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Estimation of life expectancy, loss-of-life expectancy, and lifetime healthcare expenditures for schizophrenia in Taiwan

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ABSTRACT

By employing a novel semi-parametric extrapolation method, the life expectancies after the first hospitalization for schizophrenia and the associated lifetime healthcare expenditures were both estimated. Based on the linkage between the National Health Insurance Research Database and the National Mortality Registry of Taiwan, we have established a schizophrenic cohort for 2000–2010 and followed up to 2011. Survival function was estimated through Kaplan–Meier's method and extrapolated throughout life. We applied a simple linear regression to the logit-transformed survival ratio between the schizophrenic cohort and the sex-, age-matched referents via Monte Carlo simulation from the national life table. The monthly survival probability was multiplied by the average healthcare expenditures and summed throughout life to estimate the lifelong cost reimbursed by the National Health Insurance. The results showed that patients diagnosed at age 20–29 had the highest expected years of life lost (EYLL), 15 and 9 years, in men and women, respectively, with corresponding lifetime healthcare expenditures of USD 48,000 and 53,000. Males generally had higher health cost per life-year than their female counterparts across their lifespan. We applied the same method to the first 6 years of the cohort and extrapolated to 12 years, which showed that the relative biases for different age strata were less than 5%. We thus concluded that the semi-parametric extrapolation method might provide a timely estimation of lifetime outcomes for health care planning of schizophrenia.

1. Introduction

Schizophrenia is, in many cases, chronic and disabling. Accelerating and validating the estimation of lifetime outcomes becomes timely to prioritize individual and national health actions. The shortened life expectancy (LE), also called the expected years of life lost (EYLL), of schizophrenia ranges from 7.8 to 22.5 years (Hannerz et al., 2001; Kodesh et al., 2012; Laursen, 2011; Lawrence et al., 2013; Nielsen et al., 2013; Nordentoft et al., 2013; Tiihonen et al., 2009) when compared with the general population. Most of the above studies applied life table methods on national prevalence data for years. However, life table methods usually require large, longitudinal follow-up cohorts to reflect a low incidence and chronic course of schizophrenia. Moreover, long-term outcomes estimated from incidence or treatment-/policy-naïve patients would be more accurate for showing trends and social impacts in comparison with those based on prevalent cohorts.

Costs of schizophrenia are important for healthcare resources allocation. Despite few reports on the lifetime costs of schizophrenia, prevalence-based estimates are relatively popular. The yearly costs of psychotic disorders, mostly schizophrenia, ranked the third among 19 brain disorders in 30 European countries in 2010 (Olesen et al., 2012). Langley-Hawthorne (1997) calculated LE and lifetime costs of schizophrenia by utilizing Markov models with various transitional probabilities and related costs extracted from the literature. She projected a mean LE of 31 years and approximate lifetime cost of one million dollars (36% direct costs) per patient with schizophrenia in 1995 in Australia (Langley-Hawthorne, 1997). However, these estimates of lifetime costs are still waiting for corroboration.

We have developed a semi-parametric method to estimate a lifelong survival function (Hwang and Wang, 1999), which can be multiplied with the average monthly cost of treating patients with schizophrenia to obtain lifetime costs. The method was mathematically verified to be valid, if constant excess hazard can be assumed (Fang et al., 2007),

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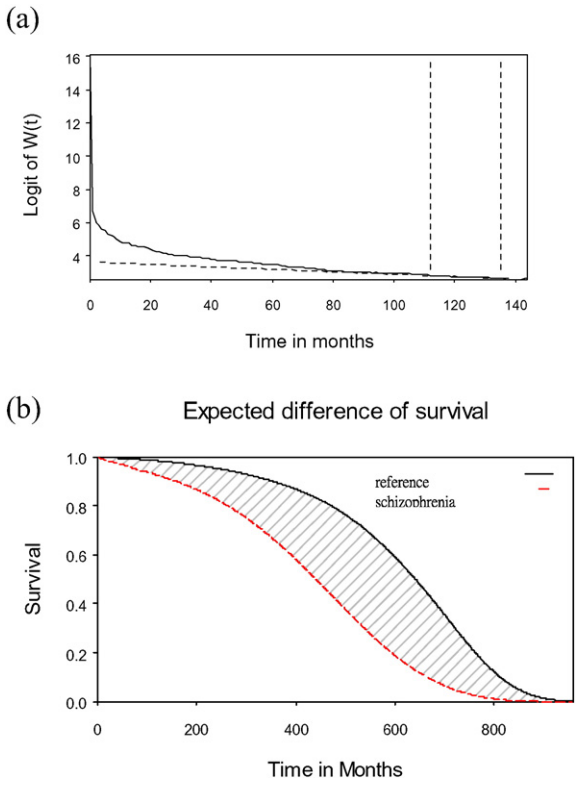

Fig. 1. (a) Logit transformation of the survival ratio W(t) between the survival functions of male patients with schizophrenia, aged 20–29, and that of the age- and gender-matched reference population generated by the Monte Carlo method. The two vertical dotted lines mark the time period when the logit survival ratio data were used for extrapolation. The bottom dotted line is the linear regression line. (b) Lifelong extrapolation to estimate the life expectancy of the 20–29 schizophrenia cohort and the corresponding reference.

and was empirically demonstrated to estimate life expectancy (LE), and by extension expected years of life lost (EYLL) on cancer cohorts with high censored rates (Andersson et al., 2013; Liu et al., 2013). Recently, it was also applied on cohorts of heroin users with relative accuracy (Chang et al., 2015). This study aims to estimate the LE, EYLL, lifetime healthcare expenditures, and cost-per-life year for a cohort of incident cases of schizophrenia followed for 12 years in Taiwan.

