## 東邦大学学術リポジトリ

Toho University Academic Repository

タイトル	Psychiatric Day Treatment Specific for Young Individuals with Early Psychosis: A Possible Contribution to Improve Their Functional Outcomes
作成者(著者)	Funatogawa, Tomoyuki / Nemoto, Takahiro / Yamaguchi, Taiju / Katagiri, Naoyuki / Tsujino, Naohisa / Mizuno, Masafumi
公開者	The Medical Society of Toho University
発行日	2020.12.01
ISSN	21891990
掲載情報	Toho Journal of Medicine. 6(4). p.164 171.
資料種別	学術雑誌論文
内容記述	Original Article
著者版フラグ	publisher
JaLCDOI	info:doi/10.14994/tohojmed.2020 014
メタデータのURL	https://mylibrary.toho u.ac.jp/webopac/TD22708302

#### **Original Article**

# Psychiatric Day Treatment Specific for Young Individuals with Early Psychosis: A Possible Contribution to Improve Their Functional Outcomes

Tomoyuki Funatogawa<sup>1)</sup> Takahiro Nemoto<sup>1)\*</sup> Taiju Yamaguchi<sup>1)</sup> Naoyuki Katagiri<sup>1)</sup> Naohisa Tsujino<sup>1,2)</sup> and Masafumi Mizuno<sup>1)</sup>

<sup>1)</sup>Department of Neuropsychiatry, Toho University Faculty of Medicine, Tokyo, Japan <sup>2)</sup>Department of Psychiatry, Saiseikai Yokohamashi Tobu Hospital, Kanagawa, Japan

#### ABSTRACT

Introduction: In recent years, various interventions for early stages of psychosis, such as first-episode psychosis (FEP) and an at-risk mental state for psychosis (ARMS), have been reported worldwide. Although the importance of psychosocial treatment has been emphasized, few studies have examined the effects of psychiatric day treatment for patients with early psychosis. The aim of the present study was to examine the effects of psychiatric day treatment, which is a comprehensive psychosocial service, for early psychosis.

*Methods*: Eighty-one subjects with early psychosis (59 FEP and 22 ARMS) who regularly participated in a psychiatric day treatment service known as "Il Bosco" were consecutively recruited. The subjects underwent various clinical assessments at baseline and after 12 months. Cognitive function, psychiatric symptoms, social functioning, quality of life (QOL), global functioning, and dosage of antipsychotics at the two time points were then evaluated.

*Results*: Significant improvements were observed in various domains, such as cognitive function, psychiatric symptoms, social functioning, QOL, and global functioning, at the follow-up time point, compared with the baseline. There were significant correlations in the frequency of attendance, with changes in memory, positive and negative symptoms, QOL, and global functioning.

*Conclusions*: Psychiatric day treatment specific for young people with early psychosis can contribute to improvements in various clinical domains.

Toho J Med 6 (4): 164-171, 2020

KEYWORDS: day treatment, early intervention, group psychotherapy, psychosis, schizophrenia

#### Introduction

Individuals with schizophrenia face various obstacles in their lives, such as social isolation and the inability to continue attending school or work.<sup>1)</sup> The illness usually develops in late puberty to early adolescence, and its various associated impairments persist throughout life.<sup>1,2)</sup> Early intervention is extremely important to improve the prognosis; reducing the duration of untreated psychosis (DUP)<sup>3)</sup> and starting intensive care within 2 years of onset, which

\*Corresponding Author: Takahiro Nemoto, 6-11-1 Omori-nishi, Otaku, Tokyo 143-8541, Japan, tel: +81-3-3762-4151 e-mail: takahiro.nemoto@med.toho-u.ac.jp

DOI: 10.14994/tohojmed.2020-014

Received July 7, 2020: Accepted Sept. 30, 2020 Toho Journal of Medicine 6 (4), Dec. 1, 2020. ISSN 2189–1990, CODEN: TJMOA2 has been identified as a critical period,<sup>4)</sup> are also vital. In Japan, an association between a poor prognosis and a delay in the treatment of psychosis has been reported,<sup>5)</sup> and various trials for shortening the DUP have been devised and implemented.<sup>6,7)</sup>

Puberty to early adolescence is extremely important in one's developmental process and education.<sup>8,9)</sup> To prevent individuals with a mental disorder from being separated from society and to promote healthy development and better education, mental health professionals need to organize appropriate early interventions. Previous studies have reported that comprehensive psychosocial treatment during the early stages of psychosis, including first-episode psychosis (FEP) and an at-risk mental state for psychosis (ARMS), has favorable effects.<sup>10-12)</sup>

Although outreach support services such as assertive community treatment are well developed in western countries, the use of psychiatric day treatment services has increased under the policy for psychiatric treatment in Japan.<sup>13)</sup> Many chronic patients, including elderly people who have been discharged from mental hospitals as a result of deinstitutionalization, have participated in psychiatric day treatment services, and these programs take patient age and physical condition into consideration.<sup>14)</sup> However, young patients experiencing an early stage of psychosis require treatment that is suitable for their age. Shek et al. (2009)<sup>15)</sup> mentioned that psychiatric day treatment may reduce hospital readmission and unemployment for patients with schizophrenia, compared with outpatient care alone. However, treatment adherence during the early stage of psychosis is often unstable, and professionals need to attract the interest of patients so as to stimulate their voluntary participation.16)

