



# Anaphylaxis and COVID-19 vaccines: Real-time interest using Google Trends

Bernardo Camacho<sup>a,b</sup>, Rita Aguiar<sup>a\*</sup>, Luciana Kase Tanno<sup>c,d,e</sup>, Ignacio J. Ansotegui<sup>f</sup> and Mario Morais-Almeida<sup>a</sup>

## INTRODUCTION

Vaccines have made an enormous contribution to global health. The year is now 2021, and once again we turn to vaccination in the midst of one of our greatest challenges in recent history. On March 11, 2020, the World Health Organization (WHO) officially announced that COVID-19 had reached the status of a global pandemic.<sup>1</sup>

Mass vaccination against COVID-19 started in December 2020, and several vaccines have been approved for worldwide usage, with 8 of them currently being administered in numerous countries. Vaccines frequently cause adverse events, although these are rarely due to an allergic reaction. Shortly after mass vaccination started with the Pfizer-BioNTech COVID-19 vaccine BNT162b2, 2 and 6 cases of anaphylaxis were reported in the United Kingdom and the United States, respectively. Since then, millions of people have been vaccinated, and anaphylaxis due to the mRNA vaccines are still uncommon events.<sup>2</sup>

However, misinformation can lead to hesitancy in regard to vaccination, and our duty as health professionals should be to provide clear, evidence-based analysis on the risks and the benefits of being vaccinated. Our goal was to understand if

the general population is overly concerned about possible severe allergic reactions, which might result in not vaccinating against this deadly disease.

The COVID-19 vaccines most frequently used worldwide are the Pfizer-BioNTech's Comirnaty, Moderna's mRNA-1273, and AstraZeneca's AZD1222, with similar mechanisms but different excipients. Several side effects have been associated with all these vaccines, the most common ones being injection site tenderness and pain, tiredness, headache, muscle pain, chills, and fever, especially after the second dose.<sup>3-6</sup> Regarding allergic reactions, namely anaphylactic reactions, there were no reports during the phase 3 testing of these vaccines, that included near 50 000 patients.

Anaphylaxis, which is defined as a "serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death", can be caused by numerous triggers and its diagnosis is based on clinical criteria.<sup>7,8</sup> Early surveillance reports have shown that, after the start of mass vaccination, anaphylaxis due to the mRNA vaccines are still uncommon events, occurring at a rate of 4.7 per million doses administered for the Pfizer-BioNTech vaccine and 2.5 per million doses administered for the Moderna vaccine.<sup>9-11</sup> The general risk of anaphylaxis due to vaccines is described as occurring at a rate of 1.31 (95 % CI, 0.90-1.84) per million vaccine doses from a large population-based studies, which indicates a relative risk increase regarding the COVID-19 vaccines, albeit the absolute risk remaining quite low.<sup>12,13</sup>

Google Trends (GT) is an online, easily accessible tool that shows how often a given search term

<sup>a</sup>Allergy Centre, CUF Descobertas Hospital, Lisbon, Portugal

\*Corresponding author. Allergy Centre, CUF Descobertas Hospital, Rua

Mário Botas, 1998-018, Lisboa, Portugal. E-mail: [ana.rita.aguiar@cuf.pt](mailto:ana.rita.aguiar@cuf.pt)

Full list of author information is available at the end of the article.

<http://doi.org/10.1016/j.waojou.2021.100570>

Received 28 March 2021; Received in revised form 3 July 2021; Accepted 12 July 2021

Online publication date 20 July 2021

1939-4551/© 2021 The Authors. Published by Elsevier Inc. on behalf of World Allergy Organization. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

is entered into Google's search engine, the most used in the world. As a result, it illustrates the popularity of top search queries across various regions and languages. With the increasing use of the Internet, it is important to have an awareness of what the general population is searching for, especially regarding controversial topics such as COVID-19 and the vaccines we have mentioned thus far. This information can be useful in order to try to face the challenges of distrust and disinformation campaigns that are ubiquitous in our current times. Our goal was to find any upsurge in online interest related with possible severe allergic reactions to the anti-COVID-19 vaccines.

