Symptomatic remission in schizophrenia affects employment outcomes; Instrumental activity of daily living is a determinant for non-remitted patients

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Abstract
Background: Remission criteria were proposed by Andreasen for classifying patients with schizophrenia according to the severity of psychopathology. Up to the present time, there have been no cohort studies exploring the association between remission status and employment outcomes in patients with schizophrenia. The study aimed to explore whether symptomatic remission is significantly associated with employment outcomes in a two-year longitudinal study, and to investigate factors associated with favorable employment outcomes for patients without symptomatic remission at baseline.

Methods: All of 525 stable patients with schizophrenia in the therapeutic community of a public mental hospital between 2013 and 2015 in Taiwan were recruited. Employment outcomes, defined as the cumulative on-the-job duration (months/per year) and income (new Taiwan dollars, NT$/per year), were investigated at the end of 1- and 2-year follow-up after enrollment. For repeated measurements, linear mixed models were constructed to examine the association between symptomatic remission and employment outcomes after controlling for potential confounding variables including age, sex, education, type and daily dose of antipsychotics, cognitive function, activities of daily living (ADL), instrumental activities of daily living (IADL), and initial employment type.

Results: The average age was 51.8 years, and 65.3% were males. Among them, 124 patients (23.6%, 124/525) met the remission criteria at baseline. The linear mixed-model analysis showed that patients who had symptomatic remission were employed 0.69 of a month longer (p = 0.04) and earned NT$2,490 more (p = 0.03) within 1 year than did those who did not show symptomatic remission. For finding factors related to employment outcomes in patients without remission, initial IADL scores were significantly associated with both outcomes (B = 0.089, p = 0.001 and B = 153, p = 0.003 for cumulative duration and income).

Conclusion: Our study suggests that assessing symptomatic remission is an useful part of monitoring treatment effectiveness for schizophrenia, and all strategies targeting the bio-psycho-social domains to attain symptomatic remission are paramount to maintain favorable employment outcomes. To enhance the level of instrumental daily activities is an important issue for schizophrenia patients to
return to the community with promising employment outcomes.

**Background**

Schizophrenia is characterized by positive and negative psychotic symptoms, such as delusions, hallucinations, disorganized behavior, blunted affect, reduced motivation, and impaired cognitive function [1–3]. The significant and permanent effects on health care could be associated with social and economic burden, not only for the caregivers but also for society as a whole [4]. In addition, schizophrenia is a severe mental disease with a chronic course, frequent relapse, and functional deterioration in many domains, such as declined occupational function [5]. Therefore, an accurate definition of symptomatic remission in schizophrenia is necessary in clinical practice. From the perspective of providing effective long-term care and supporting recovery from schizophrenia, the potential utility of consensus criteria for symptomatic remission that delineate a well-defined outcome goal can foster comparisons of effectiveness across treatment modalities and facilitate the development of appropriate rehabilitation programs [6]. Andreasen and colleagues initially defined symptomatic remission in schizophrenia, published by the Remission in Schizophrenia Working Group (RSWG) in 2005, as patients having eight core symptoms of a low severity level over a period of at least 6 months and patients with either none or mild symptoms at first episode who seem more likely to develop symptomatic remission [7].

In fact, multidimensional functional outcome measures, for example, the Global Assessment of Functioning [8–10], the Personal and Social Performance Scale [11], and the Functional Remission of General Schizophrenia scale [9, 12, 13], have been used in patients with schizophrenia to examine their personal, social, and occupational role functioning [8, 10, 14, 15]. However, few studies have investigated the relationship between symptomatic remission and employment outcomes. According to the bio-psycho-social approach in the International Classification of Functioning, Disability and Health model [16], patients with schizophrenia may exhibit difficulty related to participation in community activities, work, activities of daily life, and leisure activities. Therefore, it is suggested that researchers focus more on outcomes based on practical disabling experiences and the real-world functioning of patients instead of engaging in excessive reliance on global measures of
psychopathology and disability [17].

