

Evaluation of the disease burden of sporadic Creutzfeldt-Jacob disease with the surveillance data from 2013 to 2017 in China

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Research Article

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Abstract

Background Sporadic Creutzfeldt-Jacob disease (sCJD) is the commonest type of human prion disease and cause 100% fatality. The morbidity of sCJD is about 1 to 2 cases/million/year worldwide.

Methods In this study, the disease burden of sCJD in China was evaluated based on the data of Chinese National CJD Surveillance from 2013 to 2017.

Results The Disability-Adjusted Life Year (DALY) of sCJD was measured with 753 probable sCJD patients. The total DALY of 753 sCJD cases in the past five surveillance years was 16202.62 person-years. The Years of Life Lost (YLL) was the predominant component for DALY reaching to more than 95%, while the Years Lost due to Disability (YLD) accounted for less than 5% only. The highest DALY was noticed in the group of 45-50 year-old (6541.49), followed by the groups of 60-69 year-old (6311.25). Furthermore, the indirect economic burdens of 753 sCJD patients were estimated with the official capital data. Total indirect economic burden for five years was 372.08 million RMB (1US \$=6.9 RMB), with the average of 494,133 RMB per case. The patients aged 45-59 years old were the predominant population that accounted for approximate 73% of total indirect economic burden. Although still lacking the exact annual incidence of sCJD in China, the DALY intensity of sCJD in China could be estimated and predicted as 2.2 to 4.4 person-years /100,000 with the global morbidity of sCJD.

Conclusion This is the first disease burden assay for sCJD in China, which will supply fundamental evidence for further development of medical strategy.

Introduction

Sporadic Creutzfeldt-Jacob disease (sCJD) is the commonest subtype of human prion diseases with the estimated incidence of 1 to 2 case /million/year globally (1-3). A serial of neuropsychiatric symptoms may be noticed in sCJD patients, mainly including progressive dementia, pyramidal and extrapyramidal symptoms, myoclonus, visual or cerebellar disturbance, as well as mutism in the late stage (4, 5).

Compared with other neurodegeneration diseases, such as Alzheimer disease (AD), Parkinson disease (PD), amyotrophic lateral sclerosis (ALS), etc., sCJD usually shows rapid progression and short clinical duration. Most of the patients die within 2 years after onset and the fatality rate of sCJD is 100% (6, 7), which causes great disease burden not only on the patients and their families but also on the society.

China has started the national CJD surveillance since 2006 Up to 2018, thousands of sCJD cases and more than 150 cases of various genetic prion diseases have been diagnosed via China National surveillance for CJD (CNS-CJD) (8, 9). Like the features of sCJD globally, the prevalence of Chinese sCJD patients does not reveal any seasonal- and geographic-association. The most frequent onset age is in the group of 60-69 year-old (y). The median survival times after onset is estimated as 7 months (6).

Disability-Adjusted Life Year (DALY) is measurement of the gap between current health status and an ideal health situation, which has been widely used by countries in the evaluation of the burden of many

diseases, including neurodegenerative disorders. However, there is no special report for the DALYs of sCJD in the published literature, and the relevant data for sCJD in China remains unknown. In this study, by using the data of national CJD surveillance from 2013 to 2017, we evaluated and calculated the DALYs based on 753 Chinese probable sCJD patients, and further estimated the indirect economic burden of sCJD.

Materials And Methods

Case diagnosis

The diagnosis of sCJD in CNS-CJD was conducted based on the Diagnostic Criteria for CJD issued by Chinese National Health Commission in 2017 and relevant surveillance documents (8, 10). Briefly, possible sCJD is based on the rapidly progressive dementia, with at least two out of the following four clinical features, i.e., myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, akinetic mutism. Probable sCJD needs at least one positive result out of the following examinations or laboratory test: typical periodic sharp wave complexes (PSWC) on electroencephalogram (EEG), special abnormalities (symmetrical or asymmetrical cortical "ribbon" signs on diffusion-weighted imaging (DWI), high signal in caudate/putamen or high signal in bilateral posterior tuberosity of thalamus on proton density phase) on magnetic resonance imaging (MRI) brain scan, or positive CSF protein 14-3-3 in Western blot. Definite sCJD is still depending on the positive results of neuropathological and/or PrP^{Sc} tests in the brain tissues obtained by biopsy or autopsy. The final diagnosis was made by an expert board including neurologists, neuropathologists, epidemiologists and laboratory staff.

