

Epilepsy research output in Southeast Asian countries: A systematic review

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Abstract

Objective: Epilepsy is understudied in Southeast Asian (SEA) countries. This systematic review aimed to determine the number of epilepsy publications performed in SEA and identify factors associated with research output in this region. **Methods:** Existing academic journal article searches were performed using PubMed, Scopus, Medline and Web of Science till 1st March 2018. Openness is determined by the use of English in medical school and overseas epilepsy fellowship. **Results:** A total of 702 epilepsy articles have been published in the last 50 years in the SEA region, with an exponential increase of publications after the year 1997, with the cumulative number doubled every 5 years. Only half (54%) were published in the journals with impact factor (IF) ≥ 1 . Majority of the publications (48.2%) employed cross sectional design, followed by animal or laboratory studies (21.1%), with few randomized controlled trials and systematic review/meta-analysis studies (1.7% and 2.3%, respectively). Half (52.9%) of the publications were clinical studies. The number of papers with IF ≥ 1 correlated positively with openness to international standard ($R=0.720$, $p<0.05$), and knowledge-based economy ($p=0.01$).

Conclusion: Epilepsy research output in SEA is low in quantity and quality. The output is mainly related to the type of economy (knowledge-based or non-knowledge-based) and openness to international ideas and standard.

Keywords: Epilepsy, research output, Southeast Asia

INTRODUCTION

Epilepsy is a disease of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological and social consequences of this condition.¹ Approximately 70 million people worldwide have epilepsy, making it one of the most common neurological diseases globally.²

Southeast Asia (SEA) is a subregion of Asia geographically which consists of 11 countries: Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste and Vietnam. Ten of 11 states are members of the Association of Southeast Asian Nations (ASEAN), while Timor-Leste is an observer. In Southeast Asian countries, the estimated population is 655 million which is equivalent to 8.5% of the total world population and epilepsy affects about 1% of the population

(6.5 million). However, epilepsy is understudied and the number of publications in epilepsy is postulated to be lower compared with the other countries or regions in the world. Despite socioeconomic development in this region in the recent years and possibly leading to increase in epilepsy research, it is uncertain whether the epilepsy research output also increases consequently. There are many possible limiting factors in epilepsy research in this region, including types of economy, inadequate research funding related to low gross domestic product (GDP), lack of research interest among clinicians, low number of basic science researchers, and lack of research guidance by experienced researchers.

These postulations are neither proven nor studied previously, to the best of our knowledge. This study aims (1) to determine the number of epilepsy publications performed in SEA and (2)

to identify the factors associated with research output in this region, using a systematic review.

METHODS

Search strategy

Electronic systematic searches, which were performed using PubMed, Scopus, Medline and Web of Science for existing academic journal articles and reviews till 1st March 2018. The search terms included [epilepsy] OR [seizure*]. Author affiliations were subsequently screened and all abstracts with at least one author from any of the 11 countries in SEA region, including Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar (Burma), Philippines, Singapore, Thailand, Timor-Leste, Vietnam, were included in the initial screening. The PRISMA guidelines for conducting the review were followed.³

Inclusion and exclusion criteria

An article was included if (1) the study was performed in SEA countries, and (2) the research topic was on epilepsy, seizures or Electroencephalography (EEG). All original studies including laboratory studies, animal studies, observational studies, interventional studies and qualitative studies were included. We also included papers in other languages when the English abstract was available. We excluded book sections, literature reviews, conference presentations or abstracts, guidelines, commentaries, personal view, or studies which were performed outside SEA region.

Data collection

All abstracts were screened independently by two reviewers to determine whether they met eligibility. The full articles of eligible studies were then reviewed for eligibility again, followed by data extraction and analysis.

