Sexual Medicine

# The Impact of Testosterone Therapy on Benign Prostatic Hyperplasia in Hypogonadal Males

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**OBJECTIVE** To determine the impact of testosterone therapy (TT) on the incidence of benign prostatic hyperplasia (BPH) in a large cohort of hypogonadal males and to evaluate the relationship between TT in hypogonadal males and prostatic interventions.

**METHODS** We used the 2011-2020 International Business Machines Corporation MarketScan database to identify hypogonadal males above 18 years old and determine if they received TT. International Classification of Diseases, 9th and 10th Revisions, Current Procedural Terminology, Healthcare Common Procedure Coding System Procedure Codes, and National Drug Code (NDC) codes were used for diagnoses, interventions, and medications. We ran Cox proportional hazard models to determine the effect of TT on receiving a diagnosis of BPH and interventions. Models were adjusted for age, region, population density, and comorbidities, with TT within the last 6 months considered a time-varying covariate.

**RESULTS** In our total cohort of 882,570 hypogonadal males, 157,185 (17.8%) were diagnosed with BPH. For the first 2.5 years after hypogonadism diagnosis, there was no significant difference in the diagnosis of prostatic hyperplasia between patients on TT and those who were not (HR:1, 95%CI:0.98-1.01, $P = .66$). However, from 2.5 years onward, males who were on TT had a 32% higher risk of receiving a diagnosis of BPH (HR:1.32, 95%CI:1.28-1.36, $P < .001$). Hypogonadal males with BPH who received TT showed no significant difference in interventions compared to those who did not receive testosterone (HR:0.95, 95%CI:0.89-1, $P = .08$).

**CONCLUSION** In the long term, TT increased the risk of receiving a diagnosis of BPH in hypogonadal males. TT in hypogonadal males with BPH did not change the need for interventions. UROLOGY xx: xxx–xxx, xxxx. 

Hypogonadism affects 40% of males over 45% and 50% of males in their 80 seconds.[1] Commonly beginning in the fourth decade of life, the prevalence of hypogonadism increases with age, and blood testosterone levels generally decline over time.[1,2] Testosterone therapy (TT) is a common treatment in hypogonadal males.[2] From 2000 to 2011, the prescription of testosterone increased on a global scale, its primary spike in the United States. Food and Drug Administration-approved TT products are now available in various forms and routes of administration, including topical, nasal, oral, injections, and implants.[3]

Benign prostatic hyperplasia (BPH), like hypogonadism, is also an age-dependent condition. BPH's prevalence increases from 50% to 60% in males in their 60 seconds to 80%-90% in males 70 and older.[4]

Though TT can help hypogonadal males with the symptoms caused by low androgen levels, TT's implications in the development of BPH in hypogonadal males yield conflicting results. It was previously considered that TT increased the risk of BPH. The risk was considered serious enough for the Food and Drug Administration to issue a warning.[5] This increased risk of developing BPH from TT has been contradicted by other studies. Low testosterone levels have been associated with an increased risk of developing BPH via inflammation.[6] A randomized trial revealed that prostate androgen levels only slightly increased after 6 months of TT. Prostate tissue composition, biomarkers for cell proliferation, and gene expression were all unaltered, suggesting TT has little effect on prostate tissue androgen levels and cellular function.[7] On the other hand, it has been suggested that TT can improve lower urinary tract symptoms (LUTS) in hypogonadal males with BPH.[8]

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With this discrepancy existing in the literature, we worked to determine the impact TT has on BPH incidence in a large cohort of hypogonadal males. We also investigated the relationship between TT in hypogonadal males and the need for BPH interventions. The outcomes of this study can assist in clarifying the current inconsistency in the literature and allow clinicians to better understand the implications of TT prescription in hypogonadal males.

## MATERIALS AND METHODS

We conducted a retrospective case-control study using the 2011-2020 International Business Machines Corporation MarketScan Commercial Claims Databases. The study was exempted by the Institutional Review Board (IRB) due to the de-identified nature of the dataset under the reference number IRB_00123727. Our primary aim was to determine the prevalence of BPH in hypogonadal male patients with and without TT. Our secondary aim was to determine the rates of urological interventions and surgeries for BPH treatment.

The Marketscan database comprises de-identified health insurance claims of individuals covered by specific employer-sponsored health insurance plans. It does not contain direct personal identifiers. Thus, review by the IRB was not required. Insurance claims from 260 employers, 40 health plans, and government and public entities are included in MarketScan. The enrollment data include patient age, employment status, geographical region, sex, and insurance type. It also provides detailed inpatient and outpatient encounter information, including date and setting of service; provider type; plan- and patient-paid amounts; International Classification of Diseases, 9th and 10th Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) diagnosis and procedure codes; Current Procedural Terminology, 4th Edition (CPT-4) codes; and Healthcare Common Procedure Coding System procedure codes.

