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Course, outcome and diagnosis stability of early-onset schizophrenia in Yunnan Province, China-a three years follow-up study

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ABSTRACT

The aim of the study was to describe diagnostic stability and psychosocial outcomes of subjects with early-onset schizophrenia (EOS). All the subjects who had been hospitalized in the Department of Psychiatry of the First Affiliated Hospital of Kunming Medical University between January 2011 and July 2015 with the diagnosis of International Classification of Diseases (ICD)-10 defined schizophrenia, and discharged from the hospital for more than 12 months were enrolled to the study. The Mini International Neuropsychiatric Interview was applied for life-time ICD -10 diagnoses, and Personal and Social Performance (PSP) for global function evaluation. Altogether 249 patients were targeted for follow-up, in which 101 were followed up and the dropout rate was 59.4%. After average 37.2 ± 16.2 months, 92 patients (including 1 death) were still met the ICD-10 diagnosis of schizophrenia (F20). In terms of global functioning, 48.5% of patients had good outcome, 43.6% had moderate outcome, and 7.9% had poor outcome. A relatively high diagnostic stability of ICD-10 defined schizophrenia was obtained in the current study .Moreover, our results draw a much more optimistic picture of the outcome for EOS than what has previously been reported from Western counties.

1. Introduction

While most cases of schizophrenia manifest in early adulthood, early-onset schizophrenia (EOS) is defined as manifesting symptomatically before age 18, and can be considered a subtype of schizophrenia (Abidi, 2013). Since the Diagnostic and Statistical Manual of Mental Disorders(DSM)-III, similar criteria have been used to diagnose schizophrenia in adults and children (APA.,1980). However, unlike adult onset schizophrenia (AOS), few epidemiological studies have used standardized clinical assessments to estimate the prevalence of EOS. The prevalence of schizophrenia in children and adolescents is relatively low compared to AOS, estimated at 1.4～2.3 per 10,000 before age 15, and 1 per 10,000–30,000 before age 13(Clemmensen et al., 2012; Remschmidt and Theisen, 2012). Furthermore, among adult patients with schizophrenia, only 5～18% would have met diagnostic criteria before the age of 18, and about 1% before the age of 10 (Cannon et al., 1999; Hafner and Nowotny, 1995).

Overall, the clinical presentation of EOS resembles AOS. Nevertheless, EOS is more likely to manifest gradually rather than with an acute symptomatic episode. This makes early detection of EOS more challenging. In addition, EOS patients often have more prominent negative symptoms, more speech and language disturbances and fewer systematized delusions when compared with AOS (Abidi, 2013; Ballageer et al., 2005), and may not benefit from usual age-related gains in cognitive performance (Frangou, 2013).

The literature on outcomes of EOS is sparse. Moreover, studies examining long term outcomes are often marked by small sample sizes, low follow-up rates and conflicting findings. A systematic review by Clemmensen et al., (2012) identified 21 methodologically sound cohort studies of EOS. Among the studies selected for this review, none enrolled more than 100 subjects and only 3 enrolled more than 50. Moreover, dropout rates were higher than 30% for 10 and higher than 40% for 5 of these 21 studies. Outcome was classified as “good” for 15.4% of EOS patients, “moderate” for 24.5%, and “poor” for 60.1%. In contrast, a meta-analysis (Hegarty et al., 1994) based on 320 follow-up studies of AOS showed that 40% of cases were categorized as having a

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"good" outcome. However, in their 2-year follow-up study, Langeveld et al., (2012) conducted similar assessments on a sample of 33 EOS and 154 AOS patients. They concluded that the two groups had similar prognostic trajectories. Another line of research by Amminger et al., (2011) showed that after an average of 7.4 years, the early-onset group enjoyed a more favorable course, with fewer positive symptoms, less psychotic episodes, and better vocational and community functioning.

Diagnostic stability was another focus explored by a few follow-up studies of EOS with ambiguous findings. A nationwide register-based study (Thomsen, 1996) conducted in Denmark noted that one third of inpatients originally diagnosed with schizophrenia before age 18 were not given the same diagnosis at later admissions in adulthood, with one fifth re-labeled as having a personality disorder. However, more recent studies revealed a higher degree of diagnostic stability. One study examined fifty-one early onset psychotic disorders (18 with schizophrenia, 14 with bipolar disorder, 1 with an organic psychosis, and 11 with psychosis not otherwise specified), and showed that the diagnosis remained unchanged in over 90% patients with schizophrenia or bipolar disorder (McClellan and McCurry, 1999). In a two-year prospective study (Castro-Fornieles et al., 2011), 36 out of 40 original cases with schizophrenia spectrum disorders retained the same diagnoses at follow-up. Recently, Remberk et al., (2014) found that, over eight years, diagnostic stability for schizophrenia spectrum disorders and schizophrenia were 72% and 78%, respectively.