In 2007, we established a psychiatric day treatment center called "Il Bosco" in the Tokyo metropolitan area; this center focused on the treatment of young people between the ages of 15 and 30 years who exhibit early psychosis. <sup>17)</sup> We have provided comprehensive treatment programs including cognitive behavioral therapy and cognitive remediation performed by a multidisciplinary team based on the ideas promoted by the Optimal Treatment Project (OTP). <sup>18)</sup>

The aim of this study was to examine the efficacy and effectiveness of day treatment services for individuals with early psychosis, focusing on cognitive function, psychiatric symptoms, social functioning, quality of life (QOL), and global functioning. We investigated the longitudinal

changes in clinical variables and the associations of participation frequency with these clinical changes in patients with early psychosis.

#### Methods

#### **Participants**

Patients between the ages of 15 and 30 years with early psychosis and who attended the "Il Bosco" program between January 1, 2011, and March 31, 2014, were enrolled as subjects in this study. Their psychiatric symptoms were evaluated at baseline and at 12 months from the start of treatment. At "Il Bosco," comprehensive interventions are performed by a multidisciplinary team that includes professionals such as psychiatrists, nurses, psychiatric social workers, occupational therapists, and clinical psychologists. In the present study, patients were not required to give informed consent to the study because a clinical data set was used retrospectively. A document that declared an opt-out policy by which any possible patient and/or relatives could refuse to be included in this study was uploaded on the web page. This policy was accepted by the Ethical Research Committee of Toho University Faculty of Medicine (No. 27134).

#### Measures

We investigated the following items of demographic and clinical information at the beginning of treatment: psychiatric diagnosis according to the International Classification of Disease, 10th revision (ICD-10) criteria, history of consultation with a psychiatrist, family history, handedness using the Edinburgh Handedness Inventory, duration of untreated illness (DUI), and the DUP. The subjects with psychosis were diagnosed using ICD-10 criteria for schizophrenia, schizotypal, and delusional disorders (F20-29).<sup>19)</sup> Individuals who presented at a clinical setting with psychosis and who had never previously presented at a clinical setting with psychosis were identified as experiencing their "first-episode".20) And, we diagnosed individuals with ARMS using the Criteria of Psychosis-risk Syndrome of the Scale of Psychosis-Risk Symptoms.<sup>21)</sup> DUI was defined as the interval between the first appearance of any illnessrelated cognitive or affective complaints as well as any behavioral change from the individual's previous stable level of functioning and the initiation of treatment seeking.<sup>22)</sup> DUP was defined as the interval between the onset of psychotic symptoms and the first prescription of neuroleptics for psychosis.<sup>23)</sup> We also assessed the following items at baseline and at the 12-month time point: psychiatric symptoms using the Positive and Negative Syndrome Scale (PANSS)<sup>24,25)</sup>; cognitive function including the Letter Cancellation Test,<sup>26)</sup> Serial Seven-word Learning Test,<sup>27,28)</sup> Modified Stroop Test (color and form),<sup>29)</sup> Wisconsin Card Sorting Test,<sup>30,31)</sup> Trail-Making Test,<sup>32)</sup> and the Digit Span (chorus and reverse, Wechsler Adult Intelligence Scale)<sup>33)</sup>; social functioning (Social Functioning Scale<sup>34,35)</sup>); subjective QOL including the World Health Organization Quality of Life 26 (WHO QOL 26)<sup>19,36)</sup> and the Subjective Well-being under Neuroleptic Drug Treatment Short Form, Japanese version<sup>37,38)</sup>; and global functioning (Global Assessment of Functioning [GAF]<sup>39,40)</sup>). The average dose of antipsychotics (chlorpromazine equivalent) prescribed during the follow-up period was measured,<sup>41,42)</sup> and the number of psychiatric day treatment attendances was calculated.

#### **Statistics**

SPSS version 23.0 was used for the statistical analysis. For the changes in clinical variables from baseline to the 12-month time point, a paired t-test or Wilcoxon's signed-rank test was used as appropriate. In addition, we investigated the Spearman rank order correlations for the associations between the number of "Il Bosco" attendances and the changes ( $\Delta$ : value at 12 months minus baseline value) in clinical variables and the associations between these clinical changes and the prescribed dose of antipsychotics. To examine the differences of clinical valuables at baseline and the frequency of attendance between ARMS patients who developed and who did not develop full-blown psychosis, an unpaired t-test or the Mann-Whitney U-test was used as appropriate. A p-value <.05 was considered statistically significant.

