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Seasonal trends in tinnitus symptomatology: evidence from Internet search engine query data

David T. Plante · David G. Ingram

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Abstract The primary aim of this study was to test the hypothesis that the symptom of tinnitus demonstrates a seasonal pattern with worsening in the winter relative to the summer using Internet search engine query data. Normalized search volume for the term 'tinnitus' from January 2004 through December 2013 was retrieved from Google Trends. Seasonal effects were evaluated using cosinor regression models. Primary countries of interest were the United States and Australia. Secondary exploratory analyses were also performed using data from Germany, the United Kingdom, Canada, Sweden, and Switzerland. Significant seasonal effects for 'tinnitus' search queries were found in the United States and Australia ($p < 0.00001$ for both countries), with peaks in the winter and troughs in the summer. Secondary analyses demonstrated similarly significant seasonal effects for Germany ($p < 0.00001$), Canada ($p < 0.00001$), and Sweden ($p = 0.0008$), again with increased search volume in the winter relative to the summer. Our findings indicate that there are significant seasonal trends for Internet search queries for tinnitus, with a zenith in winter months. Further research is indicated to determine the biological mechanisms underlying these findings, as they may provide insights into the pathophysiology of this common and debilitating medical symptom.

D. T. Plante (✉)
Department of Psychiatry, Wisconsin Psychiatric Institute and Clinics, University of Wisconsin School of Medicine and Public Health, 6001 Research Park Blvd., Madison, WI 53719, USA
e-mail: dplante@wisc.edu

D. G. Ingram
Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

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Introduction

Tinnitus is a common symptom in which an individual perceives auditory sensations in the absence of corresponding external stimuli [1]. Distinguishing tinnitus from auditory hallucinations associated with psychotic disorders is the unformed acoustic nature of the sensation, classically described as a buzzing, hissing, or ringing [2]. The prevalence of tinnitus is roughly 10–15 % of the adult population, with similar estimates among countries with varied economic resources, geography, and climate; suggesting tinnitus is a worldwide problem [1]. Notably, tinnitus is also associated with significantly decreased quality of life in 1–2 % of the general population, and has been associated with increased rates of depression, anxiety, insomnia, and hearing difficulties [2, 3]. In addition, tinnitus is associated with increased risk of disability pension, underscoring the need for further research into the factors that underlie this problematic symptom [4].

The etiology of tinnitus is often multifactorial and/or not readily identifiable. Hearing loss due to presbycusis or occupational noise exposure are the conditions most commonly associated with tinnitus [5–7]. However, the relationship between hearing loss and tinnitus is not straightforward, as many with hearing loss do not report tinnitus, and conversely, many with tinnitus have audiometrically normal hearing [1]. There are myriad other diseases and/or factors associated with tinnitus, including various otological (infectious, neoplastic, and labyrinthine), neurological, rheumatological, metabolic, and psychiatric disorders, as well as head trauma and ototoxic

medications [1]. Notably, some conditions associated with tinnitus such as allergic rhinitis and mood disorders demonstrate seasonal variability [8, 9]. In addition, seasonal patterns of respiratory tract infections and their associations with acute otitis media, which can be associated with tinnitus [1], have been substantiated using viral testing [10]. It has long been clinically observed that tinnitus may worsen during changes of season, particularly during winter months [11, 12]; however, to our knowledge, there are no systematic epidemiologic studies that have examined seasonal patterns of tinnitus in large populations. Moreover, empiric studies that have examined seasonal patterns of tinnitus in association with idiopathic sudden sensorineural hearing loss, occupational exposure, or vestibular disorders, have failed to demonstrate circannual rhythms, possibly due to relatively low sample size [13–16].

Internet-based search engines represent a novel data source for examining a wide array of medical symptoms in the population. Roughly 5 % of Internet search queries are for health-related information [17], and previous investigations have leveraged this data to study seasonal or other time-varying patterns of several health conditions, including influenza [18], mental illness [9, 19], smoking habits [20], health-related behavior change [21], and sleep disorders [22, 23]. Google Trends (google.com/trends), a valuable research tool that has only recently been made available to the general public, represents a very large repository of search query data since the year 2004, and has been utilized for the majority of these prior research efforts. Google Trends may be particularly useful in studying the epidemiology of symptoms associated with otorhinolaryngological disorders, as it allows for the assessment of data from patients who visit clinicians in private practice outside of academic settings, and/or do not seek medical attention for symptoms that may resolve spontaneously [24].

The primary aim of this study was to utilize Internet search query data from Google Trends to test the hypothesis that there is seasonal variability of the symptom of tinnitus. Our hypothesis was that there would be a seasonal pattern to queries for this symptom, with increases in search volume during winter relative to summer months.

