

# Infodemiology of autoimmune encephalitis, autoimmune seizures, and autoimmune epilepsy: An analysis of online search behavior using Google Trends

Katrina T. Roberto<sup>a</sup>, Roland Dominic G. Jamora<sup>a,b</sup>, Kevin Michael C. Moalong<sup>a</sup>, Adrian I. Espiritu<sup>a,c,d,\*</sup>

<sup>a</sup> Division of Adult Neurology, Department of Neurosciences, College of Medicine and Philippine General Hospital, University of the Philippines, Manila, Philippines

<sup>b</sup> Section of Neurology, Institute for Neurosciences, St. Luke's Medical Center, Quezon City & Global City, Philippines

<sup>c</sup> Department of Clinical Epidemiology, College of Medicine, University of the Philippines Manila, Manila, Philippines

<sup>d</sup> Division of Neurology, Department of Medicine, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

## ARTICLE INFO

### Article history:

Received 8 March 2022

Revised 23 April 2022

Accepted 5 May 2022

Available online 24 May 2022

### Keywords:

Autoimmune encephalitis

Autoimmune seizures

Autoimmune epilepsy

Infodemiology

Google Trends

## ABSTRACT

**Background:** Patients and their caregivers, including clinicians and educators, use web-based search engines to access healthcare-related information from the internet. Online search behavior analysis has been used to obtain insights on health information demand.

**Objectives:** We aimed to describe the online search behavior for autoimmune encephalitis, autoimmune seizures, and autoimmune encephalitis (AE) worldwide over time through the analysis of search volumes made on Google.

**Methods:** In this infodemiological study, we retrieved search volume indices for the keyword “autoimmune encephalitis (search term)”, “autoimmune seizures (search term)”, and “autoimmune encephalitis (search term)” based on worldwide search data from January 01, 2004 to October 31, 2021, using Google Trends. We performed a descriptive analysis of search volume patterns, including related topics and queries.

**Results:** There was a progressive increase in search volume numbers over time for the keyword “autoimmune encephalitis”, “autoimmune seizures”, and “autoimmune epilepsy” with no annual seasonal variation. Peak search volumes for these keywords were recorded in July 2018, February 2005, December 2012, respectively. The greatest search volume for “autoimmune encephalitis” was recorded in Singapore, followed by Australia, the United States of America, the Philippines, and New Zealand, whereas it was highest in the United States for “autoimmune seizures” and “autoimmune epilepsy”. The most searched topics were related to definition, causes, symptoms, diagnosis, and treatment. All related topics and queries increased in volume by more than 5000-fold over time.

**Conclusions:** This study showed an uptrend in the online search interest on autoimmune encephalitis, autoimmune seizures, and autoimmune epilepsy over time, which may reflect the increased awareness of the condition by the public and the medical community. Information on online health information-seeking behavior may be obtained from Google Trends data despite its limitations.

© 2022 Elsevier Inc. All rights reserved.

**Abbreviations:** GT, Google Trends; SVI, Search volume indices; AE, Autoimmune encephalitis; HISB, Health information-seeking behavior; CSV, Comma separated values.

\* Corresponding author at: Division of Neurology, Department of Medicine, St. Michael's Hospital, University of Toronto, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada.

E-mail addresses: [ktroberto@alum.up.edu.ph](mailto:ktroberto@alum.up.edu.ph) (K.T. Roberto), [rgjamora@up.edu.ph](mailto:rgjamora@up.edu.ph) (R.D.G. Jamora), [kcmoalong@up.edu.ph](mailto:kcmoalong@up.edu.ph) (K.M.C. Moalong), [adrian.espiritu@universityhealth.to](mailto:adrian.espiritu@universityhealth.to), [aiespiritu@up.edu.ph](mailto:aiespiritu@up.edu.ph) (A.I. Espiritu).

<https://doi.org/10.1016/j.yebeh.2022.108730>

1525-5050/© 2022 Elsevier Inc. All rights reserved.

## 1. Introduction

Since the discovery of neural tissue-specific autoantibodies by Dalmau and colleagues in 2007, autoimmune encephalitis (AE) has been increasingly recognized as a neurologic disease entity [1]. It presents with a subacute progression of neuropsychiatric symptoms, a clinical picture similar to infectious encephalitis. Advances in the diagnosis and treatment of AE resulted in an increased awareness of the condition among clinicians and patients alike [2]. A population-based study showed an increase

in the incidence rate of AE from 0.4 to 1.2 per 100,000 person-years when comparing data from 1995 to 2005 versus 2006 to 2015. Previously thought of as rare, it is now considered as common as the infectious type, with the discovery of the autoantibody and increased diagnostic ability as major contributors to the uptrend [3]. While it is emphasized that early diagnosis and appropriate treatment lead to improved outcomes, some patients are left with the chronic neuropsychiatric sequelae of the disease, whereas others experience relapses based on long-term follow-up studies [4].

Epileptic seizures are considered a core symptom and frequent manifestation of autoimmune encephalitis. In this setting, seizures are said to represent an acute, symptomatic, inflammatory process in the brain and are responsive to immunotherapy [2]. Unfortunately, there are cases in which seizures are enduring and resistant to antiseizure medications and immunotherapy and, as such, are more aptly termed autoimmune epilepsy. The concept of autoimmune epilepsy was first introduced in 2002 after antibodies to GluR3 had been found in severe epilepsies, including Rasmussen's encephalitis [5]. It was included in the most recent position paper on the classification of epilepsy by the International League Against Epilepsy (ILAE) and was defined as "epilepsy with evidence of autoimmune-mediated CNS inflammation" [6]. Over the last decade, research advances on autoimmune encephalitis have contributed to the growing evidence for epilepsy with "autoimmune" as etiology. In order to provide the basis for the distinction of seizures in the context of autoimmune encephalitis, the ILAE Autoimmunity and Neuroinflammation Taskforce proposed conceptual definitions of "acute symptomatic seizures secondary to autoimmune encephalitis" and "autoimmune-associated epilepsy" in 2020 [7].

