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Research Article

Economic burden of Thai patients with inflammatory demyelinating central nervous system disorders (IDCDs)

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ABSTRACT

The economic impact has never been explored among Thai patients with inflammatory demyelinating central nervous system disorders. Thus, this study aimed to evaluate economic burden of Thai patients with inflammatory demyelinating central nervous system disorders i.e., clinical isolated syndrome (CIS), multiple sclerosis (MS), and neuromyelitis optica spectrum disorders (NMOSD) based on a societal perspective using prevalence-based approach. Data on direct medical cost were retrospectively retrieved from an electronic health record database of the patients receiving care in three specialized clinics for MS and related disorders. Data on direct non-medical and indirect costs were collected from face to face interviews using developed data collection forms. All expenses were adjusted to the 2017 year value using consumer price index. The descriptive statistical analysis was undertaken. Direct medical cost was the highest proportion (58%) of total annual average cost of MS, CIS and NMOSD patients. The annual average direct non-medical cost of all patients was 1,969±3,187 USD and informal care cost was the largest portion (56%). The total economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand was 6,287,000 USD, which NMOSD (3,447,000 USD) consumed the highest cost compared with MS (2,390,000 USD) and CIS (450,000 USD). This study demonstrated the high economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand. This would be a useful evidence which requires attention from policy makers in Thailand.

1. INTRODUCTION

Inflammatory demyelinating of central nervous system disorders i.e., clinical isolated syndrome (CIS), multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD) characterized by loss of myelin with variable loss of axons could result in a variety of neurologic manifestation in the central nervous system (CNS) i.e., brain, spinal cord, and optic nerve[1]. CIS refers to an early sign of MS or a first episode of neurologic symptoms that lasts at least 24 hours, whereas MS patients experience more than one episode. The MS diagnosis can be made when magnetic-resonance imaging (MRI) findings of CIS patients confirm that an earlier episode of damage occurred in multiple different areas in the CNS, whereas NMOSD refers to an autoimmune disorder in which

immune system cells and antibodies primarily affects to optic neuritis (blind) and/or transverse myelitis (muscle weakness on either upper extremities or lower extremities). To differentiate MS from NMOSD, anti-aquaporin 4 (AQP4) antibody is found in patients with NMOSD but not MS as there is no specific immune target identified in MS patients which indicate that MS cannot be classified as an autoimmune disease at present [1].

The prevalence of MS/CIS was higher than that of NMOSD i.e., 140 and 3.9 per 100,000 in US[2,3] or 8.5 and 4.4 per 100,000 in Japan[4,5] and this pattern was seen throughout the world. Currently MS and CIS were much well aware and disease modifying therapies (DMTs) such as immune-modulators have been approved worldwide including Thailand, while NMOSD was under investigated with promising trend in both pathogenesis and its treatment in the near future. Clinical features of inflammatory demyelinating of central nervous system disorders typically show onset of disease in the productive working age, at 20-40 years old, which predominantly occurs in females, and usually leads to disability and death in most patients developed over 10-15 years[6]. Patients with inflammatory demyelinating of central nervous system disorders on and off treatment are facing disability problems, such that it potentially leads to a decrease in their quality of life. These non-compliant patients consume a huge portion of the healthcare resource resulting to economic burden to other MS patients and their families.

Disability in inflammatory demyelinating of central nervous system disorders is commonly quantified in half-point increments using the Kurtzke Expanded Disability Status Scale (EDSS), a clinician-measured scale[7] which quantifies disability in a number of functional system and allows neurologist to assign a functional system score in a 0–10 scale. EDSS steps of 0-3.5 refer to patients who are fully ambulatory, or at most moderate disability in at least one functional system, 4.0-6.5 refers to patients who are fully ambulatory, with relatively severe disability, who need eventually constant bilateral assistance; meanwhile 7.0-9.5 refers to patients who are restricted to wheelchairs or confined to bed and 10 is death caused by MS. Consequently, patients with more disease severity spend higher healthcare costs which can affect to an increase in economic burden to their families.