Data extraction and analysis

The data of eligible articles were abstracted into variables such as country, year of publication, journal, study design and topic. The study design was classified based on the level of evidence, including: systematic reviews and meta-analysis, randomized controlled trial (RCT), non-randomized controlled trial (NRCT), cohort study, case-control study, cross sectional study, case report, and animal/laboratory study.⁴ Topics were categorized broadly into four categories

i.e. basic sciences, epidemiology, clinical and psychosocial. The subtopics included: (1) genetic, animal, technology, and pharmacology in basic sciences category; (2) epidemiology and health economics in epidemiology category; (3) diagnosis, investigation, treatment, psychiatry, status epilepticus in clinical category; and (4) psychosocial issues is categorized under one topic. The published journals were divided by impact factor (IF) into low (IF below 1) and high (IF of 1 and above) impact journal.

Information of a country was collected, which included population, gross domestic product (GDP) per capita, classification by income and a number of neurologists, number of neurologists underwent epilepsy fellowship.⁵⁻⁷ Countries were classified by income based on World Bank's data 2016, and GDP per capita were according to International Monetary Fund's October 2017.^{8,9} Economies were classified as "knowledge-based economy" and "non-knowledge-based economy". Knowledge-based economy was characterized by their emphasis on technology, knowledge and skill development with service and manufacturing account for large segment in the economy, include Malaysia, Singapore and Thailand in SEA.¹⁰ The other SEA countries were categorized under non-knowledge-based, where the economy was largely based on low-skilled agriculture, and extraction of natural resources such as oil and gas.

The term "openness" was determined whether a community is open to ideas and standard internationally. This is reflected in the use of English in medical schools and to access scientific literatures, sending epilepsy fellows for overseas training, and requirement of overseas examiners in medical examinations and post-graduate thesis. In this paper, "openness" is determined by 2 factors: (1) the use of English in medical school and (2) overseas epilepsy fellowship, given a score of 0-2 with one score granted for each factor.

For statistical analysis, student t-test was used to compare the number of papers between two groups. Correlation analysis was used to determine the relationship between number of papers and the other variables including population, GDP per capita, and number of neurologists, number of neurologists underwent epilepsy fellowship. All statistics were performed in SPSS version 22.0. Statistical significance was defined as p -value < 0.05 .

RESULTS

Study selection

The search strategy for articles up to 1st March 2018 identified 3,097 records after removing duplicates, of which 801 articles were selected for full-text assessment. Ninety-nine papers were excluded for reasons: (1) the research topic was not on epilepsy, seizure or EEG (n = 38), (2) study was performed outside SEA region (n = 41), (3) not original study, e.g. literature reviews, expert opinions, article replies (n = 20). A total of 702 articles met eligibility for data extraction. We found 656 full-text articles in English, 2 in French and 1 in Japanese. There were 43 articles that we could not assess the full-text, of which 28 of them were published before 2000. However, these studies were included if the eligibility can be determined based on abstracts and data can be extracted from the abstracts. (Figure 1)

Number of publications

A total of 702 papers on epilepsy studies performed in SEA region, published in the last 50 years, were identified. (Figure 2, Appendix 1). Of which, only 379 papers (54%) were published in the journals with impact factor 1.0 and above, which are all international journals. The oldest paper that we could find via electronic search engines was published in 1970. The total publications increased from 1 paper in the period of 1968-1972 to 292 in the past 5 years (2013-2017). The total number of papers increased exponentially after the year 1997, with the cumulative number doubled every 5 years.

The number of articles in each SEA country was shown in Table 1. According to countries in which the studies were performed, most articles were originated from Malaysia (234 articles), Thailand (210) and Singapore (173). No publication was found in Brunei and Timor-Leste. There were two increasing trends of publications in SEA region, first after 1998 in Malaysia, Thailand and Singapore, and the second increase in other countries after 2007.

