



Analysis of the reasons and costs of hospitalization for epilepsy patients in East China

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ABSTRACT

Purpose: This study aimed to assess the cause and cause-specific risks of hospitalization for epilepsy patients in East China. Further analysis was performed for inpatient hospitalization days, hospital mortality and costs.

Method: This study was performed on epilepsy patients admitted to our hospital including 21 community health centers in East China from January 2011 to April 2017. Case records including patient data, length of hospitalization, reasons for admission, hospital mortality, and the costs incurred for hospitalization of epilepsy patients were reviewed.

Results: The three principal reasons for admission were: 1) cerebral vascular disease (CVD), 2) newly diagnosed epilepsy with unknown etiology; and 3) frequent seizures including status epilepticus. The median length of hospitalization was 13 days. The three major reasons regarding inpatient days were: 1) Parkinson's Disease (PD), 2) dementia, 3) trauma. The average hospital mortality was 14.81% (17/1148) with 1) lung infection (mainly pneumonia), 2) depression (deaths occurred by suicide) and 3) frequent seizures including status epilepticus being the three top reasons. The three major financial cost incurred for in-patients with epilepsy were: 1) PD, 2) arteriovenous malformation and 3) trauma.

Conclusions: The most common hospitalized reasons for epilepsy patients were CVD, PD and dementia, which all were common diseases in the elderly. Consequently, the hospitalization days of these patients were longer and their financial burden was heavier. Epilepsy patients with comorbid depression should be closely monitored to prevent suicide from the onset of epilepsy.

1. Introduction

Epilepsy is a paroxysmal disabling brain dysfunction that affects a wide range of individuals. About 50 million people suffer from epilepsy worldwide [1]. The current global prevalence of epilepsy is approximately 1% [2]. Nearly 80% of epilepsy patients are found in developing regions, such as China and India. Epilepsy patients usually respond well to the currently available anti-epileptic drugs (AEDs). Nearly 70% of these patients only require outpatient treatment. Unfortunately, the majority of patients with epilepsy in developing countries (about 66% in China and 95% in India) do not receive regular or standard treatment for the conditions [3]. This eventually leads to severe complications in patients that require hospitalization [4]. Patients are hospitalized due to new-onset or uncontrolled frequent seizures, which are the predominant symptoms of the brain disorders due to CNS infection, stroke, or trauma; or admitted for complications or co-morbidities associated with epilepsy, such as depression and dementia. Due to these diverse reasons for the epilepsy admission, the clinical outcome and financial

burden of hospitalization may vary significantly.

Hospitalization and their costs could contribute to the giant burden of epilepsy worldwide [5]. So, it is important to clarify the reasons and reason-specific costs of hospitalization for epilepsy patients. However, till now there are few systematic studies focusing on the financial burden of patients with epilepsy based on their different causes for hospitalization. Additionally, epilepsy patients may experience a high risk of death or other unforeseen accidents. A number of reasons have been proposed to the potential causes [6]. We performed an epidemiological systematic study on these reasons, hospital mortality and the financial burden of hospitalization in epilepsy patients from the East China. It will provide evidence for correspondingly management for epilepsy patients based on analyzing their causes and cause-specific risks of hospitalization as well as their costs in the future.

2. Methods

The hospital Institutional Review Board and the Ethics Committee

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of Nanjing brain Hospital Affiliated to Nanjing Medical University approved the study, with the application number of 2017-ky007. At admission the patients were requested to sign an informed consent whether they agreed that their information during hospitalization was to use for scientific survey or research. We searched the computerized diagnosis index in our hospital including 21 community health centers in East China to identify patients who were epilepsy between January 2011 and April 2017. Nanjing brain Hospital Affiliated to Nanjing Medical University is a major neuro-psychiatric specialized institution that is located in East China and serves a population of 0.3 billion. The nature of the study was retrospective.

2.1. Diagnoses, ICD-10-CM, and electronic medical records system

Diagnoses were all based on the international classification of diseases, 10th revision, clinical modification (ICD-10-CM). All diagnosis in our electric case records were based on the ICD-10-CM. If there were handwritten medical records which were not according to the ICD-10-CM, these cases would be excluded. We searched for the following two conditions: 1) the principal diagnosis was “epilepsy” or “status epilepticus (SE)” or “frequent seizures”, and patients were unaware of the cause or requested emergency treatment; and 2) secondary diagnoses, i.e. the principal diagnosis was Parkinson's Disease (PD) and an additional diagnosis of epilepsy, or where conditions indicated the co-occurrence of two or three disease types at the time of admission with “epilepsy” as the “principal diagnosis” at that stage.