Indeed, employment is also considered a crucial predictor of better functioning for patients with psychotic disorders [15]. Although most people with psychiatric disabilities show a desire to work, they are more likely to experience adverse labor market outcomes because of symptom interference. However, employment contributes substantially to satisfaction and the meaning of life and has a very important meaning to patients with mental disorders [18]. A previous study recruiting 93 first-episode schizophrenia patients revealed that symptomatic remission was significantly related to a higher employment rate at 1-year and 12-year follow-up [19]. Patients with schizophrenia who are employed consume a lower amount of medications, have lower negative symptom severity and lower excitement symptom severity, and tend to achieve better global functioning [7, 10, 15]. Nevertheless, there were some limitations in prior studies elucidating the symptoms and employment outcomes: (1) multivariate analysis did not control for the important baseline confounders associated with psychosocial functioning that harbors a significant relationship with employment status, such as type of antipsychotics [10, 20], cognitive function [21], activities of daily living (ADL) [22–24], initial employment types [25], instrumental activities of daily living (IADL) [23], social support and skills, previous history of successful employment [26], and intrinsic/extrinsic motivation [27]; (2) a lack of clear definition of employment outcomes: previous studies defined “full-time students or paid workers” as “occupied” [19] or defined “paid employment” by asking “Did you work at a job for pay during the past 4 weeks?” [28] instead of using quantitative variables such as wages earned and tenure of job over a period of time [29]. Consequently, an important question related to employment outcomes for schizophrenia is worth exploring: “Does symptomatic remission predict employment outcomes after controlling for confounders among schizophrenia patients for a follow-up of years?” In addition, if we prove that patients with remission are more likely to have better employment outcomes, the next question is: “for patients without remission, are there any determinants associated with favorable outcomes?” A study answering these questions may illuminate key factors pertinent to employment outcomes and create more effective strategies in the future for improving the work capability of and facilitating recovery in patients with schizophrenia.
The aim of this study, therefore, was (1) to explore the association between symptomatic remission and employment outcomes, including duration and job income, with adjustments for related confounders variables including age, sex, education, type and daily dose of antipsychotics, cognitive function, ADL, IADL, and initial employment type; (2) to investigate factors associated with favorable employment outcomes for patients without symptomatic remission at baseline.

Methods

Rehabilitation model in the therapeutic community

This study was conducted in a psychiatric hospital, Yuli Hospital, Ministry of Health and Welfare, with approximately 2000 patients receiving humanistic and patient-centered professional care in eastern Taiwan. The patients in the therapeutic community at the hospital had greater access to occupational rehabilitation and worked outside the hospital while they were stable. The therapists in this therapeutic community trained the appropriate patients regularly and encouraged them to be employed in the outside labor market. This multidisciplinary rehabilitation model consisted of identifying patients’ advantaged ability, matching appropriate employment, and negotiating with employers to get reasonable salaries, especially in supported and sheltered employment. In general, the salary has remained at a fixed rate for a given job, according to predetermined agreement with employers. However, the salary may be adjusted according to a patient’s actual performance, such as efficiency, regularity, and punctuality in the workplace, based on a predefined contract among three parties: the patient, the occupational therapists, and the employers. All occupational therapists and employers reached a consensus to assist the workers according to the same standard, that is, harboring impartiality in the acceptance of workers and avoiding undue tolerance of misconduct, unjustified monetary rewards, and unreasonable harsh requirement toward the workers. If a patient expressed unwillingness to keep his or her current job, or if there were signs of unstable psychiatric condition, the intervention procedures, such as transient cessation of jobs, adjustment of medicine, or psychiatric counseling, were started. After the intervention, if the patient was still unable to meet the requirement of current work, he or she was exempted from current jobs, and the possibility of shifting to other sheltered jobs or workshops was discussed in the team meeting.
Participants

All 550 residents in the therapeutic community of Yuli Hospital from January 2013 to December 2015 were recruited for this study. Inclusion criteria were as follows: patients who were diagnosed with schizophrenia or schizoaffective disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Text Revision, Fourth Edition. Exclusion criteria included: (1) those who had an acute psychotic episode requiring transfer to acute psychiatric wards at the stage of enrollment, (2) those who refused to provide consent for evaluation, and (3) individuals with significant cognitive deficit (e.g., delirium or dementia). After the content of study procedures, benefits, and risks were fully explained to patients, informed consents were obtained. All patients who signed the informed consent underwent an initial evaluation for 1- to 2-year follow-up assessments regarding related clinical data and employment outcomes.