2. Materials and methods

2.1. Schizophrenia cohort

The National Health Insurance (NHI) in Taiwan was implemented in 1995; and since 2004, more than 99% of Taiwan citizens have been covered (National Health Insurance, 2005). The catastrophic illness system of the NHI features an up-to-date list of severe illnesses, including schizophrenia, and the system waives the co-payment for the treatment of the listed diseases. Schizophrenia healthcare that follows the formal guidelines in Taiwan is freely accessible to registered patients diagnosed and validated with code 295 based on ICD-9-CM by at least two board-certified psychiatrists. We identified a total of 58,665 patients with schizophrenia first registered with the NHI as catastrophic illness over the period of 2000–2010. Among them, 38,429 patients were hospitalized for schizophrenia for the first time. In the final analysis, only 34,658 within the age range of 20–64 when registered were included to determine if the assumption of constant excess hazard could be fulfilled among various age groups. The enrollees were either censored at death or at the end of 2011. Their survival status was verified by linkage with the national mortality registry. The health care expenditures, including the inpatient and outpatient expenditures attributed to schizophrenia and related comorbidities, were retrieved from the NHI database. Age- and gender-stratified annual incidence rates were calculated by dividing the number of new cases during the 11-year period with the total sum of the mid-year population of individual age- and gender-specific strata.

2.2. Extrapolation of long-term survival for the schizophrenic cohort

We applied Kaplan–Meier's method to estimate the time-to-mortality of the schizophrenic cohort stratified by gender and age. Lifetime survival function was estimated by a semi-parametric extrapolation method developed by Hwang and Wang (Hwang et al., 1996; Hwang and Wang, 1999; Hwang and Wang, 2004) and later mathematically validated by Fang et al. (2007). The method is briefly summarized as follows: first, hypothetical age- and gender-specific referents for each patient with schizophrenia were simulated by the Monte Carlo method conditioned on the hazard function of the life table in a given year in Taiwan. Second, the survival ratio between schizophrenic patients and referents at time t was calculated, and assumed to be one initially and gradually converge to a constant, representing the excess hazard of the premature mortality accompanying schizophrenia. Third, the survival ratio was then logit-transformed so that a simple linear regression could be applied to approximate the temporal trend of the stabilized period until the end of 2011. Accordingly, the slope of the regression line was used to extrapolate the lifetime survival of schizophrenia patients after the follow-up limit, allowing the life expectancy (LE) of an age-, gender-specific cohort to be estimated by summing up the area under the curve of the survival function throughout the patient's life. The bootstrap method of repeated sampling for 100 iterations was used to compute the mean standard error. Fig. 1(a) illustrates the slope of constant excess hazard for extrapolation (a) in male patients with schizophrenia, aged 20–29. Shaded area of the projected survival curve indicates the EYLL of 20–29 male patients (Fig. 1(b)). A software package developed by Hwang's team was used for the computation, and can be freely downloaded: Integration of Survival with Quality of Life. http://www.stat.sinica.edu.tw/isqol/ (updated on Feb. 12, 2014).

2.3. Estimation of expected years of life lost and lifetime healthcare expenditures for schizophrenia

We estimated two lifetime outcomes to assess the impact of schizophrenia. First, the expected years of life lost (EYLL) was the difference in LE between the schizophrenic cohort and the age- and gender-matched hypothetical referents, as described above. The second indicator was the average lifetime healthcare expenditure per person, for which the reimbursement data of the National Health Insurance from 2000 to 2010 included all medical expenses attributed to schizophrenia. We stratified the cohort by 10-year age and gender specific strata, and then calculated

Table 1
Annual incidence rate per 100,000, age at diagnosis and gender of cohorts.

Schizophrenia (ICD9: 295)	Gender	Total number of new cases during 2000–2010	Age at diagnosis, mean (SD)	Annual incidence rate ($\times 100{,}000^{-1}$)
20–29	Male	6372	24.72(2.89)	30.21
	Female	4197	24.85(2.84)	20.73
30–39	Male	6333	34.30(2.86)	30.47
	Female	4645	34.42(2.89)	22.77
40–49	Male	3972	43.97(2.86)	19.52
	Female	3908	44.27(2.87)	19.50
50–59	Male	1774	53.69(2.76)	12.53
	Female	2431	53.77(2.81)	16.99
60–64	Male	402	61.88(1.44)	9.23
	Female	624	61.73(1.36)	13.59
Cumulative incidence rates (CIR_{20-64})	Male			968.7
	Female			864.1