Chinese studies have reported more positive outcomes for EOS, in contrast to Western cohorts. For example, Liu et al., (2011) retrospectively evaluated Chinese Classification of Mental Disorders (CCMD-3) defined schizophrenia (onset before18 years), and found 63. 7% patients had a good prognosis, defined as a CGI (the Clinical Global Impressions Scale) score less than 4. Based on their retrospective research, Guo et al., (2001) reported an even more benign outcome for EOS compared to AOS. These younger onset patients not only met criteria for a good outcome more often (64.1% for EOS and 44.0% for AOS), they also exhibited better functioning in several daily living skills. Nevertheless, there were several limitations in the aforementioned studies. First, all these studies applied CCMD rather than the International Classification of Diseases (ICD) or DSM criteria, reducing comparability of findings. Second, the majority of studies did not define functional outcomes in a standardized manner. Furthermore, none of the studies examined diagnostic continuity from baseline to follow-up. Hence, it is difficult to draw clear conclusions about the outcome of EOS from extant studies of Chinese cohorts.

To address limitations of previous work, we applied standardized tools for assessing course and outcome in a large sample of ICD-10 defined early-onset psychosis in Yunnan, China. In addition, we will assess for diagnostic stability. By assessing the impact of a variety of prognostic factors, this study also seeks to improve our understanding of the prognosis in EOS, and therefore, to help clinicians to optimize individual treatment in their daily practice and allocate more resources to those with the worst prognosis.

2. Methods

2.1. Setting and study design

The study was done at the First Affiliated Hospital of Kunming Medical University (FAHKMU), which is based in Kunming urban area with a population of 6.67 million and typically drawing on a catchment of local citizens and patients within Yunnan province. This retrospective cohort study was conducted between July 2016 and July 2017.

2.2. Sampling

Inclusion criteria for present study is: 1) Admissions to FAHKMU (between January 2011- July 2015) with a recorded diagnosis of schizophrenia (per International Classification of Diseases, ICD-10 F20), 2) onset of psychosis before 18 years old, 3) willingness to accept evaluation by providing permission from a parent or legal guardian and/or consent/assent from patient, and 4) had been discharged from the hospital for at least 12 months.

Exclusion criteria: 1) psychotic disorder is secondary to a well-identified medical illness, or 2) drug and/or alcohol-induced psychosis, or 3) intellectual disability (IQ < 70).

Investigators initiated contact by telephone to explain the study's rationale and procedures, and to answer questions from potential participants and their families. After agreeing to participate, subjects and their parent(s) or guardian(s) were invited to FAHKMU for in-person assessments, including a survey and several structured questionnaires. For those who were unable to travel to the hospital, assessments were collected either by home visits by research staff or via telephone calls.

2.3. Assessment

We used standardized instruments to assess a variety of relevant dimensions related to baseline characteristics (at first admission to FAHKMU) and outcomes (at least one year after discharge). Assessment was conducted by two psychiatry residents after comprehensive training on study protocol and application of structured interview tools. Estimates of interrater agreement regarding the schizophrenia diagnosis revealed good reliability ($kappa = 0.815$, $P < 0.001$)

2.3.1. Assessment of first admission characteristics

All first admission (to FAHKMU) data, including socio-demographic data, premorbid history, first symptom manifestation, onset characteristics, parental education level, parent's relationship, and family history were extracted retrospectively from the medical records.

2.3.2. Self-developed survey

A structured questionnaire was developed by the investigative team to obtain relative information from the patient, available family members and medical records in the following domains: duration of untreated psychosis (DUP), treatment compliance, substance use history, any suicidal ideas or behaviors after beginning of the disease, inpatient times, and academic or occupational, marriage, and physical conditions.

DUP was determined through comprehensive consideration of information by asking family members "How long was it from the first sign of abnormality of the patient to beginning taking medication?" and information from medical record. Course of the disease was defined according to criteria of ICD-10.