Measurements of independent variables and outcomes

Demographic data, including age, sex, educational years, age at schizophrenia onset, and types and defined daily dose of antipsychotics on recruitment were abstracted from the medical records of the patients. The antipsychotics were categorized into typical antipsychotics (TAs), non-clozapine atypical antipsychotics (NCAAs), and clozapine. Patients concurrently using TAs and NCAAs were categorized as NCAAs users. Those who concurrently used clozapine and two other types of antipsychotics were categorized as clozapine users. The antipsychotics were categorized, and their dosages were converted to a defined daily dose (DDD) of antipsychotics according to a prior study [30] and from information available on the website of the Collaborating Center for Drug Statistics Methodology of the World Health Organization (http://www.whocc.no/atc_ddd_index/).

Positive and Negative Syndrome Scale (PANSS)

The psychopathology of each patient was assessed using the Chinese version [31] of the PANSS [32] (CMV-PANSS) at baseline. The PANSS ratings were based on patient interview and on information from other caregivers. This evaluation was conducted on the basis of an absolute threshold of severity for the following eight core symptoms: delusions (P1), conceptual disorganization (P2), hallucinatory behavior (P3), blunted affect (N1), social withdrawal (N4), lack of spontaneity (N6),
mannerisms/posturing (G5), and unusual thought content (G9).

**Symptomatic remission**

Symptomatic remission as defined by the RSWG in 2005 was evaluated by 4 board-certified psychiatrists using the CMV-PANSS [6]. Patients were identified to be in the state of symptomatic remission when each one of the scores of the aforementioned eight items of CMV-PANSS was less than 3 and the condition remained stable for at least 6 months. The CMV-PANSS was assessed only before the enrollment. For each patient, medical records and observation provided by medical personnel encompassing 6 months before the enrollment were examined. During the period of 6 months, stable clinical condition was defined as (1) participants did not have dominant fluctuation of psychiatric symptoms needing adjustment of psychotropic agents or (2) no transfer to or referral from acute psychiatric wards. For those whose scores on the eight items of the CMV-PANSS were less than 3 with a stable condition lasting for 6 months, the status of symptomatic remission was judged.

**Mini-Mental State Examination (MMSE)**

The Chinese version [33] of the MMSE [34] is a 33-point questionnaire used extensively in clinical and research settings to measure cognitive function. It is 3 points greater than the original version since the Chinese version added 3 questions to increase the discriminant validity in a population with relatively few years of education. Higher scores indicate better cognitive function.

**ADL and IADL**

For each patient, the IADL and ADL ratings were conducted by the patient’s charge nurse based on clinical observation and information from other caregivers. The Barthel index [35] was used for evaluating 10 variables describing ADL (feeding, bathing, dressing, toilet use, presence or absence of fecal or urinary incontinence) and mobility (transferring, walking, and climbing stairs). The Chinese version [36] of the IADL scale [37] was used to evaluate the patients’ ability to live independently in a community. This scale can measure competence in managing complex ADL, such as medication management, shopping, transportation, laundry, and social interaction. The maximum total IADL scale score is 24. The score for each IADL item ranges from one to three (1 = the patient cannot perform a specific activity at all, 2 = the patient can perform it with help or supervision, and 3 = the patient can
perform it independently).

**Rating procedure**

All raters, including one certified psychiatric nurse (Y.H.Y.) and three board-certified psychiatrists (C.H.Y., B.J.W., and S.U.), who had reached a high standard of interrater reliability (intraclass correlations ranged from 0.86-0.95) with the gold-standard raters from the Yuli Hospital research group, rated the PANSS and MMSE. The IADL and ADL scores were available from the database in the nursing department of the hospital, which required charge nurses to conduct regular evaluation with an adequate interrater reliability. All details of the interrater reliability of these ratings were described in prior studies [23, 31].

**Initial type of employment**

The participants received occupational rehabilitation in three types of employment, including (1) the hospital-based workshop (N = 323), which provides simple and repeated activities to develop work potential in patients with stable psychiatric symptoms; (2) sheltered employment (N = 68), which provides a protective workplace for the patients with work potential who cannot work in a competitive workplace, such as in a working team for cleaning (N = 37), cook assisting (N = 16), car washing (N = 8), or others (N = 7); and (3) supported employment (N = 134), which has been reported to be highly effective for patients to achieve competitive employment in regular employment in an integrated community setting [25], such as house cleaning (N = 61), document delivery (N = 34), elder care (N = 19), guarding (N = 12), painting (N = 3), and others (N = 5).