Data collection

All information of the sCJD patients came from the center of CNS-CJD, China CDC. The reporting and diagnostic procedures for various human prion diseases within CNS-CJD were described elsewhere (9). In this study, we recruited all probable-diagnostic sCJD patients from 2013 to 2017, totally 753 cases. The death times for the patients were either via the follow-up survey or via accessing into the Disease Surveillance Points System. The national population data and Gross domestic product (GDP) data are derived from the statistical yearbook of the Chinese National Bureau of Statistics (11). According to the Coale and Demeny West Level 26 Life Table, the life expectancy of women at birth is 82.5 years, and that of men at birth is 80.0 years.

Calculation of DALY for sCJD

DALYs for a disease or health condition are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality in the population and the Years Lost due to Disability (YLD) for people living with the health condition or its consequences. One DALY means a total healthy year lost. The calculations for DALY, YLL and YLD of sCJD were conducted according to the protocols described elsewhere (12, 13). Disability weights were extracted based on surveys of the experts who had a basic knowledge about prion (14).

Calculation of indirect economic burden for sCJD

Indirect economic burden = productivity weight × DALY × GDP per capita (15, 16). The productivity weight varies among the different age groups. According to the published data (17), the productivity weights of different age groups were 0.15 for the group of 0-14 year-old (y), 0.75 for the group of 15-44 y, 0.80 for the group of 45-59 y, and 0.1 for the group above 60 y.

Statistical analysis

The database was established by Microsoft Excel 2016. A descriptive analysis was applied. ArcGIS 10.3 was used to draw thematic map of Chinese sCJD patients' distribution. T-test was applied to analyze whether there were differences in DALY caused by sex.

Results

Totally, 753 sCJD patients diagnosed in the National Center for CJD surveillance network from 2013 to 2017 were recruited in this study. The case numbers from 2013 to 2017 were 108, 134, 133, 159 and 219, respectively. Up to the end of August 2018, there were 45 patients referred in 2017 still alive. The gender ratio was 1:0.9 (M:F). Majority of the patients was in the groups of 60-69 y (325, 44.2%), 45-59 y (247, 33.6%) and 70-79 y (132, 18.0%). Only small portions of the sCJD patients were younger than 45 y (31, 4.2%) or older than 80 y (18, 2.4%). Based on the permanent addresses, large portions of the patients were from the eastern and middle part of China.

DALYs for sCJD

The losses of YLL, YLD of sCJD patients each year were calculated, and then, the DALYs of sCJD patients each year were generated. As shown in Table 1, the total DALY of 753 sCJD cases in the past five years was 16202.62 person-years, showing an increased tendency along with years, which was directly due to the increased numbers of the diagnosed sCJD cases. Analysis of the components of DALYs revealed that YLLs were obviously predominant, reaching to more than 95%, while YLD accounted for less than 5% only.