It was found that all previous published studies related to economic burden in inflammatory demyelinating of central nervous system disorders were performed in MS patients. In US[8,9] and Europe[10,11], MS patients tend to be hospitalized more compared to patients with other diseases. The estimated lifetime cost of MS patients was much higher compared to other neurologic disorders[12]. Furthermore, more than half of employed MS patients left their jobs within a decade due to their disability[13,14]. A nine-fold increase in productivity loss and five-fold increase in informal care from EDSS score 0-1 to 8-9 in patients due to the neurologic disability of MS patients in Belgium[15]. Furthermore, indirect cost was the large portion of costs associated with MS. The direct medical cost was a major contributor in early stages[16] and the indirect cost was mainly attributed to early withdrawal of MS patients from active life in Canada[14,17] and Sweden[18]. It should be noted that although informal care cost i.e., the opportunity costs which caregivers or patients' relatives spend time on taking care of the patients instead of working for earning incomes, was essential to reflect true economic burden in chronic diseases, it is often neglected by researchers because such data are usually difficult to collect using face to face interviews or questionnaires compared to direct medical cost data which can easily be obtained using electronic health records at hospitals[19]. This can lead to the underestimation of the real economic impact from patients' perspective.

In Thailand, the prevalence of MS/CIS and NMOSD has been reported to be 0.203 and 0.402 per 100,000[20]– approximately 130 patients with MS/CIS and 260 patients with NMOSD based on Thai population of 65 million. Currently, there is an ongoing patient registry under Thai MS Society showing an increase awareness of Thais in inflammatory demyelinating of central nervous system disorders. However, until now the economic burden on patients and their caregivers has never been explored. Therefore, this study aimed to evaluate the economic burden of Thai patients with inflammatory demyelinating central nervous system disorders based on a societal perspective. The results from this study would provide evidence-based information to inform policy makers to recognize the level of disease burden for inflammatory demyelinating central nervous system disorders in Thai context. This could be also used as the cost information for further economic evaluation study of the treatments for patients with inflammatory demyelinating central nervous system disorders in Thailand.

2. MATERIALS AND METHODS

Prevalence-based approach was applied to estimate the total economic burden of Thai patients with inflammatory demyelinating central nervous system disorders for one year based on a societal perspective. All direct medical, direct non-medical and indirect costs were calculated. Direct medical cost included costs of diagnosis procedure, medication treatment, surgical intervention, laboratory test and alternative treatment. Meanwhile, direct non-medical cost – cost incurred by patients and families to receive treatment - included transportation cost (actual payment or approximation with public transportation type if patients could not indicate the actual expenses), additional food per day per visit for patients and caregivers, additional hotel stay or accommodation, facility modification (home alterations, ramps, stairs glides, etc.), equipment needed (wheel chairs, walkers, etc.), formal care (paid caregiver) and informal care (unpaid caregivers who spent times on taking care of patients).

Informal care cost included only time consumed on patients (preparing food, cleaning, bathing and massaging, etc.), but not for routine activities such as accompanying. Indirect cost was the productivity cost forgone from morbidity and mortality due to inflammatory demyelinating central nervous system disorders. Morbidity cost was the productivity lost from illness or early retirement due to disability, and the mortality cost was the productivity lost from premature death.

2.1 Data collection

Data on direct medical cost was retrospectively retrieved from an electronic health record (e-HR) database of patients with inflammatory demyelinating central nervous system disorders receiving care in three specialized clinics for MS and related disorders. Data on healthcare utilization and direct medical cost of patients with the ICD-10TM diagnosis as follows: G35 (multiple sclerosis) for MS or CIS, G36.0 (neuromyelitis optica) and H46 (optic neuritis) for NMOSD and G37.3 (transverse myelitis) for identifying related symptoms of MS, CIS, and NMOSD were retrospectively retrieved from the e-HR record databases during 2007-2013 from three major MS clinics and related disorders.