2.3.3. Structured diagnosis tools

The Mini International Neuropsychiatric Interview (MINI) (Si et al., 2009a) or MINI –KID (parents version) (Liu et al., 2010) was used to confirm ICD-10 lifetime diagnoses at follow-up visit. The former was applied for subjects 18 years and older and the latter for subjects between 6 and 16 years old. For subjects whose age was among 16 to 18 years old, MINI or MINI-KID (parents version) was chosen according to their level of understanding and cooperation.

Information of ICD-10 diagnosis from medical records of the first admission in FAHKMU were also recorded as baseline diagnosis for each subject.

2.3.4. Social functioning measures

The Personal and Social Performance (PSP) scale (Liu et al., 2013; Si et al., 2009b), a measure of overall severity of disturbance, was used for evaluation of global functioning. The scale has a numeric value (0 through 100) and higher scores indicate better functioning. Three categories were applied based on recommendations from a Chinese validity and reliability study for PSP (Si et al., 2009b): poor outcome (PSP-score ≤ 30), moderate outcome (PSP-score ranging from 31 to

70), and good outcome (PSP-score ranging from 71 to 100).

Educational impairment was evaluated by comparison of achieved educational status (namely, which grade at school) of subjects at follow up with norms for school-going peers. Educational impairment was defined at three levels: without any delay, mild to moderate delay (delayed ≤ 2 grades compare to peers), and severe delay (delayed ≥ 3 grades compare to peers).

2.4. Analyses (include details of all statistical tests used)

We will compare dropouts with patients who have been followed up, using chi-square tests for the categorical variable (such as, sex/family history/number of hospitalization) and Mann-Whitney-*U* tests or Independent *t*-Test for continuous variables (such as age at first admission and overall PANSS at first inpatient). Then, demographics, clinical characteristics and outcomes (including social functioning, course of illness according to ICD-10 criteria, and treatment history) will be mainly illustrated in a descriptive way. Statistical analyses were performed using SPSS version 22.0. All tests were two tailed with a level of significance of $p < 0.05$.

2.5. Ethical approval

The protocol received approval from Ethics Committee of the First Affiliated Hospital of Kunming Medical University and Yale University's Human Investigations Committee. Written (face to face interview) or oral (telephone interview) informed consent was obtained from all study participants. For patients younger than 18 years of age, a written (face to face interview) or oral (telephone interview) permission was also provided by their parents or legal guardians.

3. Results

3.1. Study sample (Table 1)

Altogether 249 patients were targeted for the present study, in which 101 (40.6%) could be reached for assessment. Reasons for loss to recruitment included inability to find accurate contact information (64, 25.7%), and refusal to participate in the study (84, 33.7%). No variables differentiated significantly between the enrolled subjects and the rest of the targeted sample (Appendix A).

Out of 101 patients (47 males and 54 females), 83 patients (82.2%) were diagnosed as schizophrenia at first onset. Mean age of patients at follow-up was 18.2 ± 2.9, while mean age of first onset of psychosis was 14.3 ± 2.3. The onset of illness was acute (less than one month) in 24 patients (23.8%), subacute (between 3 month and 6 months) in 49 patients (48.5%) and occult (more than 6 months) in 28 patients (27.7%). Besides, Mean DUP was 32.8 ± 44.9 weeks (range: 1–250), which was a large range of variation.

3.2. Social functioning

The follow-up results of the social functioning are shown in Table 2. About 48.5% of the patients had a good outcome (PSP-score ≥ 71) and 7.9% had a poor outcome (PSP-score ≤ 30). Table 2 also illustrates course of subjects and treatment history.

Among the patients who received the follow-up assessment (n = 101), 74 patients were interviewed face to face (67 at index hospital, 3 at patients' homes, and 4 at other hospitals other than index hospital), and 27 were interviewed by telephone. Face to face Interview (FI) and telephone interview (TI) did not differ in gender, age at follow-up and length of follow-up. While the latter exhibited a better general outcome defined by PSP score, a shorter delay in education, and a lower current treatment rate at follow up visit (Appendix B).

Table 1
Demographics and Clinical characteristics of study sample.

