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Consulting "Dr. Google" for Prostate Cancer Treatment Options: A Contemporary Worldwide Trend Analysis

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euo.2019.07.002.

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Abstract

Background: In the era of digital data, the Internet has become the primary source from which individuals draw healthcare information.

Objective: The aim of the present study is to determine worldwide public interest in prostate cancer (PCa) treatments, their penetrance and variation, and how they compare over time.

Design, setting, and participants: An analysis of worldwide search-engine trends included electronic Google queries from people who searched PCa treatment options from January 2004 to August 2018, worldwide. Join-point regression was performed. Comparisons of annual relative search volume (ARSV), average annual percentage change (AAPC), and temporal patterns were analysed to assess loss or gain of interest.

Outcome measurements and statistical analysis: Evaluations were made regarding (1) interest in PCa treatments, (2) comparison of people's interest, and (3) impact of the US Preventive Service Task Force (USPSTF) screening recommendation and National Comprehensive Cancer Network (NCCN) guideline endorsements on Internet searching for PCa treatments.

Results and limitations: The mean ARSV for "prostatectomy" was 73% in 2004 and decreased thereafter, reaching a nadir of 36% in 2014 (APC: −7.2%; 95% confidence interval [CI] −7.8, −6.7; $p < 0.01$). Similarly, decreased interest was recorded for radiation therapy (AAPC: −3.2%; $p = 0.1$), high-intensity focused ultrasound (AAPC: −2.3%; $p = 0.1$), hormonal therapy (AAPC: −11.6%; $p < 0.01$), ablation therapy (AAPC: −4.1%; $p < 0.01$), cryotherapy (AAPC: −9.9%; $p < 0.01$), and brachytherapy (AAPC: −8.3%; $p < 0.01$). A steep interest was found in active surveillance (AS) (AAPC: +14.2%; $p < 0.01$) and focal therapy (AAPC: +27.5%; $p < 0.01$). When trends were compared before and after NCCN and USPSTF recommendations, a consistent decrease of all the treatment options was found, while interest in focal therapy and AS showed an augmented mean ARSV (+19.6 and +31.6, respectively).

Conclusions: People are increasingly searching the Internet for PCa treatment options. A parallel decrease of interest was found for the nonmonitoring treatments, except for focal therapy, while an important growth of appeal has been recorded for AS. Understanding people inquisitiveness together with their degree of knowledge could be supportive to guiding counselling in the decision-making process and putting effort in certifying patient information.

Patient summary: In the era of digital data, patients are increasingly searching the Internet for prostate cancer (PCa) treatment options. To safeguard patients' knowledge, it is mandatory to understand how people seek healthcare information, guaranteeing certified and evidence-based information pertaining to PCa treatments options.

Keywords

Prostate cancer; Patient information; Google Trends; Prostatectomy; High-intensity focused; ultrasound; Radiotherapy; Focal therapy; Active surveillance; Hormonal therapy; Cryoablation; Brachytherapy; Living paper

1. Introduction

Prostate cancer (PCa) is the second most common tumour worldwide [1], with 164 690 estimated new cases and 29 430 death in the USA in 2018 [2].

Radical prostatectomy (RP), hormonal therapy (HTh), and radiotherapy (RTh) have been the only available treatments for PCa in the past years [3]. In the last decades, new screening methods resulted in significant stage migration towards more favourable prognoses, and a huge effort was made to develop new technologies, resulting in less invasive options that can be offered to patients [4]. Recently, it has been shown that national trends in prostate biopsy and RP volumes decreased following the US Preventive Service Task Force (USPSTF) recommendations against prostate-specific antigen (PSA) screening [5,6], leading to a reduction in overtreatment in favour of monitoring options. Nowadays, active surveillance (AS) came into play [7], becoming an initial choice for low-risk PCa patients [4].

Short- and long-term outcomes have widely been explored in clinical trials and national database analyses [8–13]. Nevertheless, no study investigated the impact of PCa treatments and the mindset shift of the knowledge and opinion of the worldwide population.

