

Public Interest in Raynaud's Phenomenon: A Google Trends Analysis

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Abstract

Introduction: Raynaud's phenomenon is a common disorder affecting body extremities. As infodemiological methods developed, online search tools could be used to explore the public interest of the disease. The study aimed to determine the annual trend, seasonal pattern, and associated topics of Raynaud's phenomenon.

Methods: Google Trends was used to collect the data. "Raynaud syndrome" was selected as the search term. Data on monthly relative search volume (RSV) were collected from 4 selected countries (United States, United Kingdom, Australia, and New Zealand) and globally. Related topics were obtained, and annual related topics were also collected for analysis.

Results: The maximum RSV appeared in January 2019, and the minimum value was observed in August 2011. The peak for RSV occurred in winter, and the bottom appeared in summer. In top related topics, "Maurice Raynaud" was the most related. In rising related topics, disease manifestations and autoimmune connective diseases were highly concerned. For annual related topics, associated diseases were attracting more attention over time.

Conclusions: The population is interested in related diseases, pathogenesis, and treatment. There was a peak in winter for searching and revealed that there might be a positive correlation between disease attack and seasonal variation.

Introduction

Raynaud's phenomenon is a common vasospasm response to cold or emotional stress, causing characteristic cutaneous color changes in the digits.^[1] It affects more women than men, and the prevalence of Raynaud's phenomenon was estimated from 3% to 5% in most population-based surveys.^[2] It can be idiopathic or secondary to another disease, including autoimmune connective tissue diseases.^[2] Primary and secondary Raynaud's phenomenon have different disease onset ages, patterns, pathogenesis, and prognosis.^[2, 3]

However, many people with Raynaud's phenomenon do not seek professional medical advice, because the damage to their quality of life might be mild.^[4] Nowadays, patients increasingly use the Internet to search for health-related information, which may influence medical decision-making.^[5] Therefore, infodemiological methods are becoming more and more competitive to estimate the disease epidemiological characteristics, to explore the public awareness of the management and treatment, and especially to detect and monitor the public interest of the disease.^[6]

Currently, the most frequently-used tool in addressing health issues related to Internet data is Google Trends. Researchers have conducted a lot of research using Google Trends in the rheumatology and immunology area, including systemic lupus erythematosus^[7], rheumatoid arthritis^[8], and multiple sclerosis^[9]. Recently, Hughes M. demonstrated that there existed a seasonal fluctuation on Internet

searches in Raynaud's phenomenon.[10] However, the overall trends, geographic distribution, and associate topics have not been completely elucidated. We collected the data from Google Trends and analyzed the trends to further illustrate the public interest.

Methods

Searching tool and Keyword selection

Google Trends was used to collect the data. Time and country could be restricted for comparison in Google Trends. A scale from 0 to 100 was used to represent the relative search volume (RSV) of a specific search term. A 100 value represents the highest RSV in a defined time period, and a value of 0 does not necessarily indicate no searches, but rather extremely low RSV.

The search term was chosen under the recommendation of a former guideline.[11] In our research, Google Trends did not provide a topic that contains the search term "Raynaud's phenomenon." Instead, "Raynaud syndrome" was given as a topic, which included all information from the search term "Raynaud's phenomenon."

Data query

The time range was set from January 2004 to December 2019. The "Health" category was selected to exclude irrelevant information like brand names. Results of regions whose RSV was lower than 5 were automatically excluded in the heat map of RSV among countries and regions. On 5 March 2020, data of the "Worldwide" RSV were exported to Microsoft Excel 2019.

Related topics of the search term from Google Trends were also extracted. Google Trends provided two types of related topics. One is the "Top related topics," defined as the most frequently searched topics within the chosen category, time, or country. The other is the "Rising related topics," which had the highest growth in volume and was presented as a percentage of fold changes. Non-related results were excluded manually. To examine the variation of the related topics over time, we further queried and analyzed the annual "Top related topics" and "Rising related topics." The top 3 topics were selected for analysis.

For seasonal variation analysis, four countries whose official language was English were included. United States, United Kingdom were the representatives from the Northern hemisphere, while Australia and New Zealand were the samples from the Southern hemisphere.

Statistical analysis

All analysis was conducted on the R software (v 3.6.2), and the graphs were directly obtained from the plotting function of R. The average monthly RSV in a year was calculated. A smooth curve was then added to the algorithm using the "spline" function in R. A cosinor model was used for seasonal analysis according to Barnett's research[12]. A "season" package was applied to produce boxplots of seasonal variation for different countries. A p-value < 0.05 was considered statistically significant.

