

Table 1
Diagnosis from case vignettes.

	COPS-A (%)	COPS-B (%)	COPS-C (%)	Full-blown schizophrenia (%)
Schizophrenia	97 (61)	110 (69)	51 (32)	147 (92)
Schizophrenia suspected	14 (9)	18 (11)	13 (8)	5 (3)
Prodrome	14 (9)	20 (13)	21 (13)	1 (1)
Mood disorders	1 (1)	15 (9)	4 (3)	2 (1)
Neurotic disorders	12 (8)	21 (13)	63 (39)	0 (0)
Others	33 (21)	27 (17)	40 (25)	8 (5)
Unknown	4 (3)	1 (1)	2 (1)	0 (0)
No reply	5 (3)	4 (3)	3 (2)	3 (2)

COPS-A: Criteria of Prodromal Syndrome-Brief intermittent psychotic syndrome; COPS-B: Criteria of Prodromal Syndrome-Attenuated positive symptom syndrome; COPS-C: Criteria of Prodromal Syndrome-Genetic risk and deterioration syndrome.

Table 2
Selected treatments for each vignette.

	COPS-A (%)	COPS-B (%)	COPS-C (%)	Full-blown schizophrenia (%)
Pharmacotherapy	124 (78)	151 (94)	125 (78)	158 (99)
Supportive psychotherapy	80 (50)	104 (65)	119 (74)	84 (53)
Family psychoeducation	32 (20)	30 (19)	19 (12)	62 (39)
CBT	5 (3)	10 (6)	17 (11)	7 (4)
Observation	57 (36)	40 (25)	65 (41)	14 (9)
Others	4 (3)	6 (4)	3 (2)	6 (4)
No reply	1 (1)	2 (1)	1 (1)	2 (1)
Not necessary	3 (2)	1 (1)	4 (3)	0 (0)

COPS-A: Criteria of Prodromal Syndrome-Brief intermittent psychotic syndrome; COPS-B: Criteria of Prodromal Syndrome-Attenuated positive symptom syndrome; COPS-C: Criteria of Prodromal Syndrome-Genetic risk and deterioration syndrome.

Table 3
Selected drugs as pharmacotherapy.

	COPS-A (%)	COPS-B (%)	COPS-C (%)	Full-blown schizophrenia (%)
Antipsychotics	118 (95)	123 (81)	66 (53)	156 (99)
Antidepressant	0 (0)	3 (2)	21 (17)	0 (0)
Mood stabilizer	1 (1)	4 (3)	0 (0)	0 (0)
Anxiolytics	2 (2)	11 (7)	33 (26)	0 (0)
Others	1 (1)	3 (2)	1 (1)	0 (0)

COPS-A: Criteria of Prodromal Syndrome-Brief intermittent psychotic syndrome; COPS-B: Criteria of Prodromal Syndrome-Attenuated positive symptom syndrome; COPS-C: Criteria of Prodromal Syndrome-Genetic risk and deterioration syndrome.

Table 4
First line drug in antipsychotics.

	COPS-A (%)	COPS-B (%)	COPS-C (%)	Full-blown schizophrenia (%)
Risperidone	62 (52)	63 (48)	24 (35)	104 (66)
Olanzapine	10 (8)	20 (15)	5 (7)	19 (12)
Aripiprazole	21 (18)	14 (11)	10 (15)	11 (7)
Perospirone	11 (9)	8 (6)	8 (12)	1 (1)
Quetiapine	2 (2)	6 (5)	4 (6)	3 (2)
Sulpiride	0 (0)	6 (5)	8 (12)	0 (0)
Others	3 (3)	4 (3)	3 (4)	7 (4)
Polypharmacy	11 (9)	9 (7)	6 (9)	13 (8)

COPS-A: Criteria of Prodromal Syndrome-Brief intermittent psychotic syndrome; COPS-B: Criteria of Prodromal Syndrome-Attenuated positive symptom syndrome; COPS-C: Criteria of Prodromal Syndrome-Genetic risk and deterioration syndrome.

Table 5
First dosage of risperidone.

	COPS-A (%)	COPS-B (%)	COPS-C (%)	Full-blown schizophrenia (%)
<1 mg	15 (24)	6 (10)	9 (38)	4 (4)
1–2 mg	28 (45)	35 (56)	9 (38)	30 (29)
2–3 mg	16 (26)	20 (32)	5 (21)	40 (38)
3–4 mg	1 (2)	2 (3)	1 (4)	22 (21)
4 mg ≤	2 (3)	0 (0)	0 (0)	8 (8)

COPS-A: Criteria of Prodromal Syndrome-Brief intermittent psychotic syndrome; COPS-B: Criteria of Prodromal Syndrome-Attenuated positive symptom syndrome; COPS-C: Criteria of Prodromal Syndrome-Genetic risk and deterioration syndrome.

Many of the psychiatrists who diagnosed the vignettes as 'suspected schizophrenia' or 'psychotic prodrome' selected 'pharmacotherapy' as their approach and 'antipsychotic' as the medication.

4. Discussion

The present results suggest that pharmacotherapy might be overused in prodromal cases, since the psychiatrists tended to prescribe neuroleptics for positive symptoms before the diagnostic criteria for schizophrenia had been fulfilled. Thus, the criteria for full-blown psychosis needs to be reexamined, the risk of transition from an at-risk mental state (ARMS) to psychosis needs to be assessed, and guidelines for pharmacological intervention for the treatment of prodromal symptoms need to be established in Japan.

Our results suggested that prodromal individuals who have experienced only brief intermittent or attenuated positive symptoms might potentially be overdiagnosed as having 'schizophrenia'. In other words, the concept of an ARMS/prodromal state has not yet been widely recognized among Japanese psychiatrists. On the other hand, it is possible that Japanese psychiatrists might be simultaneously prescribing the medication for each individual in the prodromal phase or with full-threshold schizophrenia. Even where the psychiatrists had diagnosed the patients as being prodromal, antipsychotics were being prescribed for these patients.

4.1. Japanese Society for Prevention and Early Intervention in Psychiatry (JSEIP) (<http://www.jseip.jp>)

The JSEIP is an organization for people involved in the study and treatment of psychiatric disorders in Japan. It provides a forum for members to promote practice and research into the prevention of psychiatric disorders based on medical ethics, to arrange conferences and professional meetings regarding the prevention of psychiatric disorders, to facilitate research (including multicenter trials), and to enhance other efforts to achieve its goals. The JSEIP was inaugurated in March 1996 in Okinawa, just after the first symposium on the primary prevention of schizophrenia was held at the 16th meeting of the Japanese Society of Social Psychiatry. In 2007, the 10th annual academic conference was held in Yokohama; this conference emphasized multicenter research on early psychosis in Japan. The JSEIP had more than 300 members in 2010.

The 15th annual meeting was held in December 3–4, 2011, in Tokyo. Drs. David Shiers, Louis Arsenault, Jo Smith, and Paul French have been invited as guest lecturers. Not only topics on early intervention for psychosis, but also general topics on prevention and mental health promotion were covered.

4.2. Il Bosco (<http://www.lab.toho-u.ac.jp/med/omori/mentalhealth/>)

A representative early intervention facility for young people is the "Il Bosco", where the authors of the present report and their colleagues work. This facility was founded in May 2007 at the Toho University Omori Medical Center in Tokyo. The DUP of the hospital catchment area is longer (mean: 30 months) than for other areas of Tokyo. The unit is run according to an optimal treatment project (OTP) (Falloon et al., 2004) that employs a multi-disciplinary team and utilizes the cognitive remediation-oriented method advocated by Falloon et al. (2004). The service model includes early detection and intervention, repeated assessment, and psychoeducation. Treatment strategies consist of optimal pharmacotherapy based on atypical neuroleptics, cognitive function training, cognitive behavioral therapy, and job coaching as part of the final treatment program. The cognitive function training is aimed at stimulating divergent thinking, mainly using computers. The cognitive training

program mainly targets divergent thinking deficits, since interventions for divergent thinking have been previously found to improve negative symptoms and social functioning significantly in patients with schizophrenia (Nemoto et al., 2009). Cognitive intervention to improve divergent thinking deficits during the early stage of psychosis may maximize the chance for functional recovery, and such interventions may minimize the risk of future progression in a subset of people with ARMS, since divergent thinking is critical for generating solutions to various social problems and for navigating the complexities of social interactions.

