

# Global Online Interest in Finasteride Sexual Side Effects

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## Article

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# Abstract

Prior literature has suggested that Propecia or finasteride may negatively impact men's sexual health. In 2011, the Food and Drug Administration (FDA) provided a warning on finasteride drug labels to include decreased libido and erectile dysfunction. We sought to determine global online interest in finasteride sexual side effects, their penetrance and variation, and how they compared over time. We also sought to evaluate the influence of the FDA communications on internet searches for finasteride side effects. We utilized Google search engine from January 2004 to December 2020 to include trends from web searches of Propecia or finasteride and its side effects compared amongst the United States, United Kingdom, and Australia. We performed join-point regression analysis. We compared the annual relative search volume (ARSV), average annual percentage change (AAPC), and temporal patterns to evaluate for loss or gain of interest in the respective key terms. We determined that average ARSV for "finasteride" was 15% in 2004 and increased significantly to 57% in 2020 (APC: +9.25%, 95% CI 8 to 10.5,  $p < 0.001$ ). Likewise, there was significant interest in "finasteride side effects" (AAPC: +20.7,  $p < 0.001$ ) and "post-finasteride syndrome" (AAPC: +29.2;  $p < 0.001$ ) over time. Finally, when compared trends before and after FDA communications, the average (SD) ASRV of "finasteride", "finasteride side effects", and "post-finasteride syndrome" all increased significantly ( $p = 0.001$ ,  $p = 0.014$ ,  $p < 0.001$ ), respectively. Thus, it is evident that there is a global web-based interest in finasteride and its side effects, especially after the FDA warning in 2011. These results demonstrate an increased public awareness, and thus providers should have more detailed and careful discussions with patients prior to starting treatment with finasteride.

# Introduction

The United States (US) Food and Drug Administration (FDA) approved finasteride, a 5 $\alpha$ -reductase inhibitor, for the treatment of symptomatic benign prostatic hyperplasia (BPH) in 1992 (1). Since then, its usage has grown, and it has become one of the 100 most-commonly prescribed medications in the United States (US) (1-3). This increase in finasteride usage has been attributed to several factors, including FDA approval of finasteride for androgenic alopecia in 1997 (4), the medication becoming available in a generic form since 2006 (5), and an increase in global life expectancy, with a concomitant rise in BPH prevalence (6).

Concurrently, there have also been periodic dips in finasteride consumer usage, which seem to correlate with public awareness of the medications side effects (7). Most notably, several studies have found that finasteride can have a negative, and sometimes permanent, effect on male sexual health, including impaired libido, erectile dysfunction, and ejaculatory disorders (8-11). Based on these findings, the FDA issued a warning in 2011 and expanded the drug warning label for finasteride (9, 12). It was around this time that finasteride usage had declined and briefly dropped out of the 100 most commonly prescribed medications in the US (2). Separately, a recent study of trends in medical alopecia therapies found that changes in medication prescribing patterns, including that of finasteride, paralleled these global internet search trends (7). Observations such as these raise the question of the impact of medical events,

including the sexual health warning for finasteride and online information on patient medication concerns and preferences.

Nearly all of American adults, 96%, rely on their own research when making important decisions, primarily using online resources (13). When asked about making an important life decision, 81% of Americans largely rely on their own research and only 31% rely on experts (13). Similarly, 72% of Americans look online for health information, and 77% of these used a general (non-medical) search engine such as Google, Bing, or Yahoo(14). Qualitative data have shown that patients use web-based health information for everything from direct decision making to guiding discussions with their care team (15). Understanding these patterns may facilitate a greater understanding and transparency to the patient/physician relationship (15-17).

There are currently over 3.97 billion internet users worldwide and Google is the dominant search engine, holding nearly 88% of the global search engine market-share(18). As of 2019, the distribution of internet users worldwide between 18 and 44 years old was approximately 70%, with one-third of these users between 25 and 34 years old (18). Most men who utilize finasteride for androgenic alopecia are also between this age group, making this an important population of interest. Google Trends has also been utilized to understand worldwide trends in a wide range of topics, ranging from predicting disease spread to understanding public interest in medical topics (19-22). Accordingly, Google Trends has the potential to understand patients' online behaviors and interests. For example, a study using Google Trends based data found significant difference in prostate cancer treatment search trends before and after the release of guidelines from the National Comprehensive Cancer Network and United States Preventative Services Taskforce(19).