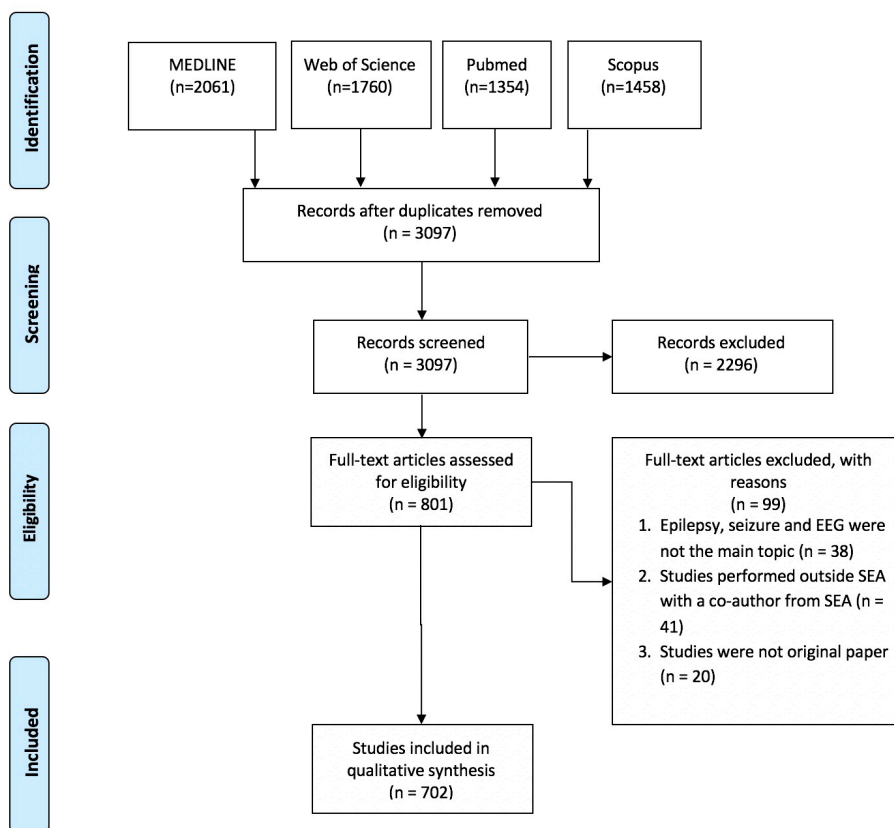


Figure 1. Flow diagram of the article selection process

Table 1: Number of epilepsy publications in each SEA countries (N=702)

Period	Brunei	Cambodia	Indonesia	Laos	Malaysia	Myanmar	Philippines	Singapore	Thailand	Timor Leste	Vietnam
1968 - 1972	0	0	1	0	0	0	0	0	0	0	0
1973 - 1977	0	0	2	0	4	0	0	4	0	0	0
1978 - 1982	0	0	1	0	6	0	0	3	1	0	0
1983 - 1987	0	0	0	0	1	0	0	8	2	0	0
1988 - 1992	0	0	2	0	4	0	1	9	4	0	0
1993 - 1997	0	0	3	0	12	0	1	13	7	0	0
1998 - 2002	0	0	2	0	10	0	1	22	27	0	1
2003 - 2007	0	0	3	3	13	0	0	30	37	0	3
2008 - 2012	0	2	4	6	59	0	0	42	38	0	7
2013 - 2017	0	3	12	2	125	1	7	42	94	0	6
2018*	0	0	1	0	4	0	0	1	5	0	0
Total	0	5	31	11	238	1	10	174	215	0	17

*Papers found up to 1st March 2018.

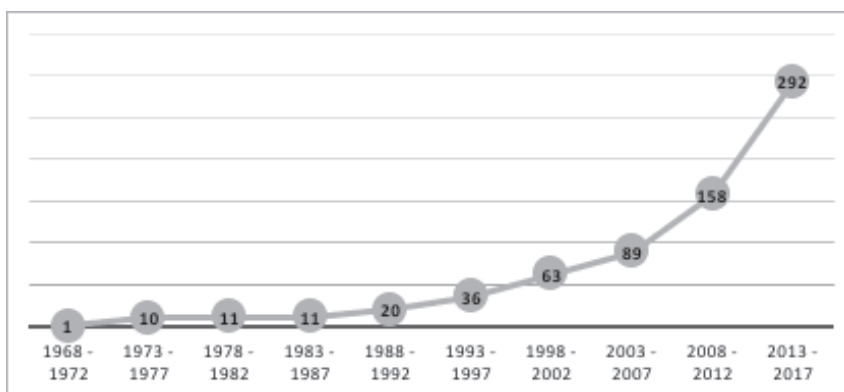


Figure 2. The trend of epilepsy publications in SEA region.

