INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 is an ongoing global health emergency. COVID-19 infection has been shown to impact multiple organ systems with varying outcomes (Zaim et al., 2020). Solutions to mitigate the impact of COVID-19 have steadily been underway, with a major focus being on the development of vaccines. Unprecedented efforts from scientists with advances in technology and government support led to the successful completion of several vaccine candidates. As a means to catalyse the utilisation of these vaccine candidates in the USA, the FDA granted Emergency Use Authorization (EUA) for the first COVID-19 vaccine on December 11, 2020. Although excitement ensued following this milestone, a significant portion of the population reports that they are unwilling to be vaccinated (Chevallier et al., 2021). While it is clear that the general public has significant hesitations with vaccination, objective information characterising the increased concern is unavailable.

Public concern regarding vaccine side effects has long been an issue encountered by healthcare providers since the advent of the
smallpox vaccine in 1798. Due to the expedited process for vaccine approval, potential harm to recipients from the vaccine is one of the most commonly reported concerns (Chevallier et al., 2021). Specifically, the impact of vaccine candidates on future fertility has been commonly raised by patients due to the lack of long-term data evaluating this outcome. While COVID-19 infection has been shown to have the ability to affect sperm parameters in the acute phase of infection, the impact on fertility from vaccine uptake is largely uncertain (Best et al., 2021). We hypothesised that irrespective of sex, fertility-related queries would markedly increase during the 48 days following Emergency Use Authorization of the coronavirus vaccine. We sought to objectively identify trends in internet search queries on public concerns regarding COVID-19 vaccine side effects on fertility that might impact vaccine uptake.

2 | MATERIALS AND METHODS

A retrospective study was conducted to investigate the influence of COVID-19 vaccine Emergency Use Authorization (EUA) on online queries regarding the coronavirus vaccine and fertility. As Google Trends is considered publicly available data, it fulfils criteria for Institution Review Board (IRB) exemption, and an IRB waiver was obtained.

2.1 | Search queries

Google Trends (https://trends.google.com/trends) (Google, 2021) is a free online tool first introduced in 2006 that provides anonymised search request made by the public on the Google Search Engine since 2004 and up to 36 hr prior to the query date (Arora et al., 2019). On February 2, 2021, we were able to investigate queries relating to the coronavirus vaccine and fertility between October 24, 2020 and January 27, 2021. The five search terms with the most interest during our established time period were identified as ‘COVID Vaccine Fertility’, ‘COVID Vaccine and Infertility’, ‘COVID Vaccine Infertility’, ‘COVID Vaccine Fertility CDC’, and ‘COVID 19 Vaccine Infertility’. Interest for a given keyword was reported as Search Volume Index (SVI) calculated as the proportion of keyword searches divided by all searches in a given location and time period (Kaleem et al., 2019). SVI may range from 0 to 100, with 100 representing the maximum search interest at that time and location selected for a given keyword. When using Google Trends, special attention was given to ensure that queries were conducted using the ‘search term’ feature that allowed for results specific to our input as opposed to the ‘topic’ feature which compiled the results of similar search terms. Google Trends allows for geographical analysis of search terms. We also queried our five established search terms globally and nationally to identify geographic regions with the highest SVI between October 24, 2020 and January 27, 2021. National results were subdivided into U.S. states and metropolitan areas (Dreher et al., 2018).

2.2 | Outcomes

With Google Trends we hoped to compare the proportion of searches or SVI for each identified search term 48 days before and after the first COVID-19 vaccine Emergency Use Authorization (EUA) in the United States. In addition, we hoped to identify the geographic distribution of each search term during this time period domestic and abroad.

2.3 | Statistical analysis plan

Mean search volume index (SVI) before and after EUA was done using paired t-test (Garijo et al., 2021). Data were analysed using Microsoft Excel Version 16.43.