Table 1
DALYs of sCJD patients from 2013 to 2017

Year	Case number	DALY	YLL	YLD	YLL/DALY(%)
2013	108	2520.959	2421.599	99.360	96.1
2014	134	3127.607	3006.167	121.440	96.1
2015	133	2789.225	2666.865	122.360	95.6
2016	159	3663.414	3517.134	146.280	96.0
2017	219	4101.412	3899.932	201.480	95.1
Total	753	16202.616	15511.696	690.920	95.7

The distributions of DALY of 753 sCJD patients in five years among the different age groups were further analyzed. As shown in Fig 1, the highest DALY was noticed in the group of 45-50 y (6541.49), followed by the groups of 60-69 y (6311.25). Total DALYs decreased apparently in the groups of 70-79 y (1594.42) and 30-44 y (1342.22), and became much less in the senior group (238.09) and young group (175.14). Subsequently, the gender was introduced into the evaluation. Both genders revealed the similar profiles of DALYs in the different age groups, with slightly higher DALYs in the female group of 45-59 y but without statistical difference (Fig 2). Those data highlight that the patients aged 45-69 y contribute mainly to the DALYs and undertake the main disease burden. Life loss is the deterministic factor for the DALYs of sCJD patients.

Indirect economic burdens for sCJD

To estimate the indirect economic burden of Chinese sCJD patients, the official capital data were introduced. The estimated indirect economic burdens of sCJD were summarized in Table 2. Total indirect economic burden for five years was 372.08 million RMB (1US \$=6.9 RMB). The average indirect economic burden per case was 494,133 RMB. As expected, the indirect economic burden each year revealed an increased trend along with years because of the increase of sCJD cases, meanwhile, did not illustrate significant difference between male and female patients by different years ($t=-0.967$, $P=0.362$).

Table 2

The estimated indirect economic burden of sCJD patients from 2013 to 2017

Year	Male	Female	Total	Per case
2013	20393184.47	31600082.91	51993267.38	481419.14
2014	43344742.26	25117569.03	68462311.28	510912.77
2015	29093147.59	27349855.36	56443002.96	424383.48
2016	37211143.41	49562003.02	86773146.43	545743.06
2017	51525375.83	56885517.08	108410892.91	495026.91
Total	181567593.57	190515027.39	372082620.96	494133.63

The indirect economic burdens in various age groups were estimated further. As expected, the patients in the age of 45-59 y were the predominant population for indirect economic burden, causing 271.49 million RMB losses that accounted for approximate 73% total indirect economic burden (Fig 3). Despite of obviously fewer case numbers (n=28), the patients in the group of 30-44 y contributed to more indirect economic burdens (51.73 million RMB) than those in the group of 60-69 y (32.71 million RMB) with the most case numbers (n=325).

Discussion

In this study, we have for the first time calculated the DALYs of Chinese sCJD based on 753 probable sCJD cases from 2013 to 2017. Overall, there are 16202.62 DALYs for 753 sCJD cases from 2013-2017, with the average annual loss of 3240.52 DALYs. Patients with the ages from 45 to 69 are the most affected populations, contributing to 79.3% of the DALYs. Moreover, YLLs each surveillance year contribute over 95% of individual annual DALY, reflecting, from another point of view, a rapid progression and short duration of sCJD.

It is well known that if the clinical course of a disease is relatively stable, the results based on the numbers of disease using are close to that of the numbers of morbidity. In general, the exact data of morbidity are relatively difficult to obtain, while the data of the people with a special disease are much easy to be acquired. We have to confess that the numbers of sCJD in this study are far below the expected morbidity, which is hard to represent the accrual DALYs of sCJD in China. However, the morbidity of sCJD is fairly stable worldwide, which maintains 1 to 2 case /million /year (18). Although the calculated incidences of sCJD in some European countries show increasing trend during the past decade, the enhanced surveillance capacities are believed to be the reason (19, 20). CJD is a spontaneous neurodegenerative disease. The current knowledge shows that its incidence has nothing to do with race and gender. In fact, based on our 10 years CJD surveillance data in Beijing, the incidence is close to 1 case/million/year (21). Taking this morbidity data and the population in China, the annual case

numbers of sCJD in China should be 1400 to 2800. Subsequently, according to the DALYs of 753 sCJD cases in this study, the average annual DALY of sCJD is estimated as 30124.36 to 60248.71 person-years. With the average population for the five years from 2013 to 2017 as the denominator, the DALY intensity of sCJD in China would be predicted as 0.022 to 0.044 person-years per 1,000 population, or 2.2 to 4.4 person-years per 100,000 populations.

