



Med J Islam Repub Iran. 2024 (12 Nov);38.131. https://doi.org/10.47176/mjiri.38.131

A Bibliometric Analysis of Testosterone Replacement Therapy Studies: Mapping the Scientific Landscape

Ali Faryabi^{1#}, Hossein Aazami^{2#}, Faezeh Norouzi³, Mohammad Reza Fattahi⁴, Hojat Dehghanbanadaki^{1*} 💿

Received: 26 Jun 2024 Published: 12 Nov 2024

Abstract

Background: Testosterone replacement therapy (TRT) is pivotal in addressing male hypogonadism, yet uncertainties persist regarding its optimal use and long-term ramifications. This study aims to explore the knowledge map of TRT.

Methods: In this bibliometric study, we searched Scopus for relevant keywords from the beginning to 2023. Our inclusion criteria were original articles and reviews and our exclusion criteria were non-English and non-related articles and document types other than original articles and reviews. Excel, VOS viewer, and Science of Science (Sci2) software were used for data synthesis.

Results: From 6712 retrieved articles, 5325 articles were included for analysis. The most productivity belonged to the USA (n=2,570 documents), the United Kingdom (n=476), and Italy (n=339). "Journal of Clinical Endocrinology and Metabolism" (n=168) had the highest participation in publishing. Also, "Journal of Clinical Endocrinology and Metabolism" and the "Journal of Sexual Medicine" exhibited significant bibliographic coupling with other journals in the TRT field. The research topics of interest were mainly related to hypogonadism, prostate cancer, and erectile dysfunction. Bursting analysis of the title and abstract revealed the TRT research prior to the year 2000 was mainly focused on castration, gonadectomy, growth, and aplastic anemia, while the focus of recent research moved towards libido, cardiovascular events, HIV, geriatric issues, diabetes, bipolar disorder, cancer, transmasculine, and transgender individuals.

Conclusion: This study highlights the growing trend of TRT research over time, with most focus on hypogonadism, prostate cancer, and erectile dysfunction. Insights gleaned from this analysis inform research priorities and resource allocation, facilitating enhanced patient care in androgen deficiency management.

Keywords: Scientometric, Bibliometric, Knowledge Map, Testosterone Replacement Therapy, TRT, Hypogonadism

Conflicts of Interest: None declared Funding: None

*This work has been published under CC BY-NC-SA 4.0 license. Copyright© Iran University of Medical Sciences

Cite this article as: Faryabi A, Aazami H, Norouzi F, Fattahi MR, Dehghanbanadaki H. A Bibliometric Analysis of Testosterone Replacement Therapy Studies: Mapping the Scientific Landscape. *Med J Islam Repub Iran.* 2024 (12 Nov);38:131. https://doi.org/10.47176/mjiri.38.131

Introduction

The multifaceted effects of testosterone envelop a wide range of benefits. These incorporate invigorating bone structure and density, simulating hematopoiesis, fostering

Corresponding author: Dr Hojat Dehghanbanadaki, dehghan.hojat@yahoo.com

Contributed equally.

- ^{1.} Tehran University of Medical Sciences, Tehran, Iran
- ^{2.} Iran University of Medical Sciences, Tehran, Iran
- ^{3.} Isfahan University of Medical Sciences, Isfahan, Iran
- ^{4.} Student Research Committee, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

sexual function and desire, creating a shield against cardiovascular risks, and supporting muscle potency (1). Testosterone replacement therapy (TRT) transpires as a prevalent

†What is "already known" in this topic:

Testosterone Replacement Therapy (TRT) is extensively used as a treatment method to remedy cases of male hypogonadism. The effects of this treatment method on bone density, sexual function, and muscle mass have been explored in earlier studies. Nevertheless, there are still uncertainties regarding the optimal use of this method, its long-term effects, and research trends in this field.

\rightarrow *What this article adds:*

What this bibliometric analysis offers is a comprehensive and inclusive overview of research trends in TRT, prominent contributors in the field, and areas with ever-growing focus. The present study also highlights the shift from earlier studies which were more focused on basic physiological studies, and mainly covers investigations on cardiovascular effects, applications in specific conditions (HIV, diabetes), and use in transgender populations, offering insights into the present situation of TRT research and directions it would follow in the future. intervention when dealing with low levels of testosterone among men, which is generally referred to as hypogonadism. The essential goals of implementing TRT revolve around returning testosterone levels to normal levels and alleviating the common symptoms that accompany low levels of testosterone, which include lessened libido, fatigue, and loss of muscle mass (2, 3). Successful and safe administration of TRT pivots on thorough and careful observation. This ordinarily includes regular blood work to determine testosterone levels and to closely watch and track for probable unfavorable side effects, which can include erythrocytosis (increase in red blood cell count) (4). Facts discovered through research highlight the potential TRT has to improve various aspects of men's well-being, covering from an increase in sexual function and expanded muscle mass and strength to improved mood and elevated levels of energy. Regardless, the investigation into the lasting effects and the most effective dosing protocols of TRT is an ongoing progress yet (1, 2, 5).