In this study, we aim to determine variation in worldwide public interest in finasteride and its related side effects over time. We secondarily aimed to detect the impact of FDA communications regarding side effects on internet searches for finasteride. Identifying patient-based finasteride side effect search trends may improve patient/physician counseling when prescribing finasteride in clinical practice.

## Methods

### *Data source*

We used Google search engine to search for worldwide trends for finasteride and its side effects. We included the search terms "finasteride," "finasteride side effects," "post-finasteride syndrome," "Propecia," and "Propecia side effects." We compared the terms annually across the US, United Kingdom (UK), and Australia from January 2004 to December 2020. We searched within "worldwide" using the "global" query category. Terms searched were assessed according to the checklist for the documentation of Google Trends use(21).

Google Trends generates results of geographical and temporal patterns according to a specific search term (21, 23). Users can input a term (or terms), and Google Trends will create a graphical representation

of interest over time, with information on individual geographical areas as well.

A relative search volume (RSV) index is assigned to each term. RSV values are scaled from 0 to 100. A value of 100 represents the highest search activity, 50 represents half of searches, and 0 representing the lowest search activity (21, 23).

### ***Statistical analysis***

We performed join-point regression analysis. We analyzed annual relative search volume (ARSV), average annual percentage change (AAPC), and temporal patterns to evaluate for loss or gain of interest. We tested the distribution of ARSV before and after the 2011 FDA warning using one-way analysis of variance.

The mean ARSV is calculated as the mean of the monthly scores within the same year as previously reported (19, 20, 24-26). The join-point regression model was used to identify significant changes in mean ARSV over time for each term. We have previously described our methodology utilizing join-point regression analysis in a series of studies utilizing Google Trends data (19, 20). Briefly, join-point regression analysis is used to better describe trends that are not constant over time and enables for evaluating statistically significant changes (join-points) in trends (23, 27). If the year(s) when changes in the trend occur (join-points) are found to be statistically significant, then linear regression techniques can be used to estimate the regression parameters (28, 29). Consequently, segmental periods are specific for each treatment/search (30).

We summarized linear trends in RSV using the estimated ARSV and annual percentage change (APC). APC was used to measure differences in ARSV between two join-points. AAPC and the respective 95% confidence intervals (CI) were estimated to summarize linear trends in ARSV during the entire period (31). We used the natural log-linear model to analyze AAPC in rate over time. A positive value of AAPC demonstrates an increasing RSV, while a negative value demonstrates decreased interest. A two-tailed test with  $p < 0.05$  was considered statistically significant. All statistical analyses were performed using SPSS v.24.0 (SPSS Inc., Chicago, IL, USA) and Join Point Trend Analysis Software V. 4.2.0.2 (Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA).

## **Results**

### ***Trend Pattern Analysis***

Table 1 summarizes the AAPC of the terms “finasteride,” “Propecia,” “finasteride side effects,” “Propecia side effects,” and “post-finasteride syndrome” compared across the US, UK, and AUS. The mean ARSV for “finasteride” was 15% in 2004 and increased significantly to 57% in 2020 (APC: +9.25%, 95% CI 8 to 10.5,  $p < 0.001$ ). Join-point regression APC curves of “finasteride” and “finasteride side effects” are demonstrated in Figure 1A-B.