Data on demographic characteristics (age, gender, clinical course, diagnosis date and date of first attack), direct medical cost (drug cost, diagnosis cost, doctor or nurse fee, hospitalization cost, drug related cost, rehabilitation cost and other medication costs), and healthcare utilization (drug quantity used, item of drug prescription, number of diagnostic procedures, number of admission and admission days) were retrieved and checked by both clinicians and researchers. Health resource utilization and cost data related to outpatient department (OP) or inpatient department (IP) visits were also collected. Moreover, diagnosis confirmation on the first attack date and diagnosis date were retrieved from medical records. In each center, the EDSS scores recorded in patient's medical chart was randomly evaluated by investigators and verified by neurologists. To ensure the validity on EDSS evaluation, the agreement between investigators and neurologists must exceed 75**%** in order to reduce inter-rater reliability of EDSS evaluation.

Furthermore, data on direct medical cost for alternative treatments spent by out of pocket, direct non-medical and indirect costs were collected from face to face interviews using developed data collection forms. Patient selection criteria were as follows: (1) Patients aged older than 15 years old with confirmed diagnosed with MS, CIS or NMOSD according to McDonald Criteria[21] - a revised diagnostic criteria for neuromyelitis optica [22] – and/or their caregivers who visited three specialized clinics for MS and related disorders during March 1, 2011 - September 30, 2014, (2) Patients and/or caregivers who agreed to participate in the study signed consent forms before conducting the study. All patients and/or caregivers were informed about the objective of study, procedure, anticipated benefit or possible risk and contact information of investigators. However, the patients who decided not to participate in the study at any time either before or during the study could withdraw from the study. Institutional Reviewing Board (IRB) Committees of three specialized clinics for MS and related disorders reviewed and approved study protocol before conducting the study.

2.2 Data analysis

Direct medical cost, the amount which hospitals charge to patients, were retrieved from e-HR and transformed to cost using the cost to charge ratio of 1.63[23]. The total average direct medical cost per patient was calculated by the average cost per unit of medical service multiplied by the number of health resources used using a bottom-up approach.

Direct non-medical and indirect costs were obtained through interview. Human capital approach was used to calculate informal care cost using the current income of caregivers multiplied by time spent for patients with inflammatory demyelinating central nervous system disorders. Morbidity cost was calculated based on loss of earning assuming that patients had income reduction once they were diagnosed with inflammatory demyelinating central nervous system disorders. Then, earning loss would be equal to income loss during the duration of disease after diagnosis through the visiting date. In addition, mortality cost due to premature death was estimated based on year of life lost (YLL), defined by life expectancy at current age according to the World Health Organization (WHO) life table criteria[24].

Meanwhile, expected age at death based on mortality study with the long-term follow up of 5,300 US veterans database, demonstrated median survival from disease onset in women (43 years) and men (34 years). To calculate cost of premature death, productivity loss using current income multiplied by YLL, especially in patients who were assumed to be dead before retirement at age of 60 years, was applied. A discount rate of 3**%** was used to adjust future cost of premature death into current year. Finally, total cost of illness or economic burden was computed through the summation of total direct medical cost spent at OP and IP visits as well as outside hospital for alternative medicines, direct non-medical cost and indirect costs multiplied by the estimated number of patients with MS, CIS and NMOSD retrieved from the multiplication of the number of Thai population[25], and also the prevalence and incidence of MS, CIS and NMOSD[26].

All costs were adjusted to 2017 values using the consumer price index (CPI) of medical expenditures[27]. Cost to charge ratio of 1.63 was based on the estimated cost to charge for tertiary care[23] and exchange rate of 35.26 Thai Baht (THB) per one USD was also applied[28] . There were no missing data with e-HR, however, missing or ambiguous data from interviewing patients were imputed by matching with patients with same disease state and resources used. Descriptive statistical analyses for all variables were performed. Assumption for normality distribution was used for continuous variables in the statistical analysis. Average and standard deviation (SD) were presented as parametric tests. Demographic characteristics, healthcare utilization, annual direct medical, direct non-medical, and indirect costs were calculated and classified by MS, CIS, and NMOSD disease groups as well as EDSS scores. STATA 13 statistical software package was used for data management and data analysis (StataCorp LP, USA).