In order to examine the literature in a particular field utilizing quantitative techniques to evaluate trends in publications, patterns of authorship, and thematic concentrations, a bibliometric study is conducted which is a structured method. When this approach is utilized, important insights into the development of research topics, the influence of different studies and the collaborative relationships between researchers and institutions are gained. Bibliometric studies can identify and isolate gaps in present-day knowledge and suggest areas that require further research by analyzing elements like the number of citations, publication rates, and the frequency with which keywords appear (6).

In our bibliometric study, we try to underline the gaps in the information that comprises the knowledge related to TRT, to emphasize the unexplored areas yet untouched by research in this field, and to encourage further research. Our goal, through this study, is to conduct a thorough scrutiny of existing information on distinctive characteristics of literature on TRT and to conduct a comprehensive scientometric analysis.

Methods

In this bibliometric study, we conducted a comprehensive search on Scopus spanning the year 2023 utilizing the following search strategy:

TITLE-ABS ("androgen therapy") OR TITLE-ABS ("androgen replacement therapy") OR TITLE-ABS ("androgen replacement therapy") OR TITLE-ABS ("testosterone therapy") OR TITLE-ABS ("testosterone replacement") OR TITLE-ABS ("testosterone replacement therapy").

The reason why we chose Scopus for our bibliometric and scientometric analysis is that, compared to alternate databases that are commonly used for conducting such studies, such as Web of Science, it provides a wider range of citations per document and also provides extensive literature coverage (7). The search was conducted on April 26, 2024, and it covered documents from the beginning to the end of 2023. The inclusion criteria were limited to original articles and review articles composed in English which were relevant to TRT. We excluded documents that did not

meet the above-stated criteria. The search results extracted from Scopus were exported from Scopus in the format of a CSV file. The various bibliometric data fields included in the exported CSV file were titles, authors, affiliations, keywords, publication year, document type, citation counts, and source titles. The above-mentioned CSV file was first imported into Microsoft Excel. In order to carry out statistical analysis and rank various bibliometric indices to determine the top 10 cited articles, top authors, countries, and journals, we processed all data utilizing Microsoft Excel. We utilized Graph Pad Prism (version 8.0.1.244) to create the line graph visualization. In order to create a visualization of the connection between terms, keywords, countries, and the rainbow density map of bibliographic coupling and journal co-citation, we utilized the VOS-viewer application (form 1.6.20). We applied a minimum threshold of 10 occurrences, documents or sources for conducting various analyses in this study, which included co-authorship networks, country collaborations, keyword occurrences, and bibliographic coupling. We selected this threshold following careful consideration and experimentation, as it proceed to provide a comprehensive yet manageable representation of the data that helped us achieve an optimal balance between inclusivity and clarity in our visualizations and analyses across different aspects of the study. Furthermore, we formed the authors' collaboration network utilizing the above-mentioned software. We made use of Science of Science (Sci2) software to create the burst analysis of words in the title and abstract.

Results

Basic Characteristics

A total of 6,712 records were collected from Scopus. After documents that were not original articles, surveys, and those not in English were excluded, a sum of 5,325 TRTrelated articles were chosen for the implementation of the bibliometric examination. Among these, the majority of 4,094 (76.88%) were original research papers whereas the remaining 1,231 (23.11%) articles were review papers. Of all the documents 2,097 (39.38%) were accessible publicly as open access.

These 5,325 documents en masse garnered 199,463 citations, which reflected the substantial impact of TRT research in the scientific community. The publications analyzed were authored by 19,073 contributors, showing that a broad array of researchers engaged in research in this field. We identified 5,696 unique author keywords, which in turn provided insights into the diverse themes and focus areas within the TRT research scope. These articles were published in 1,642 distinct sources, which shows that the TRT studies are of a multidisciplinary nature and that it is relevant across various scientific disciplines.

Chronological Publishing Trend

The publications concerning TRT illustrate noteworthy temporal dynamics from its beginning in 1938, as the process started out with a single article (Figure 1). In the following years, a gradual increase can be observed until the 1970s as during this time span, there was a distinctive surge, characterized by 27 articles in 1974 and 34 articles

^{2 &}lt;u>http://mjiri.iums.ac.ir</u> Mad. Lalam Barryh Ivan 2024 (12)

Med J Islam Repub Iran. 2024 (12 Nov); 38:131.