**Employment outcomes**

Employment outcomes as dependent variables, defined as the cumulative on-the-job duration (months/per year) and income (NT$/per year), were calculated in the first and second year after entry in this study. There were two time points for collection of outcomes: (1) Time 1: 1 year after the entry and (2) Time 2: 2 years after the entry. Dependent variables of Time 1 were cumulative employment duration and incomes from the entry of this study to Time 1. Dependent variables of Time 2 were cumulative employment duration and incomes from Time 1 to Time 2.

**Statistical analysis**
Participants were excluded from the regression model analysis if they met following conditions during the study: (1) they were proclaimed dead, (2) they were discharged to their home, (3) they were transformed from remission at baseline to acute relapse which required transferal to acute psychiatric wards afterwards. For patients with symptomatic remission at baseline, whether there were significant differences in variables between those who encountered acute psychotic relapse and those who did not would be examined.

For repeated measurements within individual patients, the association between symptomatic remission and employment outcomes was investigated using a mixed-effects model analysis [38]. Potential covariates, including age, sex, educational years, type and daily dose of antipsychotics, cognitive function, initial employment type, ADL and IADL were controlled for.

All independent variables were assessed once at the baseline except for ADL and IADL which were repeatedly collected. For ADL and IADL, their time points were (1) Time 1: at the entry of the study and (2) Time 2: 1 year after study entry. For finding factors related to employment outcomes in patients without remission, aforementioned regression models were conducted after stratifying remission status. All analyses were conducted using IBM statistics SPSS, version 19.0, and the significance level was set at two-tailed $p < 0.05$.

**Results**

At the baseline, 525 residents in the therapeutic community of Yuli Hospital, Ministry of Health and Welfare, between January 2013 and December 2015 participated in this study.

A total of 124 patients (23.6%, 124/525) met the remission criteria at baseline. The demographic and baseline clinical data are summarized in Table 1. The remission group differed significantly in terms of age, sex; education; age at schizophrenia onset; PANSS, ADL, IADL, and MMSE scores; defined daily dose of antipsychotics; and initial employment type but not in the antipsychotic type. The majority of the patients were men (65.3%). The average age of the patients was 51.8 years.

After enrollment to the end of this study, there were no subjects who were proclaimed dead or discharged to their homes. During the 2-year follow-up, there were 69 patients (13.1%, 69/525) who presented with acute psychotic relapse and were transferred to acute wards. After treatment and
clinical conditions were stabilized, all patients returned to the therapeutic community. The percentage of transformation from those who were categorized into symptomatic remission at baseline to acute relapse afterward was 8.9% \((n = 11, 11/124)\). For patients with symptomatic remission at baseline, there were no significant differences in all variables between those who encountered acute psychotic relapse and those who did not. Finally, the data collected repeatedly on the remaining 514 patients during the 2-year follow-up were analyzed in the regression model.

Table 2 shows the results of the linear mixed model. After controlling for related confounders, symptomatic remission was significantly associated with both employment outcomes. The patients who had symptomatic remission were employed 0.69 of a month longer \((p = 0.04)\) and earned NT$2,490 more \((p = 0.03)\) than patients who did not show symptomatic remission. The cumulative on-the-job duration and income were robustly associated with IADL \((p = 0.001\) and 0.01, respectively). Moreover, initial employment types were also found to be significantly associated with employment outcomes. Patients classified with the workshop had less cumulative work months and incomes than those with supportive employment and those who were classified with sheltered type. After stratifying remission status, regression models showed that initial IADL scores were significantly associated with both outcomes \((B = 0.089, p = 0.001\) and \(B = 153, p = 0.003\) for cumulative duration and income). However, for patients with remission, IADL scores were not significantly associated with both outcomes.

**Discussion**

We found that patients recruited in the therapeutic community exhibited an association between symptomatic remission and employment outcomes. This does not necessarily indicate a causal connection. However, we have the following arguments with which to corroborate such a hypothesis. First, we included only relatively stable patients with symptomatic remission from the therapeutic community. Because they were not comorbid with other major chronic diseases such as stroke and/or physical disabilities or confined to bed because of an aggravated psychiatric condition, the association would not have been confounded by these factors. Second, the significant associations between symptomatic remission and initial employment types and the employment outcomes in our
models corroborate previous reports [8, 10, 11, 39-41]. Many investigators have already emphasized that symptomatic remission can be identified as a major factor of functional outcomes in patients with first-episode psychosis [42]. Our results indicated symptomatic remission as a significant predictor of employment outcomes. These findings could be a partial validation of our final models. We not only supported the effects of symptomatic remission on functional outcomes but also extended the definitions of functional outcome by adding to employment outcomes. Third, these people were followed for 2 years and repeatedly assessed for employment outcomes at the end of each year.