In the era of digital data, the Internet has become a primary source from which individuals draw healthcare information. Information gathering by patients after the diagnoses of PCa inevitably passes through Internet surfing [14,15]. In 2018, the number of Internet users has been estimated to be 4.021 billion [11]. The use of web-derived health information is rapidly increasing, playing an important role in the decision-making process [14,16]. Moreover, patients are prepared to bypass their nearest centres to undergo treatments at more distant hospitals that better mirror their needs [17].

Google Trends (GT) is a free, easily accessible search tool that enables one to analyse worldwide “big data” on the relative popularity of search terms over a specific period of time. Its use in healthcare research is increasing, providing interesting results in terms of epidemiological surveillance, screening practices, and knowledge of therapeutic options [16,18].

The aim of the present study is to assess the interest of the worldwide population in PCa treatments to answer three key questions (KQs): KQ1: What is the worldwide interest in PCa treatments? KQ2: How peoples’ interest regarding PCa treatments is compared? KQ3: What is the impact of USPSTF screening recommendation and National Comprehensive Cancer Network (NCCN) guideline endorsements on Internet searching for PCa treatments?

2. Patients and methods

2.1. Data sources

In the present study, we included the following treatment options: RP, AS, RTh, focal therapy (FTh), high-intensity focused ultrasound (HIFU), ablation therapy, HTh, cryotherapy (CTh), photodynamic therapy, and brachytherapy (BTh).

GT generates worldwide search volume data over time since 2004, offering geographical and temporal patterns according to a specific term [16,19]. Users can input a term or a set of terms, and when enough data are available, GT will generate a “line graph”, representing how interest has increased or fallen over a period (monthly frequency), as well as the relative popularity of the search term within specific territories.

A relative search volume (RSV) index is assigned to search terms. RSV values represent the research interest regarding the highest point of the graph in relation to the region and period specified. They do not represent absolute search volume numbers, since the data are presented on a scale from 0 to 100. The value 100 indicates the highest search frequency of a given term, while 50 indicates half of the searches. A score of 0, however, indicates that sufficient data were not found for the term [16,19].

Terms searched were assessed according to the checklist for the documentation of GT use [16]. On 31 August 2018, we queried GT and downloaded the data search input for all the treatment options for PCa listed above using a combination of terms, as follows: [“treatment”] [“prostate cancer”]. We searched within “worldwide” from 1 January 2004, to 31 August 2018, using the “global” query category.

Since trends could fluctuate, we created a website (https://mistrends.wixsite.com/pcatrends) where the reader can check trends in a real-time fashion. This new supplementary feature makes the present a “living paper” that updates itself daily.

2.2. Statistical analysis

Month scores are calculated on the basis of the average relative daily search volume within the month. The mean annual relative search volume (ARSV) is calculated as the mean of the monthly scores within the same year. The joinpoint regression (JPR) model was used to identify significant changes in mean ARSV over time for each PCa treatment. The JPR model is used to better describe trends that are not constant over time and allows for evaluating statistically significant changes (join-points) in trends. 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 [20,21]. For this reason, segmental periods are specific for each treatment/search [22].

Linear trends in RSV were summarised using the estimated ARSV and annual percentage change (APC). APC was used to measure differences in ARSV between two join-points. Average annual percentage change (AAPC) and the respective 95% confidence intervals (CIs) were estimated to summarise linear trends in ARSV during the entire period [23].

The use of the natural log-linear model ($\ln[y] = xb$) enables the analysis of AAPC in rate over time. A positive value of AAPC indicates an increasing RSV, while a negative rate refers to a decreased interest. When a dependent variable was “0”, a log ($x + 1$) transformation was applied to the entire dataset. A permutation test, allowing up to four join-points, was used to evaluate any inflection points with a significant variation in the slope of the trend. A trend was defined as “nonconstant” or “constant” if slopes were identified or not identified, respectively.