The “finasteride side effects” ARSV in the US presented initially a statistically significant increase in interest between 2004 and 2010 (APC: +48.1, 95% CI 30.6 to 68,  $p < 0.001$ ), a subsequent non-statistical decrease between 2010 and 2013 (APC -17, 95% CI 060.6 to 75.1,  $p = 0.586$ ), and a significant positive increase in interest between 2013 and 2020 (APC: +18.9, 95% CI 7.6 to 31.3,  $p = 0.004$ ). This led to an overall significant overall constant increase in trend between 2004 and 2020 with a cumulative APC of +20.7 ( $p < 0.001$ ). This significant increase in trend for “finasteride side effects” was consistent across the UK and AUS between 2004 and 2020, APC +25.7 ( $p < 0.001$ ) and APC +20.1, respectively. Specifically, in the UK, the “finasteride side effects” ARSV presented initially a steep statistically significant increase between 2004 and 2009 (APC: +78.4, 95% CI 47 to 116.6,  $p < 0.001$ ), and a subsequent linear increase between 2009 and 2020 (APC +7.3,  $p = 0.023$ ). Furthermore, the “finasteride side effects” ARSV in AUS had a statistically significant increase between 2004 and 2009 (APC +82.8, 95% CI 37.6 to 142.8,  $p < 0.001$ ) and a non-significant decrease in ARSV between 2009 and 2020 (APC -0.8, 95% CI -8.9 to 8.1,  $p = 0.851$ ). Similarly, searches for the term “post-finasteride syndrome” significantly increased overall between 2004 and 2020 in the USA (APC +29.2, 95% CI 13.4 to 47.3,  $p < 0.001$ ).

There was an initial non-significant increase in “post-finasteride syndrome” between 2004 and 2009 (APC +2.9, 95% CI -12.6 to 21.1,  $p = 0.7$ ), a steep growth between 2009 and 2012 (APC +151.7, 95% CI 21.6 to 421.3,  $p = 0.018$ ), and a linear growth between 2012 and 2020 (APC +16, 95% CI 7.2 to 25.6,  $p = 0.002$ ).

On the contrary, we observed a significant decrease in “Propecia” interest over time (APC: -9.8, 95% CI -10.8 to -9.8,  $p < 0.001$ ). The interest in “Propecia side effects” significantly decreased from 2004 to 2020 (APC: -4.2, 95% CI -14.1 to 6.9,  $p < 0.001$ ) in the USA although this was not consistent in the UK (APC: -0.5,  $p = 1$ ) or AUS (APC: +10.3,  $p < 0.001$ ). In the US, the term “Propecia side effects” demonstrated three distinct points of change in trends. Between 2004 and 2012, we observed an initial non-significant increase (APC +4.7, 95% CI -2.1 to 11.8,  $p = 0.155$ ), a non-significant decrease between 2012 and 2015 (APC -27.1, 95% CI -60.3 to 33.9,  $p = 0.27$ ), and a non-significant decrease between 2015 and 2020 (APC -2, 95% CI -14.5 to 12.3,  $p = 0.743$ ). Interestingly, “Propecia side effects” ARSV significantly increased between 2004 and 2020 (APC +10.3, 95% CI -7.5 to 31.6,  $p < 0.001$ ). Between 2004 and 2006, there was an initial steep non-significant increase in interest (APC +231.2, 95% CI -25.5 to 1372.1,  $p = 0.106$ ) and a significant slight decrease between 2006 and 2020 (APC -5.7, 95% CI -12.1 to 1.1,  $p = 0.091$ ).

### ***Impact of FDA communications on finasteride side effects treatment trends***

When trends were compared before and after FDA communications in 2011(12), the mean (SD) ASRV of “finasteride”, “finasteride side effects”, and “post-finasteride syndrome” increased from 20.4 ( $\pm 5.8$ ) to 41.5 ( $\pm 10.9$ ) ( $p = 0.001$ ), from 17.6 ( $\pm 2.3$ ) to 40.2 ( $\pm 19.0$ ) ( $p = 0.014$ ), and from 2.0 ( $\pm 5.9$ ) to 36.1 ( $\pm 13.7$ ) ( $p < 0.001$ ), respectively (Figure 2).

## **Discussion**

In the present study, we evaluate worldwide public interest in finasteride and its associated sexual health side effects. In our analysis utilizing Google Trends, we found that there has been a significant increase

of interest in Internet searches for “finasteride,” “finasteride side effects,” and “post-finasteride syndrome” in the US and this was consistent with findings in the UK and AUS. Our study has several important findings.