Then, we constructed mixed-effects models to control for the demographic factors, types and daily doses of antipsychotics, cognitive function, IADL, and initial employment types. These determinants thus cannot confound the results of the final models. Therefore, we tentatively concluded that symptomatic remission is associated with better employment outcomes.

Undoubtedly, employment is not only an essential factor in people’s ability to integrate but is also a stepping stone toward recovery for these populations. There are mental health issues linked to unemployment factors, including cognitive impairment, psychotic symptoms, negative symptoms, fear of losing benefits, stigma, and lack of access to employment services [21, 43]. Past studies and meta-analyses have shown that symptomatic remission is usually associated with improved function [10, 15, 44]. A previous study enrolling 2,284 schizophrenia patients found non-remitted patients using RSWG criteria were associated with a lack of paid employment, more mental health costs, poorer quality of life, worse global functioning, and more impaired cognition at a 3-year follow-up [28]. However, while many investigators have already emphasized the importance of achieving functional improvement in addition to symptomatic remission [45, 46], our study is the first to quantitatively estimate the employment outcomes for duration and income. Because 124 of the 525 patients showed symptomatic remission in this study, which was higher in proportion to that in other studies [8, 10, 11], we had a good opportunity to observe the employment outcomes.

In addition, by controlling for other covariates in regression models, our study revealed that patients who had better IADL ability showed better work performance in the future. This finding is in accordance with other studies that found a significant relationship between IADL level and functional
outcomes in patients with schizophrenia [23, 47, 48]. Furthermore, we found an important finding that IADL scores were significantly with both employment outcomes for patients without remission. We further recoded IADL scores into whether they were greater than 14, i.e., the median of the IADL in this current study, which was seen as an indicator of better global functioning. After stratifying remission status, the mixed model revealed that among those who were without symptomatic remission, those whose IADL greater than 14 was had a positive relationship with both employment outcomes (duration of work, B = 0.81, p = 0.001; income of work, B = 1323, p = 0.017). However, in those with symptomatic remission, dichotomous IADL variable was not significantly associated with either employment outcome. This finding implies that schizophrenia patients without symptomatic remission do not necessarily have poorer employment outcomes; in fact, IADL is a major determinant for non-remitted patients for their work performance. Thus, how to tailor and carry out multi-dimensional and collaborative occupational rehabilitation programs for improving IADL ability, is pivotal to achieve favorable employment outcomes for schizophrenia patients, especially for those who are without symptomatic remission.

Strength And Limitations
Our study is the first to quantitatively estimate the employment outcomes (i.e., duration and income) using mixed-effects model analysis for patients with schizophrenia-spectrum disorders. In addition, there were no dropouts during the study, which seems be uncommon in schizophrenia studies. Employment outcomes of all patients were collected, and they all completed this study. Nevertheless, this study has the following limitations: (1) Since we recruited only stable psychiatric patients in the therapeutic community of a public mental hospital in Taiwan, and participants were assigned to work setting mainly based on staff members’ perceptions of their needs and capabilities, our results may not be generalizable to all schizophrenia patients, such as those in the community or in other treatment units. (2) Although we tried to control for as many confounders as possible in this study, we were unable to include all vocational predictors [26], such as factors related to the patients’ social support and skills, previous history of successful employment [26], and motivation [27]. (3) Schizophrenia is a disorder with dynamic changes in terms of symptomatic and functional states. Yet,
during 2-year follow-up, remission status was assessed only at baseline. The fluctuation of remission afterward possibly confounded the analysis of employment outcomes. In addition, for some patients, type and dosage of antipsychotics may be changed over a long-term period. Yet, as we know, in the current setting, participants kept almost a fixed dose and type of antipsychotics, except for those who relapsed and were transferred to acute wards. If possible, a more robust relationship between symptomatic remission and employment outcomes may be confirmed using repeated measurements of remission status as well as type and dosage of antipsychotics. (4) Moreover, rather than using an comprehensive neuropsychological battery comprising assessment of visuospatial function, attention, memory, and executive function, the current study used MMSE—for which there are a number of limitations for clinical practice. The major drawbacks of MMSE is that it exhibits ceiling effects in the detection of mild brain abnormalities; it has significant association with few disorders with cognitive impairment, such as Alzheimer's disease; and it is less sensitive to noncortical cognitive deficits [49]. Although the MMSE was used as a proxy of cognitive function for controlling the confounding in the regression model, it may be not a satisfactory measure of cognitive abilities in the context of employment. Cognitive function measured by a comprehensive neuropsychological battery may be more suitable for adjustment in the model.