Since RSV indexes fluctuate over time, data retrieved from search terms were plotted in polynomial trend lines. PCa treatment trends were compared, and the mean ARSV was computed to appreciate discrepancies over the study period (Supplementary Table 1). The Kruskal-Wallis *H* test was used to compare mean ARSV values between PCa treatments before and after NCCN AS endorsement and USPSTF recommendation.

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).

3. Results

3.1. Trend pattern analysis

Figs. 1 and 2 show the monthly ARSV for “prostatectomy”. The trend showed a nonconstant decrease with an AAPC of −3.7% ($p < 0.001$). The mean ARSV for “prostatectomy” was 73% in 2004 and decreased thereafter, touching a lower rate of 36% in 2014 (APC: −7.2%; 95% CI −7.8, −6.7; $p < 0.001$), showing an increase of interest up to 2018 (APC: +5.6%; 95% CI 3.1, 8.1; $p = 0.1$).

Fig. 1A depicts the monthly ARSV for “active surveillance” for “prostate cancer”. Globally, the trend showed a nonconstant increase with an AAPC of +14.3% ($p < 0.001$). The mean ARSV for “AS” was 8.3 in 2004, and showed a progressive nonconstant increase of interest up to 2010 (APC: +28.2; 95% CI 15.9, 41.7; $p < 0.001$) followed by a statistically nonsignificant increasing trend up to 2018 (APC: 4.9; 95% CI −1.6, 12; $p = 0.1$).

Fig. 1B displays the monthly ARSV for “radiation therapy” for “prostate cancer”. Considering the large period, it showed a decreasing trend that was not statistically significant (AAPC: −3.2%; $p = 0.1$). A detailed analysis shows a changing tendency: the mean ARSV for “radiation therapy” was 56.08 in 2004 and exhibited a nonconstant decrease until 2007 (APC: −21.6; 95% CI −27.8, −14.8; $p < 0.001$), which was then assessed in three different plateaus of interest up to 2018 (APC: +9.2; 95% CI −7.5, 28.9; $p = 0.2$; APC: −4.3; 95% CI −9.2,0.9; $p = 0.1$; and APC: +7.8; 95% CI −0.8,17.1; $p = 0.1$ up to 2010, 2015, and 2018, respectively).

Fig. 1C reveals the monthly ARSV for “hormonal therapy”. The trend showed a nonconstant decrease, with an AAPC of −11.6% ($p < 0.01$). The mean ARSV for “hormonal therapy” was 38.75 in 2004, then reduced up to 2010 (APC: −20.1; 95% CI −26.4, −13.3; $p < 0.01$), and showed a plateau with a statistically nonsignificant decreasing trend up to 2018 (APC: −4.7; 95% CI −9.6, 0.5; $p = 0.1$).

Fig. 1D shows the monthly ARSV for “focal therapy”. A nonconstant increasing trend was found with an AAPC of +27.5%. The mean ARSV was 0 in 2004, which then increased up to 2011 (APC: +27.5; 95% CI 9.1, 48.6; $p < 0.001$) followed by a plateau (APC: −6.4; 95% CI −27.0, 20; $p = 0.6$).

Fig. 2A shows the monthly ARSV for “HIFU”. The mean ARSV was 26.2 in 2004 and showed a statistically nonsignificant constant reduction of interest up to 2018 (APC: −2.3; 95% CI −5.3, 0.7; $p = 0.1$).

Fig. 2B shows the monthly ARSV for “cryotherapy” for “prostate cancer”. The mean ARSV was 31.83 in 2004, which decreased constantly up to 2018 (APC: −9.9; 95% CI −12.6, −7.2; $p < 0.001$).

Fig. 2C depicts the monthly ARSV for “ablation therapy” for “prostate cancer”. Globally, the trend showed a nonconstant decrease, with an AAPC of −4.1% ($p < 0.001$). The mean ARSV for “ablation therapy” was 42.5 in 2004, which then decreased, touching a lower rate of 12.92 in 2012 (APC: −11.5%; 95% CI −15.3, −7.5; $p < 0.001$), showing a plateau up to 2018 (APC: +6.8%; 95% CI −0.3,14.3; $p = 0.1$).