The inclusion criteria were also defined as patients with additional diagnoses, i.e., previously diagnosed as epileptic patients who had manifested mental disorders or anti-epileptic drug poisoning at time of admission. A patient could have been hospitalized several times during the observation period due to similar reasons, but only the recent admission time was considered in our present study. This included patients seeking long-term care and rehabilitation, or psychiatric patients admitted having similar psychotic relapses, or due to alcoholism or chemical dependency.

2.2. Case records

All patients with epilepsy were documented from all departments in our hospital, including the neurology department, neurosurgery department, epilepsy center, geriatrics center, children's medical center, psychiatry department, department of traditional Chinese medicine, rehabilitation department, and psychology department. The admission time defined as observation time was between January 2011 and April 2017.

General data, principal disease diagnosis and data that included their mental and somatic complications of the enrolled patients were compiled. The data included: age, gender, any metabolic diseases, frequent seizures or SE, multiple sclerosis (MS), newly diagnosed epilepsy with unknown etiology, brain tumour, autoimmune diseases, central nervous system (CNS) infection, hydrocephalus, cerebral vascular disease (CVD) including transient ischemic attack (TIA); toxins including anti-epilepsy drugs or other toxins; pleuro-pulmonary involvement (mainly lung infection); PD; dementia; and arteriovenous malformation (AVM); mental and behavioral disorders, trauma, dementia, epilepsy, and general data, which included days and the financial cost of in-hospital stay. The costs data were from finance section of our hospital and Medical Insurance Office of Nanjing city. Additional data collected included memory and cognitive difficulties, personality changes, and depression or anxiety (See Table 1).

2.3. Statistical analysis

Numerical data were expressed as mean \pm standard deviation. RMB (Chinese currency) was converted into US dollars over the same period to facilitate a better understanding of our data (for the

international scientific community). Data was analyzed using Student's *t*-test and a *p* value $< .05$ was considered statistically significance.

3. Results

3.1. Demographic characteristics of patients enrolled

During a period of over 2 yrs, 1,148 epilepsy patients were admitted to our hospital. The number of hospitalizations for epilepsy patients, by distinct age group and gender are shown in Fig. 1 and Table 2. Of these, 723 patients (62.98%) were male, aged 49.5 ± 6 yrs and 425 patients (37.02%) were female, aged 39.5 ± 6 yrs. Of the hospitalized epilepsy patients, the prominent age groups were between 18–44 yrs and 45–64 yrs.

3.2. The most common reasons for epilepsy related hospital stays

The most common reasons for hospitalization for patients with epilepsy were 1) CVD involvement including TIA, 2) newly diagnosed epilepsy with unknown etiology; 3) Frequent seizures including status epilepticus epilepsy; 4) CNS Infection; 5) brain tumour; 6) neurologic disorder including mental and behavioral disorders; 7) Lung infection and pleuro-pulmonary involvement; 8) toxins including anti-epilepsy drugs or other toxins; 9) Trauma involvement; 10) AVM; 11) Dementia; 12) hydrocephalus; 13)PD; 14)MS; 15) autoimmune diseases; 16) others (Fig. 1.2). Apart from the unknown etiologies underlying epilepsy for admission, the two main reasons for hospitalization were motor complications (37%) and psychosis (24%) (Fig. 2).

3.3. Reasons for length of hospitalization stay and financial burden for inpatients with epilepsy

Fig. 3 shows the average number of hospitalization days for epilepsy patients. As shown in Fig. 3, the top reasons were: 1) PD, 2) Dementia, 3) Trauma, 4) Neurologic disorders including mental and behavioral disorders; 5) Cerebral Vascular involvement including TIA; 6) hydrocephalus; 7) CNS Infection; 8) Toxins including anti-epilepsy drugs or other toxins; 9) lung infection; and 10) autoimmune diseases. Apart from trauma and hydrocephalus, most of the patients were inter-departmental.