#### Results

#### Clinical characteristics of participants

A total of 81 patients were registered, of which 59 were patients with FEP and 22 were patients with ARMS. Their mean age was 21.9 (SD = 3.8) years, and 31 patients (48.1%) were male. Their mean DUP was 10.0 (SD = 15.5) months, their mean DUI was 33.2 (SD = 31.8) months, and their mean antipsychotic prescription dose was 406.2 (SD = 297.7) mg chlorpromazine equivalent per day. Their mean PANSS total score was 79.4 (SD = 17.8), and their mean GAF score was 46.5 (SD = 8.0) at baseline. Eleven subjects (13.6%) dropped out from the program. There were no significant differences in the demographic information and clinical variables between the patients who completed the 1-year program and those who dropped out.

Therefore, the data for the remaining 70 (86.4%) patients (50 with FEP and 20 with ARMS) were analyzed to examine the therapeutic effects of the program.

### Changes in clinical variables and their correlations with attendance

Significant improvements in cognitive function, psychiatric symptoms, social functioning, QOL, and global functioning were observed (Table 1). Among the subjects who completed the program, the average number of attendances was 68.2 (SD = 54.7) times. Significant correlations between the attendance frequency and the following clinical measures were observed:  $\Delta$  Digit Span number forward score (r = .318, p = .049);  $\Delta$  PANSS total score (r =-.309, p = .009);  $\Delta$  PANSS positive symptoms score (r =-.238, p = .047);  $\Delta$  PANSS negative symptoms score (r =-.367, p = .002);  $\Delta$  PANSS general psychopathology score (r = -.300, p = .012);  $\Delta$  WHO QOL 26 average score (r = .330, p =.038); and  $\Delta$  GAF score (r =.401, p =.001) (Table 2). The correlation with Δ Serial Seven-word Learning Test Delayed playback (r = -.348, p = .047) was paradoxical. No correlations between these score changes and the prescribed dose of antipsychotics were observed. Regarding the transition to psychosis, three patients (15.0%) with ARMS developed full-blown psychosis. There were no significant differences in the GAF score (p = .848) and the PANSS total score (p = .337) at baseline and the frequency of attendance (p = .258) between ARMS patients who developed and who did not develop full-blown psychosis.

#### Discussion

Memory, negative symptoms, social functioning, QOL, and global functioning appeared to be significantly improved as a result of participating in the psychiatric youth day treatment at "Il Bosco." The subjects' changes were not related to the dosage of antipsychotics. Although antipsychotics did not seem to be related to the changes of clinical variables in this study, maintenance medication is thought to be important in the early phase of psychosis. 43) In this naturalistic study, we aimed to evaluate the effectiveness of the total amount of psychiatric day treatment for improving cognitive functioning, psychiatric symptoms, social functioning, QOL, and global functioning in young patients with early psychosis between the ages of 15 and 30 years. To our knowledge, only one similar study has demonstrated the effectiveness of day treatment as an early intervention for psychosis; however, the study involved elderly patients and only evaluated QOL and self-

Table 1 Changes in clinical variables during the 12-month program.

	Baseline (0M) Mean (SD)	Follow-up point (12M) Mean (SD)	<i>p</i> -value
LCT correct answers	109.9 (5.4)	111.9 (2.4)	.001 **
Serial Seven-word Learning Test	5.9 (1.2)	6.5 (0.6)	.007 **
Modified Stroop Test Part III (s)	22.1 (5.4)	19.4 (5.0)	<.001 **
WCST category achieved	4.3 (1.9)	5.3 (1.2)	.001 **
TMT Part B (s)	128.0 (49.5)	98.0 (30.4)	<.001 **
Digit Span			
Number forward score	5.9 (1.2)	6.3 (1.3)	.025 *
Number backward score	4.6 (1.3)	4.8 (1.5)	.304
PANSS			
Total score	79.4 (17.2)	71.4 (16.6)	.008 **
Positive score	17.7 (5.0)	16.3 (5.0)	.017 *
Negative score	20.0 (5.7)	17.5 (4.7)	.004 * *
General score	41.7 (8.7)	37.6 (8.8)	.030 *
SFS total score	108.2 (19.8)	126.3 (21.3)	<.001 **
QOL			
WHO QOL 26 average score	2.9 (0.6)	3.2 (0.5)	<.001 **
SWNS total score	64.3 (15.7)	74.2 (16.9)	<.001 **
GAF	45.5 (9.2)	56.2 (13.5)	<.001 **
Antipsychotics			
(mg CP equivalent/day)	401.4 (346.7)	427.1 (319.4)	.322

Abbreviations: LCT, Letter Cancellation Test; WCST, Wisconsin Card Sorting Test; TMT, Trail-Making Test; PANSS, Positive and Negative Syndrome Scale; Positive, positive symptoms; Negative, negative symptoms; General, general psychopathology; SFS, Social Functioning Scale; WHO QOL 26, World Health Organization Quality of Life 26; SWNS, Subjective Wellbeing under Neuroleptic Drug Treatment Short Form, Japanese version; GAF, Global Assessment of Functioning; CP, chlorpromazine.

For the changes in clinical variables from baseline to the 12-month time point, a paired t-test or Wilcoxon's signed-rank test was used as appropriate.