Given the debilitating nature of autoimmune encephalitis and autoimmune epilepsy, often with delayed diagnosis and treatment, patients and their caregivers may turn to other information sources such as the internet to help them in decision-making. Furthermore, given the relative infrequency of the condition, clinicians may also search the internet for medical literature to aid them in taking care of patients afflicted with the condition.

In 2004, Google Trends (GT) was released, providing an online search data mining tool that made real-time and archived

web-based search data accessible to the public. It has been increasingly used as a methodology tool over the past years in what is now called infodemiology, or the "science of distribution and determinants of information in an electronic medium, specifically the Internet, or in a population, with the ultimate aim to inform public health and public policy" [8,9].

Infodemiology was first used in predicting outbreaks of influenza and other infectious diseases and has since been applied to various medical fields [8]. Several infodemiological studies on neurologic disorders and in various fields have been published, including multiple sclerosis, epilepsy, status epilepticus, stroke, meningitis, brain tumors, polio, movement disorders, Alzheimer disease, teleneurology, and telerehabilitation [10–20]. Online search trends for neurologic disorders were found to be related to a number of factors such as real-world epidemiologic data, seasonality of the disease, news about celebrities and other prominent figures or mass-media events, patients' emotions and perceptions about their disease, and public awareness campaigns [21]. Results of infodemiologic research may provide clinicians and health educators insights on health information-seeking behavior (HISB) as an indirect method of user-based needs assessment. Accordingly, such information could serve as a basis for health information exchange program design and implementation to ultimately improve care. To date, there is no published infodemiological study on autoimmune encephalitis. In addition, although there are a number of infodemiology studies on specific epilepsy topics, none explored the infodemiology of seizures and epilepsy in relation to an autoimmune etiology. Therefore, the aim of this study was to describe the online search behavior for autoimmune encephalitis, autoimmune seizures, and autoimmune epilepsy worldwide over time through the evaluation of trends of search volumes made on Google.

## 2. Methods

The search strategy employed in this paper is summarized in Table 1 based on the methodology recommendations from a systematic review on the use of GT (Alphabet Inc, Mountain View CA, USA) in healthcare research [9]. We entered the keywords "autoimmune encephalitis" in the GT main page (available at:

**Table 1**  
Checklist for Documentation of Google Trends Use.

Section/Topic	Checklist Item		
Search Variables			
Access Date	November 6, 2021	April 15, 2022	April 15, 2022
Google Data Source	Google Trends		
Time Period	January 1, 2004 to October 31, 2021		
Query Category	“Health” query category		
Region	Worldwide		
Countries with Low Search Volume	Included		
Search Input			
Full Search Input	“Autoimmune encephalitis” as “search term”	“Autoimmune seizures” as “search term”	“Autoimmune epilepsy” as “search term”
Combination	Only one search term was used; hence no combination of terms was applied in the search input.		
Quotation Marks	Keywords were queried with quotation marks.	Keywords were not queried with quotation marks as there were no results returned for when quotation marks were used.	Keywords were queried with quotation marks.
Rationale for Search Strategy			
For Search Input	We chose this keyword to capture all search queries related to AE regardless of the language used.	We chose this keyword because there is a sufficient amount of search data available for the term for it to be analyzed by Google Trends.	
For Settings Chosen	We chose January 1, 2004 as the start date to capture baseline interest prior to the discovery of the autoantibodies attributed to the condition (2007), “worldwide” to explore regional variation in search interest, and the “health” category to assess information demand in the context of health.		

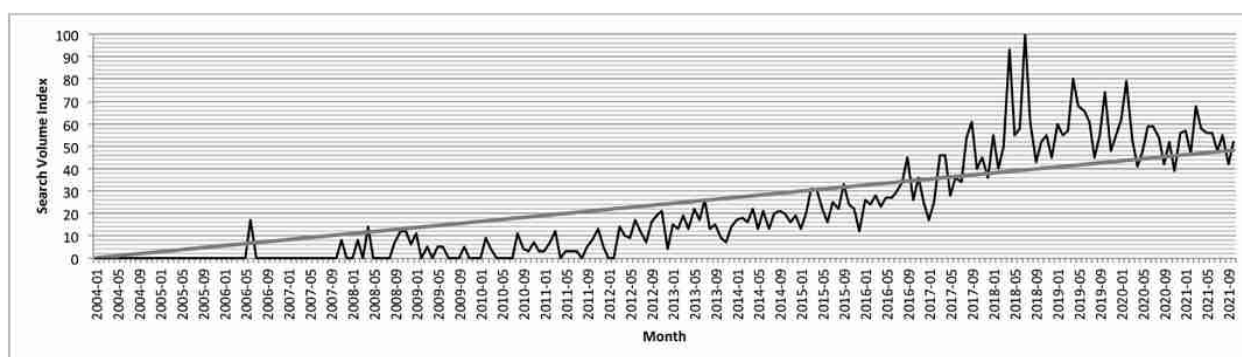
<http://www.google.com/trends>, accessed on November 6, 2021) to extract data on internet user search activities on AE. Using the GT built-in autocomplete function that suggests the most cost commonly used keyword, we selected “autoimmune encephalitis” as a “search term” to encompass all search queries that fall within the category. Worldwide search data from January 01, 2004 to October 31, 2021 were retrieved and downloaded as comma-separated value (.csv) datasets after applying the “health” category search parameter and the “web search” filter. Results were returned as search volume indices (SVI), which represent the search volume number for a particular search term relative to the overall search volume over time, expressed on a scale of 0 to 100. Similar steps were done for the keywords “autoimmune seizures” and “autoimmune epilepsy” with the same filters (available at: <http://www.google.com/trends>, accessed on April 15, 2022). Various search terms such as “autoimmune-related epilepsy”, “autoimmune-associated epilepsy”, “epileptic seizures from autoimmune encephalitis”, “seizures secondary to autoimmune encephalitis”, “seizures due to autoimmune encephalitis”, etc. were initially used to retrieve search data on “acute symptomatic seizures secondary to autoimmune encephalitis” and “autoimmune-associated epilepsy”; however, the results returned were an SVI of 0, meaning there are no sufficient data available for the search term.