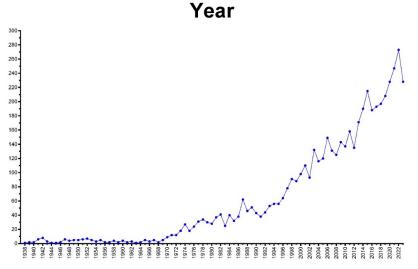


Figure 1. The trend of published studies exploring Testosterone Replacement Therapy (TRT) over time

in 1978, which translates into an increase in scholarly interest. A significantly higher number of publications started to emerge from the early 2000s onwards, which can be observed with a high record number of 132 articles in 2003. A sustained interest in this topic marked the recent years with visible peaks in 2015 (215 articles), 2020 (228 articles), 2021 (247 articles), and 2022 (273 articles), which highlight the fact that TRT is still relevant and the scholarly community is still engaging with this topic.

The Most Cited Articles

Table 1 shows the top 10 most cited research articles on TRT. Among these, 8 articles are originals, constituting 80% of the overall, while 2 articles are reviews, comprising 20% of the corpus. Notable contributions are articles by Bhasin et al.'s (2010) study on "Testosterone Therapy in Men with Androgen Insufficiency Disorders," which leads the others with 1,647 citations, and Basaria et al.'s (2010) examination of " Adverse events associated with testosterone administration," which has been cited 1,233 times.

Table 1. The 10 Most Cited Articles in Testosterone Replacement Therapy (TRT) Studies

#	Authors	Year	Article Title	No. of Citations	Average Citations per Year	Article Type	Journal Title	CiteScore 2021	IF ₂₀₂₂
1	Bhasin et al	2010	Testosterone ther- apy in men with an- drogen deficiency syndromes: An en- docrine society clin- ical practice guide- line	1647	126.6	Article	Journal of Clinical En- docrinology and Metabo- lism	9.9	5.8
2	Basaria et al	2010	Adverse events as- sociated with testos- terone administra- tion	1233	94.8	Article	New England Journal of Medicine	134.4	158.5
3	Bhasin et al	2018	Testosterone Ther- apy in Men with Hypogonadism: An Endocrine Society	973	194.6	Article	Journal of Clinical En- docrinology and Metabo- lism	9.9	5.8
4	Kaufman et al	2005	The decline of an- drogen levels in el- derly men and its clinical and thera- peutic implications	911	50.6	Review	Endocrine Reviews	46.6	20.3
5	Sih et al	1997	Testosterone Re- placement in Older Hypogonadal Men: A 12-Month Ran- domized Controlled Trial	869	33.4	Article	Journal of Clinical En- docrinology and Metabo- lism	9.9	5.8

#	Authors	Year	Article Title	No. of Citations	Average Citations per Year	Article Type	Journal Title	CiteScore 2021	IF ₂₀₂₂
6	Bhasin et al	2006	Testosterone therapy in adult men with androgen deficiency syndromes: An en- docrine society clini- cal practice guide- line	806	47.4	Article	Journal of Clinical Endo- crinology and Metabolism	9.9	5.8
7	Vigen et al	2013	Association of tes- tosterone therapy with mortality, myo- cardial infarction, and stroke in men with low testos- terone levels	796	79.6	Article	JAMA	45.4	120.7
8	Katznel- son et al	1996	Increase in bone density and lean body mass during testosterone admin- istration in men with acquired hypogonad- ism	681	25.2	Article	Journal of Clinical Endo- crinology and Metabolism	9.9	5.8
9	Kapoor et al	2006	Testosterone re- placement therapy improves insulin re- sistance, glycaemic control, visceral adi- posity and hypercho- lesterolemia in hy- pogonadal men with type 2 diabetes	655	34.47	Article	European Journal of En- docrinology	10.0	5.8
10	Fernán- dez- Balsells et al	2010	Adverse effects of testosterone therapy in adult men: A sys- tematic review and meta-analysis	601	40.6	Review	Journal of Clinical Endo- crinology and Metabolism	9.9	5.8

Bibliometric Analysis of Testosterone Replacement Therapy Studies

Fernández-Balsells et al.'s (2010) review on the "Adverse Effects of Testosterone Therapy in Adult Men" has attracted great attention with 601 citations.

The dominance of the Journal of Clinical Endocrinology and Metabolism is apparent, hosting most of the articles with high citation figures, including works by Bhasin S, Basaria S and Sih R. Bhasin appears as a particularly productive author within the confines of this corpus, with a high number of contributions, as s/he is among the authors of three of the 10 most cited articles. Other noticeable journals in this area are the New England Journal of Medicine, JAMA, and the European Journal of Endocrinology.