#### esteem.44)

The GAF scale evaluates psychological, social, and occupational functions as well as psychiatric symptoms. The more frequently the patients attended "Il Bosco," more the GAF score improved. No previous studies have examined the effectiveness of day treatment for patients with early psychosis, although one study did show a significant improvement in the GAF scores of patients with chronic schizophrenia who attended a community-based club treatment. 45) Varga et al. (2018) reported that the reason for this improvement was largely due to the rich interpersonal network and social support. Verma et al. (2012)<sup>46)</sup> and Cocchi et al. (2008)<sup>47)</sup> showed an improvement in GAF scores as a result of outreach psychosocial treatments. Verma pointed out the importance of active outreach and network construction. Cocchi et al. (2008)<sup>47)</sup> speculated on the effects of social skills training in improving the GAF scores. However, the effects of psychosocial treatment for early psychosis remain controversial. Larsen et al. (2006)<sup>48)</sup> and Nishida et al. (2018)<sup>49)</sup> failed to show any improvement in the GAF score. In our study, the improvement in the GAF score in individuals with early psychosis was obtained by providing group cognitive behavior therapy as part of psychiatric day treatment. The participants were repeatedly encouraged to enroll in schools or workplaces.

Negative symptoms were also improved by frequent treatment. Negative symptoms are predictors of functional recovery in early psychosis and important therapeutic targets.<sup>50)</sup> Several studies in Japan<sup>51,52)</sup> showed an improvement in negative symptoms among chronic patients using psychiatric day treatment. An international collaboration study on first-episode schizophrenia also showed improvements in negative symptoms and speculated that comprehensive approaches may lead to overall improvements in functioning.<sup>18)</sup> Gaynor et al. showed the effective-

<sup>\*:</sup> *p*<.05, \*\*: *p*<.01

168 (32) T. Funatogawa et al.

Table 2 Correlations between days of treatment attendance and changes in clinical variables.

	Treatment frequency Correlation coefficient	<i>p</i> -value
Δ LCT correct answers	.198	.228
Δ Serial Seven-word Learning Test		
List A Delayed playback	348	.047 *
Δ Modified Stroop Test Part III (s)	.100	.546
Δ WCST category achieved	.132	.422
$\Delta$ TMT Part B (s)	193	.259
Δ Digit Span Number forward score	.318	.049 *
Δ Digit Span Number backward score	076	.646
Δ PANSS total score	309	.009 * *
$\Delta$ PANSS Positive score	238	.047 *
$\Delta$ PANSS Negative score	367	.002 * *
$\Delta$ PANSS General score	300	.012 *
$\Delta$ SFS total score	.278	.082
$\Delta$ WHO QOL 26 average score	.330	.038 *
$\Delta$ SWNS total score	.334	.050
Δ GAF score	.401	.001 **

† Δ: 12M-0M

Abbreviations: LCT, Letter Cancellation Test; WCST, Wisconsin Card Sorting Test; TMT, Trail-Making Test; PANSS, Positive and Negative Syndrome Scale; *Positive, Positive symptoms; Negative, Negative symptoms; Genaral, General psychopathology;* SFS, Social Functioning Scale; WHO QOL 26, World Health Organization Quality of Life 26; SWNS, Subjective Wellbeing under Neuroleptic drug treatment Short form, Japanese version; GAF, Global Assessment of Functioning.

\*: p<.05, \*\*: p<.01

The Spearman rank order correlations for the associations between the number of "Il Bosco" attendances and the changes in clinical variables.

ness of group cognitive behavioral therapy for negative symptoms in patients with FEP.<sup>53)</sup> The effects of second-generation antipsychotics on negative symptoms appear to be very slight<sup>54)</sup>; therefore, approaches other than pharmacotherapy are indispensable. Frequent and continuous participation in psychiatric day treatment may be helpful.

QOL was improved, and it showed a positive relationship with the total amount of day treatment in this study. Several treatment approaches have been investigated to determine their abilities to improve social functioning and QOL. 55,56) These studies insist on the importance of improvements in daily life.

Regarding cognitive function, the Digit Span number forward score showed the improvement associating with the attendance frequency. One previous study reported an improvement in short-term memory in patients with chronic schizophrenia after 3 months of aerobic exercise training.<sup>57)</sup> Our day treatment has also adopted aerobic exercise.

The average number of day treatment attendances among the subjects who completed the program was 68.2 (SD = 54.7), which may mean that the subjects needed to participate in the day treatment more than once a week. We have focused on a cognitive function training program. Deficits in divergent thinking are closely related to social dysfunction in schizophrenia.<sup>58)</sup> Because the effect of intensive cognitive training on divergent thinking has already been revealed in our previous study,59 the "Il Bosco" program has adopted this training regimen for divergent thinking. Second, we have also incorporated the OTP, which provides comprehensive support including integrated community care and family intervention with cognitive behavior therapy. Third, "Il Bosco" provides treatment coverage for subjects in adolescence and early adulthood. Our program focuses on the mental health development of young adults by including components such as self-efficacy, which plays a role in societal skills, selfconfidence, and communication skills. Finally, we have adopted employment training as well as training to help manage oneself while in school. The day treatment program is available for 6 h/ day, 5 days a week. We have adopted case management and adjusted the content of the programs individually to make it possible for the individuals to achieve his or her goals.