The clients are restricted to ARMS patients or first-episode schizophrenia patients between the ages of 15 and 30 years. Four years have passed since the opening of "Il Bosco", and so far 112 patients (62 women and 50 men with a mean age of 20.4 ± 3.5 years) have been registered. About 80% of the patients have improved through participation in a rehabilitation program that focuses on social cognition, and this has enabled them to return to their former workplace or school. The attendance rate is better than for standard day care, which has no age limit. We are currently developing some new programs for cognitive rehabilitation and remediation as well as a psychoeducation web site for individuals with early psychosis.

4.3. Other leading centers for early intervention in Japan

Other than the above, there are several leading centers for early intervention research and practice in Japan. Most of them are driven by university departments of psychiatry with respect to both research and clinical activities. The common aims of these services are as follows: (i) to provide young people suspected of being at risk for psychosis with opportunities for assessment by specialists and the chance to receive specific intervention; (ii) to reduce the delay in accessing evidence-based treatment for persons who have already developed psychosis, especially a first episode of schizophrenia; and (iii) to develop innovative and optimized approaches for diagnosing and treating people at risk of psychosis.

4.4. Research and education for specialists

Research from Japan has also focused on both the biological and psychosocial aspects of early psychosis. Various studies have demonstrated the anatomical basis of the schizophrenia spectrum in the brain by multivariate voxel-based morphometry (Kawasaki et al., 2007), the effect of DUP on brain morphology in ultra high-risk subjects (Takahashi et al., 2007, 2008a,b) as well as the applicability of structural brain imaging to the objective diagnosis of schizophrenia (Suzuki et al., 2005; Takahashi et al., 2009a,b, 2010a,b). The influence of DUP on brain function has also been investigated (Yamazawa, 2004; Mizuno et al., 2009; Nishii et al., 2010). The development of screening methods for ARMS (Kobayashi et al., 2008), the assessment of ARMS (Miyakoshi, 2009a,b), and psychopathological studies on psychosis-like experiences have been reported (Nishida et al., 2010; Oshima et al., 2010; Kinoshita et al., 2011; Kobayashi et al., 2011), contributing to early intervention and support for adolescents in Japan. Both comprehensive and pharmacological approaches (Kobayashi et al., 2009) to treatment have been investigated. Moreover, several important English monographs about early intervention in psychiatry have been translated into Japanese by leading researchers in this field (French and Morrison, 2004; Jackson and McGorry, 2009; McGlashan et al., 2010; McGorry and Jackson, 1999).

5. Conclusion

The development of services for early intervention is expected to provide a breakthrough in the treatment of psychosis in Japan,

including a reduction in stigmatization, the prevention of suicide among young persons, and the promotion of general knowledge about mental health. It seems that there are several issues pertinent to early intervention for psychosis Asian countries – for example the format of service systems, community attitudes to psychiatric illness (including stigma), and the dependence on pharmacotherapy. An integrated approach including pharmacotherapy and psychosocial approaches might be appropriate for early intervention for psychosis in the community.

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Contributors

Masafumi Mizuno is the Grant recipient.

Conflict of interest

None.

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Lower subjective quality of life and the development of social anxiety symptoms after the discharge of elderly patients with remitted schizophrenia: a 5-year longitudinal study

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Abstract

Objectives: Remitted schizophrenic patients living in the community often encounter difficulties in their daily lives, possibly leading to the development of social anxiety symptoms. Although several studies have reported the significance of social anxiety as a comorbidity in patients with schizophrenia, few longitudinal data are available on the development of social anxiety symptoms in patients with remitted schizophrenia, especially in association with the process of “deinstitutionalization.” The aims of this study were to assess the social anxiety symptoms in remitted outpatients with schizophrenia and to examine whether the development of social anxiety symptoms was associated with psychotic symptoms, social functioning, or subjective quality of life.

Methods: Fifty-six people with schizophrenia who were discharged through a deinstitutionalization project were enrolled in this longitudinal study and prospectively assessed with regard to their symptoms, social functioning, and subjective quality of life. The severity of social anxiety symptoms was measured using the Liebowitz Social Anxiety Scale (LSAS). Global/Social functioning and subjective quality of life were evaluated using the Global Assessment of Functioning Scale, the Social Functioning Scale, and the World Health Organization–Quality of Life 26 (WHO-QOL26).

Results: Thirty-six patients completed the reassessment at the end of the 5-year follow-up period. The mean LSAS total score worsened over time, whereas other symptoms improved from the baseline. The mean WHO-QOL26 score in the worsened LSAS group was significantly lower than that in the stable LSAS group. At baseline, WHO-QOL26 scores were associated with an increase in the severity of social anxiety symptoms.

Conclusion: In community-dwelling patients with remitted schizophrenia, a lower subjective quality of life might lead to the development of social anxiety symptoms, both concurrently and prospectively. To achieve a complete functional recovery, additional interventions for social anxiety may be needed.

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1. Introduction

Recent developments in psychopharmacologic, psychological, and psychosocial treatments have made it possible

for patients with schizophrenia to achieve a symptomatic remission [1]. On the other hand, schizophrenic patients living in the community may still experience a burden imposed by their surroundings even after achieving recovery from unpleasant psychotic symptoms. These remitted patients living in the community often encounter difficulties in their daily lives, possibly leading to the development or worsening of social anxiety symptoms. Although several studies have reported the significance of social anxiety as a comorbidity in patients with schizophrenia [2–4], few

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longitudinal data are available on the development and/or worsening of social anxiety symptoms in patients with remitted schizophrenia, especially in association with the process of “deinstitutionalization.”

We previously reported a deinstitutionalization project in Japan (“the Sasagawa project”) in which a psychiatric hospital was closed in March 2002 and optimal care (rehabilitation programs, crisis intervention, and medical care management) was subsequently provided for the discharged elderly patients who began living in the community [5,6]. These apparently remitted schizophrenic patients were followed up and evaluated with regard to their symptoms; thus, longitudinal data on the development or worsening of social anxiety symptoms among remitted patients living in the community were obtained. We hypothesized that even clinically stable or apparently remitted patients with schizophrenia developed social anxiety symptoms through the process of deinstitutionalization and that their social anxiety symptoms would have a negative impact on their social functioning or subjective quality of life, as some recent studies have reported [7,8]. Furthermore, given that anxiety may underlie functional paranoia or delusional moods [9], we also assumed that the development and/or worsening of social anxiety symptoms might be associated with an increase in the severity of their psychotic symptoms.

The aims of this study were, therefore, to assess the social anxiety symptoms in remitted and clinically stable patients with schizophrenia living in the community and to examine whether the development of social anxiety symptoms was associated with psychotic symptoms, social functioning, or subjective quality of life.

2. Materials and methods

2.1. Participants

The original patient sample used in this study has been previously reported [5,6]. The study design and treatment protocols for the hospital closure, called the *Sasagawa project*, were also described in detail in our previous report. Of the 94 individuals who were discharged, 78 were independently diagnosed by 2 experienced psychiatrists as having chronic schizophrenia based on the *International Classification of Diseases, 10th Revision* criteria. These 78 patients were evaluated with regard to their symptoms or cognitive performance at the time of discharge. Two years after their discharge (ie, the baseline of the present study), 22 of the 78 outpatients could not be followed up because they were hospitalized or because they could not complete the assessments. The remaining 56 people with schizophrenia were recognized as being clinically stable or had apparently recovered; thus, they were enrolled in this study and were prospectively reevaluated after a 5-year follow-up period. Because this study targeted outpatients living in the community, subjects who were hospitalized were excluded

from this study. The subjects received rehabilitation programs, crisis intervention, and medical care management based on the Optimal Treatment Project (OTP) protocols [10], which include minimally effective antipsychotic drug strategies targeted to changing symptom profiles, education of patients and informal carers in stress management strategies, assertive case management, and goal-oriented social and occupational skills training. They also received biomedical and psychosocial treatment strategies to cope with residual psychotic symptoms as well as day-night hospital or community nurse visits, if necessary. All participants use various living supports in the community, for example, meal delivery services, visiting nursing services, and community recreation centers.

The Asaka Hospital’s Institutional Review Board approved the study protocol and the informed consent procedure. The study protocol was explained to the patients by the principal investigators. Written informed consent was obtained from all patients before their participation in the project.

2.2. Measures

The severity of social anxiety symptoms was measured using the Liebowitz Social Anxiety Scale (LSAS) [11]. This clinician-administered scale consists of 24 items, 13 describing performance situations and 11 describing social interaction situations. Each of the items is separately rated for “fear” and “avoidance” using a 4-point categorical scale. Receiver operating curve analyses have shown that an LSAS score of 30 is correlated with minimal symptoms and is the best cutoff point for distinguishing between individuals with and those without social anxiety disorder [12,13].