Table 1. Demographic characteristics of patients with inflammatory demyelinating central nervous system disorders (N=315)

Disease group	MS		CIS		NMOSD	
	N	Mean±SD	N	Mean±SD	N	Mean±SD
Age at onset (years)	104	36±14	25	44±10	186	39±13
Current age (years)	104	43±15	25	48±12	186	44±12
Disease duration after 1st attack (years)	104	7.3±6.5	25	4.1±5	186	5±5
Disease duration after 1st diagnosis (years)	104	5.1±5	25	3±4.9	186	2.2±2.7
Income at diagnosis (USD/month)	104	313±506	25	410±375	185	522±953
Current Income (USD/month)	104	234±442	25	358±396	185	368±705
EDSS	104	3.7±2.7	25	2.4±1.9	186	3.7±2.3
%Female: N (%)	80	(77)	20	(80)	168	(90)
Education N (%)						
Under 6th grade	19	(19)	4	(16)	28	(15)
6th Grade	7	(7)	5	(20)	26	(14)
Primary high school	14	(14)	2	(8)	20	(11)
High school diploma	21	(20)	3	(12)	29	(16)
Bachelor	36	(35)	5	(20)	74	(40)
Master or Ph.D.	6	(6)	6	(24)	9	(5)

Inflammatory demyelinating of central nervous system disorders, IDCDs; multiple sclerosis, MS; clinical isolated syndrome, CIS; neuromyelitis optica spectrum disorders, NMOSD; universal coverage, UC; civil servant medical benefit scheme, CSMBS; social security scheme, SSS

3. RESULTS

3.1 Demographic characteristics

Table 1 presents the demographic characteristics of patients with inflammatory demyelinating central nervous system disorders. A total of 315 patients are classified into MS (33**%**, 104 patients), CIS (8**%**, 25 patients), and NMOSD (59**%**, 186 patients). In the analysis, the average age of patients was 44 years and 85**%** (n=268) are females. Notably, the average age at onset (±SD) for patients with MS (36±14) was younger than those with CIS (44±10), but the proportion of female among three diseases seemed different. According to disease duration based on the first symptom, patients with MS had longer disease duration compared to patients with CIS and patients with NMOSD. The percentage of unemployment in patients with MS, CIS and NMOSD was 45**%**, 20**%** and 41**%**, respectively. Although the average monthly income at diagnosis among three disease

Table 2. Annual average health resource utilization and costs in patients with inflammatory demyelinating central nervous system disorders