First, search trends for “finasteride” more than tripled since 2004. As finasteride is used among younger men with androgenic alopecia as well as older men with lower urinary tract symptoms secondary to BPH, it is not surprising of the steady and steep interest in web-based searches for this term. With the steady interest in “finasteride,” our web-search analysis for “finasteride side effects” demonstrated an equally impressive growing interest over time. The growing and consistent global interest in finasteride and its sexual health side effects may be attributed to the conflicting nature of the data and studies regarding this topic. For example, Irwig et al. reported new onset sexual side effects associated with the temporal use of finasteride 1 mg for male pattern hair loss using standardized interviews with about 70 young and healthy men, in which the symptoms persisted for at least three months after stopping the medication (11). However, in a systematic review of twelve randomized trials by Mella et al. determined with moderate quality evidence that the risk of discontinuing treatment due to sexual health side effects was similar to that of placebo (10).

Second, we observed a significant interest in “post-finasteride syndrome.” There was a steep growth trend specifically between 2009 and 2012 with an average APC +151.7, which is approximately during the time of the FDA warnings on the drug labels. Post-finasteride syndrome refers to a constellation of persistent physical, psychological, and sexual adverse changes that develop during and/or after patients discontinue finasteride treatment (32). Contemporary studies predominately include low-quality evidence suggesting association between these symptoms and finasteride. Much of the medical community have yet to recognize this syndrome as a real clinical entity or even specific treatments to manage these distressing symptoms. Our web-based worldwide trend analysis indicates that, nonetheless, post-finasteride syndrome is a clearly a problem that is important to the general public that warrants intervention. Thus, it is inappropriate to dismiss this condition and more research is needed to identify which patients are at particular risk to these symptoms and information on practical recommendations and counseling.

Third, interest in “Propecia” and “Propecia side effects” significantly decreased overtime in the US. This may be attributed to Merck’s patent expiration of Propecia in 2006 in the US to allow other drug companies to market generic versions of the drug. As a result, the ARSV of “Propecia” continued to decrease while more Americans were searching for the generic form, finasteride.

Finally, when these key terms were compared before and after the FDA warning that this medication is associated with libido disorders, ejaculatory disorders, and orgasm disorders, there was a significant change of increased Google search activity. This trend demonstrates an association and increased public awareness among the FDA safety communication and patient interest in finasteride and its associated sexual health side effects. Previous studies have examined the use of Google Trends in urology ranging from oncology in prostate cancer treatment options and robotic surgery to female pelvic medicine and

reconstructive surgery (20, 33, 34). Additionally, Stone et al. evaluated impact of FDA communications on the use of surgical mesh for pelvic organ prolapse using trends in Internet search activity. Similarly, they found a significant increase in ARSV at the time of the FDA warning but also reported a poor quality of relevant health information on these Internet websites (35). Nevertheless, Google Trends remains an important aspect in healthcare gathering of information from a patient standpoint (19-22). It is also critical for providers to be aware of the public's perception of these issues to help tailor clinical counseling and discussion when prescribing these medications.

The authors of this study believe this information is critical to not only healthcare providers who commonly prescribe finasteride for lower urinary tract symptoms or androgenic alopecia, but also sexual medicine specialists who may evaluate these men with complaints of persistent sexual dysfunction after finasteride treatment. It is important to for providers to be aware of how patients are seeking healthcare information especially in today's era of digital health. This will enable physicians to be prepared for patient's complaints, better address their concerns, and provide evidence-based information in our discussion, rather than web-based medicine. With this in mind, better regulation of these Internet based web pages is needed to prevent patients from falling in the pernicious trap of "fake news" online.