Top authors, countries, and journals

We identified the top 10 authors, countries, and journals with significant contributions to the field (Table 2). Among the authors, Khera M, Bhasin S, and Morgentaler A come up as the top contributors, with 64 (1.2%), 63 (1.1%), and 63 (1.1%) publications, respectively. The United States was ahead in terms of contribution as far as authors are concerned, with 2,570 (48.2%) publications, followed by the United Kingdom (476 distributions, 8.9%) and Italy (339 distributions, 6.3%). It was observed that the Journal of Clinical Endocrinology and Metabolism, Journal of Sexual Medicine, and Endocrinology were the top journals where

research in this field was published, with 168 (3.1%), 118 (2.2%), and 94 (1.7%) publications, respectively.

Co-authorship of authors

The analysis of the co-authorship network was conducted employing a criterion of a minimum of 10 documents authored by each contributing author. Among the large pool of 19073, within the network, 91 authors met the predefined thresholds for inclusion. Nevertheless, it is worth mentioning that there were no connections between not all authors; actually, the network mesh showed fragmentation to some extent. The largest set with some coherence in this network is comprised of 75 interconnected authors, which indicates a rather strong collaboration among a good-sized subset of contributors (Figure 2). Additionally, analysis of the network exposed the existence of 8 specific clusters, which in turn is suggestive of the fact that there is thematic cohesion of collaborative patterns among authors inside these groupings.

Co-contribution of countries

We inspected global collaborations among countries in the TRT domain, focusing on observing countries with a minimum publication threshold of 10 documents. After conducting the analysis on 167 countries, it was observed

#	Author	NP* (%)	Country	NP (%)	Journal	NP (%)
1	Khera M	64 (1.2)	United States	2570 (48.2)	Journal Of Clinical Endocri- nology And Metabolism	168 (3.1)
2	Bhasin S	63 (1.1)	United Kingdom	476 (8.9)	Journal Of Sexual Medicine	118 (2.2)
3	Morgentaler A	63 (1.1)	Italy	339 (6.3)	Endocrinology	94 (1.7)
4	Davis S.R	49 (0.9)	Australia	277 (5.2)	Clinical Endocrinology	88 (1.6)
5	Saad F	49 (0.9)	Canada	266 (4.9)	Aging Male	78 (1.4)
6	Maggi M	47 (0.8)	Germany	237 (4.4)	Journal Of Urology	68 (1.2)
7	Basaria S	45 (0.8)	Japan	218 (4.0)	International Journal Of Im-	62 (1.1)
					potence Research	
8	Jones T.H	45 (0.8)	China	170 (3.1)	Andrology	55 (1.0)
9	Ramasamy R	44 (0.8)	Netherlands	132 (2.4)	Urology	51 (0.9)
10	Handelsman D.J	41 (0.7)	Brazil	117 (2.1)	Journal Of Endocrinology	49 (0.9)

NP: Number of Publications

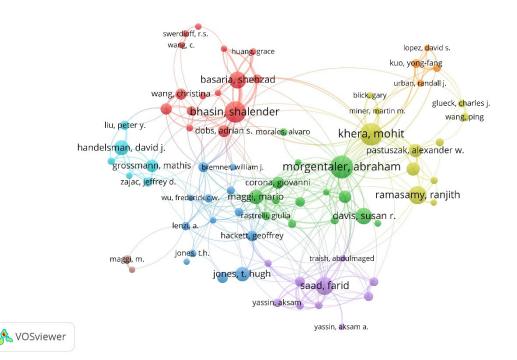


Figure 2. Mapping authors' performance clustering and their co-authorship network in publishing TRT articles. The largest co-authorship network with the most number of nodes is formed among 75 authors, each of whom contributed to at least 10 TRT articles. These authors are grouped into eight clusters that are represented by unique colors to be visible. These 75 authors are engaged in a sum of 904 collaborations.

that 49 met this threshold and this was used as the basis for our investigation. Seven distinct clusters of collaborative activity were recognized, which in turn revealed cohesive systems of scientific cooperation (Figure 3). The sum of link strengths was calculated to survey the intensity of collaborative ties between countries. The United States appeared to be the prevailing contributor with a total link strength of 694. The US was followed by the United Kingdom (369), Italy (309), Germany (301), and the Netherlands (213). Other contributors of note were Australia (169), Canada (160), Sweden (121), Belgium (106), and Switzerland (103).