Methods

The search term ‘tinnitus’ was examined using Google Trends, an Internet-based tool that analyzes Google web searches. Details regarding Google Trends are available elsewhere (support.google.com/trends). Briefly, users may enter any search term, and the tool computes how many searches have been done for that term relative to the total number of searches done on Google to estimate the likelihood that a random user will enter that particular search term at a physical location and time. The system eliminates searches that were repeated over a short period of time from the same user, and normalizes the data against total search volume. Results are displayed on a scale from 0 to 100 with individual values over time calculated by dividing each point on the graph by the highest value and multiplying by 100. Similar to prior studies [22, 23], the current study utilized monthly data that were collected by manually highlighting each data point on a given Google Trends plot and recording the value for offline analysis (12 points per year × 10 years per search query = 120 data points for each country). A screenshot was collected for each time point for record-keeping purposes. Data were crosschecked by two separate individuals to assess the veracity of the data prior to analysis. Queries were limited by country of origin (see below) within the timeframe of January 2004 to December 2013. All searches were performed between February 3rd and 18th, 2014.

Similar to prior investigations examining the seasonality of illness using Internet search query data [9, 19, 22, 23], the a priori primary countries of interest in this study were the United States and Australia. This strategy allows for evaluation of seasonal patterns of search queries that should be out of phase by approximately 6 months between these countries, since they lie on opposite sides of the equator. To substantiate findings of the primary analysis, a secondary analysis was conducted that included other countries with sufficient monthly search volume since the year 2004 for analysis. This secondary analysis included data from Germany, the United Kingdom, Canada, Sweden, and Switzerland. There were no additional countries from the southern hemisphere with sufficient search volume for secondary analysis. ‘Tinnitus’ was used as the primary search term even in countries in which English is not the popular language because equivalent non-English terms had either insufficient search volumes for analyses (i.e., Sweden: ‘öronsusning’; Switzerland: ‘acouphene’, ‘ohrgeräusche’, and ‘tinnito’) or had search volumes that were approximately 7- to 10-fold lower than ‘tinnitus’ (i.e., Germany: ‘ohrgeräusche’).

Cosinor analysis was employed to test the hypothesis that there was significant seasonal variation in normalized search volume (NSV) over time, using methods similar to prior investigations [22, 23]. This method and the software used to implement it are described in detail elsewhere [25]. Briefly, cosinor analysis fits a sinusoid to an observed time series and estimates the amplitude (A, magnitude of seasonal effect) and phase (P, timing of seasonal peak), with the length of seasonal cycle set at 12 for monthly data. Since the seasonal component of the sinusoid is composed of both sine and cosine