Our study is not without its limitations. The analysis was limited to the anonymous nature of the data obtained from Google Trends and do not allow for analysis of subpopulation groups. However, men who use finasteride for male pattern hair loss are generally younger and men who use finasteride for BPH are generally older. Although internet users tend to be younger, a significant portion of patients over 65 have been found to use the internet to access health information (36). Thus, we argue that the data captures both groups of patients. The term "Dutasteride," which may be used as second line treatment for androgenic alopecia was not assessed in this study because of the low volume of web-searches which prevented us from performing further investigations. We are also limited by inherent use of a single search engine, but Google is the most widely used search engine in the USA (18). Additionally, it is important to note that the significant interest in Internet search for finasteride may also be confounding by improved internet access in recent years. The strengths of the study include its design meticulous trend analysis providing granular data and compared across the UK and AUS for external validation.

## **Conclusion**

People are increasingly searching the web for finasteride and its potential side effects with steep interest after the FDA communications about finasteride sexual health effects. This trend demonstrates an increased public awareness, and therefore more thorough discussions prior to initiating finasteride treatment with patients may be necessary.

## **Declarations**

**Conflict of Interest:**

The authors declare that they have no competing interests.

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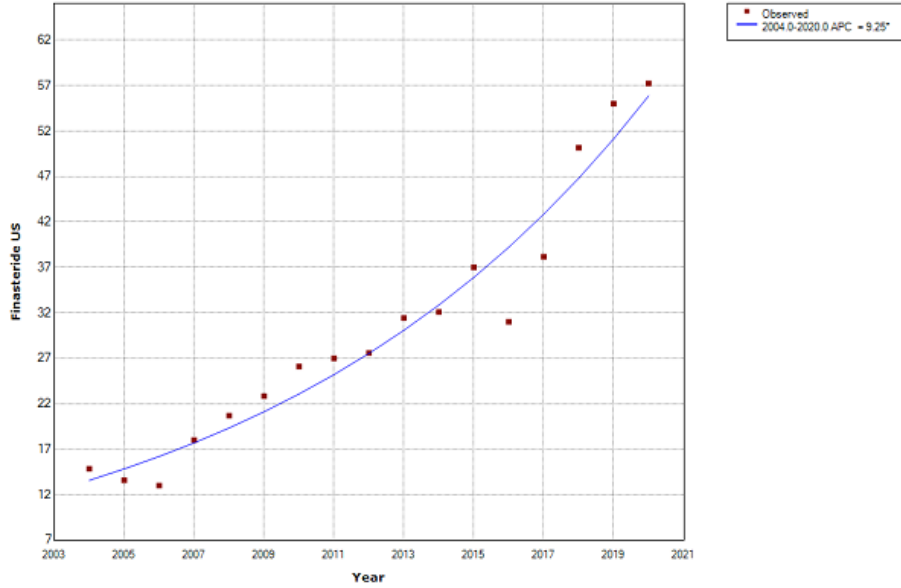
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## Tables

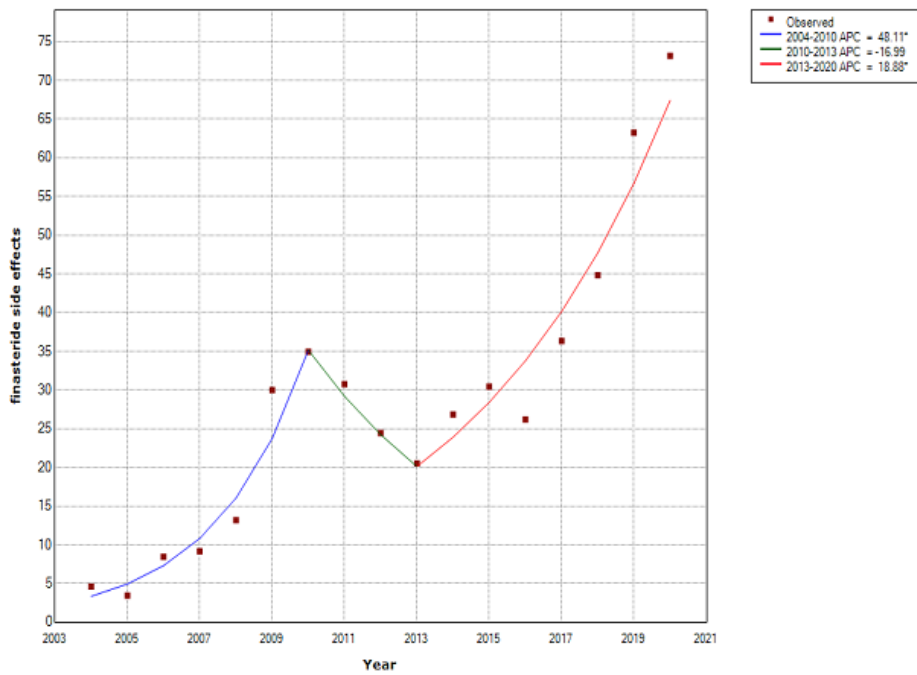
**Table 1.** (A)AAPC results of Finasteride, Propecia, and their related side effects compared across the USA, United Kingdom (UK), and Australia (AUS). *APC: Annual Percent Change; AAPC: Average Annual Percent Change. CI: Confidence Interval.*