We used ICD-9, and -10 codes to identify males above 18 years old with a hypogonadism diagnosis and used National Drug Codes and CPT/Healthcare Common Procedure Coding System procedure codes to determine if they had drug claims for testosterone, including intramuscular injection, transdermal patch, topical gel, and implantable pellet formulations. Implantable pellets were also identified using the CPT code for subcutaneous pellet implants (11,980). Individuals diagnosed with congenital genetic disorders (eg, chromosomal abnormalities), hypothalamic-pituitary disorders, or prostatic adenocarcinoma were excluded from the study cohort (Supplementary 1).

We recorded demographic and comorbidity information at the time of their initial hypogonadism diagnoses. In all patients, medical comorbidity was quantified using the Charlson Comorbidity Index. BPH diagnosis was the primary outcome of this study, and BPH treatment was the secondary outcome. We followed males with hypogonadism from their initial diagnosis to the end of their enrollment period to determine if they received a diagnosis of BPH and noted all instances of TT. For males who were diagnosed with BPH, we evaluated any records of urologic interventions for BPH treatment. We determined the time from BPH diagnosis to the first intervention in individuals with or without TT who had at least one year of enrollment following their initial BPH diagnosis. A detailed list of interventions and their associated diagnosis, procedure, and medication codes can be found in Supplementary 2.

### Statistical analysis

To investigate the effect of TT on the development of BPH, we ran a Cox proportional hazard (CPH) model from the time of initial hypogonadism diagnosis to BPH occurrence. We broke down the cohort along each demographic variable stratified by whether the person was diagnosed with BPH. Before modeling, we examined survival curves of BPH occurrence against TT status and found evidence of non-proportional effects of TT on BPH occurrence. Specifically, the direction of effect TT had on BPH survival reversed approximately 912 days (2.5 years) after hypogonadism diagnosis. Thus, we ran two CPH models for BPH occurrence, one from the first hypogonadism diagnosis to 2.5 years and one from 2.5 years to the end of enrollment.

We also used CPH models from the time of BPH diagnosis to the first intervention, to evaluate the impact of TT on BPH interventions. Receipt of TT in the last 6 months was included as a time-varying covariate in the models. In all models, we controlled for age, geographic region, population density, and comorbidities. A $P < .05$ was considered statistically significant.

## RESULTS

In our total cohort of 882,570 hypogonadal males, 157,185 (17.8%) were diagnosed with BPH. The median age was 51 (interquartile range (IQR) = 43-59) y.o. in the total cohort, 58 (IQR = 51-63) y.o. in hypogonadal males with BPH, and 50 (IQR = 41-58) y.o. in males without BPH. Hyperlipidemia was the most common comorbidity detected in 84% and 68% of hypogonadal males with and without BPH, respectively. Hypertension was detected in 56% of male patients with BPH and 34% of those without BPH (Table 1).

The mean follow-up period for the cohort was 879 days (SD = 784 days). The diagnosis of benign BPH was observed in 19.9% of males with at least one record of TT (66,331 out of 332,634), compared to 16.5% in individuals without any TT records (90,854 out of 549,936). Our multivariable regression model controlling for age, geographic region, population density, and comorbidities showed non-proportionality in the impact of TT on the occurrence of BPH. Thus, we ran two models for receiving a diagnosis of BPH, one from the first hypogonadism diagnosis to 2.5 years, and one from 2.5 years until the end of the study period. For the first 2.5 years after hypogonadism diagnosis, there was no significant difference in the diagnosis of BPH between patients on TT and those who were not on TT (HR 1.00,