We also retrieved and downloaded the.csv files of the “Top related topics,” “Rising related topics,” “Top related queries,” and “Rising related queries.” Top searches were defined as “top searches that are most frequently searched with the term entered in the same search session, within the chosen category, country, or region,” while Rising searches were “terms that were searched for with the keyword entered which had the most significant growth in volume in the requested time period” [22].

### 3. Results

#### 3.1. Search patterns for “autoimmune encephalitis (search term)”

Search volume analysis revealed a progressive increase in search volume numbers over time for the keyword “autoimmune encephalitis” with no annual seasonal variation (see Fig. 1). The first increase in online search interest since the start date was in June 2006 (17/100), followed by another increase in November 2007 (8/100). A steadily increasing trend was then seen with the peak search volume observed in July 2018 (100/100). The minimum SVI value was seen predominantly from 2004 to 2007 and finally in 2012 with a subsequent positive shift in background search volume.



**Fig. 1.** Graph showing the online search interest over time expressed as search volume index, aggregated per month, for the keyword “autoimmune encephalitis” worldwide from January 1, 2004 to October 31, 2021.

Based on regional interest, the greatest search volume for the keyword “autoimmune encephalitis” (search term) was recorded in Singapore (100/100), followed by Australia (84/100), the United States (83/100), the Philippines (79/100), New Zealand (77/100), Ireland (70/100), United Kingdom (69/100), United Arab Emirates (53/100), India (52/100), and Canada (46/100) (see Table 2).

The search queries returned for the keyword “autoimmune encephalitis” were related to AE definition, causes, symptoms, diagnosis, and treatment. In top related queries, “autoimmune encephalitis treatment” was the most related. Autoimmune encephalitis-related topics were terms corresponding to AE signs and symptoms (seizure and encephalopathy), diagnostics (cerebrospinal fluid, receptor, and Mayo Clinic), and treatment (immunoglobulin therapy and rituximab). Of note, the results returned for the keyword included only one specific type of antibody related to AE, N-methyl-D-aspartic acid or NMDA receptor. All related topics and queries had a more than 5000-fold increase in search volumes over time (see Table 3).

#### 3.2. Search patterns for “autoimmune seizures (search term)”

Analysis of online search behavior for the keyword “autoimmune seizures” demonstrated an uptrend in background search volume through time. There was also no seasonal variation displayed. The first peak in SVI was seen in February 2004 (46/100), while the maximum SVI (100/100) was in February 2005 (see Fig. 2). Search volume analysis for the keyword “autoimmune seizures” based on regional interest showed only the United States (100/100) as having the greatest tendency to search for the topic, while no other countries were returned in the results (see Table 2).

Of the top related topics, the term “seizures” was the most related (100/100). Other frequently searched topics related to the keyword “autoimmune seizures” included general terms (autoimmune disease, autoimmunity, epilepsy, immune system, immunity, brain, neurology, neurological disorder, and mental disorder) and specific autoimmune or immune-mediated diseases (systemic lupus erythematosus, multiple sclerosis, and Sjogren syndrome). Autoimmune encephalitis and encephalitis were also returned in the related topics. Terminologies on seizure semiology and epilepsy types such as generalized tonic-clonic seizure, absence seizure, focal epilepsy, and nonepileptic seizure were also frequently searched in relation to “autoimmune seizures”.

The top related queries revealed similar results. Broad topics such as autoimmune disease/s, autoimmune disorder/s, and epilepsy were frequently searched. Multiple sclerosis, fibromyalgia, autoimmune hepatitis, rheumatoid arthritis, celiac disease, and sarcoidosis were specific diseases in the list of related queries. Autoimmune encephalitis (47/100) and autoimmune epilepsy

**Table 2**

Results of search volume analysis returned for the keywords “autoimmune encephalitis”, “autoimmune seizures” and “autoimmune epilepsy” based on geographic location. SVI = search volume index.

“Autoimmune encephalitis”		“Autoimmune seizures”		“Autoimmune epilepsy”	
Country	SVI	Country	SVI	Country	SVI
Singapore	100	United States	100	United States	100
Australia	84				
United States	83				
Philippines	79				
New Zealand	77				
Ireland	70				
United Kingdom	69				
United Arab Emirates	53				
India	52				
Canada	46				
South Africa	31				
Malaysia	31				
Germany	8				
Turkey	4				
Indonesia	3				

(40/100) ranked second and fourth in the top related queries, respectively. Causes and types of seizures such as absence seizures were also frequently queried along with the “autoimmune seizures”. Of particular interest is the related query “faciobrachial dystonic seizures”, which is a distinct clinical manifestation of a specific type of autoimmune limbic encephalitis. All related topics and queries had a more than 5000-fold increase in search volumes over time (see Table 4).