3 | RESULTS

In the 48 days following the COVID-19 vaccine EUA of December 11, 2020, there was a significant increase in internet search queries related to the coronavirus vaccine and fertility. Our established search terms: ‘COVID Vaccine Fertility’, ‘COVID Vaccine and Infertility’, ‘COVID Vaccine Infertility’, ‘COVID Vaccine Fertility CDC’, and ‘COVID 19 Vaccine Infertility’ saw increases of 710.47%, 207.56%, 264.35%, 2,943.7%, and 529.26%, respectively (all p < .001) (Table 1). Collectively, the average SVI of our five search terms increased from 5.68 to 33.23 following EUA demonstrating a change of 485.04%. When observing the global distribution for our search terms the United States, United Kingdom, Canada, and Ireland appeared in the top 5 countries by SVI in more than two keywords (Table 2). On a national level, Nebraska and Ohio were the only states to appear in multiple keywords with Sioux Falls (Mitchell), SD the only metropolitan area appearing in two or more keyword searches (Table 2).

4 | DISCUSSION

The results of our study demonstrate that internet search queries in Google related to the COVID-19 vaccine and fertility significantly increased in the 48 days following Emergency Use Authorization (EUA). The search volume increase ranged from 207.56% to 2,943.7% for the most queried search terms. This increase in search volume suggests a desire for information about the vaccine’s impact on fertility potential which could be influencing public concern and hesitancy for vaccine uptake. While COVID-19 vaccine misinformation has shown to increased internet searches for topics related to infertility in the United States (Sajjadi et al., 2021) and hesitancy for uptake of the vaccine has been described in several questionnaires (Dror et al., 2020; Sallam et al., 2021), our data contribute to the body of literature which objectively describes vaccine-related fertility concerns.
In the United States, Mid-West and Eastern regions had the highest mean SVI, while on a global level our search terms were most popular in predominantly English-speaking countries which could be due to a variety of reasons including Google Trends language preferences or the overall access to the internet.

Studies thus far have demonstrated that a significant portion of the population may prefer not to receive the vaccine when available (Coustasse et al., 2020). Up to 35% of survey respondents suggested that they would not receive the vaccine, with a significantly larger portion being persons in the African American and Hispanic populations (Coustasse et al., 2020). A major concern cited by these respondents was fear from the side effects of an expedited approval process (Coustasse et al., 2020). Additionally, more than 65% of YouTube videos discouraged the use of vaccines and up to 37% of videos provided no scientific evidence (Basch et al., 2017). These results highlight the importance of the internet in the dissemination of medical information and emphasise the importance of compiling accurate information for the most salient public questions. Our results are in concordance with previous information that suggested vaccine hesitancy might be an important issue to overcome (Islam et al., 2021). This is not surprising considering the influenza vaccine which is commonly met with hesitation each year (Schmid et al., 2017).

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| TABLE 1 Results of paired t-test & Descriptive Statistics for Mean Google Trends search volume index 48 days before and after Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine | Time period relative to EUA | Mean (SVI) | Std. Deviation | Std. Error | Lower 95% CI | Upper 95% CI | % Change | t stat. | t crit. | df | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| COVID vaccine fertility | 48 days before | 5.98 | 13.47 | 13.33 | 2.07 | 9.89 | +71.047 | -11.26 | 2.01 | 47 | <0.001 |
| COVID vaccine fertility | 48 days after | 48.46 | 20.41 | 20.19 | 42.53 | 54.38 | | | |
| COVID vaccine and infertility | 48 days before | 7.44 | 19.93 | 19.73 | 1.65 | 13.22 | +207.56 | -3.25 | 2.01 | 47 | <0.001 |
| COVID vaccine and infertility | 48 days after | 22.87 | 21.90 | 21.67 | 16.51 | 29.23 | | | |
| COVID 19 vaccine infertility | 48 days before | 11.27 | 28.13 | 27.84 | 3.10 | 19.44 | +264.35 | -5.66 | 2.01 | 47 | <0.001 |
| COVID 19 vaccine infertility | 48 days after | 41.06 | 19.98 | 19.77 | 35.26 | 46.86 | | | |
| COVID vaccine fertility CDC | 48 days before | 0 | - | - | - | - | +2,943.70 | -7.64 | 2.01 | 47 | <0.001 |
| COVID vaccine fertility CDC | 48 days after | 30.44 | 27.58 | 27.29 | 22.43 | 38.47 | | | |
| COVID 19 vaccine infertility | 48 days before | 3.71 | 10.39 | 10.29 | 0.69 | 6.73 | +529.26 | -4.58 | 2.01 | 47 | <0.001 |
| COVID 19 vaccine infertility | 48 days after | 23.33 | 26.05 | 25.78 | 15.77 | 30.90 | | | |
and income level which may provide more insight into reasons for search variation also make it difficult to construct any meaningful targeted interventions. Additionally, our search queries made us incapable of differentiating sex-specific fertility concerns or those regarding a specific coronavirus vaccine brand. Furthermore, this study is limited to people with access and ability to utilise the internet and is exclusive of people that may share similar concerns but lack access to the internet. Our study was also limited to Google’s search engine and may have under-sampled geographic locations and search populations who may prefer to use alternative search engines such as Bing, Yahoo, Baidu, or Yandex. Future studies may focus on the analysis of specific demographic determinants that can lead to variations in search trends which can help us identify medical knowledge gaps and focus our resources to provide the most accurate information.

