higher in patients undergoing psychoeducation, as compared to the standard of care. More generally, this review highlighted that results on symptom improvement were very sensitive to the measurement method used (dichotomous/continuous outcome, short/mid-term end-point, CGI-S/BPRS or PANSS, etc.).

More recently, other RCTs evidenced a benefit of providing psychoeducation to patients (Hasan et al., 2015; Sharif et al., 2012) or their caregivers (McWilliams et al., 2012). Again, these trials used several measurement tools, making it difficult to interpret whether our negative results may be attributed to the method used to quantify, or simply reflect the absence of impact of psychoeducation, on symptoms improvement.
On the contrary, we evidenced that the level of improvement in terms of social autonomy was greater among patients initiating psychoeducation, than in the reference group, 3 to 5 months after the initiation of the therapy and independent of baseline confounders. This result is in line with the results of the systematic literature review (Xia et al., 2011) suggesting that psychoeducation improves social cognition and social functioning in patients with schizophrenia. Here, we provide additional evidence on the benefit of this type of therapy as provided in a real-life nationwide, hence using a wide variety of practices, study. Measuring the impact of psychoeducation on social autonomy and functioning is relevant from a physician’s perspective, because functional status is a good predictor of both relapse and remission in the long term. It has been shown that early improvement in symptoms or functioning is one of the 6 most relevant predictors of symptomatic remission in the long-term, in both first- and multiple-episode patients (Lambert et al., 2010).

4.3. Study limitations

Our results need to be interpreted in the light of certain limitations. Firstly, 1006 (17%) patients with missing data on psychosocial therapy prescription were excluded from the analyses. These patients differed from our study population: they were more often recently-diagnosed and hospitalized at study entry. This selection bias may compromise the external validity of our results, to an extent that is difficult to estimate. Secondly, the measurement scales used (CGI-S, IAQ and SAS) were not specifically developed for assessing psychoeducational therapies. However, one could argue that a global measure, here a measure of social autonomy, is a relevant outcome from a patient’s perspective. A social autonomy scale reflects what the patient is experiencing in daily life (daily activities, social life, etc.). Thirdly, the absolute difference in the mean social autonomy score between patients who underwent psychoeducation and patients who did not, was in fact
small (4.3 points). We acknowledge that the clinical relevance of a difference of this magnitude is limited, owing to the 0–100 range of the SAS scale.

Finally, because this was an observational study, the intervention was not blinded or placebo-controlled. The absence of blinding may have introduced an observation bias if the psychiatrist who prescribed the psychoeducational therapy and also rated the level of autonomy, had overestimated the effect of psychoeducation. However, the objective of the ESPASS study was not to assess the impact of psychoeducational therapy, and the prescription of a psychoeducational therapy was a piece of information collected among many others. The likelihood of the psychiatrist making a systematic error in rating the severity of symptoms or autonomy among patients undergoing psychoeducational therapy is therefore little. The absence of a “controlled arm” makes it difficult to disentangle the specific effect of psychoeducational therapy from the effect resulting from more regular interaction of the patient with healthcare providers (“placebo-effect”). In addition to the potential role played by a placebo effect as an integral component of healing practices, and regardless of the underlying mechanism of action of the therapies used, we believe that any strategy enhancing patients’ autonomy, well-being, or adherence to care should be proposed for patients with schizophrenia.

4.4. Conclusion

In routine clinical practice, psychosocial therapies are prescribed to more severe and less compliant schizophrenia patients. Among them, psychoeducational therapy provides some additional benefit in terms of social autonomy, compared to antipsychotic drugs alone. As they are therapeutic processes that actively involve the patients, psychosocial therapies could improve the patients' feeling of empowerment. This, in turn, could be a crucial step towards recovery.
The ESPASS cohort study was initiated and financed by Brystol-Myers Squibb (BMS) and Otsuka Pharmaceuticals France (data collection and data management). The database was made available to the INSERM research unit, without any particular brief. BMS and Otsuka did not take part in the design, implementation, statistical analyses, results or publication of this paper. The authors did not receive any fee from BMS or Otsuka for this work.

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Declaration of interest
Clementine Nordon is an employee of LASER, a research and consulting company, virtually collaborating with all pharmaceutical industries. Bruno Falissard has received fees from E. Lilly, BMS, Servier, SANOFI, GSK, HRA, Roche, Boeringer Ingelheim, Bayer, Almirall, Allergan, Stallergene, Genzyme, Pierre Fabre, Astrazeneca, Novartis, Janssen, Astellas, Biotronik, Daiichi-Sankyo, Gilead, MSD, Lundbeck, Stallergene, Actelion, UCB, Otsuka, Grunenthal, ViIV.