3.4. Hospital mortality

Totally 17 out of 1148 patients (14.81‰) died during hospitalization. The common causes of death were 1) lung infection (mainly pneumonia), 2) depression (death by suicide) 3) frequent seizures including SE, 4) CVD and 5) brain tumours. There were no other reportable causes of death.

3.5. Costs and charges

Total hospital fees (Chinese currency RMB) were converted to US dollars via the exchange rate over the same period in the present study. There were four different sources of payment: 1) 70% of patients had China medical insurance of urban employee and these patients only should pay 25% of their hospitalization charges; 2) 20% of patients had China new-style urban-rural cooperative medical insurance and they should pay 50% of their hospitalization charges; 3) the costs of 3% patients were absolutely paid by the commercial insurance company; 4) the residential 2% patients had to pay the costs by themselves.

As shown in Fig. 4, the top ten reasons for the highest hospital fees for inpatients with epilepsy were: 1) PD, 2) AVM; 3) Trauma; 4) Dementia, 5) brain tumour, 6) Cerebral Vascular involvement including TIA; 7) newly diagnosed epilepsy with unknown etiology; 8) lung infection; 9) hydrocephalus; 10) Neurologic disorder including mental and behavioral disorders; 11) Toxins including anti-epilepsy drugs or

Table 1
Causes of Seizures.

Condition	Examples
Autoimmune disorders	Hashimoto’s encephalopathy; lupus encephalopathy; primary cerebral vasculitis, anti-NMDA (N-methyl-D-aspartate) receptor encephalitis, multiple sclerosis
Hydrocephalus & Cerebral edema	Normal pressure hydrocephalus; eclampsia, hypertensive encephalopathy
Brain tumours	melanoma, hemorrhagic lesions, multiple metastases, slowly growing primary tumours, dysembryoplastic neuroepithelial tumours, Ganglioglioma, glioblastoma multiforme, low-grade astrocytoma, Meningioma, metastatic tumours, oligodendroglioma, gangliogliomas
CVD(only need medical treatment)	Cardiac arrhythmias, carbon monoxide toxicity, near suffocation, stroke,
Trauma	Birth injury, blunt or penetrating injuries, posttraumatic seizures occur in 25 to 75% of patients who have brain contusion, skull fracture, intracranial hemorrhage, prolonged coma, or focal neurologic deficits.
CNS infections	AIDS, brain abscess, falciparum malaria, meningitis, neurocysticercosis, neurosyphilis, rabies, tetanus, toxoplasmosis, viral encephalitis
Congenital or developmental abnormalities	Cortical malformations, genetic disorders (eg, fifth day fits, lipid storage diseases such as Tay-Sachs disease), neuronal migration disorders (eg, heterotopias), phenylketonuria
Drugs and toxins	Camphor, cocaine and other CNS stimulants, imipenem, lead, pentylenetetrazol, picrotoxin, strychnine, alcohol, anesthetics, barbiturates, benzodiazepines
AVM	Hemorrhage, hydrocephalus
Hyperpyrexia	Drug toxicity (eg, with amphetamines or cocaine), fever, heatstroke
Lung infection	Patients with lung infection may be a lead to hospitalization, or it may be prone to lung infections in patients with epilepsy
Mental and behavior disorders	Decompression illness, hyperbaric O ₂ treatments

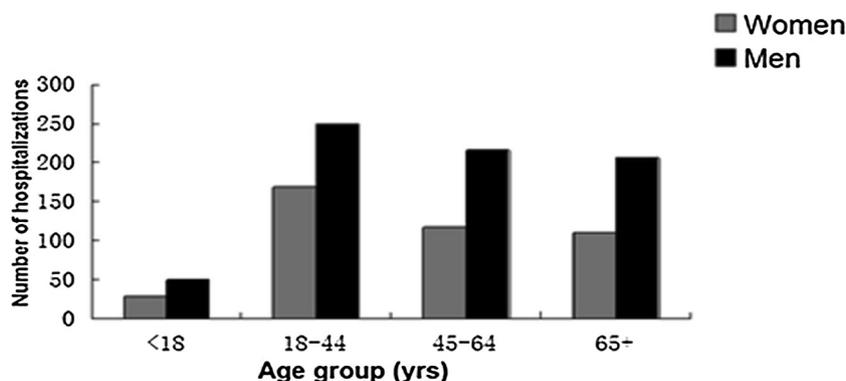


Fig. 1. Numbers of male and female hospitalized epilepsy patients by the distinct ages.