Fig. 2D reveals the monthly ARSV for “brachytherapy”. In general, the trend decreased with an AAPC of −8.3% ($p < 0.001$). The mean ARSV for “brachytherapy” was 50.25 in 2004 and declined up to 2006 (APC: −23.2; 95% CI −33.1, −11.9; $p < 0.001$), then showed a changing interest over the time without statistical significance (APC: 3; 95% CI −21.8, 35.6; $p = 0.8$; APC: −18.8; 95% CI −38.3,7; $p = 0.1$; and APC: 2.4; 95% CI −3.8, 8.9; $p = 0.4$ up to 2010, 2013, and 2018, respectively).

Fig. 2E shows the monthly ARSV for “photodynamic therapy” for “prostate cancer”. The mean ARSV was 8.33 in 2005 and no join-points were identified, which showed a constant bigger interest transversely during the study period up to 2018 (APC: 2.3; 95% CI −7.5, 13.1; $p = 0.6$)

3.2. Impact of USPSTF and NCCN recommendations on PCa treatment trends

Fig. 3A shows the mean ARSV for each treatment before and after NCCN guideline endorsement on AS in 2010. A consistent decrease of all the treatment options was found, except for FTh (5.0 vs. 19.1; $p = 0.03$), while interest in AS showed an increased mean ARSV (11.5 vs. 30.3; $p = 0.02$).

Fig. 3B depicts the mean ARSV for each treatment before and after USPSTF statement on PSA screening in 2012. Similarly, a homogeneous decrease of all the treatment options has been found, except for FTh (9.5 vs. 19.5; $p = 0.04$), and AS showed an increasing mean ARSV (16.5 vs. 31.6; $p = 0.02$).

4. Discussion

The key findings emerging from this study were that people search the Internet for PCa cancer treatments with trends that fluctuate over time. Searching for PCa curative treatments showed a downward trend, except for FTh, while monitoring option presented a growing appeal over time.

Searching trends for “prostatectomy” decreased by nearly two-thirds since January 2004. Our results mirror previous findings based on national databases. Halpern et al. [24] demonstrated that following the USPSTF recommendation, median RP volume decreased

by nearly 16% [5,25]. Tyson et al. [26] using data from the Nationwide Inpatient Sample reported a 7% decrease in the rates of RP from 1998 through 2011. However, despite the descending trend, RP still was the most searched term, compared with other treatment options. This finding is in line with the Prostate Strategic Urologic Research Endeavor (CaPSURE) study, which revealed that, though declining, RP continues to be the primary management treatment in PCa patients [9].

Interestingly, RP is the only option that showed a late increased interest. The statistically significant change of this trend matches with the peak penetrance of robotics in the field during the years 2009–2014 [27]. This finding might support the idea that people's interest could be driven by the surgical approach that is offered.

"Radiotherapy" showed a declined appeal in people searching for PCa treatments reaching a plateau after 2007, supporting previous national database [11–13] and register [8,9] analyses. Weiner et al [13] measured temporal trends in the proportion of patients with low- and intermediate-risk PCa in the USA, showing a decreasing trend of RTh in the period from 2004 to 2010. Malouff et al. [12] in a retrospective analysis of the National Cancer Database (NCD) showed a decline in the use of overall RTh and specifically for BTh. Chen et al. [11], in a population-based study evaluating the Surveillance, Epidemiology, and End Results (SEER) database between 2004 and 2013, showed a slight decrease of both RTh and BTh, which has been found to be steepest in low-risk PCa patients.

Internet searching for "hormonal therapy" displayed a downward trend over time, mirroring findings as previously described. According to the NCD (2004–2012), Gray et al. [28] showed reduced use of HTh in patients with low- and intermediate-risk disease. A declining trend in the use of HTh was also reported among patients undergoing RP, BTh, and CTh [29]. These findings might reflect the awareness about the risks of loss of libido, hot flashes, night sweats, irritability, breast development, osteoporosis, and obesity [30,31] and about quality of life [32]. In addition, the CaPSURE registry identified falling rates of primary HTh use [8,9]. As demonstrated in the review by Pagliarulo et al. [33], the benefit of HTh is very limited when used alone. HTh, in combination with external beam radiation therapy or after surgery in men with extensive lymph node invasion, has shown a strong advantage for overall survival. In this consideration, the decreased interest in HTh could be linked to the parallel decline of all curative trends.