The severity of positive/negative symptoms was rated using the Positive and Negative Syndrome Scale (PANSS) score. Global/Social functioning and subjective quality of life were evaluated using the Global Assessment of Functioning Scale (GAF), the Social Functioning Scale (SFS), and the World Health Organization–Quality of Life 26 (WHO-QOL26). These clinical assessments and the amount of neuroleptics (chlorpromazine equivalents) were measured both at baseline and at the end of the 5-year follow-up period.

2.3. Data analysis

The analyses were conducted using SPSS for Windows (version 14.0.2; SPSS Inc, Chicago, IL). For the overall sample, all the clinical variables were compared between the baseline and the end of the 5-year follow-up period using the Mann-Whitney *U* test because the size of the sample was small and the data were nonnormally distributed. To determine whether symptoms, social functioning, or quality of life were associated with the development of social anxiety symptoms, the sample was subsequently split into 2 groups according to the degree to which social anxiety symptoms had developed. Because an LSAS score of 30 has

been shown to best distinguish between individuals with and those without social anxiety disorder [12,13], individuals with both an LSAS score less than 30 at the follow-up point and an LSAS score of 30% or higher increase from the baseline value were defined as “worsened social anxiety symptoms” group (worsened LSAS group). A comparison of the clinical variables between these 2 groups (worsened LSAS group and stable LSAS group) was then performed using the Mann-Whitney *U* test. In addition, logistic regression analyses were performed both to examine whether other clinical variables at baseline can predict the development of social anxiety symptoms and to clarify whether these clinical variables at the follow-up point contribute to a worsening of social anxiety symptoms. An odds ratio and 95% confidence interval were reported. For each comparison, a value of $P < .05$ was considered statistically significant without any consideration for multiple comparisons.

3. Results

3.1. Patients

Of the 56 patients who agreed to participate and be assessed at baseline, 36 patients (64%) completed the reassessment at the end of the 5-year follow-up period. Of the 20 patients who dropped out of the study, 10 moved and could not be followed, 4 were rehospitalized mainly because of worsening physical conditions, 3 had relapsed and were rehospitalized, and 3 refused to be reassessed at the end of the 5-year follow-up period. The demographic variables, clinical assessment results, and neuroleptic dosages of the 36 patients who completed the reassessment did not differ significantly from those of the patients who dropped out of the study. The data reported hereafter are for the 36 patients who completed the final evaluation.

Most of these 36 patients were male (56%). Their mean (SD) age was 60.3 (6.2) years, they had been ill for an average (SD) of 27.6 (5.6) years, and their mean (SD) hospitalization period was 24.5 (9.5) years at the study baseline.

3.2. Social anxiety symptoms and other clinical variables

For the overall sample, the mean LSAS total score worsened over time, whereas the mean PANSS scores improved from the baseline (see Table 1). At the 5-year follow-up point, 24 patients (67%) had a mean LSAS total score higher than 30, suggesting that their social anxiety symptoms had reached a clinical level. Moreover, 2 patients (5.5%) showed a “very severe” symptom level (LSAS total score ≥ 95), 2 (5.5%) had “severe” symptoms (LSAS total score < 80), and 6 (17%) had “marked” symptoms (LSAS total score < 65) after the 5-year period, whereas only 4 (11%) patients showed a greater than marked symptom level at baseline.

To assess the contributing effect of other clinical variables to the development of social anxiety symptoms, we split the

Table 1

Means and SDs for LSAS, GAF, PANSS, SFS, and WHO-QOL across time points (N = 36)

Variables	Baseline		At the follow-up point		z score
	Mean	SD	Mean	SD	
LSAS					
Fear of social interaction	9.6	6.1	12.6	7.9	-2.81**
Avoidance of social interaction	9.7	6.3	12.2	8.3	-1.97*
Fear of performance	9.8	6.2	11.2	6.7	-1.44
Avoidance of performance	9.5	7.2	10.5	6.3	-1.28
Total	38.6	24.3	46.4	26.4	-2.17*
GAF	65.3	10.2	65.4	11.8	-0.72
PANSS					
Positive symptoms	8.7	2.5	8.4	2.0	-2.31*
Negative symptoms	14.5	5.5	14.0	5.4	-3.24**
General symptoms	22.4	5.0	21.9	4.8	-2.01*
Total	45.7	11.6	43.6	10.6	-3.09**
SFS					
Withdrawal	11.3	1.8	11.1	1.5	-0.43
Interpersonal	7.1	2.3	7.2	1.8	-0.48
Prosocial activities	11.4	7.7	9.6	7.8	-1.28
Recreation	17.5	5.9	16.7	6.5	-0.96
Independence-competence	34.6	4.3	34.0	3.9	-1.09
Independence-performance	25.2	5.9	25.1	6.0	-0.40
Employment	2.6	1.2	2.6	1.4	-0.10
Total	110.3	18.5	106.2	19.3	-1.58
WHO-QOL26					
Physical domain	22.5	2.8	21.5	2.9	-2.00
Psychological domain	18.6	3.1	18.0	3.0	-0.88
Social relationship	9.8	2.0	9.5	2.1	-0.97
Environmental domain	25.4	4.0	25.8	3.6	-0.68
General	6.2	1.1	6.2	1.2	-0.14
Total	82.2	11.3	80.9	11.6	-0.99

* $P < .05$.

** $P < .01$.

overall sample into 2 groups. Because an LSAS total score of 30 has been recommended as a cutoff point, individuals with both an LSAS total score less than 30 and an LSAS total score that had increased by less than 30% were regarded as belonging to the worsened social anxiety symptom group (“the worsened LSAS group”). Those subjects who had either an LSAS total score less than 30 or an LSAS total score that had increased by less than 30% were labeled as “the stable LSAS group.”

At the 5-year follow-up point, the mean WHO-QOL26 score in the worsened LSAS group was significantly lower than that in the stable LSAS group, whereas the differences on the PANSS or GAF were not significant between the 2 groups (see Table 2). The worsened LSAS group also had a lower score for the “employment” factor of the SFS, compared with the stable LSAS group, indicating that the patients who developed social anxiety symptoms may have been less motivated to seek employment.

As Table 3 shows, a logistic regression analysis revealed that the WHO-QOL26 scores at baseline were associated with an increase in the severity of social anxiety symptoms. The subjective quality of life at both baseline and the follow-

Table 2
Mean differences between the worsened LSAS group (an LSAS total score a $\geq 30\%$ increase) and the stable LSAS group (an LSAS total score a $< 30\%$ increase) at the follow-up point

Variables	Worsened LSAS (n = 12)		Stable LSAS (n = 24)		z score
	Mean	SD	Mean	SD	
LSAS					
Fear of social interaction	19.7	6.3	9.6	6.5	-3.56**
Avoidance of social interaction	18.4	6.8	9.4	7.5	-3.24**
Fear of performance	15.7	6.1	9.3	5.9	-2.86**
Avoidance of performance	14.4	6.2	8.8	5.6	-2.27*
Total	68.2	22.2	37.2	22.1	-3.36**
GAF	61.7	12.6	68.0	10.7	-0.62
PANSS					
Positive symptoms	8.5	2.1	8.0	1.4	-0.33
Negative symptoms	15.6	6.3	12.8	4.6	-0.39
General symptoms	23.3	4.9	21.0	4.5	-1.43
Total	47.3	12.2	41.8	9.5	-0.66
SFS					
Withdrawal	11.1	1.6	11.2	1.5	-0.17
Interpersonal	6.6	1.7	7.6	1.8	-0.71
Prosocial activities	9.3	6.7	10.0	8.6	-0.90
Recreation	15.0	7.9	17.9	5.7	-0.03
Independence-competence	33.3	2.7	34.4	4.5	-0.99
Independence-performance	24.0	5.5	25.9	6.3	-0.57
Employment	1.9	1.2	3.0	1.4	-2.01*
Total	101.2	17.8	110.0	19.6	-0.27
WHO-QOL26					
Physical domain	19.8	2.5	22.3	2.9	-1.61
Psychological domain	16.4	2.7	18.9	3.0	-2.10*
Social relationship	8.9	1.9	9.7	2.3	-1.05
Environmental domain	24.0	2.6	26.6	4.0	-2.24*
General	5.6	1.0	6.5	1.3	-1.82
Total	74.4	8.2	84.2	11.8	-2.13*

* $P < .05$.