By reviewing the published data, we have compared the predicted DALY intensity of sCJD in China with other neurodegeneration diseases, malignant tumors and some infectious diseases in China (Table 3). As expected, AD and many malignant tumors, e.g., lung cancer, liver cancer, stomach carcinoma and pancreas cancer possess much high DALYs. The DALY of sCJD seems to be comparable with those of multiple sclerosis (3.32 person-years/100,000) and myasthenia gravis (2.23 person-years /100,000). Compared with infectious diseases, the DALY of sCJD is obviously lower than that of TB, AIDS, syphilis and hepatitis B, similar as rabbis, and higher than that of hepatitis C, measles and *Shigella* dysentery. It indicates that although the morbidity of sCJD is low, its 100% fatality cause relatively high DALY.

Table 3
Comparison of the DALY intensities of different diseases

Disease	DALY intensity (person-years /100,000)
Alzheimer disease	503
Lung cancer	462
Liver cancer	325
Stomach cancer	96
Lung tuberculosis	82.3
Pancreas carcinoma	26.23
AIDS	8.2
Syphilis	7.7
Hepatitis B	6.0
sCJD	4.4–2.2
Multiple sclerosis	3.32
myasthenia gravis	2.23
Rabbis	2.2
Hepatitis C	0.3
Measles	0.3
Shigella dysentery	0.2

The total indirect economic burden of 753 sCJD patients from five years is estimated to be 372.08 million RMB (Chinese current, CNY). sCJD usually occurs in the older people. 475 of 753 sCJD patients (64.6%) in this study are over 60 years old, but account for only 11.4% of indirect economic burdens. It is understandable since we have set in this study that the main labor force for society production is the population from 14 to 59 y. However, more and more senior persons over 60 years old continue to work in China, particularly in the central cities. In addition, the retirement age in China probably will be postponed from 60 to 65 years old. Those factors will influence the estimation of indirect economic burdens of diseases, especially the diseases involving in elder population. Another issue that needs to be considered is that with the improvement of health awareness and medical conditions, the extension of people's life span will also cause the calculated DALY and indirect disease burden to be lower.

In addition to the indirect economic burden calculated by DALY and GDP, the disease burden also includes the direct economic burden, which includes various expenses directly consumed by society and families in the course of disease prevention, diagnosis, treatment, and rehabilitation. The economic status of the patient's family and the cognition of the disease affect the direct economic burden. Therefore, under certain economic conditions, increasing the public's awareness of prion disease and reasonable medical treatment can greatly reduce the financial burden of patients' families.

Conclusion

In this study, a total of 753 clinically diagnosed cases of sCJD diagnosed in China Creutzfeldt-Jakob disease surveillance system from 2013 to 2017 were included. The indirect economic burden was calculated through DALY combined with human capital method. This is the first disease burden assay for sCJD in China, which will supply fundamental evidence for further development of medical strategy.

Declarations

Ethical Approval and Consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by Ethical Review Committee of National Institute for Vial Disease Prevention and Control, China CDC. Following the principle of informed and voluntary, all signed informed consents were collected and stored by the China CJD Surveillance Center.

Consent for publication

Written informed consent for publication was obtained from all participants.

Availability of supporting data

The data and material supporting the findings could be obtained from Xiao-Ping Dong, email dongxp238@sina.com.

Competing interests

The authors declare that they have no competing interests.