Journals

Firstly, the list of journals was tabulated and sorted according to the number of papers. Among the top 20 in the list, 8 (40%) were local journals and a majority of them (12, 60%) had impact factor

below 2.0. (Table 2) In the high impact epilepsy journals (with impact factor ≥ 2.0), the percentage of papers which were performed in SEA region was very low (range from 0% to 2.69%) in the past 5 years. (Table 3)

Table 2: List of the most popular journals publishing epilepsy papers in SEA (N=313)

No	Journal	Number of articles	Impact factor*
1	Journal of the Medical Association of Thailand	78	0.42 (RG)
2	Epilepsy & Behavior	27	2.631
3	Neurology Asia	24	0.153
4	Singapore Medical Journal	24	0.667
5	Epilepsia	19	5.295
6	Epilepsy Research	18	2.367
7	Seizure	18	2.448
8	The Malaysian Journal of Medical Sciences: MJMS	17	0.73 (RG)
9	Annals Academy of Medicine Singapore	16	0.617
10	Epileptic Disorders	8	1.168
11	International Journal of Neural Systems	8	6.333
12	Brain & Development	7	1.52
13	Journal of The Neurological Sciences	7	2.295
14	Paediatrica Indonesiana	7	0.06 (RG)
15	The Southeast Asian Journal of Tropical Medicine And Public Health	7	0.655
16	Medical Journal of Indonesia	6	0.19 (RG)
17	PloS One	6	2.806
18	Journal of Paediatrics And Child Health	6	1.572
19	International Medical Journal	5	0.13
20	Archives of Disease in Childhood	5	3.786

RG: research gate data

* Impact factors in year 2018.

Table 3: The number and percentage of papers from SEA region in high impact epilepsy journal in the past 5 years

Journal	Articles in SEA per year (%)	Total articles per year
Epilepsia		
2013	5 (0.09)	5546
2014	1 (0.02)	5725
2015	0 (0)	5870
2016	2 (0.03)	6111
2017	0 (0)	6133
Seizure		
2013	5 (2.69)	186
2014	1 (0.54)	184
2015	1 (0.43)	231
2016	0 (0)	176
2017	1 (0.38)	262
Epilepsy and Behavior		
2013	5 (1.27)	393
2014	1 (0.22)	447
2015	6 (1.20)	500
2016	3 (0.68)	441
2017	1 (0.22)	460
Epilepsy Research		
2013	3 (1.36)	220
2014	1 (0.43)	233
2015	1 (0.51)	195
2016	2 (1.09)	184
2017	1 (0.49)	206

Study design

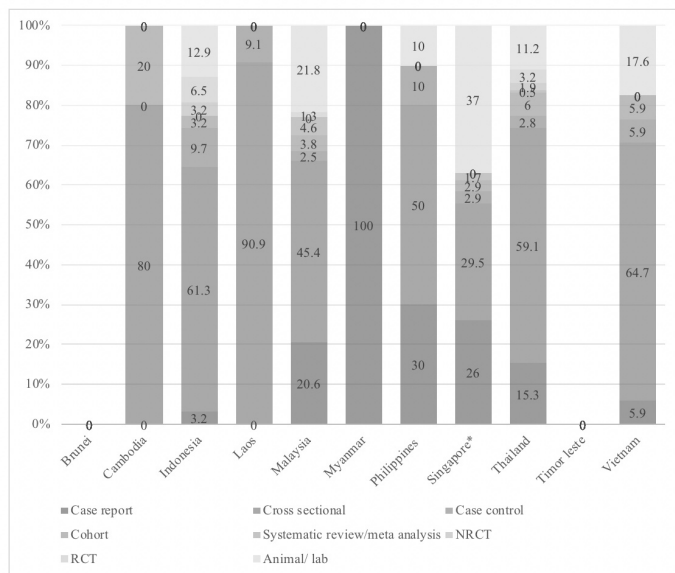
Nearly half of the published papers (48.2%) were cross sectional studies, followed by animal or laboratory studies (21.1%), whereby RCTs and systematic review/meta-analysis studies were low (1.7% and 2.3%, respectively). Sub-analysis on the types of studies performed in each country showed that animal or laboratory studies were performed and published in 6 countries, mostly in Singapore and Malaysia (37% and 21.8%, respectively). There were only few systematic review and meta-analysis studies performed in Malaysia, Singapore and Thailand (4.6%, 1.7% and 0.5%, respectively). RCT studies were found in Malaysia and Indonesia only. (Figure 3).