** $P < .01$.

up point was correlated with the development of social anxiety, and this contribution remained significant after adjusting for the LSAS total score at baseline.

On the other hand, symptoms (PANSS) and social functioning (SFS and GAF) were not significantly associated with the development of social anxiety. After controlling for the initial LSAS total score, the “independence-performance” factor of the SFS had a negative relationship with a worsening LSAS score, indicating that the worsened LSAS group was poorer at the skills necessary for independent living than the stable LSAS group at baseline.

4. Discussion

The present findings revealed that social anxiety symptoms were commonly reported among elderly patients with remitted schizophrenia after hospital discharge and that the development of social anxiety symptoms was not associated with psychotic symptoms or social functioning, but with subjective quality of life.

Several possible explanations can account for the development of social anxiety symptoms in patients with chronic schizophrenia. First, patients in a community often experience anxiety when they encounter “real world” difficulties. As hypothesized, changes in daily life (eg, discharge from hospital) could have some negative impacts on subjective quality of life, inducing social anxiety over the long term. The current study demonstrated that subjective quality of life in patients with social anxiety symptoms remained relatively low after a 5-year period.

Second, our sample might have experienced irreversible deterioration as a result of their previous long period of hospitalization. Undoubtedly, a hospitalization period of more than 20 years might cause a reduction in social functioning or social communication skills. Given that the progression of illness also causes cognitive impairment [14], the elderly patients could not sufficiently cope with their distress during daily life.

Third, the current intervention for chronic schizophrenia might have a minimal effect on social anxiety symptoms. Given that most symptoms did not worsen or even improved when compared with their baseline values, an intensive psychosocial and supportive care such as the OTP-based approach might be effective for recovering psychiatric symptoms in individuals with chronic schizophrenia who are living in the community. In addition, considering that the patients who were enrolled in this study had been hospitalized for more than 20 years on average, the effectiveness of this approach appears to be remarkable. However, the present study revealed that the development of social anxiety symptoms was independent of psychotic symptoms or social functioning; therefore, the OTP strategy alone might not be sufficient for resolving social difficulties that can induce a lower subjective quality of life or, as a result, social anxiety symptoms. Although the OTP approaches consist of cognitive-behavioral therapy, social skills training, and stress management, these approaches are designed mainly for patients with schizophrenia and not for patients with social anxiety [15].

Forth, a better understanding of social and cultural context in Japan helps explain the development and/or worsening of social anxiety symptoms in schizophrenia. Japanese psychiatry services still remain predominantly hospital based, that is, an obstacle to the development of community-based services [5]. In addition, personal stigma for chronic schizophrenia among the Japanese public was highly observed [16]. As a result, poor social networks of the long-time hospitalized and elderly patients and obstacles to social inclusion by family and community in Japan could not sufficiently support the community-dwelling patients with chronic schizophrenia.

Lastly, some studies have shown that dopaminergic agents, which are commonly used by patients with chronic schizophrenia, often worsen social anxiety symptoms [17–19]. These results suggest that not only careful medication in patients with social anxiety but also attention to changes in

Table 3
Multiple logistic regression analyses for the development of social anxiety symptoms (an LSAS total score a $\geq 30\%$ increase)

Variables	From baseline				At the follow-up point			
	Unadjusted		Adjusted ^a		Unadjusted		Adjusted ^a	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
LSAS total score	0.97	0.94-1.01	–	–	1.05*	1.01-1.09	–	–
GAF	0.97	0.90-1.04	0.96	0.89-1.04	0.95	0.90-1.01	0.94	0.88-1.01
PANSS								
Positive symptoms	0.90	0.60-1.35	0.84	0.53-1.31	0.93	0.53-1.62	0.79	0.42-1.50
Negative symptoms	1.10	0.88-1.36	1.07	0.85-1.35	1.09	0.87-1.36	1.09	0.86-1.37
General symptoms	1.02	0.79-1.32	1.15	0.85-1.55	1.05	0.81-1.36	1.18	0.87-1.59
Total	1.03	0.79-1.32	1.06	0.99-1.14	1.05	0.98-1.13	1.08	0.99-1.17
SFS								
Withdrawal	0.88	0.60-1.29	0.97	0.64-1.49	0.95	0.59-1.51	1.05	0.63-1.74
Interpersonal	0.75	0.54-1.05	0.71	0.50-1.01	0.67	0.42-1.09	0.61	0.37-1.01
Prosocial activities	0.97	0.88-1.07	0.97	0.88-1.06	0.99	0.90-1.08	0.99	0.91-1.09
Recreation	0.95	0.84-1.07	0.95	0.84-1.07	0.93	0.83-1.04	0.94	0.84-1.05
Independence-competence	1.00	0.85-1.18	0.97	0.81-1.17	0.93	0.78-1.11	0.90	0.74-1.09
Independence-performance	0.88	0.76-1.00	0.86*	0.75-1.00	0.95	0.84-1.07	0.94	0.84-1.06
Employment	0.61	0.31-1.19	0.62	0.31-1.24	0.49*	0.24-0.98	0.51	0.26-1.02
Total	0.97	0.93-1.01	0.97	0.93-1.01	0.97	0.94-1.01	0.98	0.94-1.02
WHO-QOL26								
Physical domain	0.66*	0.47-0.94	0.60*	0.41-0.90	0.65*	0.45-0.93	0.61*	0.40-0.93
Psychological domain	0.74*	0.56-0.97	0.71*	0.52-0.97	0.63*	0.43-0.92	0.57*	0.37-0.89
Social relationship	0.73	0.49-1.10	0.68	0.44-1.07	0.84	0.59-1.19	0.75	0.52-1.10
Environmental domain	0.80*	0.65-0.99	0.75*	0.58-0.97	0.78	0.60-1.01	0.68*	0.49-0.95
General	0.18**	0.05-0.61	0.10**	0.02-0.48	0.43*	0.20-0.95	0.26*	0.09-0.77
Total	0.90*	0.83-0.98	0.88*	0.79-0.97	0.90*	0.82-0.99	0.85*	0.75-0.97

^a Adjusted for the LSAS total score at baseline.

* $P < .05$.

** $P < .01$.

anxiety symptoms are important for the management of individuals with chronic schizophrenia.

The present study has some clinical implications regarding interventions for chronic schizophrenia. The association between social anxiety symptoms and a lower subjective quality of life suggests that it is clinically important to recognize the development of social anxiety. Anxiety symptoms, however, are often underdiagnosed because clinicians usually pay more attention to psychotic symptoms than these symptoms [20]. In addition, recent criteria for remission in schizophrenia mainly rely on psychotic symptoms [21,22], and therefore, the risk of underdiagnosing anxiety factors is increased. Now that the number of elderly patients with schizophrenia living in the community is increasing, it is becoming increasingly important to educate clinicians about the comorbidity of social anxiety because the underdiagnosis of anxiety symptoms can lead to insufficient intervention.

Thus, a more specific strategy, in addition to optimal care, might be needed to achieve a full recovery from illness. For example, Morita therapy involves a structured behavior program to encourage an outward perspective on life, thereby increasing social functioning. A recent review on Morita therapy in patients with schizophrenia revealed that this therapy, in addition to standard treatment, significantly improved daily living, compared with the standard treatment alone [23].

Our study has some limitations. First, the small number of subjects in this study may certainly limit the generalizability of the findings. Second, our sample comprises elderly patients and is not representative of typical patients with schizophrenia. Given that the mean age was greater than 60 years, aging might influence the worsening of not only social factors but also other symptoms. In addition, there was a substantial attrition, with some patients being rehospitalized. It may be that such long-term hospitalized patients were more vulnerable than more representative population of individuals with schizophrenia. Taken together, our results should be cautiously interpreted because we did not examine younger or short-term hospitalized patients with schizophrenia. Lastly, another methodological weakness is that we did not evaluate depressive symptoms. Although the degree to which depression is associated with social anxiety remains debatable, aging individuals often experience depression when they encounter social difficulties. Further investigations of the association between social anxiety and depression in aging schizophrenic patients are needed.

5. Conclusion

The current study provides a new and important perspective on social anxiety in individuals with schizophrenia. In community-dwelling patients with remitted schizophrenia, a

lower subjective quality of life might lead to the development of social anxiety symptoms, both concurrently and prospectively. To achieve a complete functional recovery, additional interventions for social anxiety may be needed.

