Regional and temporal awareness of alpha-gal allergy: An infodemiological analysis using Google Trends

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First officially described in 2009, alpha-gal allergy is a syndrome characterized by delayed allergic symptoms to the oligosaccharide epitope galactose-alpha-1,3-galactose present in mammalian meat.[1] Also known as mammalian meat allergy or red meat allergy, this syndrome is thought to be induced by bites of certain ticks, such as the lone star tick.[1] Alpha-gal allergy is increasingly reported in the Southeastern United States and in other parts of the world, including Western and Northern Europe, South and Central America, Japan, South Africa, Western Africa, and Australia,[1] though its true prevalence and epidemiology are unknown and difficult to ascertain. In the absence of population-level data or systematic surveillance of a rare disease such as alpha-gal allergy, "infodemiological" methods, such as online search traffic on Google, may provide a surrogate means to detect and monitor both disease interest and occurrence, including highlighting geographic areas where a disease may be emerging.[2–7] We therefore aimed to characterize regional and temporal patterns of web-based search activity for alpha-gal allergy.

We conducted an infodemiological analysis using Google Trends, an open internet search engine-based surveillance tool that provides historical and present search volume information of Google users' search queries.[4] Google search volume data are available since 2004 and can be analyzed by geographic regions. Google Trends reports its results as a "relative search volume" (RSV), which ranges from 1 to 100, and normalizes the search volume relative to a specific topic's proportion of searches on all topics examined within a specified geography and specified time period. "Search term" queries are limited to defined keywords, whereas "topic" queries encompass keywords in all search terms that share the

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same concept across languages. Up to 5 topics can be examined simultaneously. *A priori*, we selected keywords for the analysis of online queries across all Google search categories: "Alpha-gal allergy" (topic), "alpha gal allergy" (search term), "alpha gal" (search term), "meat allergy" (search term). "Chronic urticaria" (search term) was included to serve as a control search term for normalization of data, as the prevalence of this allergic disease with similar clinical features to alpha-gal allergy is believed to be stable. We also analyzed "lone star tick" (search term). Suspecting *a priori* that news reports might contribute to search activity, we entered queries into Google News to identify reports directed to a national audience that were temporally associated with sudden increases in RSV. We retrieved query data from both the United States and worldwide from January 1, 2004, to July 28, 2019. Query data were analyzed as time series, and correlations among time series were conducted using Stata 14.0 (College Station, Tex).

There is interest in alpha-gal allergy (topic) in 47 of 50 US states (Figure 1, *A*), with the highest RSV in Arkansas (100), Kentucky (79), Tennessee (65), Virginia (59), and North Carolina (54). When examined by specific search terms (alpha gal allergy, alpha gal, meat allergy), the highest RSV is similarly concentrated in the Southeast, the lower Great Plains/ Midwest, Texas, Minnesota, and New York. These regions also had the highest RSV for "lone star tick" (search term) (Figure 1, *B*). There is interest in alpha-gal allergy on 6 continents, with Sweden (100), the United States (87), Australia (63), Canada (31), and South Africa (19) having the highest RSV among countries (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org). There is an upward, nonlinear trend in RSVs for all selected alpha-gal allergy search queries in the United States since 2012, with peaks corresponding to news reports (Figure 2). RSV for the lone star tick (search term) was highly correlated with RSV for alpha-gal queries (alpha-gal allergy [topic], $R^2 = 0.83$ [$P < .05$]; meat allergy [search term], $R^2 = 0.95$ [$P < .05$]).

Google Trends has been previously used to detect incident occurrences of influenza and thunderstorm-related asthma,[5,6] as well as identifying seasonal patterns of allergic rhinitis.[7] We used Google Trends to uncover regional and temporal patterns of internet searches related to alpha-gal allergy. The regional patterns of Google searches to date support existing observations that cases of alpha-gal allergy are concentrated in the Southeastern United States and in countries where mammalian meat allergy has been reported.[1] RSV for alpha-gal terms correlates with RSV for the lone star tick, and the regional search interest for these terms corresponds to lone star tick endemic areas reflecting the suspected causal association between the lone star tick and alpha-gal allergy in the United States. In addition to regional interest, there is a growing overall interest in alpha-gal allergy over time, as reflected by increasing RSV since 2009. This is particularly salient, as it is anecdotally reported that many patients identify their diagnosis with the aid of online resources before clinical presentation.[8] Growing awareness appears to have been at least partially driven by media coverage; isolated spikes in alpha-gal-specific RSV corresponded with discrete news reports (Figure 2). It is unclear if increased public awareness is also driven by increased diagnosed cases or vice versa. In one clinical example, Pattanaik et al[9] have partly attributed the recognition of alpha-gal allergy as the leading identified cause of anaphylaxis in one Southeastern US emergency department to growing provider awareness of this condition.

We acknowledge important limitations to this analysis. Alpha-gal-specific RSV has accelerated over time, but absolute Google search volume numbers are not publicly available. We also do not know what led internet users to inquire into alpha-gal allergy, and their demographic characteristics are unknown. There is potentially a bias toward seeking information on the lone star tick when also querying alpha-gal allergy, as the association between the lone star tick and alpha-gal allergy is well known. It is possible that increased overall internet usage could possibly account for the increase in alpha-gal allergy search volume, but we think it is unlikely given that searches for our control term of chronic urticaria were only slightly increased over the same time period. Nonetheless, there has been a substantial relative increase in alpha-gal allergy search interest, though such data only provide preliminary evidence of emerging health problems and more formal epidemiologic methods are needed to estimate disease incidence and prevalence.