FTh is an emerging treatment option that involves focal ablation of PCa with preservation of surrounding healthy tissue. FTh modalities include CTh, HIFU, laser ablation, photodynamic therapy, irreversible electroporation, and radiofrequency ablation [34]. Our study showed an increased interest on "focal therapy", underlying the curiosity for all those treatments that attempt to improve the preservation of sexual and urinary functions together with oncological adequacy. Interestingly, when the search for specific FTh modalities was assessed, a slight reduction was found.

Globally, searching trends for curative treatments showed a homogenous decrease over time. These findings could be explained by the impact of USPSTF recommendation [5,24,25] on medical community. When we compared searching volume before and after USPSTF

recommendation, we found that the mean ARSV for curative PCa treatments decreased globally, while AS confirmed a growing appeal.

Our analysis showed that interest in AS increased three times since January 2004. Many centres have reported dramatic changes, with upsurges in AS of early cancers and local treatment of advanced disease. Urologists are embracing AS, and a growing literature supports its safety and efficacy for low-risk PCa. These findings reflect data from administrative and national registry databases [8,9]. Cooperberg et al. [8,9] analysed distribution data from 45 US sites that contributed data to the CaPSURE study. It has demonstrated an increase in the use of AS for patients with low-risk PCa, from a low of 6.7% in the years 1990–2009 to 40.4% in the period 2010–2013. These changing trends in the management of PCa options highlight the inversion of overtreatment, mainly confirming the findings of the CaPSURE study [9]. Moreover, in 2010, NCCN guidelines for PCa recommend the use of AS as the sole initial treatment in men with low risk and a life expectancy of <10 yr, and men with “very low risk” and a life expectancy of <20 yr [7]. The aforementioned augmented interest in AS could echo the adherence to clinical guidelines and recommendation, which play a central role in delivering day-to-day practice and efficient healthcare [35].

We demonstrated that people search for PCa treatment options on the Internet. Our findings can be used to assist physicians in knowing what the general public searches for online when explaining treatment options to patients. The Internet is an amazing informative tool with its “pro” and “cons”. Well-informed patients are better equipped to talk about issues that concern them and to share information about the way they experience their condition and treatment. However, it has been suggested that some individuals choose to rely on the Internet as their main source of information, often deterring the patient-doctor relationship [36]. The media could have a considerable impact on the public by increasing their knowledge, changing their attitudes, and influencing their health behaviour [37]. Considering the amount of “noncertified” information, it is mandatory to guarantee high-level knowledge, protecting patients from “fake news”. In this regard, the American Urological Association Care Foundation [38] and the European Association of Urology Patient Information Panel provide dependable information on urological diseases [39], translated for patients living in different countries [40] and taking into account scientific evidence and recommendations.

To the best of our knowledge, this is the first study that investigates worldwide public interest in PCa treatment options. Its strengths are the design and peculiar analysis. The opportunity to check “real-time data” in the supplementary website makes it a “living paper” that renews itself over time. Each term was searched methodically considering always “prostate cancer” and “specific treatments”. We believe that this new information is of considerable interest and practical use to the general medical community at large, who needs to be aware of contemporary option trends thereby to better advise patients seeking care for PCa.