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Clinical Practice at a Multi-dimensional Treatment Centre for Individuals with Early Psychosis in Japan

日本一所为早期思觉失调患者而设的多维治疗中心的临床实践

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Abstract

Early intervention for psychosis in Japan has lagged behind that in western countries, but has rapidly begun to attract attention in recent years. As part of a worldwide trend, a multi-dimensional treatment centre for early psychosis consisting of a Youth Clinic, which specialises in young individuals with an at-risk mental state for psychosis, and Il Bosco, a special day-care service for individuals with early psychosis, was initiated at the Toho University Omori Medical Center in Japan in 2007. The treatment centre aims to provide early intervention to prevent the development of full-blown psychosis in patients with an at-risk mental state and intensive rehabilitation to enable first-episode schizophrenia patients to return to the community. We presently provide the same programmes for both groups at Il Bosco. However, different approaches may need to be considered for patients with an at-risk mental state and for those with first-episode schizophrenia. More phase-specific and need-specific services will be indispensable for early psychiatric interventions in the future.

Key words: Cognitive therapy; Early intervention (education); Japan; Schizophrenia

摘要

虽然日本的思觉失调早期干预服务落后于西方国家，但近年开始备受注意。思觉失调早期干预已成全球趋势，有见及此，日本东邦大学大森病院于2007年成立针对思觉失调的多维治疗中心，包括为思觉失调潜伏期年青人提供服务的「青年诊所」，和以早期思觉失调患者为对象的日间精神复康中心「Il Bosco」，旨在为潜伏期患者提供早期干预以抑制典型思觉失调病发，以及为首发精神分裂症患者提供密集式复康服务，使他们能尽快重投社会。虽然Il Bosco正实施上述两种治疗计划，不过也须考虑这两类患者的需要而采用合适的治疗方案。阶段性和患者为本服务是思觉失调早期干预计划发展必不可少的部份。

关键词：认知治疗、早期干预（教育）、日本、精神分裂症

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Early Psychiatric Intervention in Japan

Early intervention for psychosis in Japan has lagged behind that in western countries because of the continued existence of hospital-based psychiatry which requires large numbers of psychiatric beds and long-term hospital stays,¹ as well as barriers resulting in delayed patient contact with psychiatric services. However, early intervention has rapidly begun to attract attention in recent years.² Despite the difficult

circumstances, reports indicated that earlier detection may enable better outcomes in addition to shortening the duration of untreated psychosis (DUP) in Japan.^{3,4} The energetic activities of the Japanese Society for Prevention and Early Intervention in Psychiatry (Website: <http://www.jseip.jp>) have also promoted early psychiatric interventions. The latest multicentre retrospective study in Japan revealed that the mean and median DUP were 20.3 and 6.0 months, respectively.⁵

When thinking about the dissemination of early intervention for mental disorders in Japan, we must consider the culture and attitudes towards mental disorders among the Japanese people. In the light of our own clinical experience, individuals with mental health problems and their families are often reluctant to seek help for various reasons, including ignorance about the features and treatability of mental disorders, beliefs that the problem should be solved by themselves, confining the problem to close relations without consulting professionals, and stigma connected with psychiatry, although Japanese people generally accept the need for medical treatment for physical problems. These obstacles may explain the long DUP and the social stigma towards mental disorders in Japan. However, the nuclearisation of families may also be affecting this delay in seeking treatment. Nishii et al⁵ reported that patients living alone in Japan had significantly longer DUP than those living with their families. These considerations should be further investigated.

Some treatment services specialising in the early stage of psychosis have recently been established in Japan, including the Tokyo Youth Club administered by the Minato Net 21 (a non-profit organisation in Tokyo), Tohoku University Hospital (Sendai at-risk mental state [ARMS] and first episode service), the University of Toyama Hospital (consultation and support service in Toyama), the University of Tokyo Hospital, Osaka University Hospital, Kochi Medical School Hospital, and the Tokyo Metropolitan Matsuzawa Hospital (Wakaba). The background and present situation of early psychiatric intervention in Japan have been detailed elsewhere.^{6,7}

Practices at the Toho University Omori Medical Center

The Toho University Omori Medical Center is located in Ota, a city with a population of about 700,000 located in the southern area of the Tokyo Metropolitan region. Our department is named the 'Mental Health Center' to avoid the stigma of psychiatry and mental disorders. About 150 outpatients visit the department each day. Having 2 psychiatric wards — a closed ward with 18 beds and an open ward with 18 beds, the Center serves psychiatric patients with physical problems as well as regular psychiatric patients. Therefore, our department shoulders the responsibility of being a core institution for mental health care in the area. The strengths of our department are early intervention for young people and cognitive

rehabilitation, which are practised at the Youth Clinic and at Il Bosco, a special day-care service. We aim at establishing a multi-dimensional treatment centre for early psychosis that encompasses symptom reduction, cognitive function, social functioning, quality of life, psycho-education, and family intervention.⁸

Youth Clinic

As part of the worldwide trend toward early psychiatric intervention, a Youth Clinic specialising in the treatment of young individuals with an ARMS was established in our department in 2007. The PRIME Screen-Revised test (PS-R)⁹ is administered to all first-time patients younger than 40 years to screen for ARMS as part of the routine preliminary examinations. The PS-R is a self-reported screening test that consists of 11 items regarding attenuated psychotic symptoms and only requires 5 minutes to complete. Patients with positive PS-R results or who are suspected of having ARMS after an examination are introduced to the Youth Clinic, where they are interviewed for diagnostic purposes using the Structured Interview for Prodromal Syndromes / Scale of Prodromal Symptoms, Japanese version.¹⁰ They are also supposed to undergo neuroimaging and cognitive testing for detailed examination. When a patient is found to meet the criteria for ARMS, treatment such as stress management, coping strategies for psychotic symptoms, and problem-solving skills is started. Medication with low-dose antidepressant, minor tranquilizer, or major tranquilizer might also be considered.

Il Bosco

Day-care Service for Patients with Early Psychosis

To develop early intervention in Japan and put it into practice, the conventional day-care service intended mainly for patients with chronic schizophrenia was terminated. In May 2007, a new day-care service, which specialises in the care and support of individuals with ARMS or first-episode psychosis aged 30 years or younger, was established. The service unit, named Il Bosco, aims at providing early intervention to prevent the development of full-blown psychosis in ARMS patients, as well as intensive rehabilitation to enable first-episode schizophrenia patients to return to the community.⁷ The staff members consist of a variety of professionals, including psychiatrists, nurses, occupational therapists, clinical psychologists, social workers, and pharmacologists. The registration period is limited to 1 year for concentrated care in principle, and can be extended up to 2 years depending on the patient's condition. Adequate medication is offered at the Youth Clinic, and intensive psychosocial treatment is provided at Il Bosco. The contents of the daily programmes are specifically considered with the intention of promoting the brain plasticity of young patients and providing an environment and atmosphere where patients can feel relieved without stigma.

Approaches and Programmes

A comprehensive support system suitable for targeted generations is indispensable to the success of psychiatric rehabilitation, and multiple and integrated approaches are administered based on the Optimal Treatment Project¹¹ at Il Bosco, in collaboration with the Youth Clinic (Fig). We offer programmes for learning and training in interpersonal relationships using worksheet and role-playing activities, practices for daily living skills such as cooking, study time for patients to keep up with their friends at school, patient-managed meetings to promote responsibilities and roles within a group, family intervention and psycho-education, as well as group therapy. We sometimes address the stigma of mental illness in the education programme.

The creation of patient goals and plans to accomplish these goals carefully and quickly is vital during the introduction period, because delays can lead to a widening distance from the community and seem to create an inferiority complex or despair, especially among adolescents. Goals can also foster hope regarding an individual's prognosis and can motivate them to join programmes. Speed is requested in every situation at Il Bosco. Young patients need to start to make a return to the community early, because they usually wish to keep their previous role in the community. Therefore, the contents of each programme must be subdivided, and frequent interviews are necessary to respond to their needs individually. We sometimes offer special programmes to only a few patients who require such programmes. Our aim is for patients to be stable not only in the day-care service unit, but also in the community.

Supporting and paying attention to patients who are building interpersonal relationships within the service is also important because young patients often quickly approach other patients in the same generation using cell phones and emails; such relationships can fail because of poor and immature interpersonal relationship skills, although some patients are obstinately hesitant to communicate with others. Efforts to handle this problem may also contribute to the low dropout rate (11.9%) at Il Bosco.