Mathieu Urbach, Arnaud Carré, Aminata Ali, Sylvie Berthoz, Massimiliano Orri, Christine Hassler and Caroline Barry have no conflict of interest to disclose.

Authors contribution
AC, AA and CN designed the study and wrote the protocol. CN and AC managed the literature searches and analyses. AA and CN undertook the statistical analysis. CN and AC wrote the draft of the manuscript. All authors contributed to and have approved the final manuscript.
Acknowledgments

References


Figure 1. Flowchart of patients included in the ESPASS study and in the study analyses

Patients included in ESPASS cohort
N=5967

- 504 (8.4%) patients with psychological therapy at baseline
- 1006 (16.9%) with information missing on psychological therapy six months
- 46 (0.8%) patients who initiated psychological therapy after 3 months

Patients included in the present study analyses
N=4411 (73.9%)

- Patients initiating psychoeducation
  N=117
- Patients in the non-intervention group
  N=4268

Propensity score matching (1:1)

“Referent patients”
N=117

Patients initiating psychoeducation
N=117

Effectiveness
Figure 2. Evolution of symptom severity and level of social autonomy over time (baseline, 1 month, 3 months and 6 months), in 117 schizophrenia patients with psychoeducation and 117 “referent patients” with no psychosocial therapy

![Graphs showing evolution of symptom severity and level of social autonomy over time.](image)

Table 1. Comparison of the schizophrenia patients present in the ESPASS cohort, included in the analyses or excluded because of missing information on exposure to psychological therapy

<table>
<thead>
<tr>
<th>Patients included in the analyses (N=4411)</th>
<th>Patients excluded from the analyses (N=1006)</th>
<th>p-values*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socio-demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1701 (38.6)</td>
<td>351 (34.9)</td>
</tr>
<tr>
<td>Age (in years), mean [SD]</td>
<td>37.3 [11.8]</td>
<td>35.6 [11.7]</td>
</tr>
<tr>
<td>Living alone (vs. not)</td>
<td>3581 (81.2)</td>
<td>868 (86.5)</td>
</tr>
<tr>
<td>Currently employed (vs. not)</td>
<td>759 (17.2)</td>
<td>158 (15.9)</td>
</tr>
<tr>
<td>Has some type of income (vs. none)</td>
<td>3852 (87.3)</td>
<td>828 (82.4)</td>
</tr>
<tr>
<td><strong>Characteristics of the disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at SCZ² onset, mean [SD]</td>
<td>27.3 (9.5)</td>
<td>26.5 (9.1)</td>
</tr>
<tr>
<td>Duration of psychiatric care &lt;1 year</td>
<td>1511 (34.3)</td>
<td>510 (51.0)</td>
</tr>
</tbody>
</table>
Table 2a. Comparisons of patient-related and disease-related characteristics at baseline, between schizophrenia patients who initiated psychological therapy (n=143) and patients who did not, before (n=4268) and after matching for propensity score (n=143)

<table>
<thead>
<tr>
<th>Characteristics of medical care</th>
<th>Patients who initiated psychological therapy (“intervention group”) (N=143)</th>
<th>Patients who did not have psychological therapy (N=4268)</th>
<th>Patients with no psychological therapy, after PS matching (“reference group”) (N=143)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>p-value*</td>
</tr>
<tr>
<td>Female</td>
<td>52 (36.4)</td>
<td>1649 (38.6)</td>
<td>0.64</td>
</tr>
<tr>
<td>Age (in years), mean [SD]</td>
<td>33.0 [12.0]</td>
<td>37.5 [11.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Living alone (vs. not)</td>
<td>122 (85.3)</td>
<td>3459 (81.0)</td>
<td>0.24</td>
</tr>
<tr>
<td>Currently employed (vs. not)</td>
<td>15 (10.5)</td>
<td>744 (17.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Has some type of income (vs. none)</td>
<td>115 (80.4)</td>
<td>3737 (87.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age at SCZ² onset, mean [SD]</td>
<td>24.6 [9.1]</td>
<td>27.3 [9.5]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* p-value of the parametric comparative tests, used as appropriate (Chi² or Fischer’s exact tests and Student’s t-tests); 1 Standard Deviation; 2 Schizophrenia; 3 Clinical Global Impression-Severity scale; 4 Investigator’s Assessment Questionnaire scale; 5 Social Autonomy Scale;
Table 2b. Comparisons of healthcare-related characteristics at baseline, between schizophrenia patients who initiated psychological therapy (n=143) and patients who did not, before (n=4268) and after matching for propensity score (n=143)