Limitations are due to the nature of GT data, which are anonymous and do not allow analysis of subpopulation groups. Moreover, we do not have access to rough data, but only

to RSV. It is important to note that the 100 reference RSV value is for the time when the search term had the highest volume "relative to all Internet searches at the same time" and a subsequent value of 50 does not represent half as many gross searches as the 100 time. It might be hypothesised that decreased barriers to entry for Internet use in developing countries have broadened potential search terms to those relevant outside western societies. The absolute number of searches in 2018 may be higher than those in 2004 because there are many more people online. Search terms in non-English languages were not captured. Search terms were selected within the "medical terminology" (eg, "prostatectomy", "photodynamic therapy", etc.). We did not consider numerous colloquial searches due to their extreme heterogeneity, which cannot be systematised (eg, "prostate removal" or "prostate cancer surgery" instead of "radical prostatectomy"). On the contrary, the strengths in using a "medical term" is based on the assumption that a search would be performed by patients or relatives after a clinical consultation, in order to get more information and make their own decision on the therapeutic indication by the urologist.

5. Conclusions

People search the Internet for PCa treatment options. A parallel decrease in relative search interest was found for curative treatments, while a growth of appeal has been recorded for FTh and AS. Understanding people's inquisitiveness together with their degree of knowledge could help guide counselling in the decision-making process and put effort in certifying patient information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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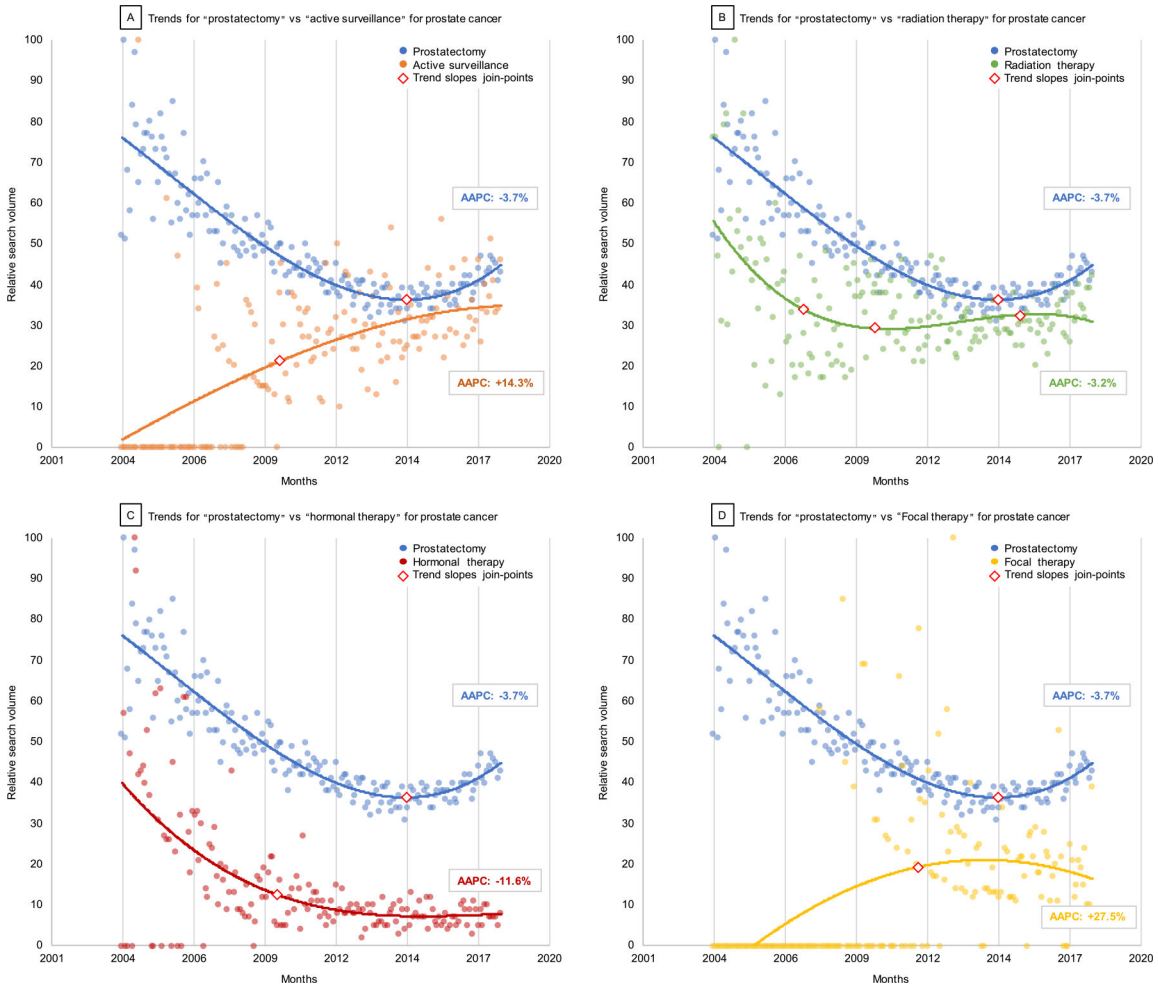

