

**Original Article**

# Duration of untreated psychosis and average 13-year outcome in first admission schizophrenia

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**Abstract**

Combining retrospectively investigated duration of untreated psychosis (DUP) and data from the previously reported 13-year outcome study of first-admission schizophrenic patients treated in Jichi Medical University Hospital, relationship between DUP and 13-year outcome was examined. The mean DUP of 62 identified patients with schizophrenia was 8.7 months, and the median was one month. The 47 followed-up subjects were divided into two groups according to their rating on Eguma's Social Adjustment Scale: a favorable outcome group and an unfavorable outcome group. In addition, they were divided into other two groups according to length of DUP (cutoff point was two weeks) : a brief DUP group and a long DUP group. However, no statistically significant relationship between both couple of groups was found, the long DUP patients tended to belong to the unfavorable group.

(Key words: duration of untreated psychosis, schizophrenia, long-term outcome)

**I. Introduction**

Schizophrenia affects a lot of young people and caused serious social disability to not a few patients. It is not too much to say that schizophrenia is a serious social problem. Since clinicians have no miracle drugs for schizophrenia once the illness starts, it is no wonder that early detection and early intervention of schizophrenia are encouraged. As for this aspect, recently clinical attentions had focused on duration of untreated psychosis (DUP).

Reports have described reduction of DUP may improve the patient's short-term outcome.<sup>1,2)</sup> However studies on relationship between DUP and long-term outcome was rarely conducted. The authors have carried out an outcome study<sup>3)</sup> of first-admission schizophrenia in which the mean follow-up period was 13 years. Then the authors added data of DUP of the subjects retrospectively obtained from clinical records, and investigated effect of DUP upon the mean 13-year outcome.

**II. Methods****A. Subjects**

The subjects were 62 first-admission schizophrenic patients, 29 females and 33 males, for an analysis of statistics of DUP, and relationship between DUP and the patients' background factors, and 47 patients (29 females and 33 males) out of 62, for an analysis of relationship between DUP and outcome, consecutively

discharged from the Department of Psychiatry, Jichi Medical University, between June 1983 and May 1988.

Jichi Medical University is located in Tochigi Prefecture, Japan, a mostly rural region about 100 kilometers north of Tokyo. The psychiatric ward of Jichi Medical University Hospital had 41 beds during the study period: nine private rooms and four ward rooms for eight persons each. During the above period, the population of the surrounding areas was not very large, and with the exception of a small number of severely excited patients, outpatients that required hospitalization could be admitted to the psychiatric ward. Some of the excited patients were hospitalized and treated in a private room that was used as an isolation room.

The subjects had been diagnosed with schizophrenia during a clinical conference of Department members based on traditional German-Japanese diagnostic convention (essentially based on Bleuler's concepts,<sup>4)</sup> and adopting Schneiderian symptomatology,<sup>5)</sup> including first-rank symptoms). The subjects were also diagnosed retrospectively by two psychiatrists who used the criteria in the *Diagnosics and Statistical Manual of Mental Disorders-IV (DSM-IV)*.<sup>6)</sup> The retrospective diagnoses were performed during another study conducted by other Department members (unpublished), and selection of the patients in the current study was based on a database prepared during that study. Thus, the diagnoses and investigation of outcome were performed according to a mutually blind procedure.

Between June 1983 and May 1988, 136 schizophrenic patients were discharged from Jichi Medical University Hospital. Sixty-eight patients with a history of psychiatric hospitalization and six patients who did not meet the DSM-IV criteria were excluded from the study, leaving 62 patients. 47 of 62 patients could be followed up.

