



Regenerative therapies for erectile dysfunction: the influence of direct-to-consumer marketing on patient interest

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Background: Despite a lack of evidence, a number of “regenerative” therapies have become popularized treatments for erectile dysfunction (ED). Platelet-rich plasma (PRP) injections and shockwave therapy have received significant attention through direct-to-consumer marketing and are advertised as viable alternatives to guideline-backed therapies. Additionally, focused low-intensity shock wave therapy (LiSWT) has become conflated with acoustic or radial wave therapy (rWT), although their mechanism of wave generation and tissue penetration is distinct. GAINSWave, a marketing platform for acoustic wave therapy, has also pervaded the marketplace. We aim to evaluate the relative impact of direct-to-consumer marketing of shockwave therapy and PRP by analyzing the quantity of Google internet search queries for selected regenerative and guideline-backed non-regenerative therapies for ED.

Methods: National Google Search trends in the United States (www.google.com/trends) were analyzed to characterize interest in different forms of therapy for ED. Search trends for PRP, LiSWT (and various iterations), intracavernosal injections (ICI), intraurethral injections (IU), vacuum erectile device (VED), and GAINSWave were analyzed. Monthly search data were compiled over multiple years, ending at 2/28/2020, just before the COVID-19 pandemic and state of emergency in the United States. Macro-level changes in public interest were quantified using yearly averages.

Results: Patterns in Google Search interest in PRP and LiSWT increased respectively by 3-fold and 275-fold over the decade, representing a larger share of Google Searches by 2020. Trends in Google Search interest in selected types of shockwave therapy for ED also show that queries for GAINSWave commanded public interest, increasing by 219-fold from 2016 to 2020.

Conclusions: Regenerative therapies for ED have produced interest surpassing other adjunct guideline-backed therapies, despite receiving the designation of “experimental” or “investigational” therapies. The establishment of GAINSWave also constitutes an inflection point for the whole shockwave market: searches for shockwave therapy increased by 782% between 2016 and 2020. Direct-to-consumer marketing of PRP and shockwave therapy has upturned the customary role of physicians in counseling patients about evidence-based therapies for ED. This increase in public interest in GAINSWave emphasizes its success as a marketing platform. The urological community should consider strategies to address misinformation, such as search-engine optimization, social media, and educational outreach.

Keywords: Erectile dysfunction (ED); Google Trends; focused shockwave therapy; direct-to-consumer marketing; regenerative therapy

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Introduction

Background

Erectile dysfunction (ED) is a common urologic condition affecting up to 47% of all men in the United States and up to 30% of men younger than 40 years of age (1). Its prevalence is projected to grow to over 320 million men worldwide by 2025 (2,3). The yearly economic burden of treating ED is projected to be upwards of \$15 billion in the United States alone, given the current prevalence (4). ED is strongly correlated with multiple co-morbidities; numerous population-level studies have found that men with self-reported ED have significantly higher rates of hypertension, angina, and high cholesterol (5,6). In addition, ED is strongly correlated with emotional distress, depression, and anxiety (7,8).

Given the economic and social burdens of ED, numerous treatment modalities have been developed. Pharmaceutical therapy with phosphodiesterase-5-inhibitors (PDE5i) represents first-line therapy (9). PDE5i are both effective and generally well tolerated, but patients with refractory ED often require supplementary treatments (10). There

are many guideline-backed, non-surgical, non-regenerative treatments in the shared-decision making pathway, including intraurethral suppositories or gels (IU), intracavernosal injections (ICI), and vacuum erectile devices (VED). These therapies have an established evidence-base and have been available to patients for several decades. Nonetheless, public interest has shifted towards a new paradigm for adjunct therapy, one that promotes the notion of rejuvenation or restoration: the use of platelet-rich plasma (PRP) and low-intensity shock wave therapy (LiSWT) is supported by a theoretical mechanism for addressing ED, based on the regeneration of tissues (11). PRP and LiSWT have been incorporated into the men's health zeitgeist in recent years partly due to a large commercial push in advertising and promotion (12). This popularity exists despite a paucity of scientific evidence supporting the use of PRP and LiSWT in treating ED. This lack of evidence has led to the designation of PRP and LiSWT as "experimental" or "investigational" therapy by both the American Urological Association (AUA) and the Sexual Medicine Society of North America (SMSNA) (10,13,14).

In recent decades, the internet has become a key tool for patients to gather health and treatment information. In 2013, it was estimated that 59% of U.S. adults had searched online for health information that year. A 2017 study found that 77% of its adult cohort utilized internet queries for health information that year (15,16). Moreover, another large population-based study in 2017 demonstrated that 45% of patients utilized the internet as their primary resource for accessing health information, compared to 13% and 8% who utilized healthcare professionals and traditional media, respectively (17).