Many patients (60.0%) have achieved their goals within 1 year since the establishment of Il Bosco; such goals include returning to school, transferring to a correspondence course school, starting to go to preparatory school, and beginning an occupation. Although many patients visit to ask for a consultation or to report on their present condition even after they have completed their course, some patients may be caught in a dilemma and may wish to forget their days at the centre. We are presently considering how to continue supporting these patients after they completed the Il Bosco programme.

Cognitive Rehabilitation

At Il Bosco, cognitive remediation, which directly targets brain function in addition to a psychosocial approach, is adopted. Both of these approaches are regarded as wheels in the promotion of early psychiatric intervention. Institutions that adopt such an approach to individuals with early psychosis are still uncommon throughout the world. Cognitive remediation has been in the spotlight as a novel approach to promoting remission and recovery

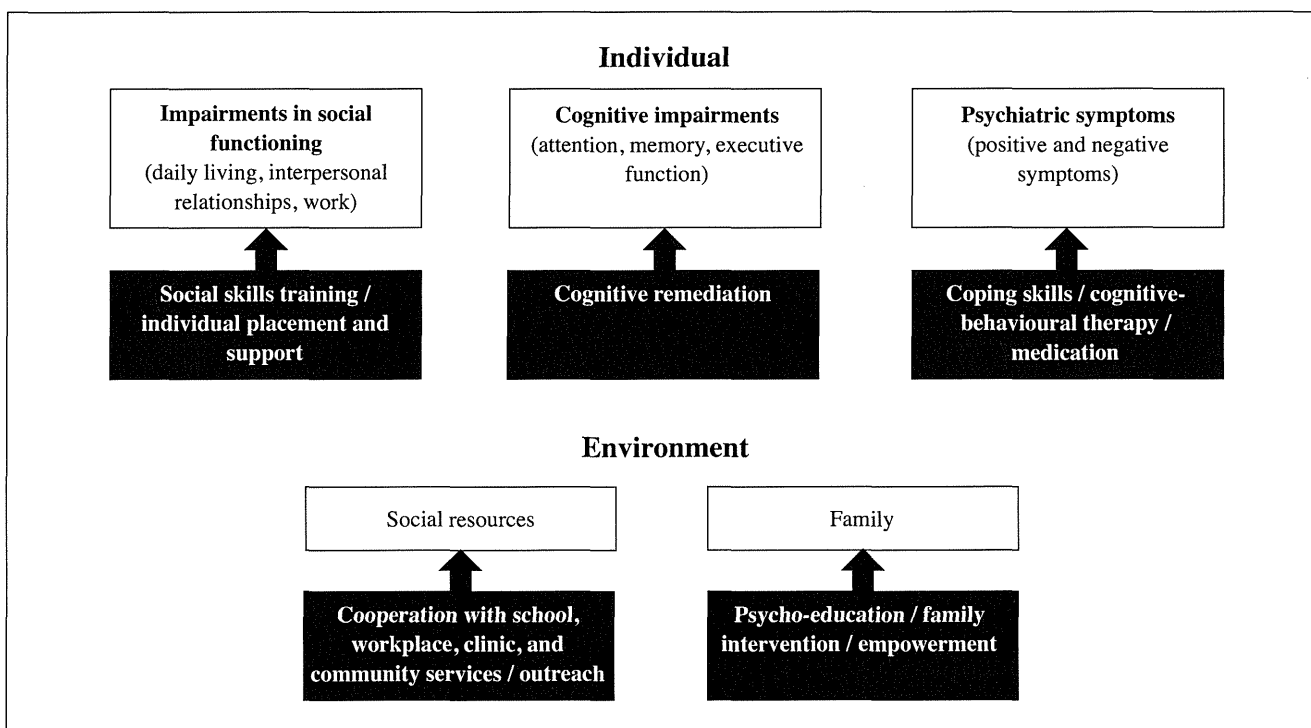


Figure. Multi-dimensional treatments provided at the Toho University Omori Medical Center.

under existing conditions in which medication is not effective for alleviating impairments in social functioning in schizophrenic patients,¹² although more empirical research is necessary to confirm the efficacy of cognitive remediation in the early course of schizophrenia.¹³ Our cognitive remediation programme mainly targets divergent thinking deficits, because it is found that cognitive training for divergent thinking leads to significant improvements in negative symptoms and social functioning of patients.¹⁴ Also, broad cognitive rehabilitation programmes are carried out and a suitable approach for young patients, such as outdoor cognitive remediation and combining cognitive remediation with physical exercise, is devised.¹⁵

Collaboration with Community Resources

We are actively engaged in activities to enlighten the community and to disseminate information on the prevention of mental disorders and to reduce the stigma associated with mental disorders. We distribute booklets and leaflets on early psychosis described in an easy and open-minded style to people in the field of education as well as to patients and their families, since collaborating with them is important for achieving early intervention. We also have many opportunities to collaborate with nursing teachers. Young people tend to stay away from medical services because of uneasiness. Therefore, a self-check sheet is offered to allow individuals to contemplate their mental condition. In addition to providing a means of introducing individuals who need help to appropriate psychiatric services, accurate psychiatric information is also available on the Il Bosco website (<http://www.lab.toho-u.ac.jp/med/omori/mentalhealth/>). Importantly, we focus not only on psychiatric symptoms, but also on patients' difficulties in daily living when starting the interventions.

Future Prospects

At present, we provide the same programmes both for individuals with first-episode schizophrenia and for those with ARMS at Il Bosco. However, ARMS patients usually maintain better cognition and social functioning than those with first-episode psychosis, and most of them are younger and are students in high school or college. Different approaches may be needed for patients with ARMS and for those with first-episode schizophrenia. More phase-specific

and need-specific services will be indispensable for early psychiatric intervention in the future.

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Early Psychosis Declaration for Asia by the Asian Network of Early Psychosis

亚洲早期思觉失调网络发表的《亚洲早期思觉失调声明》

Asian Network of Early Psychosis*

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Abstract

In line with the Early Psychosis Declaration issued by the World Health Organization and the International Early Psychosis Association, as well as the International Clinical Practice Guidelines for early psychosis by the latter in 2005, increasing interest in early intervention programmes is evident throughout Asia. Experience sharing and close collaboration that take into account the unique Asian context are needed to facilitate development of early psychosis services, education, and research in the region. The Asian Network of Early Psychosis has defined a set of Asian-specific principles to guide best practice in mental health care delivery for psychotic disorders in Asia. These principles are outlined in this paper.

Key words: Asia; Culture; Early intervention; Psychotic disorders

摘要

随着2005年世界卫生组织和国际早期思觉失调协会颁布的《早期思觉失调声明》，以及后者颁布的《国际早期思觉失调临床方针》，思觉失调早期干预在亚洲越受关注。为了促进符合亚洲人口的早期思觉失调服务的发展、教育和研究，各地的经验交流和紧密合作是必要的。亚洲早期思觉失调网络（Asian Network of Early Psychosis）近期制定一套针对亚洲人口的思觉失调护理准则，为这地区精神病人口的精神健康护理提供最佳指引。本文将概述这些准则。

关键词：亚洲、文化、早期干预、思觉失调

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Introduction

Since the introduction of the concept of 'early intervention for psychotic disorders' in the 1990s, many early intervention programmes for psychosis have taken root in western countries. In Asia, the early intervention programmes were first introduced in Hong Kong and Singapore in 2001. Since then, several other similar programmes have been set up across Asia. Increasing interest in early intervention programmes is now evident in the region, and experience sharing and close collaboration are called for to facilitate development of early intervention for psychosis services, education, and research in Asia.

The Asian Network of Early Psychosis (ANEP) is an informal network of clinicians and researchers working in early intervention for psychosis in Asia. Addressing the specific culture and values in the Asian setting, the ANEP provides a platform to facilitate development of early

intervention services in Asia through close exchanges and experience sharing across member sites. The ANEP also aims to promote research in the course, outcomes, and early intervention service delivery of first-episode psychosis in Asia, and encourage use of standardised instruments and assessment procedures for more comparable results. To date, the ANEP has contributors from cities in China, India, Indonesia, Japan, Korea, Malaysia, Singapore, and Taiwan. Through regional meetings and symposia, collaborative research, links with other regional and international networks, as well as an online discussion forum (<https://sites.google.com/site/asianearlypsychosis>), the ANEP encourages groups and researchers in the region to work together for the better care of psychosis in Asia.