Ethical requirements

This study did not involve animal experiments or clinical trials. Thus, permission from the ethical committee was not needed.

Results

Annual trends

Figure 1 shows the overall trends for RSV changing over time. The maximum RSV appeared in January 2019, and the minimum value was observed in August 2011. The average searching strength was slightly decreased before 2015 and showed an overall increasing trend after 2016.

Fig 1. The overall trends for the Relative Search Volume from 2004 to 2019.

Seasonal variation

All curves were fitted with the “cosinor” model in Figure 2 (all p-value < 0.05), which showed the seasonal variation for the RSV. The analysis revealed that the peak for the RSV in Raynaud’s phenomenon occurred in winter (February for the United Kingdom and the United States, and August for New Zealand and Australia) and a bottom in summer (February for New Zealand and Australia, and August for the United Kingdom and the United States).

Fig 2. Seasonal variation for the Relative Search Volume in New Zealand, Australia, the United Kingdom, and the United States.

Geographic distribution

France had the highest RSV (n=100), followed by Netherlands (n=94), United Kingdom (n=91), Ireland (n=86), Canada (n=83), and the United States (n=81). The geographic distribution graph was shown in Supplementary Table 1. Overall, a country or region in higher latitude may yield more RSV than that in lower latitudes.

Related topics

The related topics in Raynaud’s phenomenon from 2004 to 2019 were listed in Table 1. In top related topics, “Maurice Raynaud” was the most related (n=100), followed by “systemic lupus erythematosus” (n=26), “scleroderma” (n=23), “cold” (n=20), “lupus erythematosus” (n=13), “Sjogren syndrome” (n=11) and others. In rising related topics, “purple”, “systemic scleroderma”, “autoimmunity”, “vasculitis”, “anti-nuclear antibody”, “peripheral artery disease”, “Reye syndrome” and “connective tissue disease” were the “Breakout”. The rest of the top and rising topics were also listed in Table 1. Results

marked "Breakout" had a tremendous increase over 5000%, probably because these topics newly emerged with fewer previous searches.

Table 1. Related topics in Raynaud's phenomenon from 2004 to 2019.

The annual related topics were also summarized for comparative analysis in Table 2. The results for top related topics were consistent with the above ones. "Maurice Raynaud" had the most occurrences during the 16-year interval (16/16), and followed by "hand" (8/16), "scleroderma" (7/16), "systemic lupus erythematosus" (5/16), "syndrome" (4/16), "disease" (3/16) and others. For rising related topics, associated diseases of Raynaud's phenomenon had the most appearance, including the term "rheumatoid arthritis", "thromboangiitis obliterans", "autoimmune disease", "complex regional pain syndrome", "vasculitis", "Kawasaki disease", "giant-cell arteritis", "epileptic spasms" and so on. Manifestations and treatment options of Raynaud's phenomenon were also listed in the rising related topics, such as "paresthesia", "vibration", "chilblains", "acrocyanosis" and "endoscopic thoracic sympathectomy", "pentoxifylline", "nitroglycerin."

Table 2. Annual related topics in Raynaud's phenomenon from 2004 to 2019.

Discussion

Raynaud's phenomenon is characterized as painful vasospasm of small arteries localized in distant body extremities, and its pathogenesis has not been completely elucidated.[13, 14] The Internet is being widely used for seeking health information nowadays, with about a third of the population in the world depending on it.[15] Recently, infodemiological methods were demonstrated to be competitive in providing real-time monitoring of psychological and behavioral outcomes in the medical and health area. [16] The use of search engines is also associated with a physician visit and serves as a supplement to health care services.[17] Google Trends is particularly useful, for it offers several valuable insights into the health information-seeking behavior and collects the Internet activities concerning a specific topic.[18-20]

This study applied Google Trends to evaluate public interest in Raynaud's phenomenon. The results of our study revealed that the average number of RSV per year decreased between 2004 to 2015, and rapidly rebounded after 2016. The data indicated that this topic received more and more attention in recent years. Internet search trends may facilitate surveillance, early detection of disease patterns, and controls in healthcare settings.[21] Countries in the Northern hemisphere had higher numbers of RSV according to the rank of the searching strength divided by regions. The top 6 countries with the most RSV were all from the Northern Hemisphere, which was consistent with other previous research. [21, 22] This phenomenon could be explained by the hypothesis that the main developed and the most populous countries were in the Northern hemisphere, and the broad Internet usage or accession in proportional to the amount of Internet traffic might cause a bias. [23] Besides, a country or region with higher latitude may have RSV far more than average, for they have a lower temperature, which may be important precipitating factors of the Raynaud's phenomenon.