Conclusions
In summary, our study reveals that after controlling for major potential confounders, employment outcomes in patients with schizophrenia are associated with symptomatic remission. In the past, symptomatic remission was mainly used to assess the prognosis of chronic schizophrenia. Our findings suggest that employment outcomes should be involved in the assessment of prognosis in order to enhance the validity of symptomatic remission. Assessing symptomatic remission would be useful as a part of monitoring treatment effectiveness for schizophrenia, and all strategies targeting the bio-psycho-social domains to attain symptomatic remission are paramount to maintain favorable employment outcomes. In addition, for psychiatrists and occupational therapists, to enhance the level of instrumental daily activities for schizophrenia patients is an important issue. It would be helpful for those who have severe mental illness to return to the community with promising outcomes of regular
long-term employment.

Abbreviations

RSWG: remission in schizophrenia working group; ADL: activities of daily living; IADL: instrumental activities of daily living; TAs: typical antipsychotics; NCAAs: non-clozapine atypical antipsychotics; DDD: defined daily dose; PANSS: positive and negative syndrome scale; CMV-PANSS: Chinese version of the positive and negative syndrome scale; P: positive symptom scale; N: negative symptom scale; G: general behavior scale; FGA: first-generation antipsychotics; NC-SGAs: non-clozapine second-generation antipsychotics; Antipsychotic dose: chlorpromazine equivalent; MMSE: mini-mental state examination

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Institutional Review Board at Yuli Hospital (YLH-IRB-10310) before commencement. The survey was administered after receiving signed informed consent from each participant.

Consent for publication

The corresponding author, Dr. Jer-Hao Chang, can represent all the co-authors to give the consent for publication.

Availability of data and materials

The datasets generated and analyzed during the current study are not yet publicly available but access will be granted to those submitting a well-substantiated request, with a detailed plan to maintain the integrity and confidentiality of the data.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors were involved in study design, provided scientific oversight throughout the project, detailed comments to the paper across several drafts and edited the paper. S.P.W. designed the study, analyzed the data, and wrote the manuscript. J.D.W. designed the data analysis, and revised the study. J.H.C. assumed the corresponding author and revised the study finally. The manuscript was corrected by B.J.W.. The consultation and sources supported by T.J.W. and H.J. S.. All authors contributed to and have approved the final manuscript.

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Tables

Table 1 Characteristics at baseline and employment outcomes of subjects (N = 525)

|                                | Total       | Remission (n=124) | Nonremission (n =401) | T/Chi-square | P-value |
|--------------------------------|-------------|-------------------|-----------------------|--------------|---------|
| Age                            | 51.8±9.84   | 49.38±9.54        | 52.55±9.83            | 3.17**       | 0.002   |
| Gender (male, %)               | 343(65.3%)  | 70(56.5%)         | 273(68.1%)            | 5.65*        | 0.017   |
| Education(years)               | 9.16±3.62   | 10.7±3.48         | 8.67±3.53             | -5.40***     | 0.001   |
| Age of schizophrenia onset (years) | 22.49±6.78 | 24.22±6.80        | 21.95±6.69            | -3.06**      | 0.002   |
| PANSS                          | 74.32±17.26 | 57.90±13.4        | 79.40±15.01           | 14.29***     | 0.001   |
| P                              | 14.27±4.12  | 11.97±3.42        | 14.99±4.07            | 7.48***      | 0.001   |
| N                              | 22.79±6.49  | 16.19±4.07        | 24.83±5.69            | 18.67***     | 0.001   |
| G                              | 37.26±9.10  | 29.7±7±12         | 39.59±8.35            | 11.86***     | 0.001   |
| Antipsychotics type            |             |                   |                       | 0.17         | 0.919   |
| FGA (n, %)                     | 200(38.1%)  | 48(38.7%)         | 152(37.9%)            | 2.29*        | 0.023   |
| NC-SGA (n, %)                  | 182(34.7%)  | 44(35.5%)         | 138(34.4%)            | 0.17         | 0.919   |
| Clozapine (n, %)               | 143(27.2%)  | 32(25.8%)         | 111(27.7%)            | 3.79***      | 0.001   |
| Defined daily dose of antipsychotics | 0.83±0.73  | 0.72±0.48         | 0.86±0.79             | 2.29*        | 0.023   |
| MMSE                           | 24.98±8.76  | 29.87±3.88        | 23.46±9.30            | -11.03***    | 0.001   |
| ADL                            | 96.68±9.88  | 98.85±5.74        | 96.00±10.77           | -3.79***     | 0.001   |
| Instrumental ADL               | 13.13±5.84  | 17.61±4.35        | 11.72±5.53            | -12.18***    | 0.001   |
| Initial employment type        |             |                   |                       | 36.52***     | 0.001   |
| Hospital-basedworkshop (n, %)  | 323 (61.5%) | 48(38.7%)         | 275(68.6%)            | 0.001        |
| Sheltered (n, %)               | 68 (13.0%)  | 23(18.5%)         | 45(11.2%)             | 0.001        |
| Supported (n, %)               | 134(25.5%)  | 53(42.7%)         | 81(20.2%)             | 0.001        |
| Employment outcomes            |             |                   |                       |              |
| Cumulated duration (months) per year | 4.53±5.31  | 7.21±5.09         | 3.71±5.11             | -9.38***     | 0.001   |
| Cumulated incomes (NT dollars) per year | 5005.3±14818.5 | 11378±26836 | 3048.6±7091.2 | -4.81*** | 0.001 |