Type of utilization/cost	Mean ± SD (%)							
	N	MS	N	CIS	N	NMOSD	N	Total
Resource utilization								
Number of OP visits (times/year)	563	7±11	59	5±3	481	7±6	1,103	7±9
Duration at OP visits (days/year)	563	205±122	59	178±114	481	234±106	1,103	216±116
Number of admission (times/year)	226	1.57±1.4	13	1.15±0.41	208	1.37±0.92	447	1.46±1.15
LOS per admission (days)	354	11.2±21.1	15	9.9±6.1	287	12.0±16.0	656	11.5±18.8
Cost per admission (US$)	354	2,100±3,049	15	2,049±1,065	287	2,697±3,298	656	2,360±3,101
Direct medical cost ($US)								
Direct medical cost for OP visit	563	4,373±10,140 (57%)	59	6,250±11,589 (73%)	481	2,004±4,580 (35%)	1,103	3,440±8,391
Direct medical cost for IP visit	226	3,297±4,794 (43%)	13	2,364±1,679 (27%)	208	3,714±4,511 (65%)	447	3,464±4,604
Direct medical cost for alternative treatment	104	291±846	25	330± 818	186	328±847	315	316±842
Annual direct medical cost	**893**	**7,961±8,415 (62%)**	**97**	**8,944±9,132 (73%)**	**875**	**6,046±4,066 (52%)**	**1,865**	**7,220±6,846 (58%)**
Direct non-medical cost ($US)								
Caregivers' time at inpatient visit	104	84±333 (4%)	25	54±172 (5%)	186	131±475 (6%)	315	109±415 (6%)
Paid caregivers	104	121±611 (6%)	25	137±584 (11%)	186	136±824 (7%)	315	131±741 (7%)
Caregivers' time at outpatient visit	104	140±188 (7%)	25	216±370 (18%)	186	205±318 (10%)	315	184±287 (9%)
Patients' time at outpatient visit	104	158±229 (8%)	25	247±384 (21%)	186	230±417 (11%)	315	208±364 (11%)
Facility modification	104	214±652 (10%)	25	44±167 (4%)	186	284±1,351 (14%)	315	242±1,105 (12%)
Informal care	104	1,351±2,718 (65%)	25	494±2016 (41%)	186	1,033±2,072 (52%)	315	1,095±2,306 (55%)
Annual direct non-medical cost	**104**	**2,068±3,232 (16%)**	**25**	**1,192±2,148 (10%)**	**186**	**2,019±3,276 (17%)**	**315**	**1,969±3,187 (16%)**
Indirect cost ($US)								
Morbidity cost	104	1,099±3,258	25	830±3,527	186	2,033±9,140	315	1,629±7,341
Mortality cost	104	1,656±1,930	25	1,310±1,587	186	1,548±1,788	315	1,565±1,818
Annual indirect cost	**104**	**2,755±2,678 (22%)**	**25**	**2,140±2,735 (22%)**	**186**	**3,581±6,585 (31%)**	**315**	**3,194±5,348 (26%)**
Total cost	**1101**	**12,784±7,693 (100%)**	**147**	**12,276±7,590 (100%)**	**1247**	**11,646±4,434 (100%)**	**2495**	**12,383±6,320 (100%)**

US$= U.S. dollar, LOS = length of stay, THB = Thailand Baht, IP = inpatients, OP= outpatients, MS = multiple sclerosis, CIS = clinical isolated syndrome, NMOSD = neuromyelitis optica spectrum disorders, SD = standard deviation, LOS = length of stay, IP = inpatient

groups seemed similar, the average monthly current income seemed to be lower than those at diagnosis.

3.2 Economic burden

Table 2 shows the annual average health resource utilization and cost in patients with inflammatory demyelinating central nervous system disorders. The annual average number of OP visits seemed different among three disease groups. In comparison, the annual average duration of OP visits was longer in patients with NMOSD than those with MS or CIS (234±106 days vs 205±122 days or 178±114 days), respectively. Also, the average length of stay per admission and annual average number of admission were similar among three disease groups. Annual average direct medical cost at OP in patients with MS and CIS seemed higher than those with NMOSD (4,373±10,140 USD or 6,250 ±11,589 USD vs 2,004±4,580 USD). In contrast, the annual average IP cost was not different among three disease groups (Table 2). It can be noted that the proportion of direct medical cost for outpatient visits was the highest in patients with MS (34**%**) and CIS (52**%**), while the direct medical cost for inpatient cost was the highest proportion in patients with NMOSD (39**%**).

According to patients' interviews, annual average direct medical cost for alternative treatment spent outside hospitals by patients' out of pocket was 316±842 USD. The annual average direct non-medical cost for patients with inflammatory demyelinating central nervous system disorders was 1,969±3,187 USD. Annual average direct non-medical cost of patients with MS (2,068±3,232 USD) and NMOSD (2,019 ±3,276 USD) was similar and higher than that of patients with CIS (1,192±2,148 USD). Informal care cost (56**%**) was the largest portion of total direct non-medical cost, followed by the cost of facility modification (12**%**) and outpatient visit (11**%**) (Table 2).