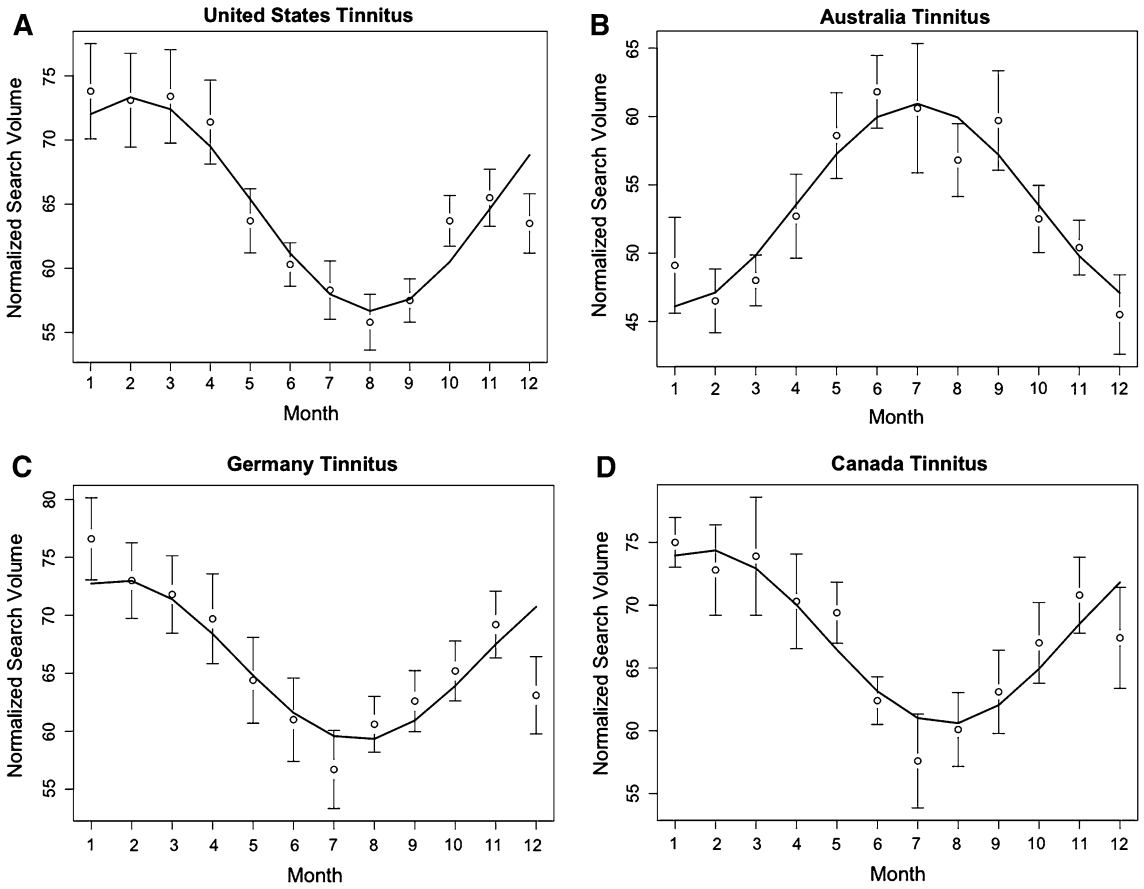

Fig. 1 Seasonal variation in normalized Internet search queries for 'tinnitus' in **a** the United States, **b** Australia, **c** Germany, **d** Canada, **e** Sweden, **f** United Kingdom, and **g** Switzerland. *Lines* indicate fitted cosinor models based on continuous data from January 2004 to December 2013. Open data points with *error bars* are monthly mean ± standard error plotted for visual purposes. Numeric values correspond to months as follows: January = 1; February = 2; March = 3; April = 4; May = 5; June = 6; July = 7; August = 8; September = 9; October = 10; November = 11; December = 12

functions, reported p values are multiplied by two for multiple comparison correction [22, 23]. Alpha was fixed at 0.05 for significance. The 'season' package in R version 2.15.2 was used to perform all cosinor analyses [25]. Additionally, similar to other investigations [26], the magnitude of seasonal effect for countries demonstrating significant seasonality of search volume was calculated as the percent change in NSV from winter months (United States: December, January, February, March; Australia: June, July, August, September) to summer months (United States: June, July, August, September; Australia: December, January, February, March).

The University of Wisconsin-Madison Health Sciences Institutional Review Board deemed this study did not constitute human subjects research as defined by 45 CFR 46.102(f) of the Health and Human Services Policy for Protection of Human Research Subjects. Consistent with institutional policy governing use of existing data sets, this study was exempt from IRB oversight.

Results

Seasonal peaks and troughs for 'tinnitus' were suggested by visual inspection of the data for both primary countries of interest. Cosinor models confirmed significant seasonal effects in both the United States ($A = 8.3$, $P = 2.1$, $p < 0.00001$) and Australia ($A = 7.4$, $P = 7.0$, $p < 0.00001$). Notably, peak searches were approximately 5 months out of phase with each other, with peaks in the winter (February for United States; July for Australia) in each country, consistent with a seasonal pattern (Fig. 1a, b).

Secondary analysis demonstrated significant seasonal effects for 'tinnitus' with peaks in winter for Germany ($A = 6.9$, $P = 1.6$, $p < 0.00001$), Canada ($A = 6.9$, $P = 1.7$, $p < 0.00001$), and Sweden ($A = 5.9$, $P = 1.5$, $p = 0.0008$) (Fig. 1c–e). Significant seasonal effects were not observed using cosinor analysis for the United Kingdom ($A = 2.6$, $P = 3.3$, $p = 0.30$) or Switzerland ($A = 3.0$, $P = 1.5$, $p = 0.18$), however, visual inspection