Fig. 1 –.

Google Trends relative search volume for PCa treatment options compared with radical prostatectomy by month, January 2004 to August 2018: (A) active surveillance, (B) radiation therapy, (C) hormonal therapy, and (D) focal therapy. PCa treatment searches were reported graphically with "radical prostatectomy" search since radical prostatectomy represents the gold standard treatment for PCa. AAPC = average annual percentage change; PCa = prostate cancer.

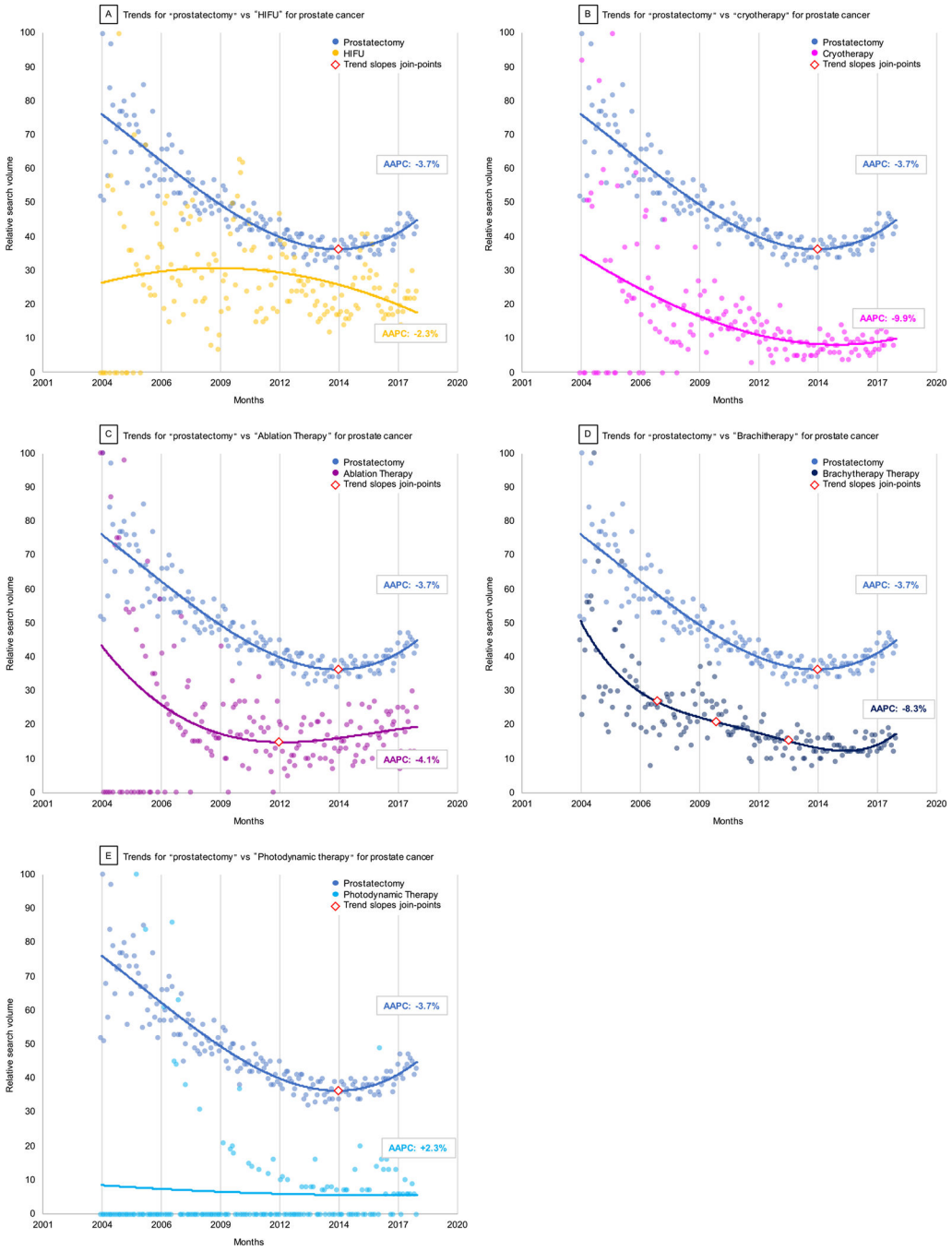

Fig. 2 –.

Google Trends relative search volume for PCa treatment options compared with radical prostatectomy by month, January 2004 to August 2018: (A) HIFU, (B) cryoablation, (C) ablation therapy, (D) brachytherapy, and (E) photodynamic therapy. PCa treatment searches