Figure 1 presents direct medical and direct non-medical costs classified by EDSS scores. It was found that higher direct non-medical costs of patients with EDSS 8.0-9.5 compared to those with other EDSS categories was also found. In addition, annual average direct non-medical cost of patients with EDSS 6.0-7.5 was higher than that of those with EDSS score <6.0. The proportion of informal care and facility management costs increased when patients reached a score of EDSS 6.0 or higher.

Moreover, higher annual average morbidity cost on patients with NMOSD (2,033 ±9,140 USD) compared to those with MS (1,099 ±3,258 USD) and CIS (830±3,527 USD) was found. Similar results of annual average mortality cost among patients with MS, CIS and NMOSD (1,656±1,930 USD, 1,310±1,587 USD and 1,548 ±1,788 USD) was also observed, respectively.

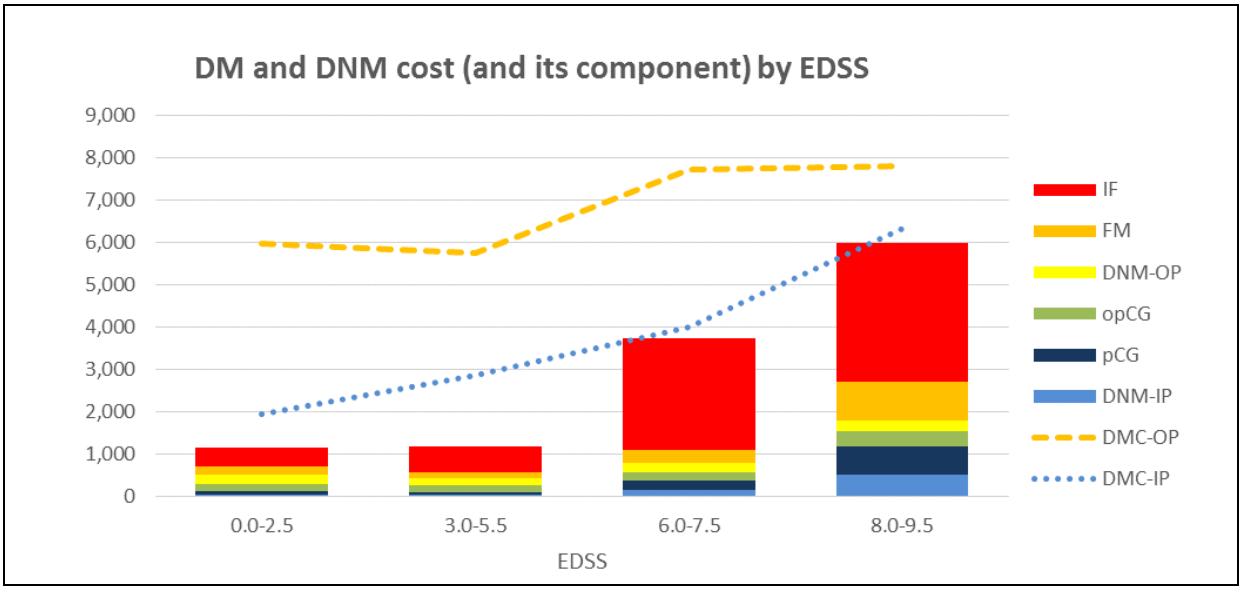

Figure 1. Describe direct medical costs (DM), direct non-medical costs (DNM) by EDSS scores. (IF= informal care cost, FM= facility modification cost, DNM-OP= direct non-medical cost for outpatient visits, opCG= time cost for caregivers accompanying patients to outpatient visits, pCG=paid caregiver cost, DNM-IP=direct non-medical cost for inpatient visits, DMC-IP=direct medical cost for inpatient visits, DMC-OP= direct medical cost for outpatient visits, EDSS= Expanded Disability Status Scale)