## MATERIALS AND METHODS

We conducted a GT worldwide search to look for any increase in Relative Search Volume (RSV) in the last 5 years regarding the search terms: "Anaphylaxis" and "Vaccine anaphylaxis". The search has been performed on February 4, 2021. RSV shows search interest over time relative to the highest point on the graph for the given region and time, but it doesn't demonstrate the absolute search volume.<sup>14</sup> Besides our worldwide search, we also analyzed the RSV regarding the search term "Anaphylaxis" in 3 European countries, with different speaking languages (Germany, Italy, and Spain) and in the United States of America (USA).

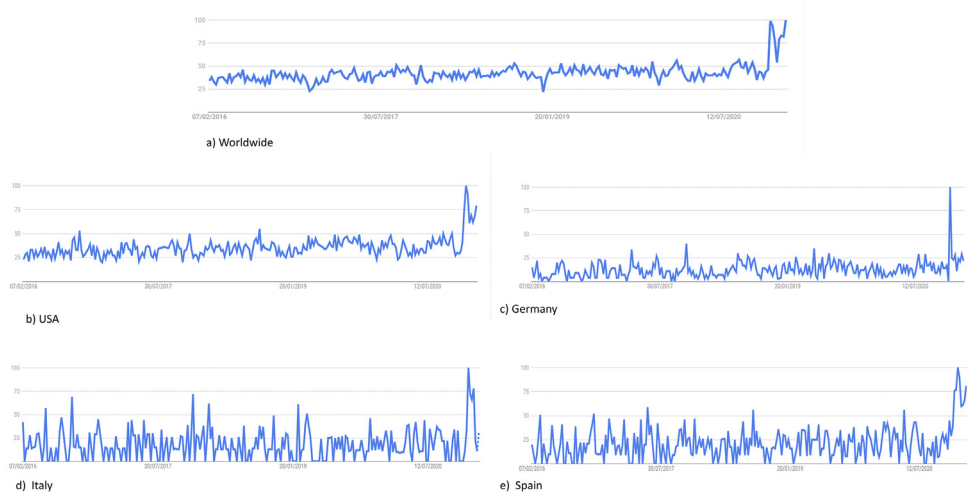
## RESULTS

We found that worldwide, there was a major increase in the "Anaphylaxis" and "Vaccine anaphylaxis" RSV in December 2020, continuing up to January 2021. We also found a similar increase in the "Anaphylaxis" RSV in the included countries. This coincides with the beginning of mass vaccination with the new mRNA vaccines and with the AstraZeneca adenovirus vector vaccine, as shown in Fig. 1 and Fig. 2.

## DISCUSSION

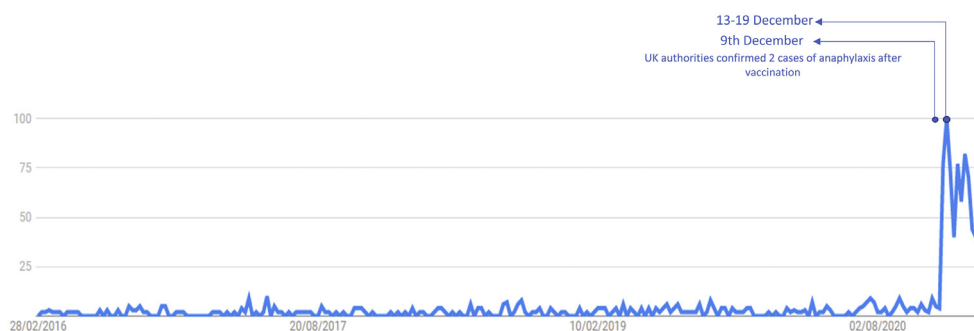
We believe this sudden interest in anaphylaxis is related to reports of some severe allergic reactions to these vaccines that were widespread through the internet worldwide. It is evident that in the last 5 years, the interest in "anaphylaxis" has never been this high, which shows that the overall population is concerned with possible severe allergic reactions and that could affect any decision-making regarding being vaccinated or not. The fact that the interest in the search term "Vaccine anaphylaxis" has also increased supports this particular concern.

