

Google Trends reveals a Temporal Correlation between A(H1N1) 2009 Influenza vaccination and Guillain-Barré Syndrome

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Abstract

Despite great concern prompted by memories of the 1976 influenza A(H1N1) outbreak and the United States mass vaccination program, which was stopped because of the emergence of increasing cases of Guillain-Barré syndrome (GBS) among vaccine recipients, a correlation between A(H1N1) 2009 influenza and an increased incidence of GBS is still matter of debate. This study aimed to interpret changes over time of web search queries for terms related to influenza and influenza vaccination and GBS in English-speaking countries in 2009, to evaluate a possible association between H1N1 vaccination and increased GBS incidence. Using Google Trends (available at: <http://www.google.com/trends>, accessed January 10, 2025), data on global search queries for terms related to GBS and influenza vaccine between January 2009 and December 2009 were analyzed. The autumnal peak for the term “Guillain-Barré” (8-14 Novembre 2009) followed of one-two week(s) that for terms related to influenza vaccination (25-31 October 2009). The increased search volumes for GBS occurred exactly one to two weeks after the peak of search terms related to influenza vaccination supports the hypothesis of a strict temporal correlation between them. Further studies are warranted to evaluate whether this temporal correlation is spurious or not.

Keywords: Epidemiology; Google Trends; Guillain-Barré; H1N1 vaccination; Influenza; Infodemiology

Introduction

Guillain–Barré syndrome (GBS) is an acute, acquired, monophasic peripheral neuropathy that is preceded by an infection in about 60% of the cases [1]. The association between an increased incidence of GBS in winter and during seasonal flu outbreaks has been widely reported in the literature [1], although the role of influenza viruses as possible triggering factors of the autoimmune response in GBS leading to diffuse peripheral nerve damage, is still matter of debate. In the recent literature there has been great discussion on the possible association between GBS and the recent pandemic influenza A(H1N1) 2009 virus infections.

Novel surveillance systems based on Internet search query data like Google Flu Trends have been suggested as useful tools to detect regional outbreaks of influenza [2]. The increasing number of online searches conducted using popular web search engines such as Google generates trend data that can be analyzed over time to detect regional outbreaks of diseases [3-4]. In this way, such meta-data can act as a real-time surveillance method to complement more traditional ones.

Google is the most popular search engine and is likely to be used by patients and physicians to look for online health-related information. Trend data generated by the number of Google searches over time can be analyzed by Google Trends, an online tool which allows users to graph the frequency of searches for single or multiple terms [2-8]. The obtained graphs are normalized on a relative basis and can focus on specific time intervals or geographic regions [4-7].

The aim of this study was to interpret changes over time of web search queries for terms related to influenza and influenza vaccination and GBS in English-speaking countries in 2009, to evaluate a possible association between H1N1 vaccination and increased GBS incidence.

Methods

The keywords “flue”, “influenza”, “influenza vaccine”, “influenza vaccination”, “flu vaccine”, “flu vaccination”, and “Guillain-Barré” were entered in the “Google Trends” main page (available at: <http://www.google.com/trends>, accessed January 10, 2025). Our search covered only the 2009 year, as we aimed to evaluate a correlation between H1N1 vaccination which was commercialized in that year, pandemic influenza A(H1N1) that occurred in 2009, and the incidence of GBS observed that year. The relative normalized search volume numbers (RNSN) were analyzed to assess changes in interest in these search terms over time [9]. All the results returned by Google Trends are normalized, with sets of data divided by a common variable to cancel out the variable's effect on the data and presented on a scale from 0-100. Doing so allows the underlying characteristics of the data sets to be compared; if this normalization was not performed and absolute rankings were used, data from regions generating the largest search volume would always be ranked highly [9]. The RNSN, i.e. the numbers on the graphs obtained by such an analysis, reflects how many searches have been performed for a particular term, relative to the total number of searches performed using Google over time [9]. Each point on the graph is divided by the highest point, which is conventionally set at 100.

Results

Main peaks in search volume numbers for the term “flu” occurred on the week 26 April – 2 May 2009 (RNSN 100/100) and on the week 25-31 October (RNSN 22/100); for the term “influenza” on 26 April – 2 May 2009 (RNSN 100/100) and 1-7 November 2009 (RNSN 18/100). Volume search numbers for the term “influenza vaccine” peaked on 26 April – 2 May 2009 (RNSN 74/100) and 25-31 October (RNSN 100/100); for the term “influenza vaccination” on 26 April – 2 May 2009 (RNSN 44/100) and 25-31 October (RNSN 100/100); for the term “flu vaccine” on 26 April – 2 May 2009 (RNSN 44/100) and 25-31 October (RNSN 100/100); for the term “flu vaccination” on 26 April – 2 May 2009 (RNSN 39/100) and 25-31 October (RNSN 100/100).

Conversely, volume numbers for the term “Guillain-Barré” peaked in 19-25 April 2009 (RNSN 100/100), 16-22 August 2009 (RNSN 41/100) and 8-14 Novembre 2009 (RNSN 93/100) (fig. 1).