Topic of epilepsy research

Half (52.8%) of the publications were clinical studies. This is followed by basic science studies (29.8%), performed mostly in the higher income countries, e.g. Singapore, Malaysia and Thailand. (Figure 4)

Factors associated with research output

The number of papers $IF \geq 1$ and the number of papers $IF \geq 1$ per neurologist were compared to the population, GDP, the number of neurologists, the number of neurologists underwent epilepsy fellowship abroad, the main language used in medical school and the openness. (Table 4) There were significant differences in number of papers $IF \geq 1$, number of neurologists per population



Study design	Number of papers (%)
Animal/ laboratory study	148 (21.1%)
Case report	132 (18.8%)
Cross sectional	338 (48.2%)
Case control	24 (3.4%)
Cohort	29 (4.1%)
Non-randomized controlled trial	3 (0.4%)
Randomized controlled trial	12 (1.7%)
Systematic review/ Meta-analysis	16 (2.3%)
Total	702

Figure 3. Study designs of epilepsy publications in SEA countries (N=702)

and number of neurologists underwent epilepsy fellowship between the countries with knowledge-based and non-knowledge-based economies. (Table 5) Openness score correlated significantly with the number of papers with high IF ($R=0.720$, $p<0.05$), and number of neurologists per 100,000 population ($R=0.663$, $p<0.05$). (Table 6)

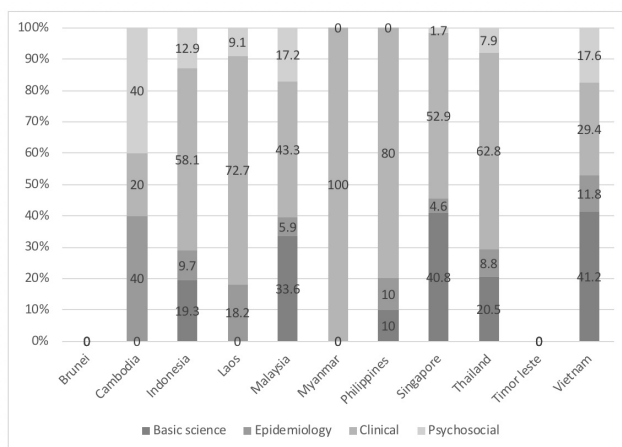
Appendix 1: List and details of all selected studies.

DISCUSSION

Low epilepsy research output in SEA countries

The research output in SEA countries was low in quantity and quality. There were only 702

epilepsy papers published in the last 50 years in the SEA region, and only 54% (379) were published in the journals with $IF \geq 1$, which are all international journals. The number of publications in high impact epilepsy journals were low (mostly below 1% of annual publications in each journal) compared to 8.5% of world population in this region. In addition, most studies performed in this region were clinical studies using cross-sectional study design, with lower level of evidence. However, there was an exponential increase in epilepsy research output after the year of 1997 in countries with knowledge-based economy (Malaysia, Thailand, Singapore), and after 2008 in Indonesia, Philippines, Laos, and Vietnam.



