



Research Paper

Three-year mortality in relation to early hospitalization and number of outpatient clinic visits in people with newly diagnosed bipolar disorder☆☆☆★



Yi-Ju Pan, M.D., Ph.D.^{a,b}, Ling-Ling Yeh, Ph.D.^c, Yu-Chun Chen, M.D., Ph.D.^{d,e,f}, Hung-Yu Chan, M.D., PhD^{g,h,*}

^a Department of Psychiatry, Far Eastern Memorial Hospital, Taipei, Taiwan

^b Department of Public Health, School of Medicine, National Yang-Ming University, Taipei, Taiwan

^c Department of Healthcare Administration, College of Health Science, Asia University, Taichung, Taiwan

^d Department of Medical Research and Education, National Yang-Ming University Hospital, Yilan, Taiwan

^e Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

^f Institute of Hospital and Health Care Administration, School of Medicine, National Yang-Ming University, Taipei, Taiwan

^g Department of General Psychiatry, Taoyuan Psychiatric Center, Taoyuan, Taiwan

^h Department of Psychiatry, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan

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ABSTRACT

Objective: Whether the early treatment pattern in people with bipolar disorder (BD) could influence later mortality remains to be determined. We aimed to explore the potential effects of early hospitalization and number of outpatient clinic visits on the 3-year mortality in patients with newly diagnosed BD.

Method: Adult participants with newly diagnosed BD were identified in Taiwan's National Health Insurance Research Database in 2008. Survival analyses were performed with this national cohort to examine the associations between the first-year treatment pattern (hospitalization and number of outpatient clinic visits) and mortality over a follow-up period of 3 years (2008–2011).

Results: A total of 15,254 participants were included. The mean age was 44.9 (S.D.=16.7) years and around 39.9% were male. The average follow-up time was 1055 days. Compared to BD patients with ≥ 7 times outpatient clinic visits within the first year, the risk of mortality was found elevated [hazard ratio=1.74; 95% confidence interval (CI), 1.40–2.15] for those who needed inpatient treatment. Number of outpatient clinic visits within the first year was found to be negatively associated with later mortality. Besides cancer (hazard ratio=2.14; 95% CI, 1.74–2.63), diabetes mellitus (hazard ratio=1.61; 95% CI, 1.38–1.89) and renal disease (hazard ratio=1.65; 95% CI, 1.36–2.00) were associated with the highest risk of mortality among the physical comorbidities. Substance use disorder stood out as the single comorbid mental illness associated with the highest mortality risk (hazard ratio=1.74; 95% CI, 1.37–2.21).

Conclusions: Early treatment pattern, including hospitalization and number of outpatient clinic visits, was associated with later mortality in BD patients. Special care should be given to enhance treatment adherence and to give psychoeducation to those with certain comorbid mental/physical illnesses to reduce health harming behavior and to improve health outcome.

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* Corresponding author at: Department of General Psychiatry, Taoyuan Psychiatric Center, No. 71, Long-Show Street, Taoyuan City 33058, Taiwan.

E-mail address: jan30@seed.net.tw (H.-Y. Chan).

1. Introduction

In comparison with the general population, mortality rate is substantially higher for individuals with bipolar disorder (BD) [1–3]. Although both natural (from disease and medical conditions) and unnatural causes of deaths (from injuries and external causes) are elevated, natural causes have accounted for around three-fourths of premature deaths in people with serious mental illnesses [1]. BD individuals have higher risk to develop cardiovascular diseases [4]. Even predating modern treatments of BD which may further influence cardiovascular risk [5,6], evidence has consistently shown a doubling of risk in cardiovascular mortality [7–10]. Independent of traditional

cardiovascular risk factors and adverse effects of psychiatric medications, manic symptom burden has been found to predict cardiovascular mortality [10], begging questions regarding alternative explanations for the elevated risk. The mechanisms are likely complex, involving the interplays between the individual's clinical symptoms, behavioral factors, treatment exposure with psychiatric medications and the underlying pathophysiology of BD [11].

Compared to the adverse effects of psychiatric medications, there has been scarce evidence addressing the impacts of clinical symptoms and behavioral patterns on the long-term mortality in people with BD. The direct effects of clinical symptoms may influence death from suicide and other unnatural causes [12]. For instance, manic symptoms increase impulsivity which, disregard of the long-term implications of one's decision, may result in risky behaviors [13]. The individual's clinical symptoms may also have impacts on natural causes of deaths, through adverse health behaviors including smoking, alcohol intake, substance abuse and lack of exercise [14,15]. On the other hand, a remaining gap exists in the knowledge regarding how the individual's treatment-seeking behavior may contribute to the excess mortality. Research showed that upward of 60% of BD patients are nonadherent to the recommended treatment [16]. The impacts of nonadherence include increased risk of relapse/recurrence [17,18] and suicide attempts [18]. However, little is known about how improvement in the treatment-seeking behavior may benefit mortality rate in people with BD, probably through better management of clinical symptoms and reduction of health harming behaviors.