In line with the Early Psychosis Declaration issued by the World Health Organization¹ and the International Early Psychosis Association, as well as the International Clinical Practice Guidelines for early psychosis by the latter institution,² and taking into consideration the unique Asian context, we have defined a set of common principles with input from regional consultants of the ANEP to guide best practice in mental health care delivery in the field of psychotic disorders in the region. The principles outlined below were first discussed at the International Conference on Early Psychosis in Asia Pacific 2012, held in Hong Kong

in January 2012. A concise summary of the statements is given in the Table.

Mental Health Policies on Psychotic Disorders

In general, Asian countries are faced with a lack of resources in early intervention for severe mental health conditions including psychotic disorders, compared with our western counterparts. Among Asian cities where early intervention programmes have commenced, high caseloads and suboptimal management remain a problem within public mental health systems. Regional and international clinical studies³⁻⁸ have provided evidence for the cost-effectiveness of comprehensive early intervention for patients with first-episode psychosis, especially during the critical period immediately following illness onset. The extra manpower and other resource input for early intervention can be offset by reduced service utilisation in terms of hospital stay and emergency services. Close collaboration between mental health policy-makers, researchers, and clinicians is needed for more informed planning in cost-effective resource allocation and achieving the best patient outcomes and mental health care at the societal level.

Clinical Care

A set of practical clinical standards for psychosis management, including pharmacotherapy and psychosocial intervention, should be developed, taking into account Asian-specific factors in terms of physiology, psychology, cultural values, and resource limitations. In particular, we sought to:

- explore and pioneer optimal interventional approaches in the context of low mental health resources and high caseload (e.g. utilisation of the primary health service in developing clinical standards, education, and training materials);
- explore and enhance Oriental cultural, societal, and familial strengths for better care of early psychosis patients;
- encourage community care instead of institutional care for early psychosis;
- understand service delivery barriers to early psychosis detection and management;

- advocate adequate consultation time for early psychosis patients; and
- develop training systems for specialised professionals working in early psychosis.

Pharmacotherapy

Antipsychotics are the mainstay of treatment for psychotic disorders. In Asia, the patients and their family’s acceptance of medication treatment remains low and should be enhanced, and clinical experience should be accumulated on the use of antipsychotics in Asian populations. There are needs to: (1) reinforce correct perception of pharmacotherapy and attitudes to medication in early psychosis patients and their families; and (2) explore how treatment response and side-effects of medication are different among Asians in terms of ethnopsychopharmacogenetics.

Psychosocial Intervention

Non-medication interventions have crucial impacts on the outcomes of patients with psychotic disorders. Provision of psychosocial intervention services should be greatly strengthened in the region. We need to:

- provide evidence-based, culturally adapted psychosocial interventions to achieve the best possible clinical outcomes during the early critical period of the illness — these may include cognitive behavioural therapy (CBT), family therapy, and multidisciplinary team approaches;
- provide active and intensive psychosocial interventions by increasing consultation time, and using case management with community service programmes;
- develop and share clinical experience in modified CBT based on Oriental thinking, such as an emphasis on awareness and perception compared with a rational approach;
- develop and share experience in the implementation of community service programmes appropriate to various Asian contexts;
- capitalise on the unique Asian value of strong familial ties by promoting family support in psychosis management, including psycho-education for family members about early detection of warning signs, and psychological support for carers; and

Table. Abbreviated Early Psychosis Declaration for Asia.

<ol style="list-style-type: none"> 1. To facilitate close collaboration between mental health policy-makers, researchers, and clinicians, in order to inform service planning and increase resources allocated for cost-effective early psychosis intervention 2. To develop a set of Asian-specific clinical practice standards for psychosis management via: <ul style="list-style-type: none"> • pharmacotherapy: to enhance acceptance of medication treatment, and to investigate pharmacological responses in Asians; and • psychosocial intervention: to strengthen the provision of evidence-based, culturally adapted psychosocial intervention services in the region 3. To understand and to raise the level of awareness in psychosis through public education tailored for Asian perspectives 4. To consolidate an Asian-specific evidence base on psychotic disorders, to promote research work and data-driven intervention in the region, and to facilitate collaborative projects in Asian populations
--

- mobilise community leaders (e.g. religious, local, or extended families leaders), an important group with great influence that can be found in most Asian cultures, as partners in psychosocial intervention.

Education and Public Awareness

The level of awareness and understanding of psychosis remains relatively low in Asia, which contributes to long delays in help seeking, barriers to treatment compliance, and extra psychological burdens to patients and their families. Efforts are required to:

- develop and share educational materials such as brochures, posters, videos, and handouts, with a focus on psychosis rather than schizophrenia, and present them to the public in an easy and acceptable fashion for Asian or Oriental perspectives;
- promote early detection of psychosis to minimise hospitalisation and chronic disability; and
- understand and address public awareness and stigma associated with psychosis in Asian populations.

Research

An Asian-specific evidence base needs to be consolidated to better inform policy-making, clinical management, and education strategies. Concerted research efforts among Asian countries and sites are needed. We aim to: (1) promote research work and data-driven intervention as an integral component of early psychosis management; and (2) pursue collaborative projects in areas of high research priority, including:

- risk population studies in Asia;
- duration of untreated psychosis and help-seeking behaviour in Asian societies;
- early intervention during the critical period (e.g. optimal duration and outcomes of the intervention service);
- efficacy of community service programmes;
- intervention for cognitive functioning;
- biomarkers of disease vulnerability and psychosis phenotypes in Asians;
- antipsychotic treatment response in Asian populations; and
- the role of sociocultural factors in the treatment of and recovery from early psychosis in Asia.

Our Visions

With this Declaration, we aim to achieve:

- enhanced communication among mental health stakeholders and policy-makers to allocate reasonable resources for cost-effective management in the early intervention of psychosis in Asia;
- development of clinical practice standards in psychosis in Asia, with an emphasis on optimal early intervention and community care;
- promotion of pharmacological and psychosocial

- management of psychosis tailored to the Asian situation;
- heightened public awareness and understanding of psychosis at a regional level; and
- consolidation of high-quality and compatible scientific data on psychotic disorders specific to Asian populations.

Conclusions

As a global direction for mental health care, developing early intervention for psychosis will continue to be a primary focus of efforts in Asian countries. Work in this area must concentrate on the 3 fronts of clinical care, education, and research. With increasing recognition of the effectiveness of early psychosis management, it is anticipated that governments and relevant authorities might contribute sufficient resources to realise the directives as outlined above. Bearing in mind the heterogeneity in many aspects, including culture, ethnicity, religion, social values, and economic development among Asian countries, joint efforts focusing on the common sets of needs, challenges, and opportunities across the region will hopefully facilitate progress in early psychosis intervention in Asia. Together, the Asia region will move towards a more preventive and cost-effective model for the management of psychotic disorders, easing the burden of the illness on patients, families, and society.

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Whither the Attenuated Psychosis Syndrome?

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After 4 years of debate, a decision has been made. The attenuated psychosis syndrome (APS) will not be a coded diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Formerly known as the psychosis risk syndrome, the proposed diagnosis was based on criteria developed in the mid-1990s that were informed by a comprehensive review of retrospective studies on the prodromal phase of nonaffective psychosis.¹ These criteria aimed to identify prospectively people in the prodrome of schizophrenia and other psychotic disorders and have been variously titled “ultra high risk (UHR),” “clinical high risk (CHR),” “at risk mental state (ARMS),” and the “prodromal stage,” and included a group with attenuated (subthreshold) positive psychotic symptoms.² The criteria are associated with rates of onset of psychotic disorder substantially higher than in the general population³ and other clinical populations.⁴ A recent meta-analysis reported the rate of onset of a psychotic disorder to be 36% after 3 years.⁵ About 73% of those developing a psychotic disorder fulfill criteria for schizophrenia spectrum psychoses.⁶ It should be noted that these data are from treated samples consisting of patients referred to specialist clinical services.

Despite the consistent finding that there is a high risk of developing a psychotic disorder associated with the APS group,⁵ there has been considerable controversy around the idea of formally codifying it into a DSM5 diagnosis. Indeed, we, the authors of this communication, all active researchers in the area, have had differences in opinion about the merits of including APS as a new diagnosis in the DSM.^{7–12}

One issue debated was the tension between the possibility of early intervention to prevent progression of disorder vs potential unnecessary diagnosis and treatment of what might be a self-limiting phase. The possibility of stigma and discrimination was also raised.^{10,11} Some speculated that a formal diagnosis would be assumed to equate to an indication for antipsychotic medication and so increase the likelihood of antipsychotic prescription.¹¹ Others argued that the absence of an APS diagnosis has led to some clinicians using the term psychosis NOS (not otherwise specified), which may lead to antipsychotic prescription. The APS as an alternative to this diagnosis could then actually reduce antipsychotic prescribing.^{9,12} Importantly, an APS diagnosis will enable evidence-based treatments to be developed, including

psychological therapies, and could therefore decrease antipsychotic use.¹²

Ultimately, the decision to exclude APS as a coded diagnosis was made not in response to any of the above issues or in the light of data addressing the principal disputes but because data on the diagnostic reliability of APS in clinical practice were limited and inconclusive.