Table 3. Total economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand

Cost types	MS (N=185)[a]	CIS (N=38)	NMOSD (N=365)	Total (N=588)
Direct medical cost at OP visits	811	235	732	1,778
Direct medical cost at IP visits	611	89	1,357	2,057
Direct medical cost for alternative treatment	54	13	120	187
Direct non-medical cost	384	45	738	1,167
Indirect cost	530	68	500	1,098
Total ('000 US$)	2,390	450	3,447	6,287

'000US$= Thousand US Dollar, IDCDs = Inflammatory Demyelinating of Central Nervous System Disorders, MS=multiple sclerosis, CIS=clinical isolated syndrome, NMOSD=neuromyelitis optica spectrum disorders, OP=out-patient, IP=in-patient, [a]=Patients no. based on prevalence estimation , Total populations based on Thailand Census Survey 2016; 65,931,550 Dept of Provincial Administration, Ministry of Interior

Total annual average cost of patients with MS and CIS seemed higher than those with NMOSD. Direct medical cost was the highest proportion of total annual average cost of patients with MS, CIS and NMOSD. However, due to higher of prevalence patients, the total cost of illness or economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand was 6,287,000 USD where NMOSD (3,447,000 USD) consumed the highest cost compared with MS (2,390,000 USD) and CIS (450,000 USD) (Table 3).

4. DISCUSSION

This study was the first to investigate the economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand and Asian countries as all published studies were conducted in the US, Australia and European counties according to the systematic review on cost of illness of MS in 2014 [29]. Direct medical, non-medical and indirect cost data were obtained from both electronic health record databases and patients' interviews from all patients receiving care at three major specialized clinics for MS and related disorders in Thailand.

As there are a total of four specialized MS and related disorders clinics in Thailand, our study represented data from a majority of patients with inflammatory demyelinating central nervous system disorders in the country. Patients with MS enrolled in the study had an average age at onset at 36±14 years, while the average current age in the cohort was 44±12 years old. This demonstrated that Thai patients with inflammatory demyelinating central nervous system disorders experienced at least mild disability in daily functioning for about a decade, according to the average EDSS scores of 3.6±2.4.

Female prevalence was also observed (85**%** or 5.7:1), and this was similar to a previous study indicating that MS was found to be more prevalent in females than males in Thailand.[30] Aligned with other studies confirming burden of MS on earning loss and employment status of patients with MS [13,14], there was a significant loss of monthly income from the onset of disease (444 USD) until at the current time of data collection (323 USD). Regarding employment status, approximately 41**%** of patients with inflammatory demyelinating central nervous system disorders were unemployed and this result was in accordance with a previous study in the Western countries [13]. The significant interval from the first onset until time to confirm the diagnosis of inflammatory demyelinating central nervous system disorders was more than two years, which could lead to a delay of diagnosis and treatment, similar to MS diagnosis globally [31].

As our study included the economic burden based on a societal perspective, direct medical, non-medical, and indirect costs were estimated. The results suggested that direct medical cost (58**%**) accounted for the highest proportion compared with direct non-medical costs (16**%**) and indirect costs (26**%**). Furthermore, patients with inflammatory demyelinating central nervous system disorders consumed similar amount of direct medical cost for outpatient (3,440 USD) to that of inpatient visits (3,464 USD).

It is noted that patients with inflammatory demyelinating central nervous system disorders had to pay drug cost through out of pocket, considering that no disease modifying therapy (DMT) which was very costly has been listed in the National List of Essential Medicine (NLEM), a drug reimbursement list for patients under all three health insurance schemes – the Civil Servant Medical Benefit Scheme (CSMBS) for government officers and their dependence, Social Security Scheme (SSS) for