### 3.3. Search patterns for “autoimmune epilepsy (search term)”

Analysis of search volumes for the keyword “autoimmune epilepsy” revealed an increase in background search volume in 2010 after two initial peaks were recorded in January 2007 (91/100) and March 2007 (85/100). The maximum SVI (100/100) for the keyword was in December 2012. An upward trend in the search volumes for the keyword was observed (see Fig. 3). As in

“autoimmune seizures”, the keyword “autoimmune epilepsy” was most frequently searched in the United States (100/100), with no other countries returned in the results of geographic search volume analysis (see Table 2).

Epilepsy and autoimmune disease (100/100) were the most frequently related topics to the keyword “autoimmune epilepsy”. Other topics were related to the definition (epilepsy, autoimmune disease, autoimmunity, seizure), pathophysiology (autoimmune encephalitis, temporal lobe, limbic system, paraneoplastic syndrome), symptoms (seizure), diagnosis (cerebrospinal fluid, antibody, Mayo Clinic, glutamate decarboxylase), and treatment of autoimmune epilepsy (intravenous immunoglobulin, immunoglobulin therapy). The top related topics returned for “autoimmune epilepsy” were similar to those of “autoimmune encephalitis”. Multiple sclerosis was also in the list for “autoimmune epilepsy” as in that for “autoimmune seizures”. There were no returned results for the top related queries for the keyword “autoimmune epilepsy”. All related topics had a more than 5000-fold increase in search volumes over time (see Table 5).

## 4. Discussion

This is the first infodemiological study to examine the online search behavior for the keywords “autoimmune encephalitis”, “autoimmune seizures”, and “autoimmune epilepsy” using GT as a data collection tool. Similar studies explored the use and role of the internet, specifically web searches in relation to HSB. The use of search volume data as a surrogate of online HSB has been suggested to provide information that is acquired traditionally from large-scale data collection via survey questionnaires and interviews that may be time-consuming and costly. The only caveat is that interpreting online search trend data requires context.

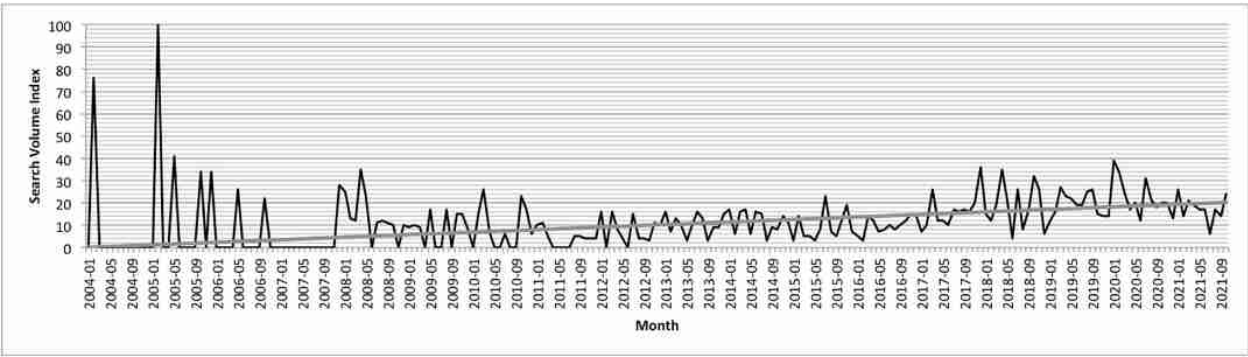
The uptrend in online search interest for AE may be explained by the increased awareness of the condition by the public and the medical community. The first increase was noted a year after Dr. Dalmau and his colleagues described four young females with neuropsychiatric symptoms, all diagnosed with encephalitis and

**Table 3**

Most frequently searched topics and queries returned for the keyword “autoimmune encephalitis” with their search volume indices. SVI = Search volume index.

Related Topics		Related Queries	
Top (SVI)	<b>Rising (% increase)</b>	<b>Top (SVI)</b>	<b>Rising (% increase)</b>
Autoimmunity (100)	Autoimmunity (>5000%)	autoimmune encephalitis treatment (100)	autoimmune encephalitis treatment (>5000%)
Autoimmune encephalitis (94)	Autoimmune encephalitis (>5000%)	autoimmune disease (83)	autoimmune disease (>5000%)
Encephalitis (26)	Encephalitis (>5000%)	autoimmune encephalitis symptoms (77)	autoimmune encephalitis symptoms (>5000%)
Autoimmune disease (11)	Autoimmune disease (>5000%)	autoimmune encephalitis panel (76)	autoimmune encephalitis panel (>5000%)
Anti-NMDA receptor encephalitis (6)	Anti-NMDA receptor encephalitis (>5000%)	what is autoimmune encephalitis (55)	what is autoimmune encephalitis (>5000%)
Antibody (5)	Antibody (>5000%)	nmda receptor autoimmune encephalitis (54)	nmda receptor autoimmune encephalitis (>5000%)
Brain (4)	Brain (>5000%)	autoimmune encephalitis causes (46)	autoimmune encephalitis causes (>5000%)
NMDA receptor (3)	NMDA receptor (>5000%)	autoimmune encephalitis icd 10 (44)	autoimmune encephalitis icd 10 (>5000%)
Seizure (2)	Seizure (>5000%)	autoimmune encephalitis mri (37)	autoimmune encephalitis mri (>5000%)
Immunoglobulin therapy (2)	Immunoglobulin therapy (>5000%)	brain on fire (26)	brain on fire (>5000%)
Encephalopathy (2)	Encephalopathy (>5000%)	anti nmda receptor autoimmune encephalitis (24)	anti nmda receptor autoimmune encephalitis (>5000%)
Rituximab (2)	Rituximab (>5000%)	autoimmune encephalitis in children (24)	autoimmune encephalitis in children (>5000%)
N-Methyl-D-aspartic acid (2)	N-Methyl-D-aspartic acid (>5000%)	symptoms of autoimmune encephalitis (13)	symptoms of autoimmune encephalitis (>5000%)
Cerebrospinal fluid (2)	Cerebrospinal fluid (>5000%)	seronegative autoimmune encephalitis (9)	seronegative autoimmune encephalitis (>5000%)
Immune system (2)	Immune system (>5000%)	autoimmune encephalitis radiology (9)	autoimmune encephalitis radiology (>5000%)
Hashimoto's thyroiditis (2)	Hashimoto's thyroiditis (>5000%)	anti-nmda-receptor autoimmune encephalitis (7)	anti-nmda-receptor autoimmune encephalitis (>5000%)
Receptor (1)	Receptor (>5000%)	brain on fire disease (4)	brain on fire disease (>5000%)
Mayo Clinic (1)	Mayo Clinic (>5000%)		
Limbic encephalitis (1)	Limbic encephalitis (>5000%)		
Limbic system (1)	Limbic system (>5000%)		