When it comes to related topics, the top is Maurice Raynaud, a French physician who discovered Raynaud's phenomenon in his doctoral thesis.[24] Besides, Raynaud's phenomenon is often the first clinical manifestation of connective tissue diseases.[25] Systemic sclerosis, Systemic lupus erythematosus, and Sjögren syndrome are the most common connective tissue diseases associated with the secondary Raynaud's phenomenon[26], which could partially explain the high relevance of these topics to the search of Raynaud's phenomenon in Google. Clinical practice indicates that the most effective therapy for Raynaud's phenomenon is the avoidance of cold.[27] The low temperature would significantly increase the severity of the disease symptoms. In cutaneous blood vessels, cold could activate vasoconstriction by selectively amplifying vascular smooth muscle constriction to norepinephrine.[28] Raynaud's Phenomenon occurs more frequently in thromboangiitis obliterans (Buerger's disease) and small/medium-sized vessel vasculitis than in large vessel vasculitis. Clinical evidence suggests that the anti-nuclear antibody may play a role in the pathogenesis of Raynaud's phenomenon.[29, 30] The vascular remodeling of Raynaud' s phenomenon is associated with the prevalence of the autoimmune antibodies and can induce endothelial apoptosis.[31, 32] Reye's syndrome may only have a similar spelling of Raynauds' syndrome, which may account for the rising search of Reye's syndrome.

Table 2 shows the trends for the evolution of associated public concerns annually. For the top topics with the highest RSV, they have subtle changes over the time frame. The hottest theme is still about Maurice Raynaud, and search on the contributions or bibliography of the scientist was highly related to Raynaud's phenomenon. In recent five years, scleroderma and systemic lupus erythematosus were attracting more attention, for they are the most common diseases that Raynaud's phenomenon is secondary to.[26] "Hand", "paresthesia", "syndrome", "disease" are the terms associated with the location or manifestation of the disease. The rising topic shows the transition of the public focus. Before 2014, people searched for more health information on the Internet concerning the manifestations and management of Raynaud's phenomenon. This was consistent with the research hot spot, for early research was always to explore and identify the clinical syndromes, such as paresthesia and acrocyanosis.[33] Therapy for this disease also attracted much attention, such as pharmacotherapy of nitroglycerin or pentoxifylline[34, 35], and surgical method like endoscopic thoracic sympathectomy[36]. In recent years, more searches focused on the pathogenesis and associated diseases. These topics were also mentioned in the publication of the latest articles which elucidated the possible molecular mechanisms and associated diseases.[25]

The seasonal analysis could provide extra evidence. The previous study had demonstrated the seasonal pattern of the RSV in Raynaud's phenomenon.[10] We separately analyzed four different countries and tried to broaden the conclusion globally. The monthly RSV shows peaks in winter for both the northern and southern hemisphere countries, with low points in summer correspondingly. This might illustrate that temperature could be a key factor leading to Raynaud's phenomenon, partially explained disease development, severity, and progression. This also demands future clinical research to evaluate the effect of seasonal variation.[10]

Although the pathogenesis of Raynaud's phenomenon has not been completely elucidated, the possible molecular mechanisms had been discussed in detail. In individuals affected by Raynaud's phenomenon, long-lasting vasoconstriction will result in clinical symptoms, ranging from general discomfort to serious, disabling conditions.[2] Dysregulation of autonomic and small sensory nerve fibers, involving the abnormal release of several chemical substances (calcitonin gene-related peptide, neurokinin A, substance P, vasoactive intestinal peptide, adrenergic agonists and nerve growth factor), leads to abnormal vasoconstriction of peripheral small vessels.[25] The severe fibrotic proliferation of the intima and other structural abnormalities secondary to connective tissue diseases are the fundamental changes causing secondary Raynaud's disease.[37] Increased levels of endothelin-1 (ET1), one of the most potent endogenous vasoconstrictors released by the endothelium during cell injury,[38] contribute to the progressive obliteration of the vessel lumen with other inflammatory mediators.[39] Platelet activation and oxidative stress resulting in hyperviscosity and leukocyte activation are possible pathogenic factors for Raynaud's disease.[25] These results also appeared in the related topics with high RSV annually and reflected the public interest.