Despite the numerous platforms available, Google Search represents the most popular internet search engine, accounting for nearly 90% of all online searches worldwide (8,11,18). Google Trends, a search analysis tool, tracks internet-user interests in various search terms over time. Researchers have recently started analyzing Google Trends data in an attempt to understand patients' approach to seeking health information on a population level (11,19-23). The illuminating results of these studies have prompted a formalization of this new area of research, "infodemiology", defined as the study of distribution and determinants

Highlight box

Key findings

- Direct-to-consumer marketing appears to play an outsized role in influencing public interest in non-surgical treatments for erectile dysfunction.
- Public interest trends assessed via Google Search parallel marketing campaigns rather than data-driven guidelines.

What is known and what is new?

- Interest in adjunct non-guideline-backed regenerative therapies for erectile dysfunction such as platelet-rich plasma and shockwave therapy has increased in recent years.
- Marketing platforms have shifted public interest away from guideline-backed therapies for erectile dysfunction furthering the consumerization of men's health.

What is the implication, and what should change now?

- The urologic community should employ approaches to correct misrepresentations of health data, including advice for optimizing internet searches, social media campaigns, and robust educational outreach.

of information through an electronic medium and its subsequent impact on public health and policy (21).

Objective

This infodemiologic study will shed light on the recent trend towards regenerative therapies for ED. This will be the first study of its kind to investigate the patterns of internet-user interest in second-line, non-surgical treatments for ED. Our goal is to better understand what factors may influence population-level interest in non-first-line therapies for ED and whether this interest corresponds with AUA and SMSNA guidelines regarding ED treatment. By quantifying the frequency of internet search queries for regenerative ED therapies, we aim to evaluate the impact of direct-to-consumer marketing on public interest.

Methods

We utilized Google Trends to analyze population-level Google Search trends in the United States. These trends were analyzed to describe internet-user interest in non-surgical adjunct therapies for ED. The Google Trends inquiry tool restricts a comparative search of up to five distinct search queries. Thus, unique search terms were used to compare trends for five non-surgical, non-first line therapies: PRP, LiSWT, ICI, IU, and VED. Multiple iterations of each term were produced and combined into a distinct search, as subsequently listed.

The amalgamated search terms for PRP included: “*P shot*”; “*Priapus shot*”; “*Platelet rich plasma for ED*”; “*Platelet rich plasma for erectile dysfunction*”. The search terms for LiSWT included: “*Shockwave therapy for ED*”; “*Shock therapy for ED*”; “*Low intensity shock therapy for ED*”; “*GAINSWave*”. The search terms for ICI included: “*Intracavernosal injections*”; “*Trimix*”; “*Bimix*”; “*Edex*”; “*Caverject*”. The search terms for IU included: “*Intraurethral alprostadil*”; “*MUSE ED*”; “*MUSE erectile dysfunction*”. The search terms for VED included: “*Vacuum erectile device*”; “*Vacuum device for ED*”; “*Vacuum device for erectile dysfunction*”. Unique search terms were limited by word count.

In order to shed light on the effect of direct-to-consumer marketing, we examined GAINSWave, a provider database and marketing platform. A second, distinct Google Trends comparison was therefore performed specifically comparing the four aforementioned iterations of LiSWT to each other, in addition to “*Radial wave therapy for ED*”; “*Acoustic wave therapy for ED*”; “*Focused shockwave therapy for ED*”;

“*Focused shock therapy for ED*”. Of note, GAINSWave, a popular radial-wave therapy that is categorically different from traditional LiSWT, has been marketed to the general population as “shockwave therapy”. Given that search trends are an appropriate proxy for patient-interest, GAINSWave was included in our search terms in order to understand the effect of marketing on consumers in this space.

Google Trends data is tabulated on a relative scale of 0–100, referred to as a “search volume index”, with “100” representing the search term with the highest search prevalence over a specified time interval and all other numbers being relative to the peak frequency. We compiled the monthly Google Trends data for the past decade [2010–2020] and subsequently calculated yearly averages to quantify macro-level changes in patient interest. In order to avoid confounding, the selected endpoint for data abstraction was February 28, 2020, as it represents the onset of the COVID-19 pandemic in the United States, marked by the subsequent state of emergency in March 2020.