In this study, 11 patients (13.6%) dropped out of the program before the 12-month completion point. This rate is similar to that reported in previous studies. At the Early Psychosis Prevention and Intervention Center in Australia, the drop-out rate was 23.3% after an 18-month intervention. At an early intervention service provided in New Zealand, the drop-out rate was 24.6% after a 12-month intervention. Therefore, our result appears to be roughly equivalent to those of previous studies.

Three of the 20 (15.0%) ARMS patients developed psychosis. These cases who transitioned to psychosis were between the ages of 15 and 19 years and seemed to have a low attendance frequency in the "Il Bosco" program when considered their risk, although this rate was similar to that of previously reported data in Japan. Although the three patients' GAF and PANSS scores were not significantly different from those of patients who did not develop psychosis, the insufficient attendance may not lead to the prevention of the onset of psychosis. Further research is needed to improve young patients' adherence to and motivation toward psychosocial treatment. Although the sevention of the onset of psychosocial treatment.

In the present study, however, several limitations should be mentioned. First, this was a single-arm study. Although it is difficult to conduct randomized trials in the clinical settings, a randomized trial will be needed in the future. Second, in this study, we used chlorpromazine equivalent as an index of medication. However, the profile of each antipsychotic is needed to be considered in the future.

In conclusion, the present study indicated that psychiatric day treatment for 12 months led to improvements in memory, negative symptoms, QOL, and global functioning in young people with early psychosis. The improvements were associated with the frequency of psychiatric day treatment attendance.

**Disclaimer:** Masafumi Mizuno is one of the Editors of Toho Journal of Medicine. He was not involved in the editorial evaluation or decision to accept this article for publication at all.

Contributors: Study Design: T.F., T.N., and M.M.; Data Collection:

T.F., T.Y., N.K., and N.T.; Data Analysis: T.F. and T.N.; and Writing the Manuscript and Revision: T.F., T.N., and M.M.

**Acknowledgements:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Conflicts of interest: None declared.

#### References

- McGlashan TH. The chestnut Lodge follow-up study. II. Long-term outcome of schizophrenia and the affective disorders. Arch Gen Psychiatry. 1984; 41 (6):586-601. doi: 10.1001/ archpsyc.1984.01790170060007, Pubmed: 6732419.
- Häfner H, an der Heiden W. Epidemiology of schizophrenia. Can J Psychiatry. 1997; 42 (2):139-51. doi: 10.1177/ 070674379704200204, Pubmed: 9067063.
- Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship Between duration of untreated psychosis and outcome in first-episode schizophrenia: A critical review and meta-analysis. Am J Psychiatry. 2005; 162 (10): 1785-804. doi: 10.1176/appi.ajp.162.10.1785, Pubmed: 16199825.
- Birchwood M, Todd P, Jackson C. Early intervention in psychosis. The critical period hypothesis. Br J Psychiatry Suppl. 1998; 172 (33): 53-9. doi: 10.1192/S0007125000297663, Pubmed:9764127.
- 5) Yamazawa R, Nemoto T, Kobayashi H, Chino B, Kashima H, Mizuno M. Association between duration of untreated psychosis, premorbid functioning, and cognitive performance and the outcome of first-episode schizophrenia in Japanese patients: prospective study. Aust N Z J Psychiatry. 2008; 42 (2): 159-65. doi: 10.1080/00048670701787537, Pubmed:18197512.
- 6) Harada M, Maegawa S, Hama Y, Adachi T, Iwasa T, Kurita K, et al. An implementation model for early intervention in Japan (in Japanese). Jpn J Clin Psychiatry. 2012; 41: 1481-8.
- Matsumoto K, Miyakoshi T, Ito F, Omuro N, Matsuoka N. Therapeutic intervention for group with risk of psychosis - Sendai Atrisk Mental State and First Episode. (in Japanese). Psychiat Neurol Jap. 2009; 111: 298-303.
- Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustün TB. Age of onset of mental disorders: a review of recent literature. Curr Opin Psychiatry. 2007; 20 (4): 359-64. doi: 10.1097/ YCO.0b013e32816ebc8c, Pubmed: 17551351.
- Patel V, Flisher AJ, Hetrick S, McGorry P. Mental health of young people: a global public-health challenge. Lancet. 2007; 369 (9569): 1302-13. doi: 10.1016/S0140-6736(07)60368-7, Pubmed: 17434406.
- 10) Craig TK, Garety P, Power P, Rahaman N, Colbert S, Fornells-Ambrojo M, 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. doi: 10.1136/bmj.38246.594873.7C, Pubmed:15485934.
- 11) Petersen L, Jeppesen P, Thorup A, Abel MB, Øhlenschlaeger J, Christensen TØ, 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. doi: 10.1136/ bmj.38565.415000.E01, Pubmed:16141449.
- 12) McGorry PD, Edwards J, Mihalopoulos C, Harrigan SM, Jackson