	Early onset schizophrenia (n = 101)	
	n	%
Demographics and premorbid variables		
Male/Female	47/54	46.5/53.5
Han Chinese/ minority Chinese	86/15	85.1/14.9
Less than 9 years education of father	46	45.5
Less than 9 years education of mother	62	61.4
Poor relationship of parents	24	23.8
Poor learning ability of patients at onset	11	10.9
Poor living ability of patients at onset	8	7.9
Clinical features		
Type of onset		
less than 1 week	12	11.9
less than 1 month	12	11.9
1–3 months	27	26.7
3–6 months	22	21.8
6–12 months	9	8.9
more than1year	19	18.8
Original symptom(s) at the first episode		
Attention disorder	84	83.2
Delusion	83	82.2
Formal thought disorder	81	80.2
Hallucinations	76	75.2
Affective flattening	67	66.3
Poverty of speech or speech content	65	64.4
Bizarre behavior	58	57.4
Depression	58	57.4
Anhedonia	43	42.6
Anergia	41	40.6
Schizophrenia diagnosis at first onset	83	82.2
	Mean ± SD	Range
Age at follow up (years)	18.2 ± 2.9	9 − 23
Length of follow-up(months)	37.2 ± 16.2	12 − 73
Age at first onset (years)	14.3 ± 2.3	7 − 17
Age at first antipsychotic treatment(years)	14.8 ± 2.4	7 − 19
Duration of untreated psychosis DUP (weeks)	32.8 ± 44.9	1 − 250

3.3. Diagnostic stability

A comparison of the life-time ICD-10 diagnoses of the total sample (n = 101) at follow-up with their ICD-10 diagnoses made at first admission (baseline diagnosis) revealed a diagnostic stability in 92 (91.1%) and a change of diagnosis in 9 (8.9%) cases. Nine patients were given different diagnoses at follow up (4 bipolar affective disorder, 1 malingering, 1 major depressive with psychotic symptoms, 1 schizoaffective disorder, 1 obsessive compulsive disorder and 1 dissociative disorder), and 1 patient was deceased (Table 3).

4. Discussion

4.1. General outcome

The major findings of the present study are that (i) the prognosis of EOS is better than previously reported from western counties and (ii) our study sample reveal a good diagnostic stability for EOS.

EOS is usually considered as a more severe form of the disorder than adult-onset schizophrenia, and is considered to have poorer prognosis and outcome than its adult-onset counterpart. In the current study we applied PSP to evaluate general functioning, and discovered that 48.5% of early onset psychosis experienced a “good” outcome, 43.6% experienced a “moderate” outcome, and only 7.9% experienced a “poor” outcome. Clearly, our findings revealed a better outcome compared to that of systematic review by Clemmensen et al., (2012)which indicated that 15.4% of EOS patients had a rather unfavorable prognosis. The relatively better outcome in the current study compared to Western cohorts may reflect progress in the treatment of schizophrenia for the past decades, including widespread application of second-generation

Table 2
Outcomes of Early Onset Schizophrenia (EOS).

	Early onset schizophrenia($n=101$)	
	n	%
Social Functioning		
General outcome[a]		
Good(100 − 71)	49	48.5
Moderate(70 − 31)	44	43.6
Poor(30 − 0)	8	7.9
Living situation		
With parents	79	78.2
With partner	21	20.8
Day and night hospital	1	1.0
Occupational or scholastic situation		
At school or employed	64	63.4
Unemployed	37	36.6
Delay in educational level[b]		
Without any delay	16	15.8
Mild delay	43	42.6
Severe delay	42	41.6
Having source of income and support himself/herself	7	6.9
Course of illness according to ICD–10 criteria		
0.00 continuous	6	5.9
0.01episodic	17	16.8
0.02 episodic with stable residual symptoms	13	12.9
0.03 episodic with inter-episode progressive recession	3	3.0
0.04 partial remission	39	38.6
0.05 full remission	23	22.8
Suicidal behavior (plans or attempts)	36	35.6
Plans	28	27.7
Attempts	8	7.9
Treatment History		
Hospitalization for schizophrenia[c]		
One time	42	41.6
Two times	40	39.6
Three times or more	19	18.8
Current on medication	78(31)	77.2(30.7)

[a] General outcome defined according to the of the Personal and Social Performance, and the deceased subject was defined as “poor outcome”

[b] Mild delay (delayed ≤ 2 grades compare to their normal peers), severe delay (delayed ≥ 3 grades compare to their normal peers).