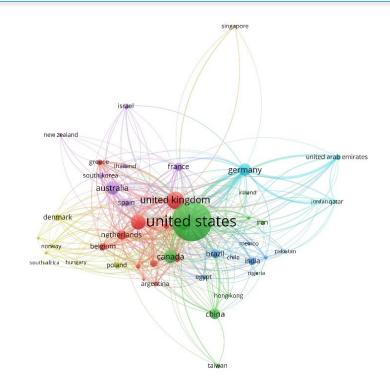
Frequent author's keywords

We conducted an analysis of author keywords within a TRT domain, focusing on those with a minimum occurrence threshold of 10 instances. Out of 5696 keywords examined, 189 met this criterion (Figure 4). Analysis of the data showed eight clusters, each representative of a main topic: reproductive health and hormonal changes, effects of androgens and hormone replacement therapy, prostate cancer and its impact on quality of life, aging and its implications on male health, connections between metabolic syndrome and cardiovascular health, testosterone therapy in various contexts, hypogonadism and testosterone replacement therapy, and apoptosis and heart failure. Among these, the top 10 co-occurrences were identified, including "Testosterone" (1401 occurrences), "Hypogonadism" (619 occurrences), "Androgen" (249 occurrences), "Prostate cancer" (231 occurrences), "Testosterone replacement therapy" (225 occurrences), "Erectile dysfunction" (136 occurrences), "Testosterone therapy" (131 occurrences), "Androgen receptor" (112 occurrences), and "Testosterone deficiency" (107 occurrences).

Frequent terms

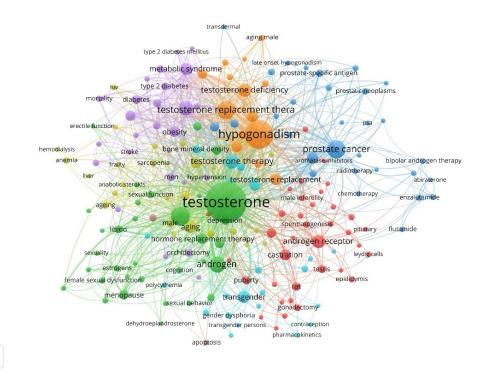
In our analysis, we examined the frequency of the occurrence of terms used by authors and limited the span of the

5



🙈 VOSviewer

Figure 3. Analysis of the network of global collaborations among 49 countries, each with at least 10 documents in the field of TRT, is depicted. This network analysis revealed a total of 1,939 collaborations, and as is visible, the strongest collaboration watched was observed between the United States, Canada, and China.

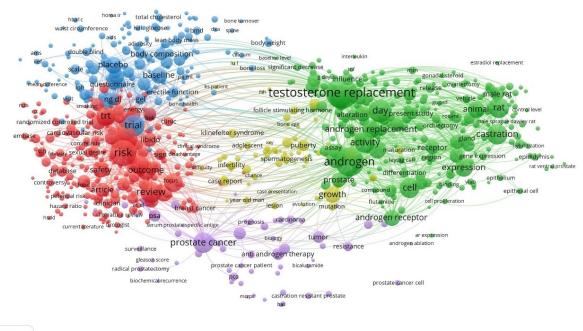


A VOSviewer

Figure 4. Illustrates the network of connections among author keywords, each with at least 10 co-occurrences. Among the 5,696 keywords examined, we selected 189 to be included in this network. The keywords were afterward clustered into 8 distinct groups, each group shown by a different color.

scrutiny to the context of testosterone-related research. Out of a total of 78,598 terms analyzed, 1,369 met the threshold we predefined and occurred at least 20 times (Figure 5).

Notable terms with the highest frequency included "Testosterone replacement" (1,247 occurrences), "Androgen" (1,068 occurrences), "Risk" (886 occurrences), "Symptom"



A VOSviewer

Figure 5. Illustrates the linkage established between nodes that represent terms that were used at least 20 times in the titles and abstracts. Out of a total of 78,598 terms, 1,369 met the criteria for this network and were included. These terms were afterward sorted into 5 clusters, and each was marked by a different color.

(696 occurrences), "Day" (673 occurrences), "Control" (659 occurrences), "Trial" (633 occurrences), "Review" (598 occurrences), "Castration" (570 occurrences), and "Activity" (569 occurrences).

Bibliographic coupling and co-citations analysis of journals

One of the methods used to measure the similarity between different sources, such as journals or articles, is bibliographic coupling where the studied media is compared based on the references they share. In our study, we adopted this method and in order to conduct bibliographic coupling analysis, we decided to set a minimum threshold of 10 documents for each source. Out of a total of 1,642 sources we examined, 94 met this criterion and were included in the analysis (Figure 6a).

It is important to mention that although some of these 94 sources were interconnected nodes, forming a network of related literature, others showed no connection and remained isolated. Within the boundaries of our analysis, the largest cohesive network consisted of 92 interconnected sources, which shows they have a robust thematic connection among them.

Particularly, we found in the context of our study on TRT that two journals, namely, the "Journal of Clinical Endocrinology and Metabolism" and the "Journal of Sexual Medicine" showed significant bibliographic coupling with other journals in the field of TRT. This implies that these two journals share common references and themes related to TRT research.