Therefore, the current study, using the claims data from the National Health Insurance Research Database (NHIRD) in Taiwan, sought to explore the impacts of the individual's clinical symptom and treatment pattern on the later mortality over a period of three consecutive years. By taking hospitalization as a proxy for clinical symptom severity and appointment-keeping behavior as a proxy for level of adherence to treatment, we explored the relative impacts of these factors on the 3-year mortality in a nationally representative sample of people with newly diagnosed BD in 2008.

2. Methods

2.1. Setting

Taiwan is a country with population of around 23 million. National Health Insurance (NHI) in Taiwan is a single-payer compulsory social insurance system, which centralizes the disbursement of healthcare funds and guarantees equal access to health care for all citizens and legal foreign workers. In 2008, a total of 22.9 million individuals are enrolled in Taiwan's NHI program with a coverage rate of 99.5% [19]. The NHIRD consists of data characterizing healthcare utilization of insured residents, including expenditures, medical procedures/treatments and basic demographic characteristics. Diagnosis in NHIRD is given with the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnoses. All participants in this study are first identified from the NHIRD and the index date is defined as the date on which the participant is first diagnosed of BD (*ICD-9-CM* codes: 296.0, 296.1, 296.4–296.7) in 2008. Data on all NHI information for each participant are extracted for the 1 year preceding and 3 years following the index date.

2.2. Participants

All participants meeting the following criteria in NHIRD are qualifying:

They are diagnosed with BD in 2008.

Aged 18 years or over on the index date. They do not have a diagnosis of BD in the preceding year of the index date.

Data are available for a minimum of 12 months before and 36 months after the index date.

2.3. Sociodemographic data and comorbid physical/mental illnesses during the preceding year

Because sociodemographic data, household income, comorbid mental and physical illnesses can have impacts on the mortality in people with BD, we extract data on age, gender, physician specialty and type of mood episode on the index date as well as socioeconomic variables, including low-income household, insurance premium (the monthly salary-based income of the insured, categorized into four levels: above New Taiwan Dollar (NTD) 72,801, NTD 36,301–72,800, NTD 17,281–36,300, below NTD 17,280 (International Dollar 1=NTD 16.99)) [20], and urbanization level of residence [21] on the index date. For all participants, comorbidities of mental and physical illnesses, healthcare utilization and expenditure are traced back for the 12 months prior to the index date.

2.4. Hospitalization and number of outpatient clinic visits within the first year of index diagnosis

Given our focus on the relationship between the early treatment pattern – in terms of hospitalization and adherence to outpatient appointment – and later mortality, treatment pattern is operationally defined by whether the individual receives inpatient treatment as well as the frequency of outpatient clinic visits for BD treatment within the first year of diagnosis. Because the individuals who need inpatient treatments may differ largely from those receiving treatments exclusively at outpatient settings, we categorize study participants into four mutually exclusive groups: (1) those who have been admitted for inpatient treatments of BD, (2) those having ≥ 7 times outpatient clinic visits but no inpatient treatments, (3) those having four to six times outpatient clinic visits but no inpatient treatments, and (4) those having one to three outpatient clinic visits but no inpatient treatments.

2.5. Mortality

Death status in this study is defined as the withdrawal of the person from the NHI program and without reuse of any healthcare services since. There are three kinds of situations when a person withdraws from the NHI program of Taiwan: (1) death, (2) missing for more than 6 months and (3) disqualification as an insurance applicant of the NHI program such as immigration and the expiration of the duration of stay of aliens. Missing for more than 6 months is closely related to death and the percentage of disqualification as an insurance applicant is relatively minimal given the fact that foreigners constitute only around 2% of all insured individuals of Taiwan's NHI [22]. Previous studies have used withdrawal from the NHI program of Taiwan as the definition of death [23,24].

2.6. Statistical methods

Demographic/clinical data, socioeconomic variables, comorbid mental/physical conditions, healthcare utilization pattern for the preceding year and deaths over the three consecutive years were described for the overall sample of participants with newly diagnosed BD and compared among groups based on the first-year hospitalization and outpatient treatment pattern after index diagnosis. Survival analyses with Kaplan–Meier curves and Cox regressions were employed to estimate the effects of hospitalization and number of outpatient visit on the hazard ratios of mortality over the 3 years following the index diagnosis. The considered confounders included basic demographic/clinical factors, socioeconomic factors and comorbidities of physical and mental illnesses during the preceding year. Interaction terms such as physician specialty $\times$ treatment pattern and gender $\times$ treatment pattern were tested for presence of effect modification. Alpha level was set at .05 (*P* value) for statistical significance for all statistical analyses, performed with SPSS version 17.0 (Chicago, IL, USA).

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