All things considered, COVID-19 has killed millions of people worldwide, and only a very small sample of vaccinated persons has had to deal with severe complications, meaning that in almost all of the cases, the benefits severely outweigh the risks. Apart from patients with previous reactions to the



**Fig. 1** Relative search volume over time in the past 5 years (February 2016 until January 2021) of the search term "Anaphylaxis": a) worldwide; b) in the USA; c) in Germany; d) in Italy; e) in Spain. The highest interest on a search query is quantified as 100 relative search volume (RSV), decreasing to 0 RSV, indicating no interest

50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65  
66  
67  
68  
69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84  
85  
86  
87  
88  
89  
90  
91  
92  
93  
94  
95  
96  
97  
98  
99  
100



**Fig. 2** Relative search volume over time in the past 5 years (February 2016 until January 2021) of the search term “Vaccine anaphylaxis”, worldwide. Data source: Google Trends (<https://www.google.com/trends>)

COVID-19 vaccine components, recent reports suggest that there is no clear indication that previous allergic reactions (including anaphylaxis) to any type of food, insect stings, and drugs (where the trigger has been identified), family history of allergies, previous non-systemic reaction to a vaccine, asthma, or allergic rhinitis, produces an incremental risk for an adverse reaction of any kind to COVID-19 vaccination.<sup>13,15</sup> Anyone who gets vaccinated against COVID-19 should be monitored on site. There are also algorithms set in place in all the vaccination centers so that in case any of these reactions occur, a timely response ensues. Vaccination providers should have the appropriate personnel, medication, and equipment, and should immediately treat patients experiencing anaphylaxis with an intramuscular injection of epinephrine.

In conclusion, anaphylaxis awareness is apparently the highest it has ever been, and we should take this opportunity to encourage patients to look for health care professionals if there is any uncertainty about any past allergic reactions, allowing for correct anaphylaxis management. From an international perspective, the World Allergy Organization (WAO) addressed the goal of increasing awareness of anaphylaxis during World Allergy Week 2021. Only a very small percentage of the population have real contraindications to vaccination, so we must prevent as many people as we can from deciding against vaccination due to misinformation.<sup>13,15</sup> The increased interest and concern of the population in this particular topic should be a wake-up call to health care professionals to increase their preparedness to better advise patients.

The limitations of our study should also be taken into account, given that data from GT should not be interpreted as epidemiologically accurate. The exact

volumes of queries are not known, limiting the way that the data can be processed and as this field of research is relatively new, there is no standard way of reporting, resulting in the same meaning of different terms between different reports.

Last but not least, it is imperative that notification and surveillance of allergic/anaphylactic reactions to these novel COVID-19 vaccines proceed to narrow down the scarce group of patients for whom the vaccine will be contraindicated and not to exclude those who could receive the vaccine uneventfully and be protected against this life-threatening disease.<sup>16</sup> With this in mind, we believe that more research is needed to find the real cause of anaphylaxis and that usage of this vaccine is still in the early stages. Millions of people have perished to COVID-19, and given that only a very small percentage of the population has had severe complications associated with vaccination, it is vital that we try to lessen the impact of vaccine hesitancy.

**Abbreviations**

GT, Google Trends; RSV, Relative Search Volume; USA, United States of America; WHO, World Health Organization.

**Availability of data and materials**

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

**Statement of ethics**

Ethics approval was not required.

**Funding sources**

No funding was received in the publication of this letter.

52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65  
66  
67  
68  
69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84  
85  
86  
87  
88  
89  
90  
91  
92  
93  
94  
95  
96  
97  
98  
99  
100  
101  
102

## Author contributions

BC, RA, and MMA participated in study design and conception. BC performed data analysis and drafted the first manuscript. All authors provided critical review of the manuscript and approved the final draft for publication.

## Authors' consent for publication

All the authors consent to the publication of the manuscript.

## Declaration of competing interest

The authors have no conflicts of interest to declare.

## Acknowledgments

There are no acknowledgments to be mentioned.

