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Original article

# Estimate dynamic changes of dysfunction and lifelong spent for psychiatric care needs in patients with schizophrenia

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ABSTRACT

*Background:* Disturbance of functionality is one of the core features of schizophrenia, and has deleterious effects on a patient's employment, increased healthcare costs, and a large societal burden. Thus, if a patient's disability status could be predicted, and interventions needed identified in advance, poor outcomes could be prevented. To achieve this aim, we developed a method by which to assess dynamic changes of dysfunction and estimate the lifetime duration of disability in patients with schizophrenia, as a proxy for assessing their specialized healthcare needs.
*Methods:* The proposed method was developed based on a nationwide database and a cross-sectional survey. The primary analysis investigated the dynamic change in the proportion of patients with manifested disability over time, while the secondary analysis estimated the lifetime duration of disability, obtained as the proportion of patients with manifested disability multiplied by the survival probability throughout the life of patients.
*Results:* The average lifetime duration of manifested disability of global functioning was estimated to be 20.9 years, which represents approximately 73% of the whole lifetime of patients. The duration of disability in socially-useful activities was estimated to be 15.6 years, while that in personal and social relationships was 17.5 years. The female patients had a longer duration of manifested disability (22.9 years) than the male patients (19.5 years).
*Conclusions:* The developed method of analysis indicated that the longest lifetime durations of manifest disability were observed in the areas of socially-useful activities and personal and social relationships, and the proportions of patients with these disabilities rapidly increased at 200 months after diagnosis.


## 1. Introduction

Schizophrenia is a disabling and severe mental disorder with a chronic clinical course, often resulting in progressive loss of self-care and psychosocial functions in affected individuals. The lifetime prevalence of schizophrenia is approximately 0.8–1% [1]. In the care of such patients, clinicians must continually assess their functionality to monitor progress and long-term prognosis in order to modify the treatment if necessary. Previous studies have indicated that a poor functional outcome was significantly associated with higher subsequent direct/indirect costs [2–4] and increased healthcare utilization [2]. In other words, if a patient's functional disability status could be predicted, and interventions that might be required to improve functionality are identified in advance, poor outcomes could be prevented and healthcare resources could be saved. Furthermore, if the lifelong years for which a patient with schizophrenia suffers manifested disability could be measured beforehand, the healthcare resources for patients with schizophrenia could be appropriately allocated at different stages of prognosis by policy-makers, and the cost-effectiveness of care could be improved [5–7].

In order to achieve this aim, a method that relies on a nationwide database and a cross-sectional survey was developed to explore dynamic changes of functional disability in patients with schizophrenia over time and estimate the lifetime duration of

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disability in personal and social functioning in patients with schizophrenia, as a proxy for assessing their specialized healthcare needs.

## 2. Material and methods

### 2.1. Schizophrenia cohort

The research protocol was approved by the Ethical Committee for Human Research at the National Cheng Kung University. The Taiwanese National Health Insurance (NHI) program is a universal health program that was introduced in March 1995. By the end of 1999, approximately 99% of the Taiwanese population had enrolled in the NHI program. Therefore, the NHI database is representative of the entire Taiwan population. The NHI databases include a registry of beneficiaries, ambulatory care claims, inpatient claims, prescriptions dispensed at pharmacies, a registry of medical facilities, a registry of board-certified specialists and a registry of catastrophic illnesses. After careful review and approval by the Institutional Review Board, these databases were linked to individual personal identification numbers (PINs) to provide patient-level information on demographic characteristics, and PINs were then encrypted prior to data release for research purposes. The registry of catastrophic illnesses features up-to-date information regarding severe illnesses, including schizophrenia, dementia, end-stage renal disease, cancer, etc. In general, a patient must be evaluated and diagnosed by a board-certified physician in the specific field in order to write a certificate for an application, which then must be validated by another specialist before approval for registration as a victim of such illnesses. For patients with a catastrophic illness, co-payments for outpatient or inpatient care can be waived. We identified 52,299 patients who were diagnosed with schizophrenia (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM], code 295) from the catastrophic illness register of the NHI during the period of 2000–2008. The index date of follow-up was defined as the date of the first application for a catastrophic illness certificate. In order to match the cross-sectional survey data in terms of age (the patient age of diagnosis ranged from 15 to 50 years in the survey data), we restricted the cohort to within the age range of 15–50 years, resulting in a final cohort of 42,339 patients. The all-cause mortality was extracted from the catastrophic illness records, which noted the occurrence of death. The NHI administration regularly checks patient status (death or invalidity) and notes these checks in the catastrophic illness records every month.