[c] Numbers of hospitalization at any hospitals before follow-up assessment

Table 3
Diagnostic stability.

Items	n	%
Baseline diagnosis (F20. Schizophrenia)	101	100
Follow-up diagnosis		
F20. Schizophrenia (deceased)	92 (1)	91.1 (1.0)
F31.9 Bipolar affective disorder	4	4.0
Z76.5 Malingering	1	1.0
F32.3 Major depressive with psychotic symptoms	1	1.0
F25.9 Schizoaffective disorder	1	1.0
F42.9 Obsessive compulsive disorder	1	1.0
F44.9 Dissociative disorder	1	1.0

antipsychotics, deinstitutionalization movement and development of community services. 13 out of 21 studies in Clemmensen et al., (2012)'s review were conducted before 2000, with 14 studies evaluating baseline data in the 1980′s, while all the subjects of our study were hospitalized after 2011. Moreover, outcome differences may also reflect duration of follow-up: outcomes deteriorated with longer follow-up periods (> 10 years) in the samples reviewed by Clemmensen et al., (2012). The duration of follow-up for this study is only around three years [37.2 ± 16.2 months]; whereas among the studies from Clemmensen et al., (2012)'s review, only 3 studies followed their subjects shorter than 5 years and as many as 12 studies revisited their subjects 10 years later (two as long as 42 years). Besides, different clinical characteristics of the samples, different outcome measures and remission criteria used may also account for the differences in results.

However, previous follow-up studies from China reported a much more favorable outcome of EOS compared to our study. Liu et al., (2011)reported that 63. 7% of patients behaved and functioned properly 2 to 4 years from start of the illness reflected in a CGI (the Clinical Global Impressions Scale) score less than 4. In the study by Zhu et al., (2006), 124 EOS and 120 AOS were followed up after 10.3 ± 2.1 and 11.2 ± 4.3 years respectively, which showed that good outcomes were more frequent in the EOS group (78.4% vs. 57.0% in AOS). Different subjects source may explain the difference between the present and the above two studies to some extent. Our sample were from psychiatry department of general hospital with an average admission time of 20 days, while those of the above two studies were admitted to mental health hospital with an average admission time as long as 60 days. In the latter circumstances, more firm doctor-patient relationship may be set up and the caregivers of the schizophrenic patients may be more aware the condition of patients and more compliant to the treatment, which could be reflected by a lower attrition rate of the follow-up (only 9.8% and 6.5% respectively in Liu and Zhu's study). However, this interpretation is only an assumption that needs further examination.

4.2. Social functioning

Our results resemble some other western studies to show that EOS exert a negative impact on subjects' social functioning in several ways. In our sample, as high as 36.6% of patients cannot engage in a productive life, either cannot go to work or cannot go to school. Regarding the academic achievement, only 16 subjects (15.8%) could keep up with the pace of their age-matched normal peer, i.e., there was no delay in their school grades. Our results is along with the previous studies (Hassan and Taha, 2011; Hollis, 2000) which detected an obvious academic functioning impairment in this group of population, suggesting extra rehabilitation training (both on academic and occupational) in this area is needed to prevent EOS from those adverse consequences.

4.3. Diagnostic stability

Although it was considered that schizophrenia is the most stable diagnosis among the early-onset non-affective psychosis (Remberk et al., 2014), there were controversial findings regarding diagnosis stability in previous studies as some studies reported one third of inpatients originally diagnosed with schizophrenia before 18 years were not given the same diagnosis at later admissions in adulthood. On the contrary, Some studies concluded that once the diagnosis of schizophrenia below age 18 is made it is relatively stable. For example, in a two-year prospective study (Castro-Fornieles et al., 2011), 36 out of 40 original cases with schizophrenia spectrum disorders retained the same diagnoses at follow-up.

It seems that the longer the duration of the study the lower the diagnosis stability. Another reason for these result discrepancy may result from different classifications of diseases applied across baseline and end-point assessments in different studies. Therefore, the diagnosis change may reflect changes in the classification of schizophrenia either in the ICD or the DSM over the past three decades other than change of the illness. This haslimited inferences about diagnostic stability.

In the present study, after 37.2 ± 16.2 months, 92 out of 101 subjects were given a schizophrenia (F20.) diagnosis at follow-up, yielding a diagnosis stability as 91.1%. Despite relatively high diagnostic stability of EOS observed in the current study, the clinicians still need to pay attention to the development of symptoms to detect the subgroups that exhibited altered clinical manifestation over time, and among those mainly is bipolar disorder in present sample.