Results

Population-level interest in non-regenerative, guideline-backed, adjunct therapies (IU, ICI, VED) remained relatively flat over the last decade. Interest in PRP and LiSWT, in comparison, increased by 3-fold and 275-fold, respectively, over the same time period. ICI represented the most searched term over the entire decade. However, ICI lost a large share of internet-user interest over the study period; ICI encompassed 79.4% of searches in 2010 vs. 50.3% in 2020. In contrast, PRP comprised 11.2% of searches in 2010, growing to 26.1% by the end of the study period. Likewise, LiSWT comprised 0.1% of searches in 2013, increasing to 20% by 2020. The quantity of internet searches for both IU and VED decreased significantly from 2010 to 2020 (–34.7% and –31.4%, respectively). The macro-level trends in non-surgical, second-line therapies for ED are displayed in *Figure 1*.

Notably, this increase in interest in LiSWT coincided with the establishment of GAINSWave, a marketing platform for radial shockwave therapy as a treatment for ED. In 2017, searches for shockwave therapy increased by 3,842.9% compared with other second-line therapies between 2016 and 2020. This recent surge represents a 219-fold increase relative to IU. Within the shockwave-related searches enumerated in *Figure 2*, GAINSWave dominated over all alternative terms. There was an 6237.5% increase

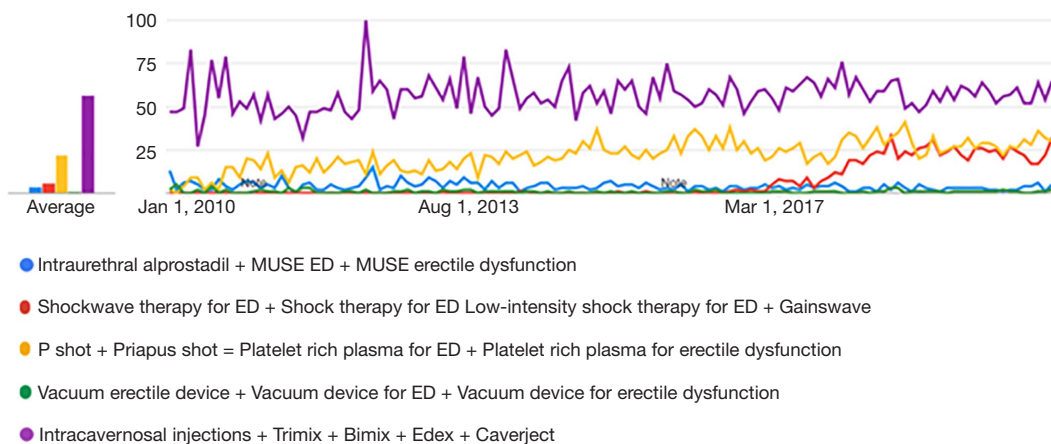


Figure 1 Google search trends for second-line, non-surgical treatments of erectile dysfunction [data source: Google Trends (<https://www.google.com/trends>)]. ED, erectile dysfunction.

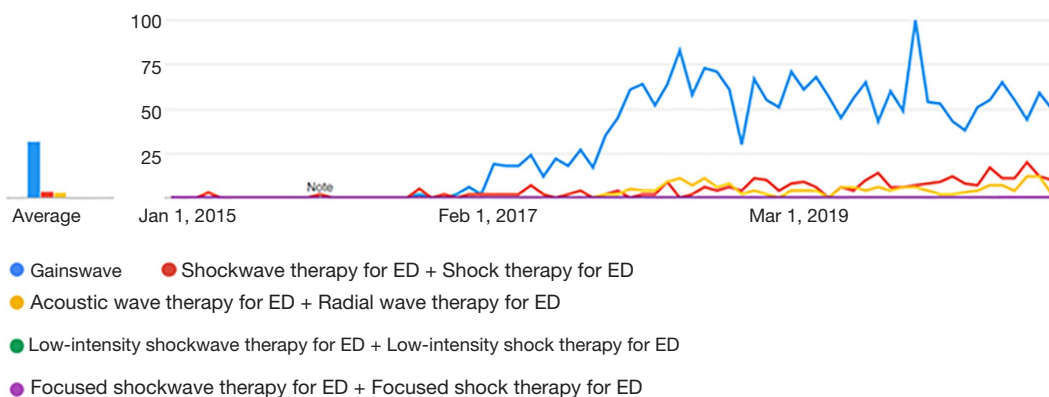


Figure 2 Google search trends for shock and acoustic wave therapy for erectile dysfunction [data source: Google Trends (<https://www.google.com/trends>)]. ED, erectile dysfunction.

in searches for “GAINSWave” from 2016 to 2020. This far exceeded the parallel but generic searches such as “Shockwave therapy for ED” and “Shock therapy for ED”, which had a concomitant combined rise of 912.5% within the same time interval.