employees, and Universal Coverage Scheme (UCS) for non CSMBS or SSS, which covers 16**%** , 9**%** and 75**%** of Thai populations, respectively[32]. This could lead to a huge economic burden for patients and their families[33]. Among types of direct non-medical costs, informal care cost had the highest proportion (55**%**) for caregivers and patients with inflammatory demyelinating central nervous system disorders. Informal care cost in this study was in line with other studies which revealed that informal care cost ranged between 17**%** and 67**%** [29]. In the survey, most of patients with inflammatory demyelinating central nervous system disorders always accompanied with one caregiver and spent approximately 12 hours during each outpatient visit for traveling to the hospital and waiting for physicians. This could be explained by the only four MS and related disorders clinics in the country and three study sites in this study were among those four referral centers which could provide diagnosis and treatment for Thai populations at the provincial level. In addition, the proportion of informal care varied among studies due to a difference in family structure and cultural norm in each country[15,34,35]. Thai cultural norm, same with other Asian countries, usually spend time giving care for their family members rather than using the institutional care which would be different from the care provided by patients' families[17,35-37].

Moreover, the indirect cost of patients with inflammatory demyelinating central nervous system disorders, which included morbidity and mortality costs, accounts for 25**%** of total cost. In this study morbidity cost was computed by estimating the earnings lost from the starting income of the patients at the time of first attack and current income on the time of data collection – to know the real burden of patients with inflammatory demyelinating central nervous system disorders in Thailand. However, earnings lost from average gross national income (GNI) and current income was not calculated, which seems more acceptable according to the current Thai Health Technology Assessment Guidelines[23]. In addition, mortality cost due to premature death was estimated based on a valued time aspect referred to the patients' latest income with average wage of 8.50 USD/day[38]. Nevertheless, the cost of premature death using productivity time aspect referred to the GNI irrespective of socioeconomic status of patients might better represent economic burden in Thai population. These could be room for further studies. However, both morbidity and morbidity costs in our study could demonstrate a hidden economic burden which might be overlooked by health decision makers in Thailand.

To add, the total cost of illness among patients with MS (12,784±7,693 USD), CIS (12,276±7,590 USD) and NMOSD (11,646 ±4,436 USD) was different, and the proportion of direct medical costs at inpatient and outpatient visits as well as direct non-medical costs were also quite diverse. CIS patients had the highest proportion of direct medical costs at outpatient visits (73**%**) followed by MS (57**%**) and NMOSD (35**%**) because currently, there has been no approved drug for NMOSD patients, yet. Therefore, these patients would be more likely incur cost during inpatient visits, while MS and CIS patients would receive approved drugs at outpatient visits. In addition, patients with CIS had less severity than those with MS or NMOSD, thus direct medical costs of CIS in inpatient visits were lower than those of MS and NMOSD. There are two limitations in this study. First, we could include only three out of four MS and related disorders clinics due to data limitation. However, it was estimated that 70**%** of total patients in the country were collected, which could represent the economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand. Secondly, we did not provide total mortality cost for lifetime period (data from lost on lifetime was available, but it was divided into annual cost), due to lack of specific data for life expectation at specific age in Thailand.

5. CONCLUSION

The results from this study would provide a useful information on the economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand. Although the economic burden information may not be directly applied for health policy decision making, the results from this study may be still helpful to provide the best evidence on the economic impact of diseases. It would be helpful to compare with the economic burden of other diseases or countries for better understanding the element on economic burden of patients with inflammatory demyelinating central nervous system disorders. This study demonstrated the high economic burden of patients with inflammatory demyelinating central nervous system disorders in Thailand which required the attention from policy makers.

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Conflict of interest

SS has received funding for travel and speaker honoraria from Merck Serono, Pacific Healthcare (Thailand), Menarini (Thailand), Biogen Idec, UCB (Thailand) and Novartis. NP has received funding for travel and speaker honoraria from Bayer Schering Pharma, Eisai Inc, Pfizer Pharmaceutical Company Limited, Novartis, Sanofi-Aventis. CC, PP, MA, MT, AR and UC has no conflict of interests.

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Ethical approval

This ethical approval was granted by the Institutional Reviewing Board (IRB) Committees of three specialized clinics for MS and related disorders i.e., Siriraj Hospital (Si634/2011), Chiangmai university (203/2556), and Prasat Neurological Institute (57020) before conducting this research.

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