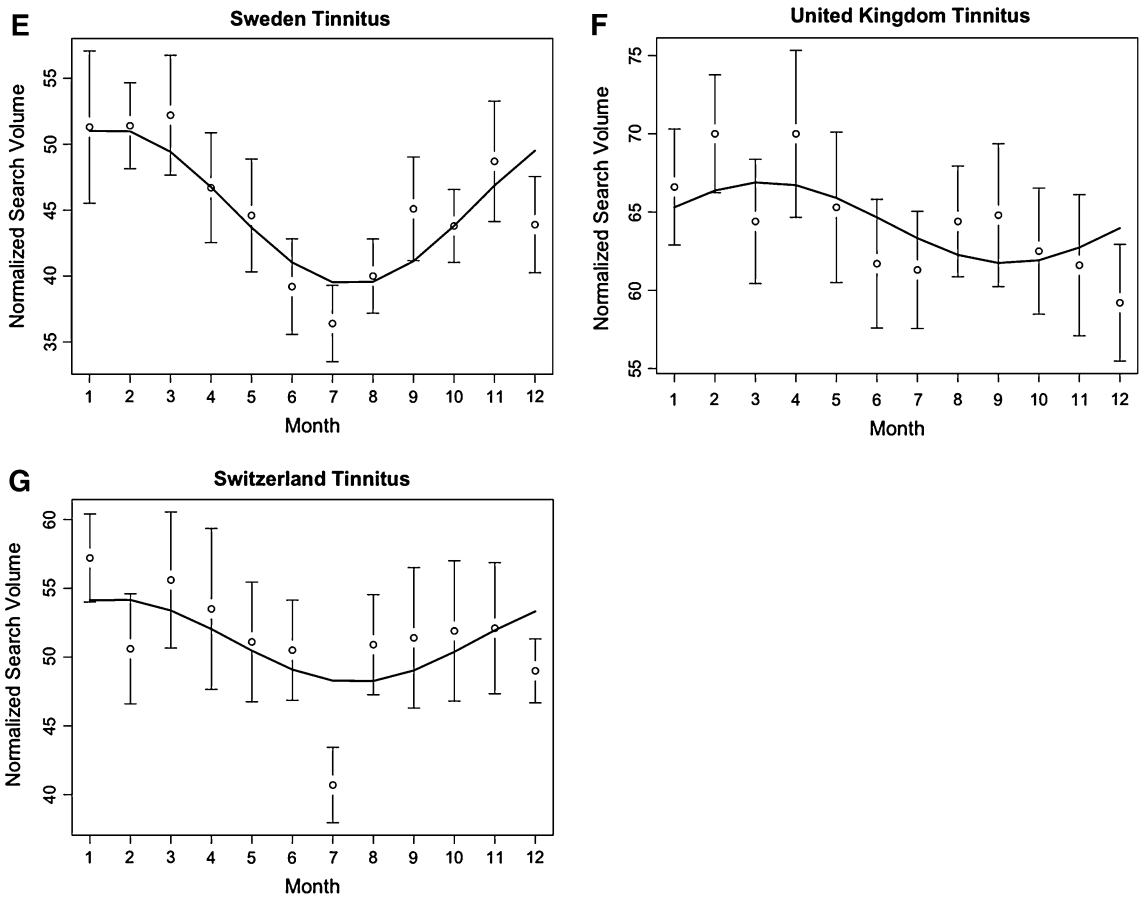

Fig. 1 continued

of the data demonstrated patterns of higher NSV for tinnitus in winter relative to summer months (Fig. 1f, g).

The magnitude of seasonal effect, as operationalized by percent change in search volume from winter to summer months, were as follows (mean, 95 % CI): United States 17 % (14–21 %), Australia 20 % (15–24 %), Canada 15 % (10–20 %), Germany 15 % (11–19 %), and Sweden 18 % (15–22 %).

Discussion

The current study examined seasonal variability in Internet search queries for tinnitus across several countries. In accordance with our hypothesis, results demonstrated a significant seasonal pattern for these searches with peaks in the winter and troughs in the summer in the primary countries of interest (the United States and Australia), as well as the majority of countries examined on an exploratory basis to corroborate findings. Our results contribute to the literature on the epidemiology of tinnitus, by demonstrating that Internet-based search queries for tinnitus vary significantly by season.

Although the methods used in this study are not able to identify the mechanisms that underlie seasonal patterns of tinnitus, it is likely that there are myriad factors that may contribute to increased search volumes for this symptom in the winter. In terms of infectious etiologies and their treatments, it has long been appreciated that pediatric viral respiratory illnesses, such as respiratory syncytial virus (RSV) and influenza, are more common in the winter [27]. In addition, seasonal patterns of viral respiratory tract infections and their associations with acute otitis media, which can be a cause of tinnitus [1], have been demonstrated, particularly for RSV, human metapneumovirus, and influenza A [10]. However, because advancing age is a risk-factor for tinnitus [28], it is unlikely that increases in pediatric respiratory viruses and associated otological disorders would solely account for increased search volumes for the symptom in winter. Notably, although acute otitis media is less common in adults, it has been associated with both tinnitus and sensorineural hearing loss in retrospective studies [29]. In a related vein, it is plausible that increased use of macrolide antibiotics, which are commonly used for a number of respiratory tract infections and in some instances to treat otitis media, may contribute to increases

in tinnitus search queries in the winter. Macrolide antibiotics are associated with ototoxicity [30], and prescribed more frequently in the winter relative to the summer in both the United States and Europe [31, 32].