Fundings

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Authors' contributions

CG, LZ and XPD designed the study. KX and WZ collected the data. YW and CC analyzed the available data. CG and LZ prepared the manuscripts. QS and XPD reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Figures

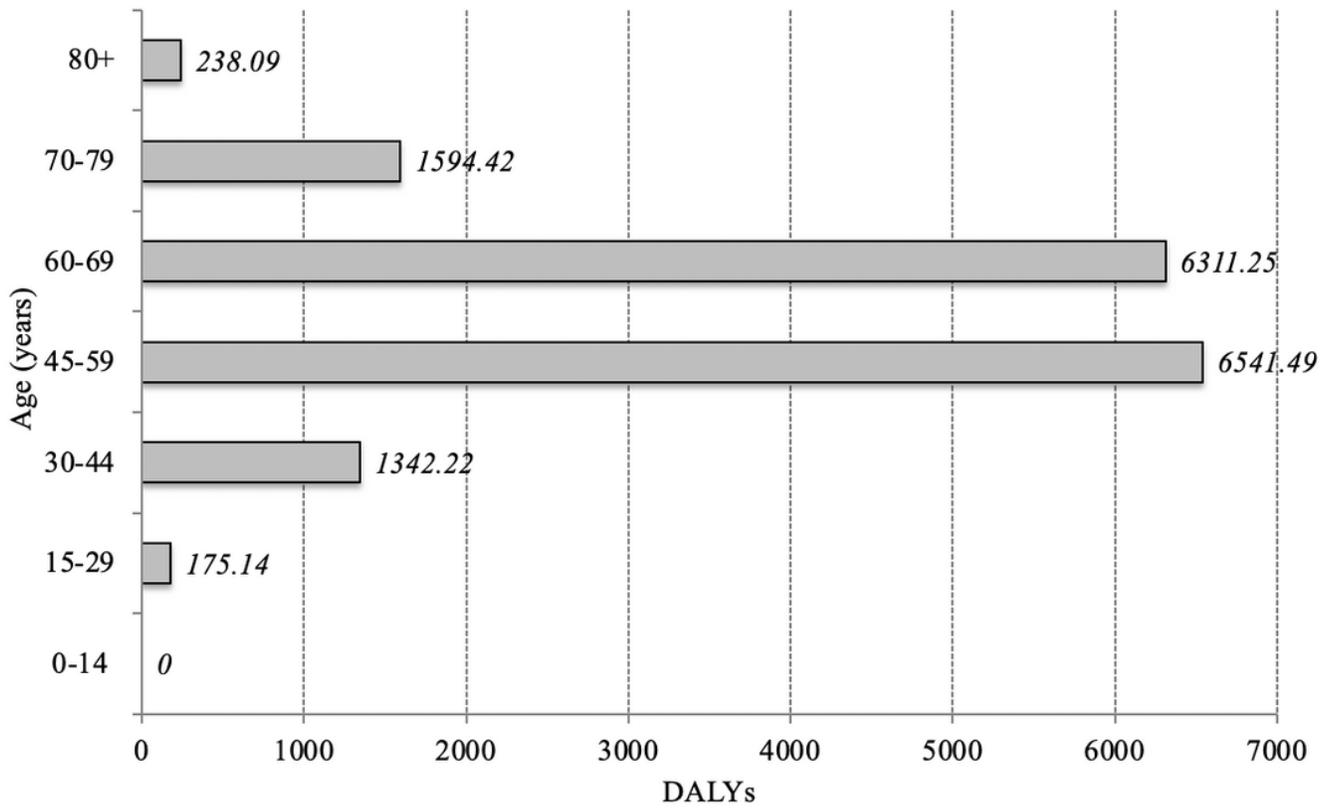


Figure 1

DALYs caused by the sCJD patients in different age groups. DALYs are showed in X axis and the age groups are showed in Y axis.