<u>Search term</u>	<u>Segments</u>	<u>Lower endpoint</u>	<u>Upper endpoint</u>	<u>(A)APC</u>	<u>Lower CI</u>	<u>Upper CI</u>	<u>Test-statistic</u>	<u>P-value</u>
<b>Finasteride (USA)</b>	overall	2004	2020	9.2	8	10.5	16.4	<0.001
	1	2004	2020	9.2	8	10.5	16.4	<0.001
<b>Finasteride side effects (USA)</b>	overall	2004	2020	20.7	5.6	37.9	2.8	<0.001
	1	2004	2010	48.1	30.6	68	7	<0.001
	2	2010	2013	-17	-60.6	75.1	-0.6	0.586
	3	2013	2020	18.9	7.6	31.3	3.9	0.004
<b>Finasteride side effects, (UK)</b>	overall	2004	2020	25.7	17.8	34.3	6.9	<0.001
	1	2004	2009	78.4	47	116.6	6.5	<0.001
	2	2009	2020	7.3	1.2	13.7	2.6	0.023
<b>Finasteride side effects (AUS)</b>	overall	2004	2020	20.1	9.1	32.2	3.7	<0.001
	1	2004	2009	82.8	37.6	142.8	4.6	0.001
	2	2009	2020	-0.8	-8.9	8.1	-0.2	0.851
<b>Post-finasteride syndrome (USA)</b>	overall	2004	2020	29.2	13.4	47.3	3.8	<0.001
	1	2004	2009	2.9	-12.6	21.1	0.4	0.701
	2	2009	2012	151.7	21.6	421.3	2.9	0.018
	3	2012	2020	16	7.2	25.6	4.2	0.002
<b>Propecia (USA)</b>	overall	2004	2020	-9.8	-10.8	-8.8	-20.3	<0.001
	1	2004	2020	-9.8	-10.8	-8.8	-20.3	<0.001
<b>Propecia side effects (USA)</b>	overall	2004	2020	-4.2	-14.1	6.9	-0.8	<0.001
	1	2004	2012	4.7	-2.1	11.8	1.6	0.155
	2	2012	2015	-27.1	-60.3	33.9	-1.2	0.27
	3	2015	2020	-2	-14.5	12.3	-0.3	0.743
<b>Propecia side effects (UK)</b>	overall	2004	2020	-0.5	-7.1	6.6	0.1	1
	1	2004	2020	-0.5	-7.1	6.6	-0.1	0.885
<b>Propecia side effects (AUS)</b>	overall	2004	2020	10.3	-7.5	31.6	1.1	<0.001
	1	2004	2006	231.2	-25.5	1372.1	1.7	0.106

# Figures



\* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level. Final Selected Model: 0 Joinspoints.



\* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level. Final Selected Model: 2 Joinspoints.

Figure 1

(A) Annual percent change (APC) of “finasteride” in the US from 2004 to 2020 demonstrating significant interest over time.

(B) Annual percent change (APC) of “finasteride side effects” in the US from 2004 to 2020 demonstrating a steep significant interest from 2004-2010 (blue), non-significant decreased interest from 2010-2013 (green), and significant interest from 2013-2020 (red).