In conclusion, Google search query data reflect a growing regional and population-level interest in alpha-gal allergy. By characterizing health-information–seeking behaviors on the internet, Google Trends and other infodemiological methods may provide clues for diseases that are increasingly being recognized or whose epidemiology expresses a geographic pattern. Clinicians should be prepared to direct patients to reputable web-based resources regarding alpha-gal allergy and management, as they are already seeking this information independently. Systematic case reporting and population-based surveillance methods are needed to understand the true epidemiology of this emerging allergic disease.

Queries and Answers

Query: If there are any drug dosages in your article, please verify them and indicate that you have done so by initialing this query

Answer: N/A - EAI

Query: Please check and confirm the city and state added to each affiliation.

Answer: Corrected abbreviation: Tenn --> TN

Query: Please provide department/division for affiliation c.

Answer: School of Information and Library Science, University of North Carolina at Chapel Hill, Chapel Hill, NC. The School of Information and Library Science does not have departments/divisions

Query: Please confirm that the funding and conflicts of interest statements are both complete and accurate.

Answer: I confirm that funding and conflicts of interest statements are complete and accurate.

Query: Please check whether the text under the Acknowledgments section is okay as set.

Answer: The text under the acknowledgments section is OK as set.

Query: Have we correctly interpreted the following funding source(s) and country names you cited in your article: NIH, United States?

Answer: Yes

Query: Please confirm that given names and surnames have been identified correctly and are presented in the desired order and please carefully verify the spelling of all authors' names.

Answer: Yes

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Clinical Implications

- Internet search query data via Google Trends demonstrate a growing regional and population-level interest in alpha-gal allergy. Clinicians should be prepared to direct patients to reputable online sources, as patients are seeking this information independently. Formal epidemiologic surveillance is needed.
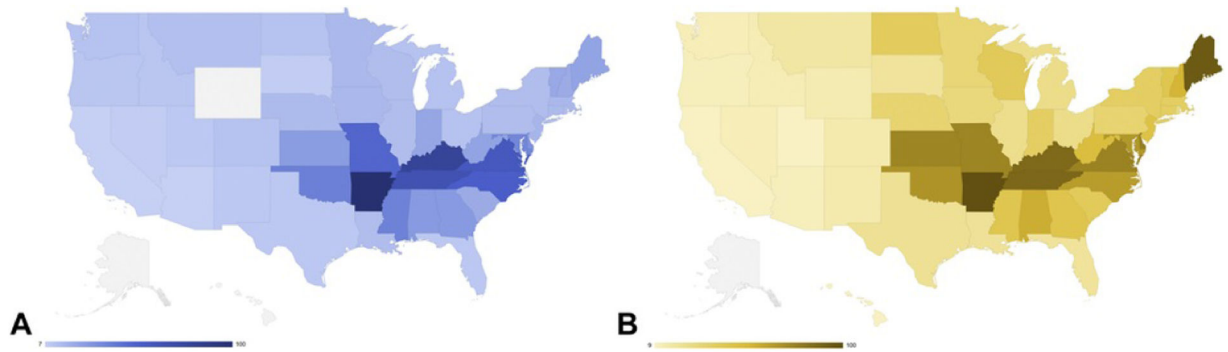
Figure 1.
Heat maps of relative search volume (RSV) in the United States, 2004–2019. **A**, Alpha-gal allergy (topic). Highest RSV was in the following states: Arkansas, Kentucky, Tennessee, Virginia, North Carolina, and Missouri. **B**, Lone star tick (search term). Highest RSV was in the following states: Arkansas, Maine, Tennessee, Kentucky, Delaware, Virginia, Missouri, and Kansas.
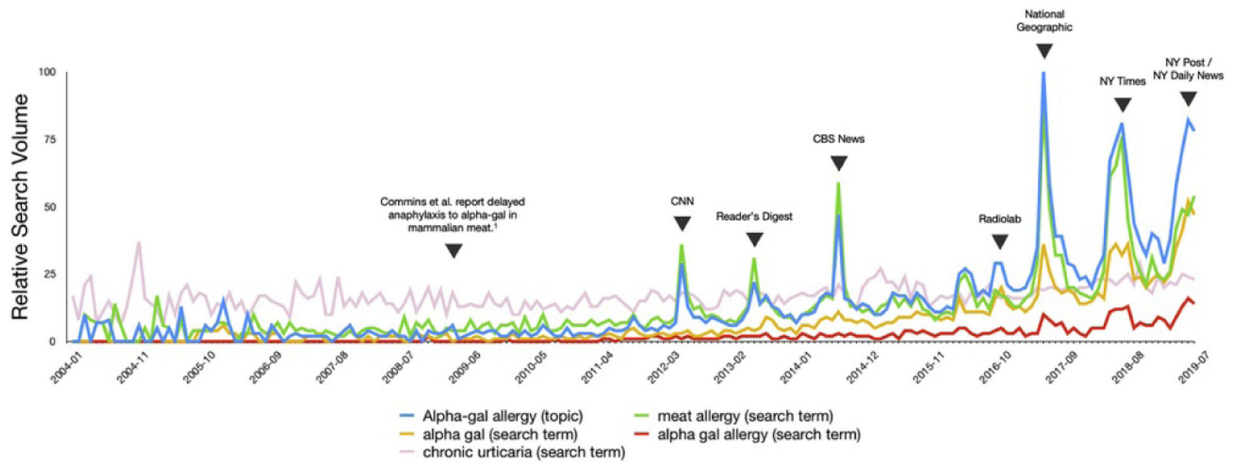
Figure 2.
Relative search volume of alpha-gal allergy queries in the United States, 2004–2019.
Increasing relative search volume over time for alpha-gal allergy search queries. News
media coverage coincides with search query peaks. A selected sampling of news reports are
shown for clarity.