In Figure 2, iterations of LiSWT and radial wave therapy (rWT) were compared to each other between 2015 to 2020. Following the introduction of GAINSWave in 2017, there was a large increase in both searches for shockwave therapy and radial/acoustic wave therapy at 614.3% and 2,667%, respectively. In 2020, GAINSWave made up 75.6% of all related searches. However, shockwave therapy represented 15.7% of searches while acoustic/rWT only encompassed

8.7% of searches. Search results incorporating the “low-intensity” and “focused” alternatives of shockwave therapy were zero for the entire time interval, relative to the other searches.

Discussion

The health and economic burden of ED in the United States has driven the development of numerous treatment modalities. Recently, the desire to “cure” ED has buoyed a new treatment paradigm that promotes regenerative therapies. This study highlights the current state of public interest in second-line, non-surgical treatments for ED,

showing an unparalleled surge in searches for regenerative treatments over the past decade. Further, this work demonstrates that direct-to-consumer marketing represents a strong force in this market landscape that appears to outweigh data-driven guideline recommendations.

The internet has become a powerful and widely-used resource for patients and consumers seeking health information. Research utilizing Google Trends in healthcare is in its infancy but is quickly gaining traction. The tool has been primarily employed as a surveillance tool to understand disease epidemiology and to compare real-world trends with search interest, and has successfully found strong correlations between established surveillance datasets and Google Trends (19,24). While the need for standardized and transparent procedures for employing Google Trends amongst different research topics is evident, the platform has undeniable potential as an accessible method for viewing population-level trends. This infodemiologic approach is novel within the field of urology; the few studies involving Google Trends have included correlating internet searches for kidney stones with real-life prevalence, tracking population-level interest in kidney stones over the decade, and attempting to understand general consumer knowledge about prostate artery embolization (PAE) (20,22). Notably, Dreher *et al.* used Google Trends to uncover that online interest in specific procedures for nephrolithiasis did not reflect the current clinical recommendations and frequency of procedures (18). Our study similarly sheds light on the relationship between public interest and clinical recommendations; internet-user interest in non-first-line therapies for ED does not align with the current clinical guidelines set by the AUA and SMSNA (10,13). The etiology of this discordance between patient interest and guideline-based treatment algorithms for both kidney stones and ED is likely multifactorial. The data in this study suggest that direct-to-consumer marketing drives patient interest in the ED space, but it is unclear if this dynamic also drives patient interest in the various treatments for nephrolithiasis. For ED therapies, consumer marketing is prevalent because of the significant financial incentives tied to out-of-pocket reimbursement for said treatments (23). Utilizing Google Trends data to shed light on public interest in treatments is important as it allows opportunities for patient education and permits a more nuanced patient-centric, shared-decision making approach.

Regenerative therapies for ED have seized an increasingly large share of public interest over the past decade (24). Providers and websites offering PRP and

LiSWT promote tissue regrowth and resolution of the symptoms of ED (8). However, these claims are not backed by current guidelines. After review of the current literature, the AUA guideline recommendation classifies PRP as an experimental therapy and LiSWT as an investigational therapy (6). Similarly, the SMSNA guidelines designate both PRP and LiSWT as experimental therapies due to the lack of rigorous experimental data. No level 1 evidence supports the use of PRP in the treatment of ED. The PRP literature lacks not only placebo trials, but studies comparing PRP efficacy to the gold standard, PDE5i (15,18). Of note, some institutions have started double-blind, placebo-controlled trials to further attempt to understand the efficacy of PRP (25). While there have been systematic reviews on the efficacy of focused LiSWT, due to significant limitations and variations in study design, the impact of LiSWT is also inconclusive (16,18). Nonetheless, despite being classified as “experimental” or “investigational” therapies by both the AUA and SMSNA, our results indicate that both PRP and LiSWT have created significantly greater online interest than that of two guideline-backed therapies (IU and VED). Thus, it is evident that online health-information seeking is motivated by factors beyond clinical trials and guideline recommendations from governing bodies in the field.