As a bibliometric analysis, co-citation is a method where the frequency with which two sources (such as journals or articles) are cited together by other publications is examined. What is measured with this method is the association between two sources based on the number of times they are referenced together in the citation lists of other publications. This method provides an understanding of the semantic or thematic links between sources since frequent co-citation signifies a shared relevance or influence within a particular research domain.

In order to conduct the co-citation analysis, we set a minimum threshold of 100 citations per source. Out of the 24,529 sources we examined, 248 met the threshold and were incorporated into the analysis, and eventually, 9 clusters were formed (Figure 6b).

The analysis indicated that "Journal of Clinical Endocrinology and Metabolism" (n=14441), Endocrinology (n=3492), "Journal of Urology" (n=3423), "Journal of Sexual Medicine" (n=3195), "New England Journal of Medicine" (n=2973), JAMA (n=2115), "aging male" (n=1859), "European Journal of Endocrinology" (n=1707), Diabetes Care (n=1665) and Circulation (n=1619) had the highest citations in the reference list of articles related to TRT.

Burst detection analysis

Figure 7 illustrates temporal analyses showing the patterns of bursting words that were found within the titles and abstracts of articles on TRT. The bursting words in titles and abstracts indicated that, prior to 2000, the focus of research was on the impact of TRT on castration, gonadectomy, growth, and aplastic anemia, whereas in the course of the recent years, TRT research has moved towards the effects of TRT on libido and cardiovascular events along

Bibliometric Analysis of Testosterone Replacement Therapy Studies

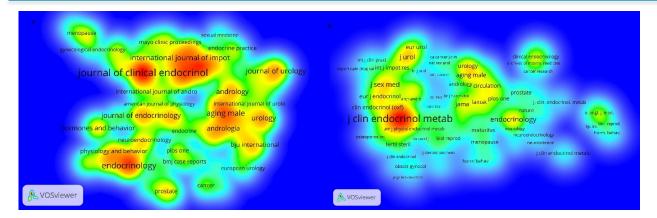


Figure 6. a. Illustrates the bibliographic coupling network among journals with a minimum of 10 documents related to TRT. b. The co-citation rainbow density of journals with a minimum of 100 citations across TRT literature.

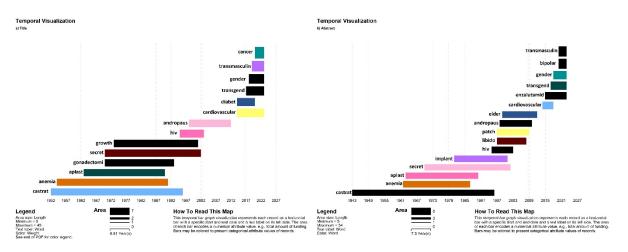


Figure 7. a. The temporal distribution of the most prominently emerging words used in a) titles and b) abstracts of TRT studies.

with its effects during specific conditions, such as HIV, age-related diseases, diabetes, bipolar disorder, and prostate cancer, or on specific populations such as transmasculine and transgender individuals.

Discussion

The present bibliometric study offers a comprehensive analysis of the landscape that surrounds TRT research, directing the spotlight toward its evolution, leading and influential contributors, and collaborative networks and focusing on certain thematic areas. By examining factors such as publication trends and bibliographic coupling, we acquire valuable insights into the existing state and future directions and the course of this field.

One of the most prominent findings of the present study is the momentous escalation in TRT publications, which began in the early 2000s, culminating in outstanding peaks in recent years (2015, 2020-2022). This surge in research output can be associated with the increasing recognition that androgen deficiency is a prevalent condition and also aligns with the increasing interest in strategies to manage it, as perceived in previous bibliometric studies on topics such as male hypogonadism (8, 9). The publication trajectory that was observed suggests that TRT has earned substantial scientific attention, which is likely due to factors such as aging populations, improved diagnostic methods, and the development of innovative therapeutic approaches (10). The supremacy of the United States in TRT research, where nearly half of the total contributed literature is produced, is a recurrent pattern that is observed when conducting bibliometric analyses of andrology-related fields (8, 9). The substantial research funding and infrastructure available in developed nations, as well as the high prevalence of androgen deficiency and associated conditions in these populations, can be categorized as causes of this dominance. Nevertheless, it is heartening to note the significant contributions from other countries, including the United Kingdom, Italy, and Australia, indicating a worldwide interest in this area.