Note

PANSS: Positive and negative syndromes scale; P: positive symptom scale; N: negative symptom scale; G: general behavior scale; FGA: first-generation antipsychotics (typical antipsychotics); NC-SGAs: second-generation antipsychotics (non-clozapine atypical antipsychotics); Antipsychotic dose: chlorpromazine equivalent; MMSE: mini-mental state examination; ADL: activities of daily living; Instrumental ADL: instrumental activities of daily living

* p<0.05; ** p<0.01; *** p<0.001
Table 2 Linear mixed-effects model for yearly employment outcomes in a 2-year follow-up study (N = 514)

| Independent variable                  | Cumulative work months | Cumulative work incomes |
|---------------------------------------|------------------------|-------------------------|
| B (S.E.)                              | B (S.E.)               |
| Age                                   | 0.00 (0.01)            | -79.1 (46.9)            |
| Gender                                | -0.03 (0.27)           | -268.1 (907.4)          |
| Male (reference level)                |                        |                         |
| Education(years)                      | 0.06 (0.04)            | 160.4 (139.6)           |
| Antipsychotics type                   | 0.19 (0.33)            | 353.9 (1111.1)          |
| FGAs                                  |                        |                         |
| NC-SGAs                               | 0.37 (0.32)            | 69.6 (1059.0)           |
| Clozapine(reference level)            |                        |                         |
| Defined daily dose of antipsychotics  | 0.28 (0.23)            | -839.9 (785.2)          |
| MMSE                                  | 0.01 (0.02)            | 20.5 (61.7)             |
| ADL                                   | 0.01 (0.01)            | 64.7 (61.3)             |
| Instrumental ADL                      | 0.07 (0.02) **         | 279.9 (108.4) **        |
| Initial employment types              |                        |                         |
| Hospital-based workshop               | -8.68 (0.32) ***       | -10,743.6 (1105.8) ***  |
| Sheltered                             | 0.63 (0.32) *          | -6,497.1 (1376.0) ***   |
| Supported (reference level)           |                        |                         |
| Symptomatic remission                 | 0.69 (0.34) *          | 2490.1 (1145.9) *       |
| Nonremission (reference level)        |                        |                         |
| Time effect                           |                        |                         |
| Time 1 (first year)                   | 0.32 (0.15) *          | 1770.3 (1772.1)         |
| Time 2 (second year) (reference level)|                        |                         |

Note.

FGA: first-generation antipsychotics (typical antipsychotics); NC-SGAs: second-generation antipsychotics (non-clozapine atypical antipsychotics); Antipsychotic dose: chlorpromazine equivalent; MMSE: mini-mental state examination; ADL: activities of daily living; Instrumental ADL: instrumental activities of daily living

Age, sex, education, antipsychotic types, antipsychotic dose, MMSE, and initial employment type were controlled for.

* p < 0.05; ** p < 0.01; *** p < 0.001; B = estimated coefficient; S.E. = standard error