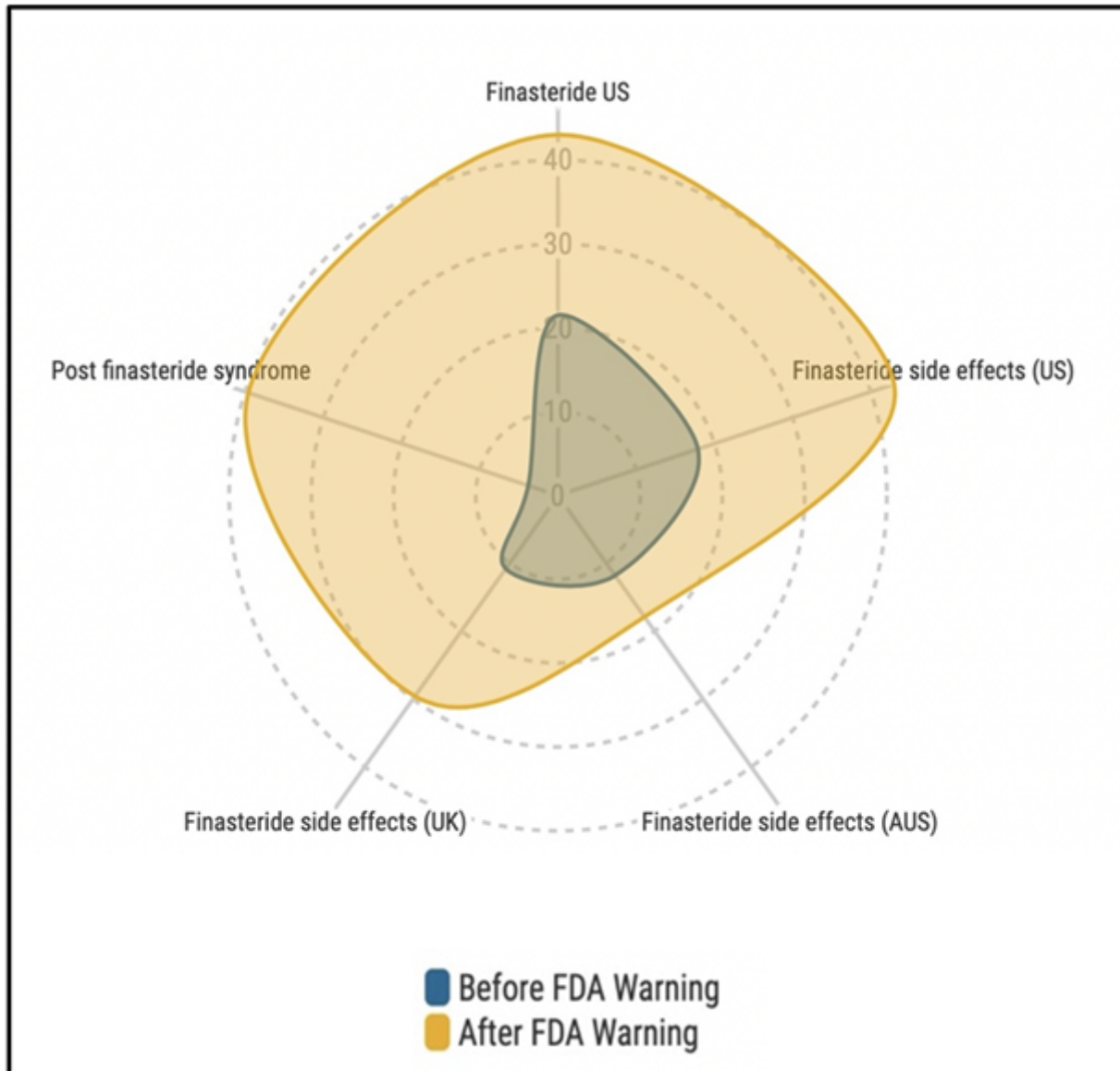


Figure 2

Finasteride-related web searches performed before (2004- 2012) blue area) and after (2012-2021 yellow area) the FDA warning

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [GoogleFinasterideVisualAbstract.pdf](#)