## B. Investigation

The 62 patients were located as 33 outpatients, six inpatients, two patients who died sudden deaths, seven suicides, eight patients not receiving medical treatment, and six lost. The investigation of the subjects' outcome was conducted between January and May 1999. The average interval between first admission and follow-up was 13 years 2 months. After obtaining their informed consent, the subjects were interviewed directly, if possible, and information was also obtained from their families and the psychiatrists in charge. Information on eight patients not receiving medical treatment was obtained from the family by telephone after obtaining the family's informed consent. Full details are mentioned in another paper.<sup>3)</sup>

## C. Assessment and Definition of Groups

Social outcome was measured using Eguma's Social Adjustment Scale,<sup>7)</sup> which contains five categories: self-supportive, self-semi-supportive, socially adjusted to family or community, maladjusted, and hospitalized (Table 1). The subjects were divided into two groups according to their rating on Eguma's Scale: a favorable outcome group composed of those in the self-supportive and self-semi-supportive categories, and an unfavorable outcome group composed of those in the socially adjusted to family or community, maladjusted, and hospitalized categories.

Data on the following were obtained from clinical records and analyzed: sex, family history of mental disorders, educational background (high school graduates or below), job experience, marital status,

age at the time of their first contact with a psychiatrist, age at the time of their first hospitalization, and symptoms at the time of their first hospitalization (delusions, hallucinations, disorders of ego consciousness, thought disorders, emotional disturbances, lack of spontaneity, catatonic symptoms, hypochondriac-cenestopathic symptoms, disorganized behavior, and suicide attempts). Again, full details are mentioned in another paper.<sup>3)</sup>

**Table 1. Eguma's Social Adjustment Scale**

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<i>A. Self-supportive</i>	
1.	Has returned to a level of social functioning similar to that prior to onset of illness.
2.	Maintains an independent social life with or without asking for advice from psychiatrists or acquaintances.
3.	Maintains a normal family life (housewife, for example).
<i>B. Semi-self-supportive</i>	
1.	Displays vocational ability, with some occasional failures.
2.	Maintains a positive attitude towards work, but needs supervision and guidance.
3.	Maintains a normal life at home, but hesitates to return to the job held prior to the onset of illness.
<i>C. Socially adjusted to family or community</i>	
1.	Works when encouraged, with continuous significant support from others.
2.	Needs more time before being ready to return to previously held job.
3.	Able to work continuously, if the work level is kept simple.
<i>D. Maladjusted</i>	
	Social adjustment impossible.
1.	Non-productive life (able to be cared for at home).
2.	Anti-social (admission to psychiatric hospital necessary).
<i>E. Hospitalized</i>	
	In a psychiatric hospital.

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Data of DUP was investigated retrospectively from clinical records. The DUP was defined as the duration between the time of the onset of a psychosis, and the time of the start of appropriate treatment. The onset of a psychosis is defined as the time when (1) obvious delusions, (2) persistent or intermittent hallucinations, or (3) disorganized behaviors are firstly observed. For example, the time when first-rank symptoms of Schneider,<sup>5)</sup> or nine symptoms listing in ICD-10<sup>8)</sup> as significant symptoms for diagnosing schizophrenia were observed, is identified as onset of a psychoses. The start of appropriate treatment means the time when the patient began to be under continuous treatment as an inpatient or an outpatient.

While DUP in patients with a short DUP could be often identified in the order of weeks, or days as the case may be, accuracy of a DUP in the patients with a long DUP was questionable and could be identified only in the order of months or even years. So DUPs were estimated with the unit of month, and the

mean DUP was calculated. For example, a DUP under two weeks was identified as 0 month, rounding off the fractions. To offset inaccuracy of DUP, especially in the patients with a long DUP, the subjects were divided into two groups according to length of a DUP, with the cutoff point of two weeks. Patients with a DUP under 2 weeks were classified a brief DUP group, while patient with a DUP of 2 weeks or longer were classified a long DUP group.

#### D. Data Analysis

The data for the brief and the long DUP groups were compared using Fisher's exact probability test or Mann-Whitney's  $U$  test.

Then the two couples of groups, the favorable and the unfavorable outcome groups and the brief DUP and the long DUP groups, were compared using Fisher's exact probability test.

The study was performed in adherence with the guidelines of the Declaration of Helsinki.

### III. Results

The DUPs in 62 patients were ranged from 0 month to 84 months. The mean was 8.7 month (SD 17 months), and the median was one month. While about a half subjects have DUPs of 0 month and 1 month, the rest dispersed in a wide range.