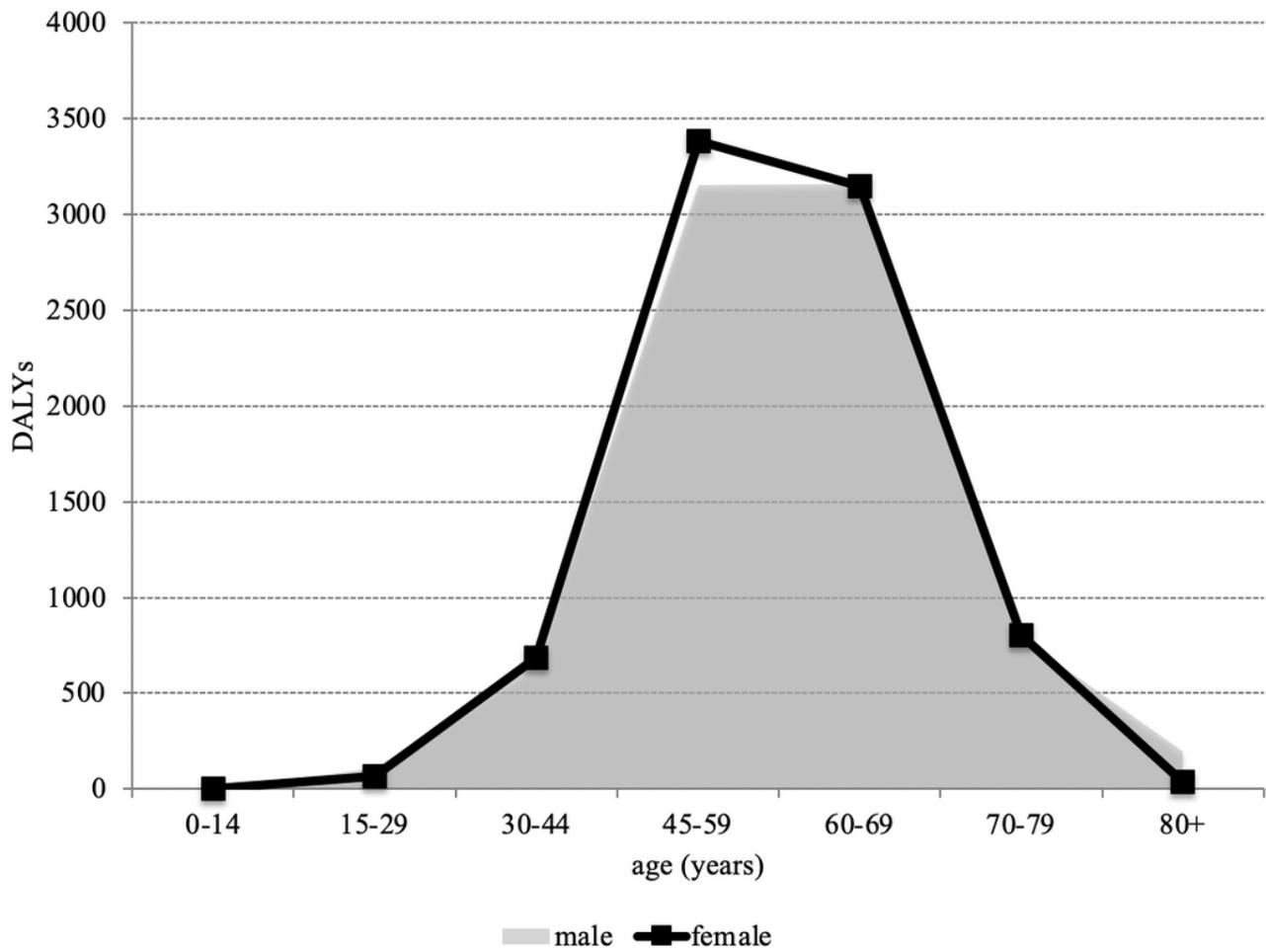


Figure 2

DALYs caused by male and female sCJD patients in different age groups. DALYs are indicated in Y axis and the age groups are showed in X axis.