- HJ. EPPIC: an evolving system of early detection and optimal management. Schizophr Bull. 1996; 22 (2): 305-26. doi: 10.1093/schbul/22.2.305. Pubmed:8782288.
- Yamane H. Turning point of psychiatric day care has come. (in Japanese). The Jpn J Occup Ther. 1995; 29: 532-7.
- 14) Nemoto T, Niimura H, Ryu Y, Sakuma K, Mizuno M. Long-term course of cognitive function in chronically hospitalized patients with schizophrenia transitioning to community-based living. Schizophr Res. 2014; 155 (1-3): 90-5. doi: 10.1016/j. schres.2014.03.015, Pubmed: 24725850.
- 15) Shek E, Stein AT, Shansis FM, Marshall M, Crowther R, Tyrer P. Day hospital versus outpatient care for people with schizophrenia. Cochrane Database Syst Rev. 2009; 4 (4): CD003240. doi: 10.1002/14651858.CD003240.pub2, Pubmed:19821303.
- 16) O'Brien A, Fahmy R, Singh SP. Disengagement from mental health services. A literature review. Soc Psychiatry Psychiatr Epidemiol. 2009; 44 (7): 558-68. doi: 10.1007/s00127-008-0476-0, Pubmed:19037573.
- 17) Mizuno M, Nemoto T, Tsujino N, Funatogawa T, Takeshi K. Early psychosis in Asia: insights from Japan. Asian J Psychiatr. 2012; 5 (1): 93-7. doi: 10.1016/j.ajp.2012.02.004, Pubmed: 26878953.
- 18) Falloon IR, Montero I, Sungur M, Mastroeni A, Malm U, Economou M, et al. Implementation of evidence-based treatment for schizophrenic disorders: two-year outcome of an international field trial of optimal treatment. World Psychiatry. 2004; 3 (2): 104-9. Pubmed:16633471.
- World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research;2. 1993.
- 20) Breitborde NJK, Srihari VH, Woods SW. Review of the operational definition for first-episode psychosis. Early Interv Psychiatry. 2009; 3 (4): 259-65. doi: 10.1111/j.1751-7893.2009.00148.x, Pubmed: 22642728.
- 21) Miller TJ, McGlashan TH, Rosen JL, Cadenhead K, Cannon T, Ventura J, et al. Prodromal assessment With the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. Schizophr Bull. 2003; 29 (4): 703-15. doi: 10.1093/oxfordjournals.schbul.a007040, Pubmed: 14989408.
- 22) Beiser M, Erickson D, Fleming JA, Iacono WG. Establishing the onset of psychotic illness. Am J Psychiatry. 1993; 150 (9): 1349-54. doi: 10.1176/ajp.150.9.1349, Pubmed: 8352345.
- 23) Yamazawa R, Mizuno M, Nemoto T, Miura Y, Murakami M, Kashima H. Duration of untreated psychosis and pathways to psychiatric services in first-episode schizophrenia. Psychiatry Clin Neurosci. 2004; 58 (1): 76-81. doi: 10.1111/j.1440-1819.2004.01196.x, Pubmed: 14678461.
- 24) Igarashi Y, Hayashi N, Yamashina M, Otsuka N, Kuroki N, Anzai N, et al. Interrater reliability of the Japanese version of the Positive and Negative Syndrome Scale and the appraisal of its training effect. Psychiatry Clin Neurosci. 1998; 52 (5): 467-70. doi: 10.1046/j.1440-1819.1998.00425.x, Pubmed:10215006.
- 25) Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. Schizophr Bull. 1987; 13 (2): 261-76. doi: 10.1093/schbul/13.2.261, Pubmed:3616518.
- 26) Diller L, Weinberg J, Gordon W, Goodkin R, Gerstman LJ, Ben-Yishay Y. Studies in cognition and rehabilitation in hemiplegia. 1974
- 27) Kashima H. The application of neuropsychology to rehabilitation