Table 2
Number and rate of hospitalizations for epilepsy.

Age (yrs)	Women	Men	Total
	No.	No.	
< 18	29	50	79
18–44	169	250	419
45–64	117	216	433
65+	110	207	317
Total			1148

other toxins. Of these patients, AVM, trauma, brain tumour and hydrocephalus were the main reasons for surgery, while PD, dementia, CVD, infection and mental and behavioral disorders were treated in the neurology department.

4. Discussion

Epilepsy is one of the most common chronic disorders worldwide and often results in several serious problems and complications [7]. It affects the quality of life and impairs work and social activities, particularly in developing countries. Patients with epilepsy have high morbidity and mortality compared to several other diseases. Although some types of epilepsy have no identifiable etiology, and are termed idiopathic epilepsy, recent studies have demonstrated that several epilepsy types have specific underlying mechanisms for seizures occurring. To better understand epilepsy and manage them in future, it is critical to

analyze patients with epilepsy that are hospitalized for different reasons. The present study investigated the causes and risk factors leading to hospitalization in a very large cohort of adult epilepsy patients (1148). In addition, we investigated the costs, the length of hospitalization and patient mortality. From our results, young and middle-aged patients formed the majority of our inpatients.

There are several causes of epilepsy and were mainly due to genetic or metabolic dysfunctions [8,9]. In our present study, we found that CVD was the major reason observed in epilepsy patients for hospitalization. This trend will increase, especially in the developing countries like China that has a high incidence of stroke but a relatively high cure rate. Our current results are consistent with previous studies [10]. Prognostic interactions with CVD and epilepsy have been demonstrated. Epilepsy is one of the most common disorders after stroke, and includes early-onset seizures and late-onset epilepsy. Conversely, epilepsy increases the chance of developing stroke based on previous research [11]. As the population ages, the association between CVD and epilepsy will increasingly become more prominent [12]. In addition, special attention should be paid regarding the adverse effects of certain antiepileptic drugs to increase the risks of myocardial infarction, CVD, and mortality in patients with or without stroke [13,14].

In the present study, PD was the major reason for inpatient hospital stay and costs of epilepsy. It is well known that neuro-degenerative diseases, such as PD and Alzheimer’s disease (AD), account for the highest global disease burden. As with stroke mentioned above, age-related neurodegenerative disease is one of the leading causes of inpatient hospitalization of epilepsy. China has a rapidly aging population. Currently, 12.5% of the Chinese population is over 65, and this

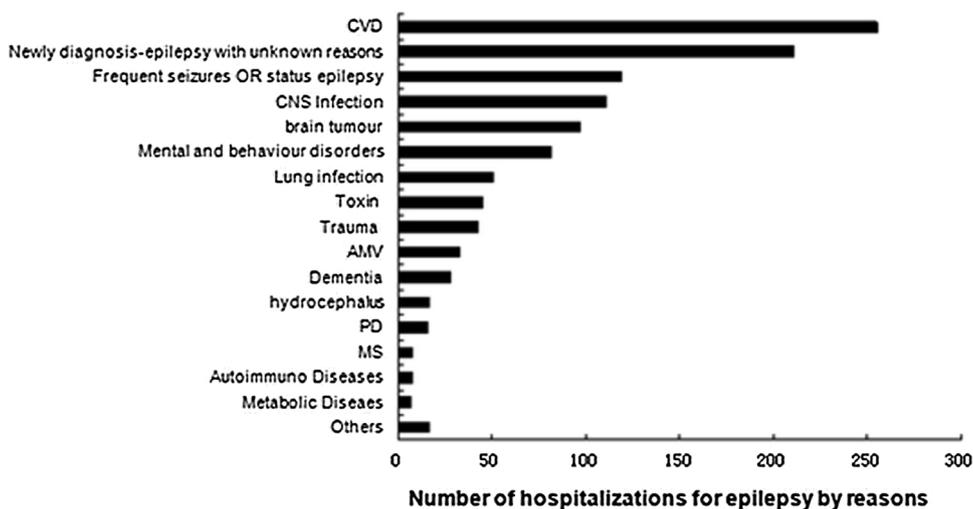


Fig. 2. Numbers of the hospitalized patients with epilepsy by the different reasons.