Several limitations should be addressed in this study. First, the search may not be completely queried by the patients but the population who are interested in the field. Second, there may exist a selective bias, because the disease did not attract enough attention in the underdeveloped areas. Third, some people may use other search engines instead of Google to search for health information, but such data were not included.

Conclusions

Google Trends was used to examine the trends and related topics over time in Raynaud's phenomenon. Many people are interested in related diseases, pathogenesis, and treatment. There was a peak in winter for searching and revealed that there might be a positive correlation between disease attack and seasonal variation. The study of underlying mechanisms of seasonal variation in Raynaud's phenomenon is needed. Further studies of pathogenesis, comorbidity, and treatment are also highly warranted.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

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Competing interests

The authors declare that they have no competing interests.

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Not applicable

Data availability

All data could be accessed from Google Trends. (<https://trends.google.com/>)

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Tables

Top Related Topics	Relative Search Volume	Rising Related Topics	Changing Fold
Maurice Raynaud	100	Purple	Breakout
Systemic lupus erythematosus	26	Systemic scleroderma	Breakout
Scleroderma	23	Autoimmunity	Breakout
Cold	20	Vasculitis	Breakout
Lupus erythematosus	13	Anti-nuclear antibody	Breakout
Sjogren syndrome	11	Peripheral artery disease	Breakout
Thromboangiitis obliterans	8	Reye syndrome	Breakout
Autoimmune disease	7	Connective tissue disease	Breakout
Phenomenon	7	Cold	1050%
Glove	7	Lupus erythematosus	650%
Nifedipine	6	Maurice Raynaud	350%
Purple	5	Thromboangiitis obliterans	350%
Systemic scleroderma	4	Autoimmune disease	300%
Autoimmunity	4	Sjogren syndrome	300%
Vasculitis	4	Glove	300%
Anti-nuclear antibody	3	Systemic lupus erythematosus	250%
Peripheral artery disease	3	Nifedipine	200%
Reye syndrome	3	Scleroderma	190%
Connective tissue disease	3	Phenomenon	100%

Table 1. Related topics in Raynaud's phenomenon from 2004 to 2019.

Year	Top Related Topics	Growth	Rising Related Topics	Growth
2004	Maurice Raynaud	100	Paresthesia	Breakout
	Scleroderma	56	Rheumatoid arthritis	Breakout
	Paresthesia	34	Autoimmune disease	Breakout
2005	Maurice Raynaud	100	Thromboangiitis obliterans	Breakout
	Systemic lupus erythematosus	33	Vibration	Breakout
	Hand	28	Biofeedback	Breakout
2006	Maurice Raynaud	100	Connective tissue disease	Breakout
	Scleroderma	35	Complex regional pain syndrome	Breakout
	Hand	33	Glove	Breakout
2007	Maurice Raynaud	100	Vasculitis	Breakout
	Scleroderma	35	Anti-nuclear antibody	Breakout
	Hand	35	Chilblains	Breakout
2008	Maurice Raynaud	100	Endoscopic thoracic sympathectomy	Breakout
	Hand	44	Nitroglycerin	Breakout
	Scleroderma	34	Vascular disease	Breakout
2009	Maurice Raynaud	100	Kawasaki disease	Breakout
	Syndrome	69	Giant-cell arteritis	Breakout
	Hand	39	Epileptic spasms	Breakout
2010	Maurice Raynaud	100	Rett syndrome	Breakout
	Syndrome	59	Pentoxifylline	Breakout
	Hand	36	Compartment syndrome	Breakout
2011	Disease	100	Pentoxifylline	Breakout
	Maurice Raynaud	69	Reye syndrome	300%
	Syndrome	47	Glove	250%
2012	Disease	100	Chilblains	250%
	Maurice Raynaud	72	Telangiectasia	250%
	Syndrome	39	Guillain-Barré syndrome	170%
2013	Maurice Raynaud	100	Systemic scleroderma	250%
	Syndrome	48	Carpal tunnel syndrome	140%
	Hand	32	Hand	60%
2014	Maurice Raynaud	100	Acrocyanosis	160%
	Hand	29	Calcium channel	90%
	Scleroderma	19	Erythromelalgia	90%
2015	Maurice Raynaud	100	Vasodilation	200%
	Cold	19	Circulation	200%
	Scleroderma	18	Vibration	170%
2016	Maurice Raynaud	100	Glove	130%
	Systemic lupus erythematosus	42	Lupus erythematosus	110%
	Scleroderma	34	Autoimmune disease	50%
2017	Maurice Raynaud	100	Cryoglobulinemia	100%
	Systemic lupus erythematosus	41	Mixed connective tissue disease	100%
	Scleroderma	34	Peripheral artery disease	90%
2018	Disease	100	Dermatomyositis	140%
	Maurice Raynaud	23	Vascular disease	110%
	Systemic lupus erythematosus	10	Erythromelalgia	100%
2019	Maurice Raynaud	100	Systemic scleroderma	60%
	Systemic lupus erythematosus	45	Vibration white finger	50%
	Scleroderma	35	Not available	-