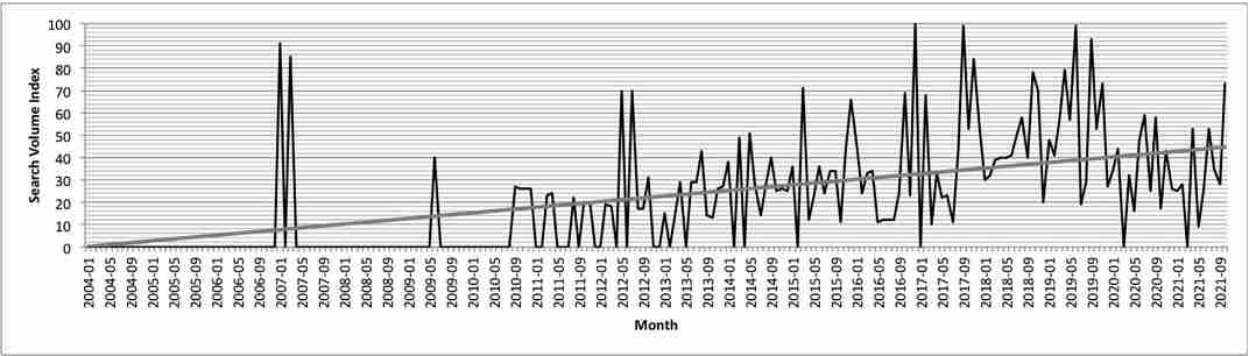


**Fig. 2.** Graph showing the online search interest over time expressed as search volume index, aggregated per month, for the keyword “autoimmune seizures” worldwide from January 1, 2004 to October 31, 2021.

**Table 4**

Most frequently searched topics and queries returned for the keyword “autoimmune seizures” with their search volume indices. SVI = Search volume index.

Related Topics		Related Queries	
Top (SVI)	Rising (% increase)	Top (SVI)	Rising (% increase)
Seizure (100)	Autoimmunity (>5000%)	autoimmune disease 9100)	autoimmune disease (>5000%)
Autoimmune disease (82)	Disease (>5000%)	autoimmune encephalitis (47)	autoimmune encephalitis (>5000%)
Autoimmunity (59)	Cause (>5000%)	autoimmune diseases (43)	autoimmune diseases (>5000%)
Disease (50)	Autoimmune encephalitis (>5000%)	autoimmune epilepsy (40)	autoimmune epilepsy (>5000%)
Epilepsy (18)	Systemic lupus erythematosus (>5000%)	epilepsy (40)	epilepsy (>5000%)
Cause (17)	Brain (>5000%)	autoimmune disorders (35)	autoimmune disorders (>5000%)
Autoimmune encephalitis (13)	Encephalitis (>5000%)	autoimmune disorder (30)	autoimmune disorder (>5000%)
Systemic lupus erythematosus (8)	Multiple sclerosis (>5000%)	lupus (22)	lupus (>5000%)
Brain (8)	Focal epilepsy (>5000%)	causes of seizures (22)	causes of seizures (>5000%)
Encephalitis (7)	Nonpileptic seizure (>5000%)	autoimmune disease in dogs (9)	seizures in dogs (>5000%)
Immune system (5)	Neurology (>5000%)	absence seizures (8)	autoimmune disease in dogs (>5000%)
Multiple sclerosis (5)	Neurological disorder (>5000%)	multiple sclerosis (7)	absence seizures (>5000%)
Focal epilepsy (4)	Mental disorder (>5000%)	autoimmune limbic encephalitis (7)	multiple sclerosis (>5000%)
Nonpileptic seizure (4)	Causes of seizures (>5000%)	types of seizures (6)	autoimmune limbic encephalitis (>5000%)
Neurology (4)	Generalized tonic clonic seizure (>5000%)	fibromyalgia (6)	types of seizures (>5000%)
Neurological disorder (3)	Antibody (>5000%)	autoimmune hepatitis (6)	fibromyalgia (>5000%)
Mental disorder (3)	Sjogren syndrome (>5000%)	faciobrachial dystonic seizures (5)	autoimmune hepatitis (>5000%)
Causes of seizures (3)	Human brain (>5000%)	rheumatoid arthritis (4)	faciobrachial dystonic seizures (>5000%)
Generalized tonic-clonic seizure (3)	Absence seizure (>5000%)	celiac disease (4)	rheumatoid arthritis (>5000%)
Antibody (3)	Immunity (>5000%)	sarcoidosis (4)	celiac disease (>5000%)
Sjogren syndrome (3)			sarcoidosis (>5000%)
Human brain (3)			
Absence seizure (3)			
Immunity (3)			



**Fig. 3.** Graph showing the online search interest over time expressed as search volume index, aggregated per month, for the keyword “autoimmune epilepsy” worldwide from January 1, 2004 to October 31, 2021.

ovarian teratoma. The succeeding increase in November 2007 was the same year when anti-NMDA (N-methyl-D-aspartic acid) receptor was identified [1]. The same explanation could be given for the increasing tendency to search for “autoimmune seizures” and

“autoimmune epilepsy” through the years. As physicians also turn to the internet to gain medical information, their queries may have also contributed to the upward search trends. The increasing search interest paralleled the rise in the number of publications

**Table 5**

Most frequently searched topics returned for the keyword “autoimmune epilepsy” with their search volume indices. SVI = Search volume index.