There were no significant differences in sex, family history of mental disorders, premorbid character, educational background, marital status, job experience, age at first contact, age at first hospitalization, type of onset, and symptoms at the time of the first hospitalization, between the brief DUP group and the long DUP group in 62 patients (Table 2).

**Table 2. Premorbid status and situation at onset**

	the brief DUP ( $< 2$ wks) group (n=11)	the long DUP ( $\geq 2$ wks) group (n=36)	P
Sex			
Female	6	23	N.S.*
Male	12	13	
Family history of mental disorders			
In one or more members	3	17	N.S.*
None	10	32	
Family history of schizophrenia			
In one or more members	2	7	N.S.*
None	11	42	
Premorbid personality			
Sociable	5	15	N.S.*
Unsociable	8	34	
Educational background			
High school or under	8	35	N.S.*
College or higher	5	14	
Job experience			
One or more jobs	7	25	N.S.*
None	6	24	
Marital status			
married	0	8	N.S.*
unmarried	13	41	
Age at first contact (SD)	22.5 (5.6)	24.8 (7.9)	N.S.**
Age at first hospitalization (SD)	23.7 (5.6)	25.6 (7.8)	N.S.**
Symptoms at the time of the first hospitalization			
Hallucinations	7	36	N.S.*
None	6	13	
Delusions	10	39	N.S.*
None	3	10	
Disorders of ego consciousness	2	15	N.S.*
None	11	34	
Thought disorders	1	5	N.S.*
None	12	44	
Emotional disturbances	1	8	N.S.*
None	12	41	
Lack of spontaneity	3	22	N.S.*
None	10	27	
Catatonic symptoms	2	2	N.S.*
None	11	47	
Hypochondriac-cenestopathic symptoms	3	15	N.S.*
None	10	34	
Disorganized behavior	4	15	N.S.*
None	9	34	
Suicide attempts	0	7	N.S.*
None	13	42	

\* Fisher's exact probability test; \*\* Mann-Whitney's *U* test

Comparing the brief and the long DUP groups and the favorable and the unfavorable groups in 47 followed-up patients, there was a tendency for patients with a brief DUP to belong to the favorable outcome group, but no significant differences ( $p=0.083$ ) (Table 3).

**Table 3. Relationship between DUP and outcome**

	the brief DUP ( $< 2$ wks) group ( $n=11$ )	the long DUP ( $\geq 2$ wks) group ( $n=36$ )	P*
the favorable outcome group ( $n=22$ )	8	14	0.083
the unfavorable outcome group ( $n=25$ )	3	22	

\* Fisher's exact probability test

#### IV. Discussion

This study is preliminary and insufficiently, but a rare report concerning to the relationship between DUP and long-term outcome.<sup>9)</sup> The subjects in this study were first-admission schizophrenic patients in a medical university hospital. During the study period, the psychiatric ward of Jichi Medical University accepted almost all outpatients who needed hospitalization except severely excited patients. Thus our subjects were supposed to be not largely distinct from general population with schizophrenia.

In the clinical conference at the psychiatric ward of Jichi Medical University Hospital, the Department chief (the professor) examined patients along with the discussion among the members, and the patients were diagnosed from the viewpoint of the traditional and consistent diagnostics. Furthermore, the patients were doubly diagnosed using criteria in DSM-IV. So, it is no exaggeration to say that we extracted doubtlessly diagnosed schizophrenic patients in this procedure.

But, in the context of studied on DUP, our samples were not ordinary population, because the target of the DUP study must be "early psychosis",<sup>2)</sup> which does not yet met the criteria in DSM-IV<sup>6)</sup> with the duration of six months of schizophrenic symptoms, or the criteria in ICD-10<sup>8)</sup> with the duration of a month. Since our subjects are schizophrenia which met the criteria in DSM-IV, patients with early psychosis who were successfully treated within six months were methodologically excluded.