The top 10 highly cited articles show a balanced blend of original research (60%) and review articles (40%), which highlights the value of both primary studies and synthesized evidence in TRT-related research. The eminence of authors like Khera M, Bhasin S, and Morgentaler A, who together account for over 3% of the total publications, underlines the instrumental role of key researchers in influencing the TRT literature. The dominance of Bhasin et al.'s pivotal work on testosterone therapy in dealing with androgen deficiency syndromes, with 1,647 citations (11), and his two other highly cited articles highlight his influential

role (12, 13). Basaria et al.'s study on adverse events (1,233 citations) has been widely recognized, most probably due to examining the risks involved with the therapy (14). The Journal of Clinical Endocrinology and Metabolism hosted most top-cited articles, including Bhasin's, Basaria's, and Sih's which reflect its standing in the scope of endocrinology and TRT research. The inclusion of Fernández-Balsells et al.'s review on adverse effects (601 citations) emphasizes the importance of broad and comprehensive reviews in synthesizing evidence and guiding the course of future studies (15). Despite the fact that topics were diverse, it was observed that there was a common focus on therapy efficacy, risks, and clinical implications. This emphasis supports efforts to ensure safe, effective TRT use at the same time as improving understanding across patient populations. The presence of high-impact general medical journals like the New England Journal of Medicine and JAMA in the scope of TRT research strengthens the multidisciplinary nature of TRT research.

The analysis of author keywords and frequent terms gives insights into the major research themes in TRT. The focus on androgen deficiency, its management, and associated conditions, such as prostate cancer and erectile dysfunction, is in accordance with the research trends that were identified in bibliometric studies of related domains (8, 9). Furthermore, the bibliographic coupling and co-citation analyses further highlight the thematic links between journals in the field of TRT, with prominent endocrinology and general medical journals showing significant coupling and cocitation.

A fact that was revealed by the analysis of bursting words was that one of the concerning topics during the past few decades was the adverse effect TRT has on cardiovascular events. The most cited article on this topic, published by Vigen R et al. in JAMA, showed that as far as men with hypogonadism were concerned, TRT was 23% more likely to develop adverse outcomes such as all-cause mortality, myocardial infarction, and ischemic stroke after 3 years of follow-up (hazard ratio= 1.29; 95% CI: 1.05, 1.58) (16). Another area TRT research focused on during recent decades was gender-affirming hormonal care among transmasculine individuals. For example, findings of one of the recent studies showed that 33% of amenorrheic transmasculine individuals on TRT showed ovulatory activity (17). Moreover, the effects of gender-affirming hormone therapy, including testosterone, on mental health outcomes such as anxiety and depression among transgender individuals have been investigated in research (18). What this growing body of work puts emphasis on is the importance of understanding the specific needs and experiences of transgender individuals in terms of TRT and gender-affirming care (19). In addition, recent TRT research demonstrated that the implementation of TRT in men with hypogonadism was not associated with an increase in the risk of prostate cancer (20).

While this bibliometric analysis provides a comprehensive synopsis of TRT research, it is of great importance to recognize potential limitations. The present study relies on data from the Scopus database, which may not encapsulate and record all pertinent publications, particularly those that appear in non-indexed sources. Even so, we propose that the Scopus database incorporates a large number of esteemed journals. Furthermore, when it comes to bibliometric analysis, Scopus holds precedence compared to alternative databases like Web of Science (WoS) and Google Scholar. Besides, Scopus boasts of having the widest coverage of scholarly literature in terms of citation count and average citations per publication (21). This analysis is centered on quantitative metrics and as a result, may not completely depict the nuances and qualitative aspects of the entire research landscape. Relevant research in the future could explore more granular aspects of TRT literature, such as specific therapeutic approaches, demographic characteristics of patient populations, or investigated clinical outcomes. Furthermore, integrating qualitative analyses or incorporating expert opinions could provide added insights into the research trends, challenges, and the course this field could take in the future.

Conclusion

In conclusion, this bibliometric study underlines the evergrowing scientific momentum in the scope of TRT research. The spotlights of TRT research were on hypogonadism and prostate cancer populations. Recent research focused more on the impact of TRT on cardiovascular events, transmasculine individuals, and conditions such as HIV, age-related diseases, diabetes, bipolar disorder, and prostate cancer. The findings emphasize the instrumental role of key authors, institutions, and journals, along with the dominance of developed countries in shaping the research landscape. These insights can inform research priorities, allocation of resources, and collaborative endeavors, all of which, in due course, would improve our understanding and management of androgen deficiency and the conditions associated with it.

Authors' Contributions

AF and HA conceived the study design, conducted data analysis, and drafted the initial manuscript. HA developed the search strategy and performed the systematic literature search. FN and MRF made substantial contributions to study methodology, data interpretation, and critical revision of the manuscript for important intellectual content. HDB critically reviewed the manuscript, provided substantial intellectual input, and supervised the research process. All authors participated in revising and approving the final manuscript.

Ethical Considerations

As this study involves a bibliometric analysis of existing research, ethical approval, and participant consent are not required.

Acknowledgment

None.

Conflict of Interests

The authors declare that they have no competing interests.