Related Topics	
Top (SVI)	Rising (% increase)
Autoimmune disease (100)	Autoimmune disease (>5000%)
Epilepsy (100)	Epilepsy (>5000%)
Autoimmunity (19)	Autoimmunity (>5000%)
Seizure (13)	Seizure (>5000%)
Antibody (8)	Antibody (>5000%)
Mayo Clinic (8)	Mayo Clinic (>5000%)
Autoimmune encephalitis (7)	Autoimmune encephalitis (>5000%)
Encephalitis (6)	Encephalitis (>5000%)
Immune system (6)	Immune system (>5000%)
Neurology (5)	Neurology (>5000%)
Immunoglobulin therapy (4)	Immunoglobulin therapy (>5000%)
Intravenous immunoglobulin (4)	Intravenous immunoglobulin (>5000%)
Immunity (3)	Immunity (>5000%)
Microsoft PowerPoint (3)	Microsoft PowerPoint (>5000%)
Assessment (2)	Assessment (>5000%)
Multiple sclerosis (2)	Multiple sclerosis (>5000%)
Paraneoplastic syndrome (2)	Paraneoplastic syndrome (>5000%)
Glutamate decarboxylase (2)	Glutamate decarboxylase (>5000%)
Temporal lobe (2)	Temporal lobe (>5000%)
Encephalopathy (2)	Encephalopathy (>5000%)
Cerebrospinal fluid (2)	Cerebrospinal fluid (>5000%)
Immunotherapy (2)	Immunotherapy (>5000%)
Limbic system (2)	Limbic system (>5000%)

over time on these topics, as noted after searching biomedical databases such as Pubmed and Scopus. This observation of expanding research interest in conjunction with higher search volumes was demonstrated in an infodemiology study on another rare autoimmune disorder, antiphospholipid syndrome [23]. Because user characteristics querying the web engine cannot be identified through GT, it is uncertain whether the upward tendency of search interest may be attributed to increased HISB of patients and their relatives or clinicians and researchers.

The maximum SVI for “autoimmune encephalitis” was recorded in July 2018. A Google search for peak-related news headlines using a custom date range and “news” filter showed the release of a biographical film of a New York Times writer named Susannah Cahalan afflicted with AE entitled “Brain on Fire” on an online streaming service on June 22, 2018, which can probably account for this peak in search interest. A positive shift in the background search volume for “autoimmune encephalitis” was seen in 2012, which was the year when the said writer released her book on AE. This is consistent with the results of previous studies that showed the effect of news headlines or mass media events on online search volumes [15,16]. This increase in online search behavior for health-related terms was labeled as the “Robin Williams’ phenomenon” based on the recorded Google search peak on the keyword “Parkinson’s disease” after the news on the actor’s disease was released [15,16,24,25]. Notably, “brain on fire” was also included in the returned search queries for the keyword “autoimmune encephalitis”, further suggesting the increased search interest driven by mass media. As for the keywords “autoimmune seizures” and “autoimmune epilepsy”, the maximum SVIs were recorded in February 2005 and December 2012, respectively. Unlike AE, these peaks in search interest did not seem to be temporally related to any news headlines.

Aside from long-term longitudinal trends, infodemiology reveals temporal patterns in HISB within a single year. In this study, no annual seasonal variation in search interest for “autoimmune encephalitis”, “autoimmune seizures”, or “autoimmune epilepsy” was observed, suggesting the possible lack of seasonality of the disease. This is in contrast to the findings of prior research demonstrating a cyclical trend of interest in relation to seasonal variation of a particular disease, e.g., influenza, multiple sclerosis

[15]. Analyzing temporal trends would help determine optimal times for public health education and promotion campaigns. The impact of public health education activities may be gauged by evaluating the change in online search interest in relation to the campaign launch. This effect of awareness campaigns to increase online HISB was suggested in infodemiological studies on epilepsy and colorectal cancer [10,26]. Whether the same can be said for AE and autoimmune epilepsy is unknown as there is limited information on specific awareness campaigns for these conditions. For instance, a global awareness day on encephalitis of both infectious and autoimmune types, a rare disease day featuring AE, and international epilepsy day, which all fall in February, did not coincide with any peaks in search activity on autoimmune encephalitis and autoimmune epilepsy.

Higher SVIs for AE were recorded from developed countries. There is no available epidemiology study on the geographical distribution of AE to suggest a possible disease-specific explanation for the regional trend. Better internet access and literacy may still be a plausible reason for the greater online search interest in developed countries. Interestingly, Singapore and the Philippines emerged with a relatively high SVI for AE. A possible explanation would be the relatively high percentage of internet users in Singapore at 75.88% and the Philippines at 46.88%, based on the most recent statistical report by the World Bank [27]. Due to the lack of available information on awareness campaigns on AE, it is difficult to elucidate the influence of awareness campaigns to account for the huge search volumes from these two countries. In addition, there were no news headlines of celebrities or prominent figures in these countries that could possibly contribute to the increased online search interest.