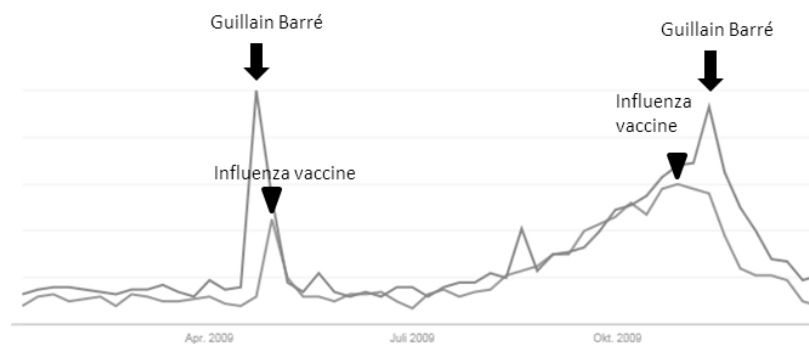


Figure 1: Google Trends graph depicting tendency over time of internet search queries for the terms “influenza vaccination”, and “Guillain-Barré” worldwide from January to December 2009. Results are expressed as relative normalized search volume numbers.

Discussion

Despite great concern prompted by memories of the 1976 influenza A(H1N1) outbreak and the United States mass vaccination program, which was stopped because of the emergence of increasing cases of GBS among vaccine recipients, a correlation between A(H1N1) 2009 influenza and an increased incidence of GBS is still matter of debate.

A European multinational case-control study found no differences in GBS occurrence between A(H1N1) 2009 vaccine recipients and controls [10], and the US vaccine surveillance program showed only a slightly increased risk of GBS after influenza A(H1N1) 2009 vaccination (odds ratio 1.77) [11]. A modest risk of Guillain-Barré syndrome attributed to Influenza A (H1N1) 2009 vaccination was found in a recent Italian study [12] (relative risk of 2.1; 95 % CI 1.1-3.9), and in a meta-analysis of the literature (incidence rate ratio 2.35, 95% CI 1.42-4.01) [13].

Overall considered, the highest search volume numbers for terms related to flu/influenza occurred one week (26 April- 2 May 2009) after the peak for the term “Guillain-Barré” (19-25 April 2009). This increased amount of Web searches for GBS preceding that for influenza, rules out a causal correlation between previous influenza infection and the subsequent occurrence of GBS. Conversely, the autumnal peak for the term “Guillain-Barré” followed of one-two week(s) that for terms related to flu/influenza and vaccine/vaccination “25-31 October”.

The outbreak of A/H1N1influenza was declared pandemic by the WHO on 11 June 2009, and on 25 October H1N1 was declared by US President Barack Obama a national emergency. The Food and Drug Administration (FDA) licensed the first 2009 influenza A(H1N1) monovalent vaccines ("H1N1 vaccines") on September 15, 2009 [14].

The first article published in MEDLINE in 2009 concerning both H1N1 influenza and GBS was published on 1 August 2009 [12]. This article alerted about the risk of a possible association between flu vaccine and Guillain-Barré syndrome, as documented in the 1976 National Influenza Immunization Programme against "swine flu" [15]. In a subsequent article published on 11 December 2009, it was reported that, as of November 24, the U.S. Vaccine Adverse Event Reporting System had received 12 reports of possible GBS [16]. After chart review, four of these 12 reports (all after receipt of influenza vaccination) met internationally accepted diagnostic criteria for GBS, four did not meet the criteria, and four were under review [16].

During October 1, 2009-May 10, 2010, a total of 529 reports of potential GBS were identified by Surveillance Systems, of which 326 met the GBS case criteria. Of the 326 persons with GBS, 27 had documentation of 2009 H1N1 vaccination in the 42 days preceding illness onset, 274 did not receive vaccine, and the vaccine status of 25 was either unknown (6 patients) or pending ascertainment (19 patients) [11].

Conclusion

Correlation does not mean causation. However, the high-volume numbers for the term “Guillain-Barré” occurring precisely one to two weeks after the peak of search volume for terms related to flu/influenza and vaccine/vaccination is hardly to be explained as due to chance alone. Furthermore, the marked increase in search volume for “Guillain-Barré” before medical community reported the first cases of GBS possibly associated with A(H1N1) influenza vaccine (11 December 2009) indicates that the increased searches related to GBS in Google were not driven by medical literature, but possibly reflected an actual increase in GBS incidence.

The increased search volumes for GBS occurred exactly one to two weeks after the peak of search terms related to influenza vaccination supports the hypothesis of a strict temporal correlation between them. Further studies are warranted to evaluate whether this temporal correlation is spurious or not.

Declarations

Conflict of Interest

The Authors declare that there is no conflict of interest.

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The authors have no funding sources to report.

Author Contributions

Francesco Brigo: Conceptualization, Methodology, Investigation, Supervision, Data curation, Writing-Original draft preparation; **Stanley C. Igwe:** Supervision; **Raffaele Nardone:** Supervision.

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