figure is expected to reach 33% by 2030 [15]. Neurodegenerative diseases are usually debilitating and largely untreatable conditions that are strongly associated with age [16]. Epilepsy had been recognized as an uncommon comorbidity of PD and the coexistence had only been found in several cases considered not direct association between them [17]. The reason for this may be that non-motor seizures in PD were missed, or the rhythmic jerking was misdiagnosed as motor symptoms of PD [18]. Currently, PD and other neurodegenerative disorders have also been reported to increase the incidence of epilepsy [19]. Gruntz K et al [20] had reported that the OR of epileptic seizures was 1.68 in PD patients compared with PD-free individuals suggesting that incident PD is associated with an increased risk of incident epileptic seizures. Epilepsy patients with these neuro-degenerative diseases will be harder to treat due to their chronic and incurable conditions, which results in longer hospital stays. In our present study, the financial burden of PD and cognitive disorders were high. Our data only included the cost of treatment for these brain disorders with epilepsy, and did not account for the loss in productivity in patients with epilepsy and for their caregivers. The financial burden would be much higher if the loss in productivity was considered.

Additionally, brain tumour was another common reason for epilepsy. Over 1/3 of patients newly diagnosed with brain tumours develop epileptic seizures [21]. In our hospital, astrocytoma and meningioma were the two most common brain tumours that caused

epilepsy. Brain tumours, vascular malformation congenital abnormalities, and AVMs often require surgery. Hospitalization time is generally not very long, however the cost is very high often with poor prognosis.

Epilepsy may be the initial or even the dominant manifestation of systemic immune disorders [22,23]. “Autoimmune epilepsy” is a new research area, that is currently been actively studied by several researchers in the field of epilepsy. It is defined as the occurrence of seizures mediated by systemic immune responses with early immunotherapy showing good efficacy and prognosis [24,25]. In our study, the higher immune-inflammation that occurred in the brain resulted in seizures with a frequency that was dependent on the type of inflammatory disease, as follows: Hashimoto’s encephalopathy; systemic lupus erythematosus; primary cerebral vasculitis, anti-NMDA receptor encephalitis, multiple sclerosis; Sjögren’s syndrome, primary angitis of the CNS, and demyelinating disorders-MS.

CNS or severe systemic infection could also cause chronic epilepsy or result in acute seizures, especially frequent seizures or SE. Epilepsy risk from CNS infection in our present study was mainly due to viral encephalitis or meningoencephalitis, which is in line with previous studies [26,27]. From our current study, CNS infection was the fourth major reason and the third most cost for epilepsy hospitalization.

In addition to the direct causes of epilepsy, the concomitant disease, complications or comorbidities of epilepsy also lead them to hospitalization. In our present study, lung infection was the primary reason for

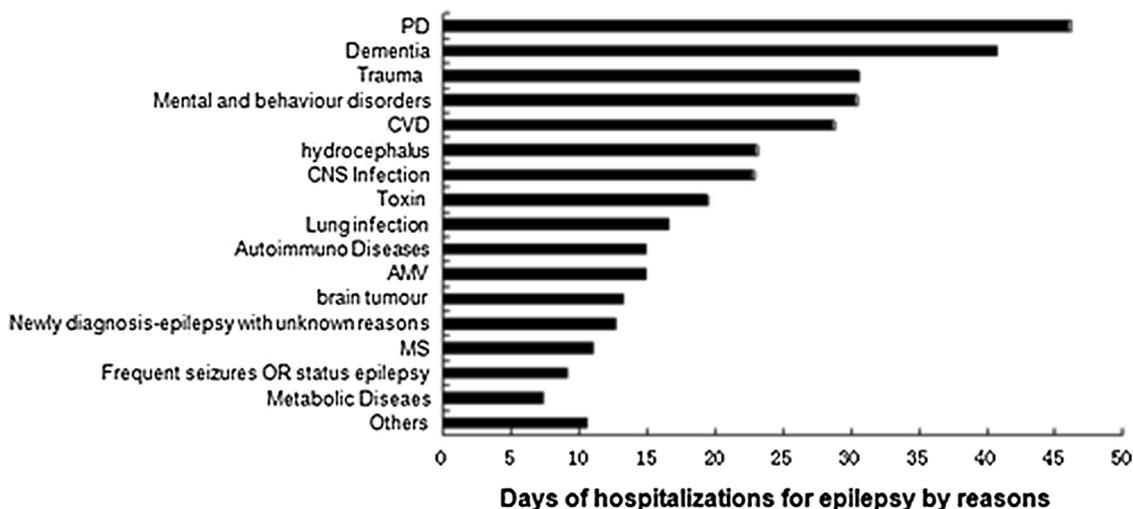


Fig. 3. The hospital days of the epilepsy patients by the different reasons.