## Author details

<sup>a</sup>Allergy Centre, CUF Descobertas Hospital, Lisbon, Portugal. <sup>b</sup>Pediatrics Department, Central Hospital of Funchal, Funchal, Portugal. <sup>c</sup>University Hospital of Montpellier, Montpellier, France. <sup>d</sup>Desbrest Institute of Epidemiology and Public Health, UMR UA-11 INSERM, University of Montpellier, France. <sup>e</sup>WHO Collaborating Centre on Scientific Classification Support, Montpellier, France. <sup>f</sup>Department of Allergy & Immunology, Hospital Quironsalud Bizkaia, Bilbao, Spain.

## REFERENCES

1. WHO Novel Coronavirus (2019-nCoV) Situation Report - 51(11 March 2020). Geneva: World Health Organization; 2020 [cited Feb 6]. Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19>.
2. Turner PJ, Ansotegui IJ, Campbell DE, et al, WAO Anaphylaxis Committee. COVID-19 vaccine-associated anaphylaxis: a statement of the World Allergy Organization Anaphylaxis Committee. *World Allergy Organ J.* 2021 Feb;14(2):100517. <https://doi.org/10.1016/j.waojou.2021.100517>.
3. Fact Sheet for Recipients and Caregivers: Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 16 Years of Age and Older [cited Feb 6]. Available from: <https://www.comirnatyeducation.pt/resources>.
4. Fact Sheet for Recipients and Caregivers: Emergency Use Authorization (EUA) of the Moderna COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 18 Years of Age and Older [cited Feb 6]. Available from: <https://www.modernatx.com/covid19vaccine-eua/>.
5. Summary of the COVID-19 Vaccine from AstraZeneca [cited Feb 6]. Available from: [https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement\\_en](https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement_en).
6. Blumenthal KG, Freeman EE, Saff RR, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. *N Engl J Med.* 2021;384:1273-1277.
7. Turner PJ, Worm M, Ansotegui IJ, et al, WAO Anaphylaxis Committee. Time to revisit the definition and clinical criteria for anaphylaxis? *World Allergy Organ J.* 2019 Oct 31;12(10):100066. <https://doi.org/10.1016/j.waojou.2019.100066>.
8. The challenge of establishing the burden of anaphylaxis: some recent Trends. *Curr Treat Options Allergy.* 2020;7:441-456. <https://doi.org/10.1007/s40521-020-00257-9>.
9. CDC COVID-19 Response Team; Food and Drug Administration. Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine—United States, December 14–23, 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(2):46–51.
10. CDC COVID-19 Response Team; Food and Drug Administration. Allergic reactions including anaphylaxis After receipt of the first dose of Moderna COVID-19 vaccine—United States, December 21, 2020–January 10, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(4):125–129.
11. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis After receipt of mRNA COVID-19 vaccines in the US, December 14, 2020–January 18, 2021. *J Am Med Assoc.* Feb 2021. <https://doi.org/10.1001/jama.2021.1967>.
12. McNeil MM, DeStefano F. Vaccine-associated hypersensitivity. *J Allergy Clin Immunol.* 2018;141(2):463–472. <https://doi.org/10.1016/j.jaci.2017.12.971>.
13. Greenhawt M, Abrams EM, Oppenheimer J, et al. The COVID-19 pandemic in 2021: avoiding overdiagnosis of anaphylaxis risk while safely vaccinating the World. *J Allergy Clin Immunol Pract.* 2021 Jan 30;S2213–2198(21):80–85.
14. Barbosa MT, Morais-Almeida M, Sousa CS, Bousquet J. The “big five” lung diseases in CoViD-19 pandemic—a Google Trends analysis. *Pulmonology.* 2021;27(1):71–72. <https://doi.org/10.1016/j.pulmoe.2020.06.008>.
15. Banerji A, Wickner PG, Saff R, et al. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. *J Allergy Clin Immunol Pract.* 2020 Dec 31;S2213–2198(20):31411–31412. <https://doi.org/10.1016/j.jaip.2020.12.047>.
16. Turner PJ, Ansotegui I, Campbell DE, et al. COVID-19 vaccine-associated anaphylaxis: A statement of the World Allergy Organization Anaphylaxis Committee. *World Allergy Organ J.* 2021;14:100517. <https://doi.org/10.1016/j.waojou.2021.100517>.