**CONFLICT OF INTEREST**
The authors have nothing to disclose.

**TABLE 2**
Results of Mean Google Trends search volume index by geographic region 48 days after Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine

| Keyword                  | US State (SVI) | Metropolitan Area (SVI) | Country (SVI) |
|--------------------------|----------------|-------------------------|---------------|
| **COVID vaccine fertility** |                |                         |               |
|                          | 1. South Dakota (100) | 1. Sioux Falls (Mitchell), SD (100) | 1. United Kingdom (100) |
|                          | 2. Nebraska (50)       | 2. Lincoln & Hastings-Kearney, NE (98)   | 2. Ireland (74) |
|                          | 3. Maine (39)          | 3. Dayton, OH (92)          | 3. United States (74) |
|                          | 4. Connecticut (32)     | 4. Des Moines-Ames, IA (82)   | 4. United Arab Emirates (29) |
|                          | 5. Montana (26)        | 5. Champaign & Springfield-Decatur, IL (71) | 5. Canada (26) |
| **COVID vaccine infertility** |                |                         |               |
|                          | 1. Nebraska (100)      | 1. St. Louis, MO (100)      | 1. United States (100) |
|                          | 2. Wisconsin (83)      | 2. Hartford & New Haven, CT (75) | 2. Ireland (50) |
|                          | 3. Indiana (77)        | 3. Indianapolis, IN (49)     | 3. United Kingdom (44) |
|                          | 4. Iowa (67)           | 4. Boston, MA-Manchester, NH (41) | 4. Canada (31) |
|                          | 5. Ohio (62)           | 5. Cleveland-Akron(Canton), OH (36) | N/A |
| **COVID vaccine infertility CDC** |                |                         |               |
|                          | 1. North Dakota (100)  | 1. Sioux Falls(Mitchell), SD (100)   | 1. United States (100) |
|                          | 2. Nebraska (99)       | 2. Wichita-Hutchinson, KS (99)   | 2. Ireland (63) |
|                          | 3. Vermont (90)        | 3. Omaha, NE (87)            | 3. United Kingdom (56) |
|                          | 4. Delaware(70)        | 4. Cedar Rapids-Waterloo-Iowa City & Dubuque, IA (67) | 4. Canada (30) |
|                          | 5. New Hampshire (62)  | 5. Little Rock-Pine Bluff, AR(62) | N/A |
| **COVID 19 vaccine infertility** |                |                         |               |
|                          | 1. Pennsylvania (100)  | 1. Philadelphia, PA(100)     | 1. United States (100) |
|                          | 2. New York (91)       | 2. Chicago, IL (82)          | 2. United Kingdom (33) |
|                          | 3. Ohio (69)           | 3. Atlanta, GA (79)          | 3. Canada (23) |
|                          | 4. Colorado (65)       | 4. Boston, MA-Manchester, NH (74) | N/A |
|                          | 5. Virginia (63)       | 5. Denver, CO (73)           | N/A |

**DATA AVAILABILITY STATEMENT**
The data that support the findings of this study are available in Google Trends in the public domain: https://trends.google.com/trends/ (search terms and parameters provided in the Methods).

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