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Patients who initiated a psychological therapy (“intervention group”) (N=143)</th>
<th>Patients who did not have a psychological therapy (N=4268)</th>
<th>Patients with no psychological therapy, after PS matching (N=143)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td><strong>n (%)</strong></td>
<td><em><em>p</em>-value</em></td>
<td><strong>n (%)</strong></td>
</tr>
<tr>
<td>Characteristics of the psychiatrist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13 (39.4)</td>
<td>286 (33.3)</td>
<td>41 (39.4)</td>
</tr>
<tr>
<td>Age, mean [SD]</td>
<td>44.1 [9.2]</td>
<td>45.6 [8.2]</td>
<td>44.1 [7.8]</td>
</tr>
<tr>
<td>Care setting</td>
<td>Full-time hospitalization (vs. not)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>71 (49.7)</td>
<td>1269 (29.7)</td>
<td>69 (48.3)</td>
</tr>
<tr>
<td>Psychotropic medication before baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main antipsychotic drug</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st generation antipsychotic (FGA)</td>
<td>21 (14.7)</td>
<td>1192 (27.9)</td>
<td>15 (10.5)</td>
</tr>
<tr>
<td>2nd generation antipsychotic (SGA)</td>
<td>64 (44.7)</td>
<td>2139 (50.1)</td>
<td>66 (46.1)</td>
</tr>
<tr>
<td>No antipsychotic medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotic drug-naive (vs. not)</td>
<td>58 (40.6)</td>
<td>937 (22.0)</td>
<td>62 (43.4)</td>
</tr>
<tr>
<td>Antipsychotic drug-naive (vs. not)</td>
<td>18 (12.6)</td>
<td>324 (7.6)</td>
<td>9 (6.3)</td>
</tr>
</tbody>
</table>

* p-value of the parametric comparative tests, used as appropriate (Chi² or Fischer’s exact tests and Student’s t-tests); 1 Standard Deviation; 2 Schizophrenia; 3 Clinical Global Impression-Severity scale; 4 Investigator’s Assessment Questionnaire scale; 5 Social Autonomy Scale;
Prescription of antidepressants

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (N=117)</th>
<th>Referent group (N=117)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean [SD]</td>
<td>Mean [SD]</td>
<td></td>
</tr>
<tr>
<td>Symptoms at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGI-S¹ score</td>
<td>5.02 [0.96]</td>
<td>5.03 [0.92]</td>
<td>0.94</td>
</tr>
<tr>
<td>IAQ-4² score</td>
<td>11.54 [2.61]</td>
<td>11.62 [2.58]</td>
<td>0.80</td>
</tr>
<tr>
<td>Item “negative symptoms”</td>
<td>3.05 [1.10]</td>
<td>3.15 [1.04]</td>
<td>0.50</td>
</tr>
<tr>
<td>Item “positive symptoms”</td>
<td>3.19 [1.13]</td>
<td>3.25 [1.02]</td>
<td>0.67</td>
</tr>
<tr>
<td>SAS³ score</td>
<td>50.58 [18.39]</td>
<td>52.06 [18.80]</td>
<td>0.54</td>
</tr>
<tr>
<td>Symptoms at 6 months</td>
<td></td>
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</tr>
<tr>
<td>CGI-S¹ score</td>
<td>3.82 [1.25]</td>
<td>4.02 [1.22]</td>
<td>0.22</td>
</tr>
<tr>
<td>IAQ-4² score</td>
<td>7.92 [2.92]</td>
<td>8.17 [2.10]</td>
<td>0.80</td>
</tr>
<tr>
<td>Item “negative symptoms”</td>
<td>2.12 [0.92]</td>
<td>2.27 [0.87]</td>
<td>0.19</td>
</tr>
<tr>
<td>Item “positive symptoms”</td>
<td>1.90 [0.94]</td>
<td>2.10 [0.99]</td>
<td>0.12</td>
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<tr>
<td>SAS³ score</td>
<td>35.94 [20.06]</td>
<td>40.19 [19.24]</td>
<td>0.005</td>
</tr>
</tbody>
</table>

* Comparisons were performed using Student’s paired t-test; ¹ Standard Deviation; ² Clinical Global Impression-Severity scale; ³ Investigator’s Assessment Questionnaire scale; ⁴ Social Autonomy Scale

Table 3. Severity of symptoms and level of autonomy in 117 schizophrenia patients who initiated psychoeducation and 117 schizophrenia patients with no psychological therapy during the study, matched on propensity score

Highlights

- Randomized controlled trials do not always reflect routine practice
- The effectiveness of psychoeducation was explored in patients with schizophrenia
- Psychoeducation may improve social autonomy of patients with schizophrenia