Aside from the socioeconomic-related digital divide contributing to higher search volumes from developed countries, another reason may be the greater scientific productivity in high-income countries. There is no published paper on research productivity by country or bibliometric analysis on autoimmune encephalitis, autoimmune seizures, and autoimmune epilepsy; however, a search in a citation database (Scopus) showed that the greatest number of articles on these keywords originates from the United States. This unequal global distribution of search interest and research publications was likewise observed in a study on antiphospholipid syndrome infodemiology [23].

With regard to spatial bias, a Google search returned news articles on AE published online from countries with high search volumes, namely Singapore, Australia, United States, Ireland, United Kingdom, and India. As aforementioned, a film release coincided with the highest peak in search interest on AE in the United States. However, the influence on search interest based on the geographic origin of the news report for the countries with the highest search volumes is uncertain, as further analysis of the temporal relationship between increased search volumes and the release of news reports from the same country of origin was not done in this study. Because the news articles did not involve celebrities and prominent people, the role of mass media may not be considered the main driver of the relatively great online search interest on AE, as was demonstrated for other condition in a previous study [15].

Most terms associated with the search queries for AE were related to causes and symptoms. In accordance with a similar publication, our results confirm that most people look for definitions and symptomatology regardless of the chronicity of the condition [15]. We also hypothesize that the heterogeneity of AE presentation is another reason for this need for clarification of the definition and symptoms. The top related search query was “autoimmune encephalitis treatment” with immunoglobulin therapy and rituximab emerging in the list. These are used as first- and second-line treatment options for AE, which may explain the frequency by which these are queried.

As for “autoimmune seizures” and “autoimmune epilepsy”, the terms “autoimmunity” and “autoimmune” were related terms frequently searched. We speculate that the complexity of the disease process is the possible reason which causes patients and caregivers to search for more information to increase their understanding of autoimmunity. Most search terms were also related to definition, symptoms, causes, diagnosis, and treatment. This is similar to the findings of a previous infodemiology study on epilepsy in general [28]. Notable is the inclusion of other specific autoimmune diseases, such as systemic lupus erythematosus and multiple sclerosis, in the list of related search queries. This does not come as a surprise as these conditions are the more common autoimmune diseases. Among the results for related search queries for autoimmune seizures, “faciobrachial dystonic seizures” is the only specific semiology that is distinctly associated with a particular autoimmune limbic encephalitis [29].

This study has some limitations inherent to infodemiological studies using web search engine trends. One limitation is intrinsic to the online search analysis tool used, that is, the data provided GT are normalized or relative, and thus are non-absolute search volumes. The online search queries sampled by GT are based only on data collected through Google. Although Google is the most popular search engine worldwide, the online search activity using other web search engines was not included in the analysis. Another limitation is the lack of demographic information regarding the users of the web search engine and the purpose of their search queries. Because our search employed English terms, only search volumes from English-speaking countries were analyzed. The results thus reflect online search behaviors of English-speaking internet users and this further limits the generalizability of the results. This study may not reflect real-world epidemiologic data due to the lack of precision in the use of internet metrics and traffic, but it could serve as indirect evidence of information demand and health information gaps. While causality testing cannot be done using data from GT, it may still be used for hypothesis generation and descriptive analysis. Despite these limitations, the use of infodemiology as a research method allows a quick and easy way to study the online behavior of millions of internet users worldwide.

## 5. Conclusion

To our knowledge, this was the first descriptive analysis of online search behavior related to autoimmune encephalitis, autoimmune seizures, and autoimmune epilepsy. This study showed an increasing online interest in autoimmune encephalitis over time, with most search queries related to symptoms, diagnosis, and treatment. The increased tendency to search online for autoimmune seizures and autoimmune epilepsy was also demonstrated. Information on online health information-seeking behavior from GT data may provide insights into the unmet needs related to health information and may serve to inform health information exchange policies and awareness campaigns.

## 6. Sources of support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CRediT authorship contribution statement

**Katrina T. Roberto:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.  
**Roland Dominic G. Jamora:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.

**Kevin Michael C. Moalong:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.  
**Adrian I. Espiritu:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.