Table 2. Annual related topics in Raynaud's phenomenon from 2004 to 2019.

Figures

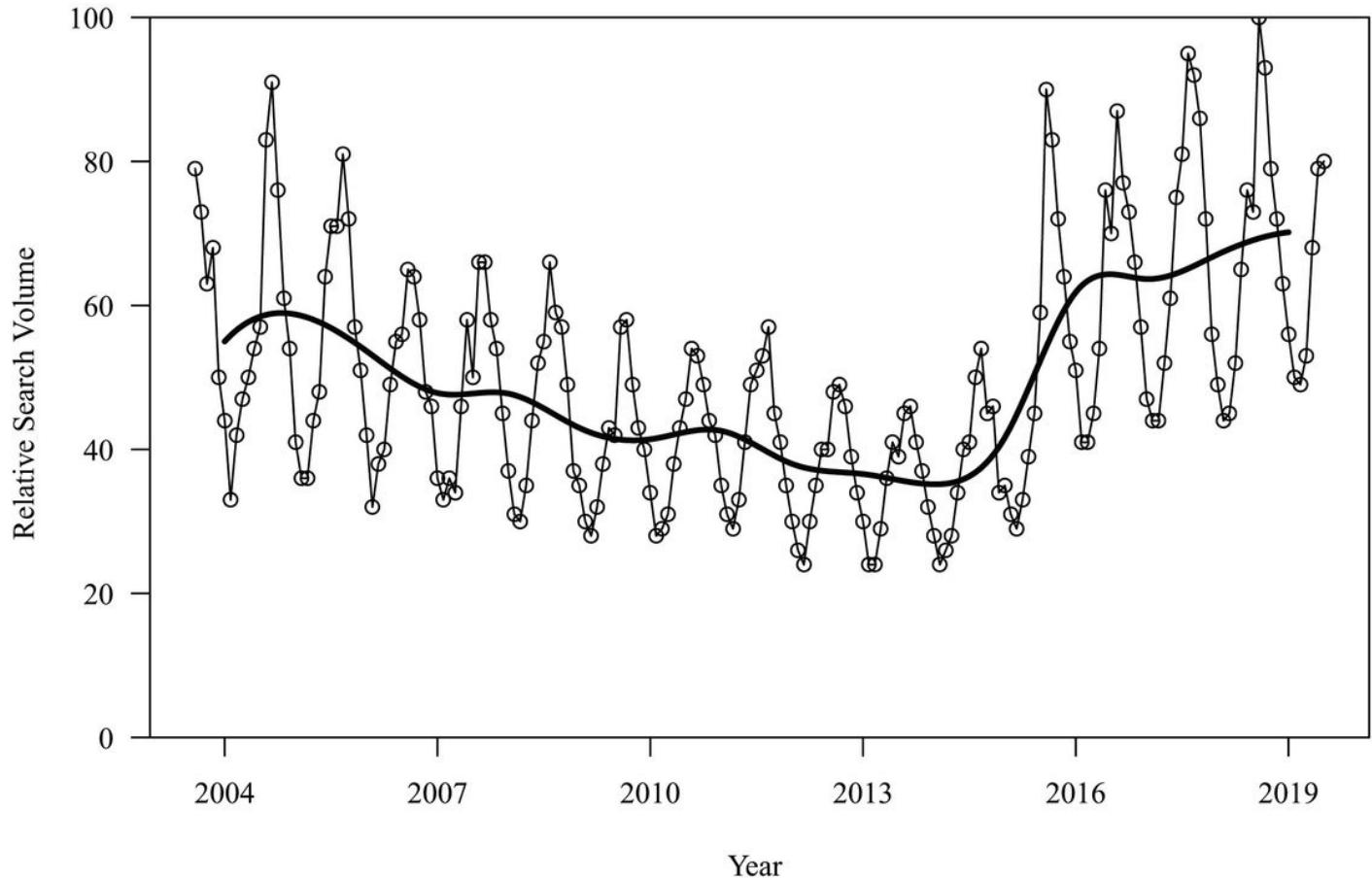


Figure 1

The overall trends for the Relative Search Volume from 2004 to 2019. Seasonal variation