References

- 1.Gruenewald DA, Matsumoto AM. Testosterone supplementation therapy for older men: potential benefits and risks. J Am Geriatr Soc. 2003;51(1):101–15.
- Hassoun O, Starostka M, Shearer H, Millar A, Hassoun S, Isles C. Improving the annual monitoring rates of testosterone replacement therapy patients in primary care. BMJ Open Qual. 2022;11(3):e001784.
- Araujo AB, Esche GR, Kupelian V, O'Donnell AB, Travison TG, Williams RE, et al. Prevalence of symptomatic androgen deficiency in men. J Clin Endocrinol Metab. 2007;92(11):4241–7.
 Pérez-Luis J, Adolewska PD. ODP412 High Frequency of
- 4. Pérez-Luis J, Adolewska PD. ODP412 High Frequency of Erythrocytosis in Hypogonadal Men on Testosterone Replacement Therapy. J Endocr Soc. 2022;6(Supplement_1):A661–2.
- Margiana R, Abdullah MF, Ilhamsyah I, Supardi S, Narulita P. Comparison of short and long-acting testosterone replacement therapy for better sperm production and testosterone levels in male late-onset hypogonadism. JAMA. 2009;
- Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: An overview and guidelines. J Bus Res. 2021 Sep 1;133:285–96.
- Kulkarni A V, Aziz B, Shams I, Busse JW. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. JAMA. 2009;302(10):1092–6.
- Zhang J, Shen Y, Li G, Zhang F, Yang A, Li J, et al. Bibliometrics and visualization analysis of literature on male hypogonadism from 2000 to 2023: research focus and frontiers. Int J Impot Res. 2023;1–12.
- Zhang Y, Xiao F, Lu S, Song J, Zhang C, Li J, et al. Research trends and perspectives of male infertility: a bibliometric analysis of 20 years of scientific literature. Andrology. 2016;4(6):990–1001.
- Mahmoud RH, Cardoso O, Colombo A, Constantinescu D, Deebel NA. Research trends in testosterone deficiency and management: A bibliometric analysis approach to quality improvement in urology resident education. Urologia Journal. 2023;03915603231217353.
- 11. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab [Internet]. 2010;95(6):2536–59. Available from: https://doi.org/10.1210/jc.2009-2354
- Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab [Internet]. 2006;91(6):1995–2010. Available from: https://doi.org/10.1210/jc.2005-2847
- Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, et al. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab [Internet]. 2018;103(5):1715–44. Available from: https://doi.org/10.1210/jc.2018-00229
- Basaria S, Coviello AD, Travison TG, Storer TW, Farwell WR, Jette AM, et al. Adverse events associated with testosterone administration. N Engl J Med. 2010;363(2):109–22.
- Fernández-Balsells MM, Murad MH, Lane M, Lampropulos JF, Albuquerque F, Mullan RJ, et al. Clinical review 1: Adverse effects of testosterone therapy in adult men: a systematic review and metaanalysis. J Clin Endocrinol Metab. 2010;95(6):2560–75.
- Vigen R, O'Donnell CI, Barón AE, Grunwald GK, Maddox TM, Bradley SM, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. JAMA. 2013;310(17):1829–36.
- Asseler JD, Del Valle JS, de Sousa Lopes SMC, Verhoeven MO, Goddijn M, Huirne JAF, et al. One-third of amenorrheic transmasculine people on testosterone ovulate. Cell Rep Med. 2024.
- Amand CS, Fitzgerald KM, Pardo ST, Babcock J. The Effects of Hormonal Gender Affirmation Treatment on Mental Health in Femaleto-Male Transsexuals. J Gay Lesbian Ment Health [Internet]. 2011;15(3):281–99. Available from: https://doi.org/10.1080/19359705.2011.581195
- Lo Moro G, Brescia V, Scaioli G, De Angelis A, Siliquini R, Bert F. Mapping research on LGBT+ persons' health: a bibliometric analysis. Perspect Public Health. 2024;144(3):174–81.
- 20. Bhasin S, Travison TG, Pencina KM, O'Leary M, Cunningham GR, Lincoff AM, et al. Prostate Safety Events During Testosterone Replacement Therapy in Men With Hypogonadism: A Randomized Clinical Trial. JAMA Netw Open. 2023;6(12):e2348692–e2348692.
- 21. Martín-Martín A, Thelwall M, Orduna-Malea E, Delgado López-

10 <u>http://mjiri.iums.ac.ir</u>

Med J Islam Repub Iran. 2024 (12 Nov); 38:131.

Cózar E. Google Scholar, Microsoft Academic, Scopus, Dimensions, Web of Science, and OpenCitations' COCI: a multidisciplinary comparison of coverage via citations. Scientometrics. 2021;126(1):871– 906.