Topic	Subgroup	Number of papers (%)
Basic science (209, 29.8%)	• Genetic	61 (29.2)
	• Animal	54 (25.8)
	• Technology	86 (41.1)
	• Pharmacology	8 (3.8)
Epidemiology (51, 7.3%)	• Epidemiology	43 (84.3)
	• Health economics	8 (15.7)
Clinical (371, 52.8%)	• Diagnosis	146 (39.2)
	• Investigation	47 (12.6)
	• Treatment	139 (37.6)
	• Psychiatric	13 (3.6)
	• Status epilepticus	26 (7.0)
	• Psychosocial issue	71 (10.1%)
Total		702

Figure 4. Topics of epilepsy publications in SEA countries (N=702)

Table 4: The number of papers IF \geq 1 in relation to the socio-economic and medical characteristics of SEA countries (N=11)

Country	Population (million)	GDP nominal per capita (USD)	Number of neurologists	Number of neurologists per 100,000 population	No of neurologists underwent epilepsy fellowship	Main language used in medical school	Papers with IF \geq 1	Number of papers with IF \geq 1 per neurologist	Number of papers IF \geq 1 per 1 million population	Openness
Knowledge-based-economy										
Malaysia	31.187	9,659	120	0.38	10	English	128	1.07	4.10	2
Singapore	5.607	53,880	100	1.79	10	English	127	1.27	22.65	2
Thailand	68.864	6,336	645	0.94	10	English	93	0.14	1.35	2
Non-knowledge-based economy										
Brunei	0.423	27,893	2	0.47	0	English	0	0	0	1
Cambodia	16.013	1,389	5	0.03	2	Cambodian	5	1.0	0.31	1
Indonesia	261.115	3,858	1,150	0.44	10	Indonesian	7	0.01	0.03	2
Laos	6.758	2,567	3	0.04	0	Laos	7	2.33	1.04	0
Myanmar	52.885	1,272	23	0.04	0	Burmese	0	0	0	0
Philippines	103.320	3,022	425	0.41	10	English	2	0.004	0.02	2
Timor-Leste	1.269	2,208	0	0	0	Portuguese	0	0	0	0
Vietnam	92.701	2,306	800	0.86	10	Vietnamese	10	0.01	0.11	1

Table 5: Comparison between countries with knowledge-based (N=3) and non-knowledge-based economies (N=8)

	Knowledge-based, (Mean ± SD)	Non-knowledge-based (Mean ± SD)	<i>p</i> value
Population, millions	35.22 ± 31.82	66.81 ± 88.51	0.572
GDP per capita	23,291 ± 26,542	5,564 ± 9,060	0.367
Number of neurologists	288 ± 309	301 ± 450	0.966
Number of neurologists per 100,000 population	1.03 ± 0.71	0.29 ± 0.31	0.030
Number of neurologists underwent epilepsy fellow	10.0 ± 0.0	4.0 ± 5.0	0.012
Number of papers IF≥1	116.0 ± 19.9	3.8 ± 3.9	0.01

Factors affecting epilepsy research output

There are various factors affecting research output in SEA countries, including knowledge-based economy, research personnel and skill development, and openness to international standard.

Knowledge-based economy

Economic type might be the most important factor determining the research output of a country. In SEA region, Malaysia, Singapore and Thailand are considered to have knowledge-based economy. In these countries, technology, knowledge and

Table 6: Correlations analysis among publication output socio-economic variables. (N=11)

	Population (million)	GDP per capita (USD)	Number of neurologists	Number of neurologists per 100,000 population	Number of neurologists underwent epilepsy fellow	Openness	Number of papers IF≥1
Population (million)	1	-0.315	0.901*	0.031	0.529	0.215	-0.192
GDP per capita (USD)	-0.315	1	-0.24	0.773*	0.180	0.267	0.553
Number of neurologists	0.901*	-0.24	1	0.275	0.690*	0.352	-0.036
Number of neurologists per 100,000 population	0.031	0.773*	0.275	1	0.655*	0.616*	0.663*
Number of neurologists underwent epilepsy fellow	0.529	0.180	0.690*	0.655*	1	0.886**	0.575
Openness	0.215	0.267	0.352	0.616*	0.886**	1	0.720*
Number of papers IF≥1	-0.192	0.553	-0.036	0.663*	0.575	0.720*	1