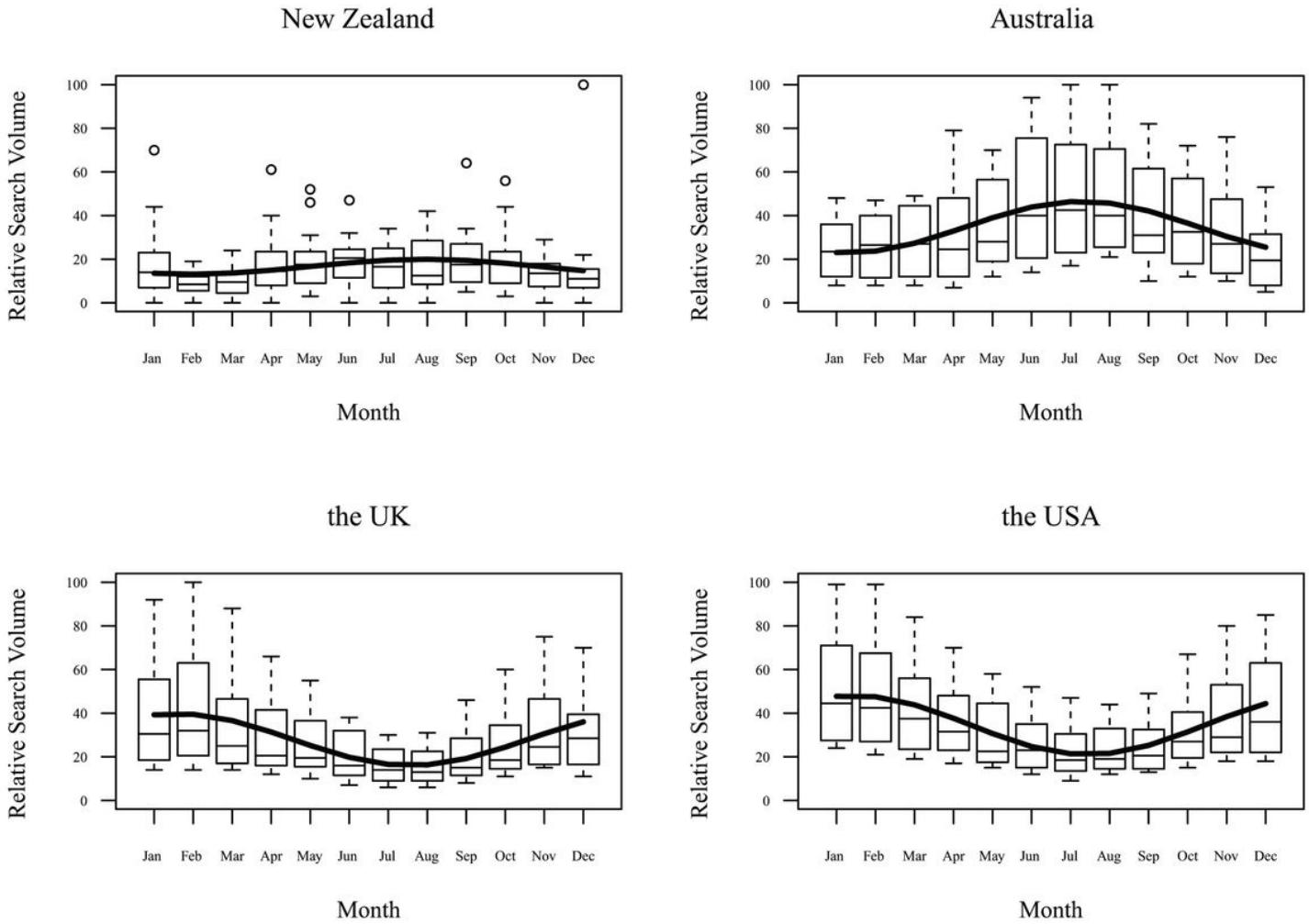


Figure 2

Seasonal variation for the Relative Search Volume in New Zealand, Australia, the United Kingdom, and the United States.