Principle findings

The impact of direct-to-consumer advertising is observable in the LiSWT trend. LiSWT has been discussed as a potential second-line ED treatment modality as early as 2012, but search interest remained minimal until 2016 (26). The distinct inflection point in 2017 coincides with the introduction of the marketing platform, GAINSWave. As seen in *Figure 2*, GAINSWave-specific searches continue to dominate over all other iterations of LiSWT search terms, accounting for 80.5% of all LiSWT-related searches in 2020. However, internet-user interest in the other shockwave related search terms also increased from 2017 and onward, suggesting that the marketing push for GAINSWave increased overall awareness of the use of LiSWT as a treatment for ED, thus driving behavior. Importantly, the literature distinguishes between radial/acoustic wave therapy and authentic shockwave therapy. Available efficacy data from shock wave trials exclusively analyze focused or LiSWT; there is scarce research on the effectiveness of rWT (27,28). Despite only preliminary studies comparing acoustic and LiSWT, the two therapies have been conflated by marketing platforms (29). In fact,

the results of this population-based search analysis suggest that GAINSWave has become synonymous with shock wave therapy in the eyes of the general public as shown in *Figure 2*. Despite GAINSWave being a form of radial/acoustic wave therapy rather than focused low-intensity shockwave therapy, its tremendous rise is closely followed by a parallel increase in patient interest in authentic LiSWT therapy; prior to the introduction of GAINSWave in 2017, patient interest in shock therapy was negligible, thus supporting our hypothesis of the conflation of GAINSWave and LiSWT by the targets of direct-to-consumer marketing. As such, we believe that direct-to-consumer marketing is a key factor in driving population-level interest in these regenerative therapies for ED.

It is important to note that despite its current “experimental” status, focused LiSWT appears to have the potential to become an accepted and viable second-line therapy (26). Recently published papers in the field of urology specifically support the efficacy of focused LiSWT, rather than unfocused acoustic/radial shockwave therapy. While all forms of shockwave therapy inherently use acoustic or sound waves as their modality of treatment, rWT and focused shockwave therapy use distinctly different methods of sound waves. Focused LiSWT employs a similar mechanism to the shockwave lithotripsy used in the treatment of urolithiasis, which sends out acoustic waves that can be directed and focally penetrate to a greater depth (29). In contrast, rWT utilizes acoustic waves that disperse outwards and penetrates to a more shallow depth than focused LiSWT (29,30). In recent literature, Kalyvianakis *et al.* performed the first rigorous double-blind randomized, sham-controlled study to evaluate the efficacy of focused LiSWT on patients with moderate vasculogenic ED (31). Their findings excitingly suggest that there is strong evidence of efficacy of LiSWT in treating vasculogenic ED. The distinction between the two forms of shockwave therapy remains clinically important and therefore, the field must reconcile the notion that marketing platforms appear to be reaching patients more effectively than well-versed urologists. As research continues to illuminate the efficacy and safety of LiSWT, it is more important than ever for urologists to make the distinction between the types of shockwave therapy clear to their patients. We believe it is critical for evidence-based messaging to reach patients, particularly given the out-of-pocket costs associated with non-guideline backed therapies.

Limitations

A limitation of this study is that only English-language searches in the United States were tracked, and only one internet search engine, Google, was utilized. Additionally, due to the restricted word count in Google Trends, there were limited permutations of each unique search subject. Google Trends only provides tracking for various metropolitan areas and at the state level. Thus, trends at the rural level may be overlooked and different from the overall larger trend. Of note, PDE5i was not incorporated as a search term due to its significantly higher search volume relative to that of any other ED therapy. We believe this intentional omission does not take-away from the findings here, as this study aimed to specifically highlight trends in second-line, non-surgical therapies. One other notable limitation of the Google Trends search function, is its inability to provide demographic information of its users. As such, we are unable to comment on the influence of different demographic populations in searching for the terms included in our study. Finally, the study uses patient interest in these therapies as a proxy for patient use, which is a limitation. However, studies show that patients are now paying significant out-of-pocket costs for regenerative therapies, suggesting that interest is in fact translating to use (32,33).

Despite the mentioned limitations, our study sheds light on the importance of understanding patient interest in ED treatment modalities. Despite being classified as an experimental therapy by the AUA and SMSNA, PRP and LiSWT have garnered significantly more interest than IU and VED. Clinicians who manage ED should be aware of the increased patient interest in the non-guideline-backed therapies for ED and proactively discuss these procedures and their limitations with patients. Future directions include investigating the quality of health information surrounding regenerative therapies that are available for patients online and better characterizing of cost, provider credentials, and treatment protocols.

Conclusions

This descriptive approach of analyzing population-level interest using Google Trends may illuminate how consumer marketing can impact the decision-making of individuals seeking non-surgical adjunct therapy for ED.

Understanding the driving forces behind internet search behavior may provide novel opportunities in targeting patient engagement.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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