- medicine.(in Japanese). General Rehabilitation. 1985; 13: 11-8.
- Kashima H. Neuropsychological assessment of dementia. (in Japanese). Ronen Seishin Igaku Zasshi. 1992; 3: 253-60.
- Stroop JR. Studies of interference in serial verbal reactions. J Exp Psychol. 1935; 18 (6): 643-62. doi: 10.1037/h0054651.
- Heaton RK. A manual for the Wisconsin Card Sorting Test. Psychological Assessment Resources. Odessa, FL: 1981.
- Kashima H. Wisconsin card sorting test (Keio Version)(KWCST) (in Japanese). Brain Sci Ment Disord (Tokyo). 1995; 6: 209-16.
- 32) Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. Percept Mot Skills. 1958; 8 (3): 271-6. doi: 10.2466/pms.1958.8.3.271.
- Scale Wechsler D. Wechsler adult intelligence. WAIS-R Manual. Psychological Corporation. New York: 1981.
- 34) Nemoto T, Fujii C, Miura Y, Chino B, Kobayashi H, Yamazawa R, et al. Reliability and validity of the Social Functioning Scale Japanese version (SFS-J). (in Japanese). Jpn Bull Soc Psychiatry. 2008; 17: 188-95.
- 35) Birchwood M, Smith J, Cochrane R, Wetton S, Copestake S. The Social Functioning Scale: the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. Br J Psychiatry. 1990; 157: 853-9. doi: 10.1192/bjp.157.6.853, Pubmed: 2289094.
- Tazaki M, Nakane Y. Guideline for WHO QOL 26 Japanese Version. (in Japanese). Tokyo: Kaneko Shobo; 1997.
- 37) Naber D, Moritz S, Lambert M, Pajonk FG, Holzbach R, Mass R, et al. Improvement of schizophrenic patients' subjective well-being under atypical antipsychotic drugs. Schizophr Res. 2001; 50 (1-2):79-88. doi: 10.1016/s0920-9964(00)00166-3, Pubmed: 11378316.
- 38) Watanabe M, Matsumura H. Reliability and validity of Subjective Well-being under Neuroleptic drug treatment Short form, Japanese version (SWNS-J). Jpn J Clin Psychopharmacol. 2003; 6: 905-12
- 39) Bell CC. DSM-IV: diagnostic and statistical manual of mental disorders. JAMA. 1994; 272 (10): 828-9. doi: 10.1001/jama.1994.03520100096046.
- Takizawa R. The handbook of psychiatric and psychological assessment. (in Japanese). 2015.
- 41) Inada T, Inagaki A. Psychotropic dose equivalence in Japan. Psychiatry Clin Neurosci. 2015; 69 (8): 440-7. doi: 10.1111/pcn.12275, Pubmed: 25601291.
- 42) Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. J Clin Psychiatry. 2003; 64 (6): 663-7. doi: 10.4088/jcp.v64n0607, Pubmed: 12823080.
- 43) Hui CLM, Honer WG, Lee EHM, Chang WC, Chan SKW, Chen ESM, et al. Long-term effects of discontinuation from antipsychotic maintenance following first-episode schizophrenia and related disorders: a 10 year follow-up of a randomised, double-blind trial. Lancet Psychiatry. 2018; 5 (5): 432-42. doi: 10.1016/S2215-0366(18)30090-7, Pubmed: 29551618.
- 44) Šago D, Lovretić V, Habuš K, Ivezić E, Bogović Dijaković A, Đogaš VV, et al. Improving the quality of life during treatment in the Day hospital for early intervention in Psychiatric Hospital "Sveti Ivan". Psychiatr Danub. 2019; 31 (Suppl 2): 190-5. Pubmed: 31158121.
- 45) Varga E, Endre S, Bugya T, Tényi T, Herold R. Communitybased psychosocial treatment has an impact on social processing and functional outcome in schizophrenia. Front Psychiatry. 2018;

- 9: 247. doi: 10.3389/fpsyt.2018.00247, Pubmed:29937739.
- 46) Verma S, Poon LY, Lee H, Rao S, Chong SA. Evolution of early psychosis intervention services in Singapore. East Asian Arch Psychiatry, 2012; 22 (3): 114-7. Pubmed:23019285.
- 47) Cocchi A, Meneghelli A, Preti A. Programma 2000: celebrating 10 years of activity of an Italian pilot programme on early intervention in psychosis. Aust N Z J Psychiatry. 2008; 42 (12): 1003-12. doi: 10.1080/00048670802512032, Pubmed: 19016088.
- 48) Larsen TK, Melle I, Auestad B, Friis S, Haahr U, Johannessen JO, et al. Early detection of first-episode psychosis: the effect on 1-year outcome. Schizophr Bull. 2006; 32 (4): 758-64. doi: 10.1093/schbul/sbl005. Pubmed:16809640.
- 49) Nishida A, Ando S, Yamasaki S, Koike S, Ichihashi K, Miyakoshi Y, et al. A randomized controlled trial of comprehensive early intervention care in patients with first-episode psychosis in Japan: 1.5-year outcomes from the J-CAP study. J Psychiatr Res. 2018; 102:136-41. doi: 10.1016/j.jpsychires.2018.04.007, Pubmed: 29653344.
- 50) Best MW, Grossman M, Oyewumi LK, Bowie CR. Examination of the Positive and Negative Syndrome Scale factor structure and longitudinal relationships with functioning in early psychosis. Early Interv Psychiatry. 2016; 10 (2): 165-70. doi: 10.1111/ eip.12190, Pubmed:25277757.
- 51) Someya T, Anzai N, Ikebuchi E, Ozawa M, Harada S, Ueda T, et al. Negative symptoms and the course of social adjustment in schizophrenia. (in Japanese). Clin Psychiatry. 1986; 28: 1229-36.
- 52) Suzuki A. Evaluation of day care effects: using Wing's scale. (in Japanese). Jpn J Socpsychiatry. 1984; 7: 67-73.
- 53) Gaynor K, Dooley B, Lawlor E, Lawoyin R, O'Callaghan E. Group cognitive behavioural therapy as a treatment for negative symptoms in first-episode psychosis. Early Interv Psychiatry. 2011; 5 (2): 168-73. doi: 10.1111/j.1751-7893.2011.00270.x, Pubmed: 21535424.
- 54) Fusar-Poli P, Papanastasiou E, Stahl D, Rocchetti M, Carpenter W, Shergill S, et al. Treatments of negative symptoms in schizophrenia: meta-analysis of 168 randomized placebo-controlled trials. Schizophr Bull. 2015; 41 (4): 892-9. doi: 10.1093/schbul/sbu170, Pubmed: 25528757.
- 55) Štrkalj-Ivezić S, Vrdoljak M, Mužinić L, Agius M. The impact of a rehabilitation day centre program for persons suffering from schizophrenia on quality of life, social functioning and selfesteem. Psychiatr Danub. 2013; 25 (Suppl 2): S194-9. Pubmed: 23995175.
- 56) Weldon E, Clarkin JE, Hennessy JJ, Frances A. Day hospital versus outpatient treatment: a controlled study. Psychiatr Q. 1979; 51 (2): 144-50. doi: 10.1007/BF01064563, Pubmed:482458.
- 57) Pajonk FG, Wobrock T, Gruber O, Scherk H, Berner D, Kaizl I, et al. Hippocampal plasticity in response to exercise in schizophrenia. Arch Gen Psychiatry. 2010; 67 (2): 133-43doi: 10.1001/archgenpsychiatry. 2009.193, Pubmed: 20124113.
- 58) Nemoto T, Kashima H, Mizuno M. Contribution of divergent