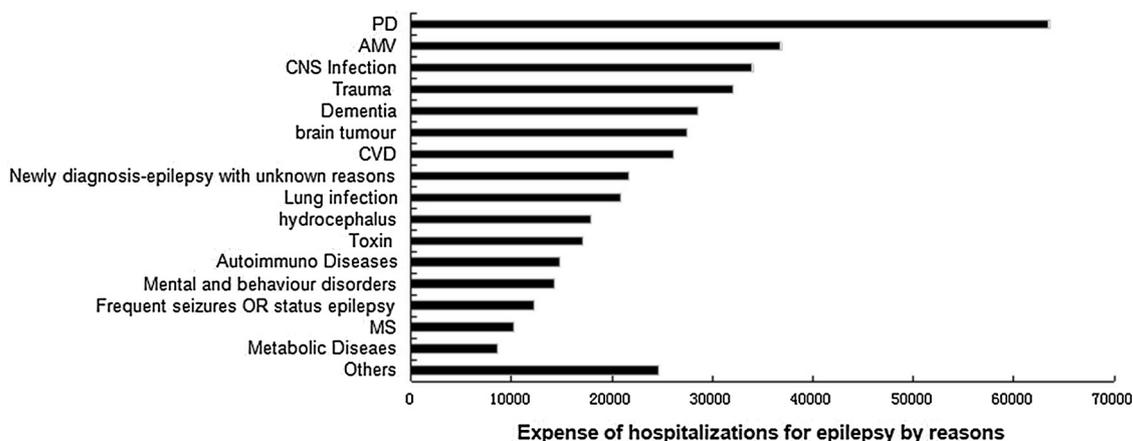


Fig. 4. The hospitalization costs of the epilepsy patients by the different reasons.

patients with epilepsy to be admitted to our hospital. This could be explained by; 1) lung infection usually causes hypoxia and hypercapnia resulting in respiratory insufficiency; 2) seizures lead to lung infections [28,29].

Although previous studies on mortality in patients with epilepsy have been performed, only a few studies specified the causes for epilepsy [30]. In our study, epilepsy patients with lung infection or frequent seizures had the highest death rate, and hence needs early therapeutic intervention. However, psychiatric disorders in patients were an unexpected significant factor for mortality (death by suicide). Patients with epilepsy have a higher risk of suicide [31]. Epilepsy patients with depression were prone to accidental deaths, which should be monitored closely to prevent from death the initial stage. Using a large sample, the application of our results to a wider epilepsy population is of decreased doubtful validity.

These reasons for the hospitalization of epilepsy patients in our present study were not exactly similar to the previous epidemiological studies on the etiology of epilepsy, which were due to infectious, genetics, immune-related or metabolic. In addition to the etiology of epilepsy for hospitalization, the comorbidity and complications of epilepsy are other important factors for hospitalization. Hence our study significantly demonstrates the actual reasons for hospitalization, as well as demonstrating the significant financial burden for epilepsy patients.

5. Conclusions

Taken together, apart from the stigma and discrimination, epilepsy patients and their families also have to deal with long inpatient hospital stays, high hospital mortality and costs. Our study showed that young and middle-aged epilepsy patients were more likely to be inpatients. There were several different reasons for hospitalization. Initial admission only accounted for 13% after diagnosis, which was basically due to frequent seizures including SE. However, in subsequent admissions, the most common reason was CVD, PD, dementia, infection and toxins. Consequently, the hospitalization days of these patients were high with the subsequent high hospitalization costs. Particular attention should be paid to epilepsy patients with SE, lung infection or depression due to a higher risk of death. They should be closely monitored to prevent suicide from the onset of the disease and given prompt intervention.

Declaration of Competing Interest

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personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled.

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