Following this decision, some critics have been quick to denounce the whole APS/ultra high-risk/clinical high-risk/prodromal concept.^{13–15} We, therefore, feel it is timely, as a group involved in high-risk (prodromal) research, to document some points of consensus between us and highlight areas for future research.

Points of Consensus

Attempts to recognize the prodrome of schizophrenia prospectively have been active for nearly 20 years.² Many samples of persons meeting high-risk criteria have been seen and evaluated. A strong consensus exists that individuals meeting APS criteria (which includes a criterion for help-seeking) are symptomatic and in need of clinical care.^{16–18} People meeting the criteria do in fact fulfill the broad definition of mental disorder: “a clinically significant behavioral and psychological syndrome or pattern ... that is associated with present distress ... or disability ... or with a significantly increased risk of suffering death, pain, disability, or an important loss of freedom,”¹⁹ (p. xxi). Thus, treatment is clearly justified, regardless of the justification of reduction of risk or prevention. We agree that this treatment should include monitoring of mental state, supportive therapy, and attention to current practical needs. Cognitive therapy and omega-3 fatty acids may also be helpful. On current evidence, antipsychotic medication is no more effective than other more benign treatments and so is typically not recommended.²⁰

A second point of consensus is that people meeting APS criteria have a greatly increased risk of developing a psychotic disorder within a brief time frame.^{3,5,21,22} Despite evidence that the transition rate (conversion from high-risk state to first-episode psychosis) may be declining in the short term²³ and the finding of low rate of psychosis in recent intervention trials,^{24,25} its magnitude is similar to other risk syndromes,^{26,27} and still in the order of hundreds fold above the risk of the general population. Given this, we agree that regular assessment of mental state to detect first episode of psychosis is indicated. The monitoring of mental state and early detection of psychosis allow prompt treatment and the minimization of the duration of untreated psychosis, which, if prolonged, is harmful to both patients and their families and is known to be associated with a poor outcome.^{28,29}

Finally, we agree that more research into the APS is needed. We support the Psychotic Disorders Workgroup in its recommendation to include the APS as a category

in the appendix (Section 3) of DSM-5 as a condition for further study.

Collectively, we have devoted many hours into thinking about this condition. Through our research and clinical experience with these patients, we have evolved our thinking and our conceptualization of APS. Initially, the high-risk criteria were developed, as the name suggests, to detect individuals at high risk of psychotic disorder. However, the use of the criteria should not be thought of as identifying and treating an asymptomatic group at risk of a poor outcome, analogous to detecting and treating hyperlipidemia to prevent myocardial infarction (MI). APS patients are symptomatic and distressed. Thus, angina may be a more apt analogy. However, better still is to think of the criteria as detecting chest pain. The condition is distressing, symptomatic, and leads to help seeking. It may indicate the early signs or risk for a serious cardiac disease such as MI, a serious but noncardiac disease, such as pneumonia or a benign self-limiting condition such as esophageal spasm or costochondritis. Likewise, APS may indicate the early signs or risk for illnesses such as nonaffective and affective psychotic disorder, presence or risk for a serious but nonpsychotic illness such as severe unipolar depression, or it may indicate something that is not serious and which may resolve, with or without treatments such as psychological support, stress reduction family interventions, and practical help.

This way of conceptualizing APS leads to many different paths for research. Suggestions for the future research agenda follow.

Expanding the Range of Outcomes to Be Studied

Investigation of different outcomes in both the short and long term including psychotic disorders, nonpsychotic disorders, persistence or remission of APS, and social and cognitive functioning is needed. Refining risk factors for these different outcomes is another avenue of research. It may be that added criteria are necessary to enrich the sample for schizophrenia, such as basic and negative symptoms and decline in cognitive and social skills.^{30,31} Other methods of enrichment for other outcomes can also be studied, including multiple subclinical symptoms plus depression,³² presence of personality disorder, family history of mental disorder, and childhood trauma and adversity.³³

Examining recovery and remission of the high-risk state as outcomes is another area that is currently understudied. Searching for predictors of these positive outcomes can then lead to adding such factors to ascertainment criteria as exclusions, which would result in a reduced false positive rate and increased positive predictive power.

Searching for Markers of Different Trajectories

Examining associated neurobiological,^{34–36} cognitive,³⁷ physiological,³⁸ metabolic,³⁹ and genetic^{40,41} associations

with the APS and its different outcomes is needed so that subgroups can be more sharply delineated. Longitudinal follow-up is needed to elucidate whether the biological markers that are observed in the APS group are indicative of a trait vulnerability to psychotic disorder or whether they are state markers. Comparison with other psychiatric groups without APS will determine whether biological findings are specific to APS and represent a continuum with psychotic disorders such as schizophrenia or whether they are associated with general psychiatric distress.

Stigma and the Effect of Symptoms and Diagnosis

Research is also needed as to what harms and benefits are associated with an APS diagnosis. This should include assessing any perceived stigma, and comparison made with the stigma, stereotypes, and wish for social distance associated with overt psychiatric symptoms that may occur prior to help seeking and diagnosis. Whether clinical care that provides information, treatment, and hope of a good outcome can minimize stigma should also be studied. The effects of creating a new diagnosis, on patients, their families, and the wider health system, needs to be better understood.

Reliability and Clinical Utility

While reliability of assessment has been demonstrated in previous studies using structured interviews,^{42,43} the clinical utility and reliability of assessment in routine practice needs to be assessed and improved and the impact of the proposed diagnosis on prescribing practice examined. Investigation of factors that lead APS patients to seek help will also be useful. Currently, it is unclear how much of the distress that leads to seeking help is related to the psychotic-like symptoms or to associated nonpsychotic mental disorders, such as depression and anxiety.⁴⁴ Little is known about the prevalence of APS in adolescent and adult clinical populations and in the general community and this also needs further study.

Treatment Trials

Further intervention research is also needed. Omega-3 fatty acids have shown promise in reducing symptoms as well as decreasing the risk of transition to psychotic disorder in one study.⁴⁵ This requires replication. Other novel treatments such as psychological treatments, vitamin D, glycine, and other neuroprotective agents are also worth testing.

Possibility of a Pluripotent Risk Syndrome

Finally, with increasing the knowledge of risk factors for different outcomes (see above), the APS model could also be extended to a more general a strategy for early intervention

in a range of mental disorders. It may be that many disorders develop from initial nonspecific symptoms and syndromes, from a background of specific and nonspecific risk factors (such as genes and early environment). Worsening of symptoms and acquisition of new symptoms may occur, together with progressive neurobiological abnormalities, and related neurobehavioral deficits, until clear-cut recognizable mental disorders appear.⁴⁶ Progression of symptoms and neurobiological abnormalities could continue after “threshold” diagnosis, with development of chronic symptoms, relapses, and ongoing functional deterioration. Transition from one stage to the next is not inevitable, either due to different risk and resilience factors or due to nonspecific or specific intervention. Thus, preventive possibilities exist across this spectrum of evolving illness.

This concept of a pluripotent risk syndrome opens up a range of research possibilities. Studying genetic and environmental risk factors and gene and environment interactions for different outcomes, further work on resilience and protective factors, and examination of different trajectories are all future avenues of research. Whether any specific markers for particular course and outcome can be detected early is another area and leads to the possibility of early specific treatments. Novel methods such as multimodal imaging and neurocognitive analysis, single subject methods to predict individual disease course are also possible.

Conclusion

APS concept remains a useful one. It identifies people with significant mental health problems that justify treatment in their own right, as well as having a higher likelihood of developing a psychotic disorder (mostly schizophrenia) within a few years. Research into this group will increase our understanding of psychotic-like symptoms and their trajectories and the emerging phase of psychotic disorders. The APS concept is consistent with the continuum view of psychosis and is probably a reflection of biologic reality. Outcomes other than psychotic disorder are also clearly worthy of study. The placement of APS in the DSM-5 appendix should be a clarion call to the field to focus attention on these patients and families in need.

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