Beyond seasonal changes in infectious disorders and their treatments, it is also possible that circannual modification of steroid-mediated functions may contribute to seasonal patterns of tinnitus. In humans, serum cortisol is higher in winter compared to summer [33]. Notably, cochlear glucocorticoid receptors are expressed in both inner and outer hair cells [34], and can modulate hearing sensitivity in response to acoustic trauma [35]. Patients with tinnitus with normal hearing thresholds frequently have outer hair cell damage [36]; while deafferentiation of inner hair cells in tinnitus has been suggested in studies of animals and humans [37]. Recent data suggest patients with tinnitus may also have altered glucocorticoid sensitivity [38]. Thus, although speculative, seasonal alterations in cortisol and/or changes in sensitivity to glucocorticoids may contribute to circannual patterns of tinnitus observed in this study. Beyond glucocorticoids, it is noteworthy that testosterone exhibits a seasonal pattern in humans, with a peak in fall and early winter, and nadir in the summer [39]. Interestingly, the magnitude of cochlear response to auditory stimuli also exhibits a seasonal pattern, with greatest responses in the fall, and with higher levels of testosterone in the summer inversely associated with response to auditory stimuli [40]. However, because data that connect androgens and/or glucocorticoids to seasonal patterns of tinnitus are circumstantial, future research that examines associations between circannual patterns of steroid-activity and production of tinnitus may be a fruitful area of investigation.

Importantly, pathophysiological models of tinnitus must also account for affective changes in the central nervous system associated with the phenomenon [2]. Increased activity in limbic structures such as the amygdala, anterior cingulate cortex, insula, and parahippocampal areas has been described in patients with tinnitus and associated high distress [41, 42]. Interestingly, seasonal changes in serotonin-1A receptor binding in many of these limbic structures have also been described, with increases in binding during summer months with increased light exposure [43]. Notably, mental changes induced by stress may contribute to the onset or exacerbation of tinnitus [44]. The auditory and limbic systems are connected via the medial geniculate body in the thalamus, with projections to the amygdala [37]. The amygdala plays a key role in the regulation of negative emotion, and demonstrates increased activity induced by negative images in fMRI paradigms [45]. Moreover, individuals who are more successful at diminishing negative affect, as evidenced by lower amygdala activation, exhibit a more normative decline in diurnal salivary cortisol [46]. Thus, the regulation of affect by limbic structures may be affected by factors such as cortisol and serotonin receptor binding that may be modulated seasonally. Albeit indirect, such observations may connect larger epidemiologic studies demonstrating seasonal worsening of depression in the winter [9, 19], with similar circannual increases in tinnitus search volume observed in this study.

Despite our novel findings and the potentially important insights to be gleaned from this investigation, there are inherent limitations to our study that warrant discussion. First, the data available through Google Trends do not include demographic characteristics of the user performing the search query, and thus important covariates (e.g., age, gender) that may relate to the probability of utilizing Internet-based health information, and specifically those searching for 'tinnitus', cannot be assessed. Second, inherent to research paradigms that utilize Internet search query data in the study of human disease is the assumption that such queries are representative of prevalence and/or severity of a given symptom, the veracity of which cannot be definitively established. Third, the use of data from a single search engine could result in selection bias; however, this risk is mitigated by the fact that over two-thirds of all Internet searches are performed using Google [47]. Fourth, only normalized (rather than raw) search volumes are available from Google Trends for analysis, and thus we were not able to control for other factors (e.g., national/religious holidays) that may influence the total number of Internet searches. Finally, while our results support population-level seasonal trends of tinnitus; they may not apply at the level of the individual patient, who may experience no (or opposite) seasonal patterns in terms of the severity or incidence of tinnitus to those observed in this investigation.

In summary, Internet search queries for tinnitus exhibit significant seasonal variability, with a zenith in winter months, and nadir in the summer. The seasonal trends for tinnitus observed in this study may be due to circannual patterns of associated disorders and/or side effects of their treatments. Not exclusive to this possibility, is that seasonal patterns of tinnitus may reflect functional interactions in otological and/or neuroendocrine factors related to tinnitus that vary by season. Further research is indicated to clarify the mechanisms underlying seasonal patterns of tinnitus in the population, as they may inform the pathophysiology of this common and frequently debilitating medical symptom, and lead to new insights regarding its treatment.

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