**p*-value < 0.05

***p*-value < 0.01

skill development play more important roles in economy, as compared to other countries focus on extraction of natural resources, traditional agriculture using low-skilled labour. Studies with higher level of evidence such as basic science studies, systematic review and meta-analysis or RCT were performed more often in these countries with knowledge-based economy. These studies depend on intellectual capital, leveraged science and technology. Thus the emphasis on publication is a reflection of the overall values placed on acquisition of knowledge and development of skills in these countries.

The number of neurologists per population and the number of epilepsy fellows were higher in countries with knowledge-based economy, reflecting how human capital development influences the research output. In SEA region, only a few institutions offer epilepsy fellowship training (Thailand: 4, Malaysia: 3, Singapore: 2, Indonesia and Vietnam: 0) compared with the other Asian countries (Taiwan: 9, Japan: 112, South Korea: 20).⁵ Academic institutions offer not only professional training but also encourage and support research activities, including research methodology training, research expert consultation, multi-disciplinary collaboration and research grant opportunities. Inadequate emphasis and support for research activities limits the quality and scope of research. From personal communication with the regional leaders, research is part of neurology training in most countries, including Myanmar and Indonesia, but most of the research outputs are not published. In addition, some neurologists who had fellowship training in developed countries may be involved in research during their fellowship. However, they may not continue the research upon return to their own countries after completion of fellowship, probably limited by local funding, laboratory and personnel support and research culture. Lower number of neurologists per population in this region also implies more clinical workload and thus less time for research.

Openness

Openness score reflects how much a country opens to international standard and ideas. In this study, openness is measured by use of English in medical school and sending fellows for further training abroad. In this study, we have found openness correlated positively with high impact research output. The link between openness would be stronger if the measurement to quantify

openness can be more comprehensive, such as use of English to access scientific literature and continuing medical education, and requirement of overseas examiners in certifying examinations and post-graduate thesis.

One may argue that the strong motivation for publication in high IF journals is instead the competition to raise the international ranking of the universities. Nevertheless, even the motivation to raise university ranking through the emphasis to publish in high IF journal is also reflective of the importance the universities placed on the assessment by the international peers, i.e., openness.

If the purpose of research is to evaluate and create new knowledge, surely whether the new knowledge is shared to wider readership internationally is just as important as just having the work documented, published and made accessible. This again reflect the value placed on openness; though here, the emphasis is on sharing rather than receiving. Many research projects conducted in SEA region were published in local journals, which were in native languages, such as Ho Chi Minh city Medical Journal (in Vietnamese language), Laos Medical Journal (in Laos), or Journal of the Medical Sciences (in Indonesian). As the readership of these journals are limited to the nationals in these countries, the impact factor is also low. Epilepsy investigators in SEA should place higher priority, and strive to have their research published in the international journal to reach out to wider readership, to enhance the values of the efforts they have invested in the study.

Future implications

This study indicates the need to encourage research activities in the region. In order to bridge the epilepsy research gap between SEA and other regions, international collaborations with guidance from more established research centers should be encouraged. Besides identifying novel research projects, the quality of research can be improved through international collaborations, leading to higher opportunities to publish in international journals. Availability of regional or international funding, or support from local funding agencies is another predicting factor. In addition, cultivating interest of local clinicians and scientists, and providing protected research time are additional steps to improve the situation.

Limitations

This systematic review only focuses on studies performed in the region. Many researchers in SEA countries may have contributed data in an oversea-based research project, or participated in research when they reside overseas, but these papers were not captured in the review. This exclusion is to depict a clearer picture on local research output and quality.

Conclusion

Epilepsy research output in ASEAN is low in quantity and quality, and mainly related to type of economy of the country, and openness to international ideas and standard.

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DISCLOSURE

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