4.4. Strengths and limitations

The current study is the first one in China to elucidate the prognosis of EOS who admitted to a psychiatry department of general hospital. Besides, unlike the previous follow-up studies in which CCMD system were employed, we applied the ICD classification system across the baseline and endpoint, which make our results more comparable to those from western counties. We hope that the results from the current study could enable the clinician to a better understanding of the course and then refine treatment for this group of population with serious disorder.

However, several limitations should be noted. First, even though high attrition rates are very common in EOS follow-up study with estimated rates ranging between 0 and 59% and a median of 29% (Clemmensen et al., 2012), that for present study was relatively high (59.4%). Among those who were attrited from the original cohort, 25.7% were unable to reach, which may mirror the dramatic social and cultural changes, and urbanization for the past one to two decades in China. People tend to move from one place to another, and change the cell phone number more frequently than before. When considering the impact of dropout rates, in Clemmensen et al., (2012)'s observation they found that higher attrition rate was associated with higher percentage of poor outcome and lower percentage of moderate outcome, whereas there was no attrition effect on the rate of good outcome . If that's the case, the present study may overate the percentage of poor outcome, and thus the overall prognosis of our sample may be more positive.

Furthermore, the results of the present study are limited by its retrospective design rather than longitudinal study and this may be the case in most of previous studies concerned with retrospective data. Therefore, details about early development and medication history can be subjected to different kinds of bias such as recall bias or regency effect; Another limitation of the study is an uncertain reliability of telephone visit data (accounting for 26.7% of the followed samples), especially concerning psychiatric diagnosis. In the current study we tried to minimize these effects through depending on retrieving the information from more than one source (doctor in charge, family members, medical reports, etc), but definitely we didn't exclude the bias entirely; Finally, as the subpopulation of general hospital hospitalized EOS subjects is usually among high social-economic class and are more urban residents with a shorter admission duration compared to subjects from mental health hospital, a generalization of our findings to other type of patients may not be warranted.

Summing up, the present study draws a much more optimistic picture of the outcome in EOS than what has been previously seen at western counties, and good outcome of patients with early onset schizophrenia is attainable in 48.5% of current samples who once have been hospitalized in the past 2–5 years,with 77.2% under medication at follow-up. Furthermore, our data indicate a higher diagnostic stability of schizophrenia in adolescents than what have been reported previously. Further understanding on the long-term outcome of EOS might benefit from the prospective study design, low attrition rates of the sample, repeated and standardized instruments assessing outcome, and varieties of samples from different type of institutions involved.

Declarations of interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.11.013.

Appendix A. Comparisons of study sample vs. those lost to recruitment (LTR)

	Follow-up (n = 101)	LTR (n = 148)	Analysis χ^2	p
Gender(male/female)	47/ 54	59 / 89	1.092	0.296
Family history of mental disorders(yes/no)	22 / 79	26 / 122	0.685	0.408
Number of hospitalization (one /multiple)[a]	74 / 27	117 / 31	1.125	0.289
	Mean (SD)	Mean (SD)	t	p
Age of onset (years)	14.3 (2.4)	14.7 (2.1)	−1.657	0.099
Overall PANSS[b] at first inpatient admission	80.8 (16.6)	82.2 (15.1)	0.594	0.553

[a] number of hospitalization in First Affiliated Hospital of Kunming Medical University between January 2011 and July 2015.
[b] Positive and Negative Syndrome Scale (PANSS)

Appendix B. Follow-up Characteristics of Interview Group and Telephone Interview Group

	Face to face interview n = 74	Telephone interview, n = 27	p-value
Male/Female	35/39	12/15	0.799[a]
Age at follow-up(year)	18.1 ± 3.1	18.5 ± 2.3	0.511[b]
Length of follow-up(months)	36.8 ± 16.5	38.6 ± 15.6	0.617[b]
PSP	67.2 ± 20.3	80.4 ± 11.7	0.002[b]
Delay on education(year)	2.7 ± 1.9	1.8 ± 1.9	0.040[b]
Current on treatment	63 (85.1%)	15 (55.6%)	0.002[a]

[a] pearson Chi-square;
[b] t test;

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