## Declaration of competing interests

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## References

- [1] Dalmau J, Tüzün E, Wu H-Y, Masjuan J, Rossi JE, Voloschin A, et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007;61:25–36. <https://doi.org/10.1002/ana.21050>.
- [2] Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, Cellucci T, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol* 2016;15(4):391–404. [https://doi.org/10.1016/S1474-4422\(15\)00401-9](https://doi.org/10.1016/S1474-4422(15)00401-9).
- [3] Dubey D, Pittock SJ, Kelly CR, McKeon A, Lopez-Chiriboga AS, Lennon VA, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. *Ann Neurol* 2018;83(1):166–77.
- [4] Gibson LL, McKeever A, Coutinho E, Finke C, Pollak TA. Cognitive impact of neuronal antibodies: encephalitis and beyond. *Transl Psychiatry* 2020;10. <https://doi.org/10.1038/s41398-020-00989-x>.
- [5] Levite M. Autoimmune epilepsy. *Nat Immunol* 2002;3:500. <https://doi.org/10.1038/ni0602-500>.
- [6] Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia* 2017;58:512–21. <https://doi.org/10.1111/epi.13709>.
- [7] Steriade C, Britton J, Dale RC, Gadot A, Irani SR, Linnoila J, et al. Acute symptomatic seizures secondary to autoimmune encephalitis and autoimmune-associated epilepsy: Conceptual definitions. *Epilepsia* 2020;61(7):1341–51.
- [8] Eysenbach G. Infodemiology and infoveillance: Framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the internet. *J Med Internet Res* 2009;11:1–10. <https://doi.org/10.2196/jmir.1157>.
- [9] Nuti S V, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, et al. The use of Google trends in health care research: A systematic review 2014;9. <https://doi.org/10.1371/journal.pone.0109583>.
- [10] Moalong KMC, Jamora RDG, Roberto KT, Espiritu AI. Patterns of Google search behavior for epilepsy and seizures in the Philippines: An infodemiological study. *Epilepsy Behav* 2021;125. <https://doi.org/10.1016/j.yebeh.2021.108377>.
- [11] Coreia F, Budincevic H, De Marchis GM, Nasr N, Rutovic S, Zedde M. Outlining stroke infodemiology. *Telemed e-Health* 2020;26(4):380–1.
- [12] Mondia MWL, Espiritu AI, Jamora RDG. Brain tumor infodemiology: worldwide online health-seeking behavior using Google Trends and Wikipedia Pageviews. *Front Oncol* 2022;12. <https://doi.org/10.3389/fonc.2022.855534>.
- [13] Luigi N, Bacigaluppi S, Robba C, Nardone R, Trinka E, Brigo F. Infodemiology of status epilepticus: A systematic validation of the Google Trends-based search queries. *Epilepsy Behav* 2016;55:120–3. <https://doi.org/10.1016/j.yebeh.2015.12.017>.
- [14] Perez JALS, Espiritu AI, Jamora RDG. Google search behavior for meningitis and its vaccines: an infodemiological study. *BMC Neurol* 2021;21:1–7. <https://doi.org/10.1186/s12883-021-02258-w>.
- [15] Brigo F, Lochner P, Tezzon F, Nardone R. Web search behavior for multiple sclerosis: An infodemiological study. *Mult Scler Relat Disord* 2014;3:440–3. <https://doi.org/10.1016/j.msard.2014.02.005>.
- [16] Brigo F, Erro R. Why do people google movement disorders? An infodemiological study of information seeking behaviors. *Neurol Sci* 2016;37:781–7. <https://doi.org/10.1007/s10072-016-2501-5>.
- [17] Layug EJV, Espiritu AI, Calotes-Castillo LV, Jamora RDG. The association of online search interest with polio cases and vaccine coverage: an infodemiological and ecological study. *Eur J Pediatr* 2021;180:2435–41. <https://doi.org/10.1007/s00431-021-04049-4>.
- [18] Piamonte BLC, Anlacan VMM, Jamora RDG, Espiritu AI. Googling Alzheimer disease: an infodemiological and ecological study. *Dement Geriatr Cogn Dis Extra* 2021;11:333–9. <https://doi.org/10.1159/000520692>.
- [19] Lechico CFD, Austria EM, Espiritu AI. Global online interest in telehealth, telemedicine, telerehabilitation, and related search terms amid the COVID-19 pandemic: an infodemiological study. *Acta Med Philipp* 2021;1–10. <https://doi.org/10.47895/amp.vi0.3037>.
- [20] Alonto AHD, Jamora RDG, Lechico CFD, Espiritu AI. Low online search interest in teleneurology before and during COVID-19 pandemic: an infodemiological study. *Neurol Sci* 2022;43(5):2929–34. <https://doi.org/10.1007/s10072-022-05902-6>.

- [21] Moccia M, Brigo F, Tedeschi G, Bonavita S, Lavorgna L. Neurology and the Internet: a review. *Neurol Sci* 2018;39:981–7. <https://doi.org/10.1007/s10072-018-3339-9>.
- [22] Mavragani A, Ochoa G. Google trends in infodemiology and infoveillance: Methodology framework. *JMIR Public Heal Surveill* 2019;5:1–15. <https://doi.org/10.2196/13439>.
- [23] Sciascia S, Radin M, Unlu O, Erkan D, Roccatello D. Infodemiology of antiphospholipid syndrome: merging informatics and epidemiology. *Eur J Rheumatol* 2018;5(2). <https://doi.org/10.5152/eurjrheum.2018.17105>.
- [24] Bragazzi NL, Watad A, Brigo F, Adawi M, Amital H, Shoenfeld Y. Public health awareness of autoimmune diseases after the death of a celebrity. *Clin Rheumatol* 2017;36:1911–7. <https://doi.org/10.1007/s10067-016-3513-5>.
- [25] Mahroum N, Bragazzi NL, Sharif K, Gianfredi V, Nucci D, Rosselli R, et al. Leveraging Google Trends, Twitter, and Wikipedia to investigate the impact of a celebrity's death from rheumatoid arthritis. *J Clin Rheumatol* 2018;24:188–92. <https://doi.org/10.1097/RHU.0000000000000692>.
- [26] Kaminski M, Marlicz W, Koulaouzidis A. Googling on colonoscopy: A retrospective analysis of search engine statistics. *Clin Exp Gastroenterol* 2020;13:397–405. <https://doi.org/10.2147/CEG.S266546>.
- [27] Bank W. Individuals using the internet (% of population) - Philippines, Singapore n.d.
- [28] Brigo F, Igwe SC, Ausserer H, Nardone R, Tezzon F, Bongiovanni LG, et al. Epilepsy & Behavior Why do people Google epilepsy ? An infodemiological study of online behavior for epilepsy-related search terms. *Epilepsy Behav* 2014;31:67–70. <https://doi.org/10.1016/j.yebeh.2013.11.020>.
- [29] Irani SR, Michell AW, Lang B, Pettingill P, Waters P, Johnson MR, et al. Faciobrachial dystonic seizures precede Lgi1 antibody limbic encephalitis. *Ann Neurol* 2011;69(5):892–900. <https://doi.org/10.1002/ana.22307>.