- thinking to community functioning in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2007; 31 (2): 517-24. doi: 10.1016/j.pnpbp.2006.12.001. Pubmed: 17218048.
- 59) Nemoto T, Yamazawa R, Kobayashi H, Fujita N, Chino B, Fujii C, et al. Cognitive training for divergent thinking in schizophrenia: a pilot study. Prog Neuropsychopharmacol Biol Psychiatry. 2009; 33 (8): 1533-6. doi: 10.1016/j.pnpbp.2009.08.015, Pubmed: 19733608.
- 60) Conus P, Lambert M, Cotton S, Bonsack C, McGorry PD, Schimmelmann BG. Rate and predictors of service disengagement in an epidemiological first-episode psychosis cohort. Schizophr Res. 2010; 118 (1-3): 256-63. doi: 10.1016/j.schres.2010.01.032, Pubmed: 20206475.
- 61) Turner MA, Boden JM, Smith-Hamel C, Mulder RT. Outcomes for 236 patients from a 2-year early intervention in psychosis service. Acta Psychiatr Scand. 2009; 120 (2): 129-37. doi: 10.1111/ j.1600-0447.2009.01386.x, Pubmed:19392808.
- 62) Matsumoto K, Ohmuro N, Tsujino N, Nishiyama S, Abe K, Hamaie Y, et al. Open-label study of cognitive behavioural therapy for individuals with at-risk mental state: feasibility in the Japanese clinical setting. Early Interv Psychiatry. 2018; 0.
- 63) Nemoto T, Takeshi K, Niimura H, Tobe M, Ito R, Kojima A, et al. Feasibility and acceptability of cognitive rehabilitation during the acute phase of schizophrenia. Early Interv Psychiatry. 2020 Mar 26; doi: 10.1111/eip.12955. Online ahead of print. Pubmed: 32219993
- 64) Nemoto T, Uchino T, Aikawa S, Matsuo S, Mamiya N, Shibasaki Y, et al. Impact of changes in social anxiety on social functioning and quality of life in outpatients with schizophrenia: A naturalistic longitudinal study. J Psychiatr Res. 2020; 131: 15-21. doi: 10.1016/j.jpsychires.2020.08.007, Pubmed: 32911206.
- 65) Nemoto T, Uchino T, Aikawa S, Saito J, Matsumoto H, Funato-gawa T, et al. Social anxiety and negative symptoms as the characteristics of patients with schizophrenia who show competence-performance discrepancy in social functioning. Psychiatry Clin Neurosci. 2019; 73 (7): 394-9. doi: 10.1111/pcn.12848, Pubmed: 30968478.
- 66) Uchino T, Nemoto T, Yamaguchi T, Katagiri N, Tsujino N, Murakami Y, et al. Associations of personality traits with the capacity-performance discrepancy of functional outcome in patients with schizophrenia. Neuropsychiatr Dis Treat. 2019; 15: 2869-77. doi: 10.2147/NDT.S218738, Pubmed:31632034.
- 67) Tobe M, Nemoto T, Tsujino N, Yamaguchi T, Katagiri N, Fujii C, et al. Characteristics of motivation and their impacts on the functional outcomes in patients with schizophrenia. Compr Psychiatry. 2016; 65: 103-9. doi: 10.1016/j.comppsych.2015.10.006, Pubmed: 26773997.

©Medical Society of Toho University. Toho Journal of Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).