Besides, retrospective procedure of this study possibly damaged reliability of the DUP. However, the clinical records relied on the memory of the patients' family at the time of first contact have certain reliability, so far as using our definition of DUP based on first obvious psychotic symptoms observed by the family. No wonder the family of patients with a brief DUP had good memory of the onset of illness. While the memory of family of patients with a long DUP must have been doubtful, dichotomy between the brief DUP group and the long DUP group got rid of this uncertainty.

Larsen et al<sup>2)</sup> illustrate that the DUP have a mean of 1-2 years and a median of 26 weeks. There are also reports showing that the mean DUP is 30 weeks or 32 weeks,<sup>1)</sup> which are close to our data, 8.7 months. As for Japanese population, there is few reports concerning DUP, for example, Yamazawa et al.<sup>10)</sup>

reported that mean DUP of first episode schizophrenia was 13.7 months.

Even if there is relationship between DUP and the outcome, it must not be linear relationship, namely relationship that the longer DUP is, the worse outcome is. In this aspect, we employed the categorization of the brief DUP group and the long DUP group, however where the cutoff point had to be set was problematic. Although in several studies<sup>11-14)</sup> the cutoff points were set to the median DUP, we chose two weeks as the cutoff point, because we supposed very early intervention only affects long-term treatment outcome. Actually, there were no patients with a DUP of 8-13 days in our subjects, and the brief DUP group consisted of patient with DUP of seven days or less.

DUP is supposed not to be an independent variable, but to be affected by premorbid adjustment, individual variations of the illness, family's understanding of or prejudice against psychoses, cultural environment, social resources, and so on. But there were no significant differences in the patients' background factors, including premorbid status, situation at onset, and symptom at the time of first admission, between the brief and the long DUP groups.

Now, we focused on relationship between DUP and the mean 13-year outcome in this study. Considerable researchers investigated relationship between DUP and 12-month or 24-month outcome, and concluded that patients with a short DUP tend to have more favorable outcome, however there are a few different opinions.<sup>1,15)</sup> Just de Haan et al.<sup>16)</sup> and Bottlender et al.<sup>17)</sup> focused on relationship between DUP and long-term outcome as far as we know. De Haan et al compared two groups, patients with a DUP of 3 months or less and patients with a DUP of 16 months or longer, and concluded that there were no significant differences between the groups on any of the outcome measures 11.1 years after the first psychotic episodes. Contrarily, Bottlender et al. concluded that a longer DUP was associated with a lower global functioning 15 years after the first psychiatric admission.

We found no statistically significant relationship between brief and long DUPs and 13-year outcome. Even if DUP plays a very important role in the outcome of schizophrenia, many factors, possibly related to the long-term outcome, may cover the effect of DUP. However, a relatively small amount of P-value ( $P=0.083$ ) in this study suggests that the increase of sample size would reveal statistically significant relationship.

It seems that evidence of relationship between DUP and outcome up to 2 years is nearly established.<sup>15)</sup> Yet relationship between DUP and long-term outcome is still uncertain.<sup>18)</sup> De Haan et al.<sup>19)</sup> presented the concept of delay in intensive psychosocial treatment (DIPT), and emphasized that DIPT may be a more important predictor of negative symptoms at outcome than is DUP, actually, defined as delay in treatment with antipsychotic medication. The concept of DUP may be insufficient for a long-term outcome predictor.

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# 初回入院統合失調症患者の精神病未治療期間と 13年予後

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## 抄 録

自治医科大学精神科への初回入院統合失調症患者の平均13年予後研究のデータを用い、そこに後方視的に調査した精神病未治療期間 (DUP) を加えて、DUP と患者の背景因子・病像、DUP と13年予後の相関を検討した。DUP の平均は8.7カ月、中央値が1 カ月であった。検討に当たっては、DUP の長短に応じて、

DUP が14日未満 (実際には数日以内に収まる) の無 DUP 群と、14日以上の有 DUP 群との二群で比較した。DUP と背景因子の関連、DUP と病像の関連ともに、有意な所見はなかった。DUP と予後の関係については、統計的有意ではないが、無 DUP 群に予後良好な症例が多い傾向がみられた。