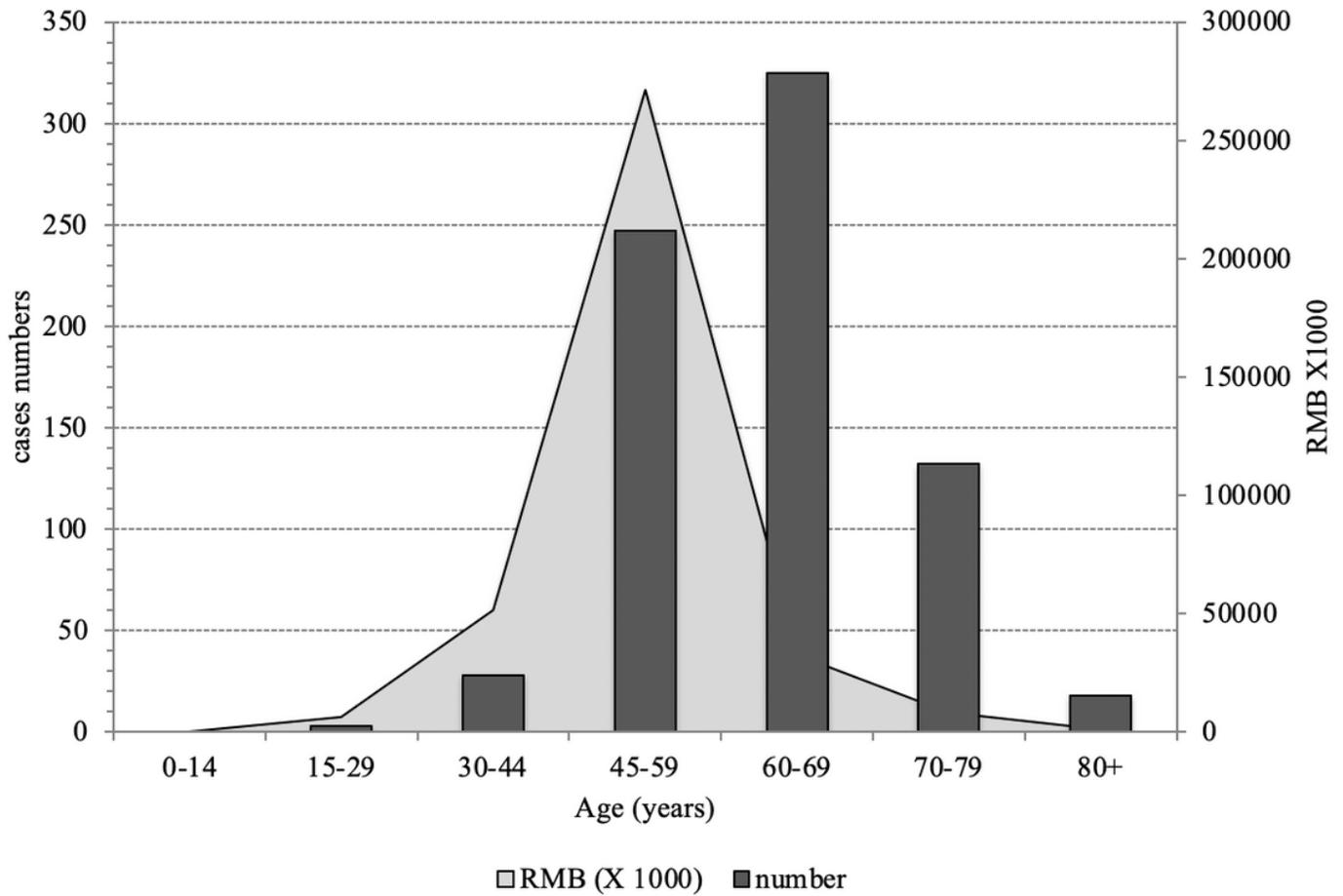


Figure 3

Indirect economic burdens of sCJD patients in different age groups. Case numbers in different age groups are showed in the left Y axis and the indirect economic burdens are showed in the right Y axis. The age groups are indicated in X axis.