were reported graphically with “radical prostatectomy” search since radical prostatectomy represents the gold standard treatment for PCa. AAPC = average annual percentage change; HIFU = high-intensity focused ultrasound; PCa = prostate cancer.

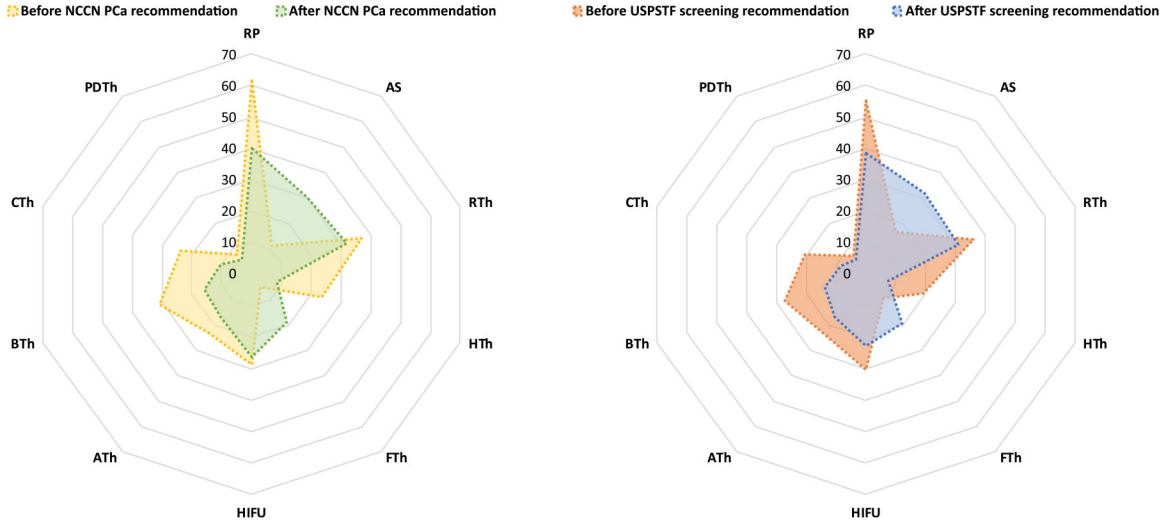

Fig. 3 –.

Mean ARSV PCa treatment comparison before and after NCCN guidelines and USPSTF screening recommendation. AS = active surveillance; ATh = ablation therapy; BTh = brachytherapy; CTh = cryotherapy; FTh = focal therapy; HIFU = high-intensity focused ultrasound; HTh = hormonal therapy; NCCN = National Comprehensive Cancer Network; PCa = prostate cancer; PDTh = photodynamic therapy; RP = radical prostatectomy; RTh = radiation therapy; USPSTF = US Preventive Service Task Force.