### 2.2. Collection of data regarding functionality and functional levels

Functionality was measured by conducting a cross-sectional survey of patients with schizophrenia analyzed after the date of first diagnosis. The sample size was 230 patients from 2 medical centers and one mental hospital in Taiwan (day-care wards, community rehabilitation centers, outpatient clinics). The inclusion criteria were: patients meeting the DSM-IV criteria for schizophrenia, and currently aged 20–60 years (age of diagnosis from 15 to 50 years). The exclusion criteria were: a) a severe and unstable major medical disease or a history of neurological disease; b) a history of alcohol or substance dependence or abuse, except for nicotine dependence; c) a history of head injury; d) receipt of electroconvulsive therapy within the previous 6 months; e) an intelligence quotient <70; f) severe vision deficiency, e.g., color blindness or any corrected visual acuity <0.5; and g) illiteracy or disability, and inability to read traditional Chinese characters.

The tool applied for assessment of the patients was the Personal and Social Performance scale (PSP), administered by psychiatrists in each hospital during the one-year study period. The PSP was developed based on the social functioning component of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and the social occupational functioning assessment scale (SOFAS). The reliability and validity of the PSP have been investigated in previous studies, and high test–retest reliability, a good inter-rater reliability [8], and high levels of correlation with the Global Assessment of Functioning (GAF) scale, the Activities of Daily Living (ADL) scale, the SOFAS scale and the Positive and Negative Syndrome Scale (PANSS) were observed [9,10]. The PSP consists of four domains: socially-useful activities; personal and social relationships; self-care; and disturbing and aggressive behaviors. Each domain is rated on a six-point Likert scale from 1 to 6, representing absent, mild, manifest but not marked, marked, severe and very severe. Higher domain scores indicated poorer functioning in that particular domain. A global score, which reflected global functioning, was derived from the levels of impairment in each of the four domains, ranging from 1 to 100. Higher global scores indicated better functioning on the global level. In this study, functional disability was measured according to the scores for each domain (a higher score indicating poorer functioning) and the global score (a lower score indicating poorer functioning).

### 2.3. Survival analysis and extrapolation to estimate life expectancy and expected years of life lost

We applied the Kaplan-Meier method to estimate the time-to-death of the schizophrenia cohort (obtained from the NHI catastrophic illness database). Lifetime survival was estimated using the semi-parametric extrapolation method [11,12]. The lifetime survival of the schizophrenia cohort was estimated for up to 900 months using a simple linear regression extrapolation of a logic transformation curve to assess the survival ratio between the schizophrenia cohort and a year-, age- and gender-matched reference population, which was generated by the Monto Carlo simulation method from life tables for the general population of Taiwan. The survival ratio between the schizophrenia cohort and the reference population assumed a constant excess hazard, the detailed method and mathematical proof of which have been described in a previous study [13]. The standard error of survival estimate was obtained through a bootstrap method of repeated sampling with replacement from a real dataset 100 times. The life expectancy (LE) of the schizophrenia cohort was estimated by summing the area under the estimated lifetime survival curve. The expected years of life lost (EYLL) was calculated as the difference in LE between the schizophrenia cohort and the age- and gender-matched reference population.

To validate the extrapolation method, the relative bias between the predictions and real values was estimated: the LE estimate (using extrapolation based on the first 5 years of follow-up) was compared with the Kaplan Meier estimate based on the actual 9-year follow-up period. The relative bias was less than 1% for the whole study population and for gender-stratified groups. The details are presented in Supplementary Table 1.

### 2.4. Estimations of proportions of patients with functional disabilities at different functional levels

Functional disability does not remain constant over time in patients with schizophrenia, and changes according to the duration of illness; therefore, a kernel-smoothing method was used to estimate the dynamic changes in functional disability [11]. To synchronize with clinical significance, we converted a patient's PSP score into two functional levels: less (mild) difficulty (global score: 71–100; domain score: 1–2) and manifested disability (global score $\leq$70; domain score: 3–6). We classified the indicator