**Table 1.** Demographic breakdown of cohort.

| Variables | BPH | No BPH | Full cohort | Statistics |
|---|---|---|---|---|
| No. participants | 157,185 (17.81%) | 725,385 (82.19%) | 882,570 (100%) | |
| Age; median (IQR) | 58 (51-63) | 50 (41-58) | 51 (43-59) | X2 = 6626; $P$ < .001 |
| *Region* | | | | X2 = 5763; $P$ < .001 |
| Northeast | 30,251 (19.25%) | 89,125 (12.29%) | 119,376 (13.53%) | |
| Midwest | 24,639 (15.68%) | 119,153 (16.43%) | 143,792 (16.29%) | |
| South | 78,084 (49.68%) | 380,187 (52.41%) | 458,271 (51.92%) | |
| West | 22,811 (14.51%) | 127,108 (17.52%) | 149,919 (16.99%) | |
| Other | 1400 (0.89%) | 9812 (1.35%) | 11,212 (1.27%) | |
| Population density (urban) | 136,404 (86.78%) | 624,936 (86.15%) | 761,340 (86.26%) | X2 = 43; $P$ < .001 |
| *Comorbidities* | | | | |
| Diabetes mellitus | 60,911 (38.75%) | 195,076 (26.89%) | 255,987 (29%) | X2 = 8822; $P$ < .001 |
| Hyperlipidemia | 132,928 (84.57%) | 497,229 (68.55%) | 630,157 (71.4%) | X2 = 16,238; $P$ < .001 |
| Peripheral vascular diseases | 11,879 (7.56%) | 17,239 (2.38%) | 29,118 (3.3%) | X2 = 10,867; $P$ < .001 |
| Cardiovascular disease | 36,070 (22.95%) | 68,139 (9.39%) | 104,209 (11.81%) | X2 = 22,790; $P$ < .001 |
| Hypertension | 88,092 (56.04%) | 248,721 (34.29%) | 336,813 (38.16%) | X2 = 25,909; $P$ < .001 |
| BMI 30-40 | 28,483 (18.12%) | 92,813 (12.79%) | 121,296 (13.74%) | X2 = 3091; $P$ < .001 |
| BMI 40 and higher | 8126 (5.17%) | 34,915 (4.81%) | 43,041 (4.88%) | X2 = 35; $P$ < .001 |
| Smoking | 33,397 (21.25%) | 120,013 (16.54%) | 153,410 (17.38%) | X2 = 1989; $P$ < .001 |
| Alcohol abuse | 5628 (3.58%) | 23,099 (3.18%) | 28,727 (3.25%) | X2 = 64; $P$ < .001 |
| drug abuse | 8312 (5.29%) | 33,075 (4.56%) | 41,387 (4.69%) | X2 = 153; $P$ < .001 |
| Renal diseases | 20,372 (12.96%) | 37,171 (5.12%) | 57,543 (6.52%) | X2 = 13,015; $P$ < .001 |
| Chronic pulmonary diseases | 43,924 (27.94%) | 124,237 (17.13%) | 168,161 (19.05%) | X2 = 9800; $P$ < .001 |
| Liver diseases | 17,873 (11.37%) | 44,177 (6.09%) | 62,050 (7.03%) | X2 = 5510; $P$ < .001 |
| Depression | 37,375 (23.78%) | 146,528 (20.2%) | 183,903 (20.84%) | X2 = 1002; $P$ < .001 |
| Anxiety disorders | 33,849 (21.53%) | 120,742 (16.65%) | 154,591 (17.52%) | X2 = 2137; $P$ < .001 |
| Bipolar disorders | 2561 (1.63%) | 9378 (1.29%) | 11,939 (1.35%) | X2 = 109; $P$ < .001 |
| Injury | 60,186 (38.29%) | 186,928 (25.77%) | 247,114 (28%) | X2 = 10,045; $P$ < .001 |
| Autoimmune diseases | 70,934 (45.13%) | 212,109 (29.24%) | 283,043 (32.07%) | X2 = 14,967; $P$ < .001 |

BMI, body mass index; BPH, benign prostatic hyperplasia; IQR, inter-quartile range. Continuous variables are presented as median (with IQR). Categorical variables are presented as the number of patients (with percentage of group). The "Statistics" column gives univariable tests of variation between all treatment groups using Kruskal-Wallis tests (for continuous variables) and Chi-squared tests (for categorical and binary variables).

95%CI 0.98-1.01, $P$ = .66). However, from 2.5 years onward, males who were on TT had a 32% greater chance of receiving a diagnosis of BPH (HR 1.32, 95%CI 1.28-1.36, $P$ < .001) (Figure 1, Table 2).

Hypogonadal males with BPH who received TT showed no significant difference for BPH interventions compared to those who were not on TT (HR 0.95, 95%CI 0.89-1, $P$ = .08) (Table 3). However, the time until intervention for hypogonadal males diagnosed with BPH, based on whether they received TT or not, showed that those who did not undergo TT experienced an average time of 485 days until intervention, whereas those who received TT had a statistically significant longer average time of 581 days before intervention was needed ($P$ < .001).

## DISCUSSION

In this study, our findings indicated that TT did not alter the risk of BPH in hypogonadal males within the initial 2.5 years. However, hypogonadal males undergoing TT for more than 2.5 years demonstrated a 32% higher risk of receiving a diagnosis of BPH, suggesting potential

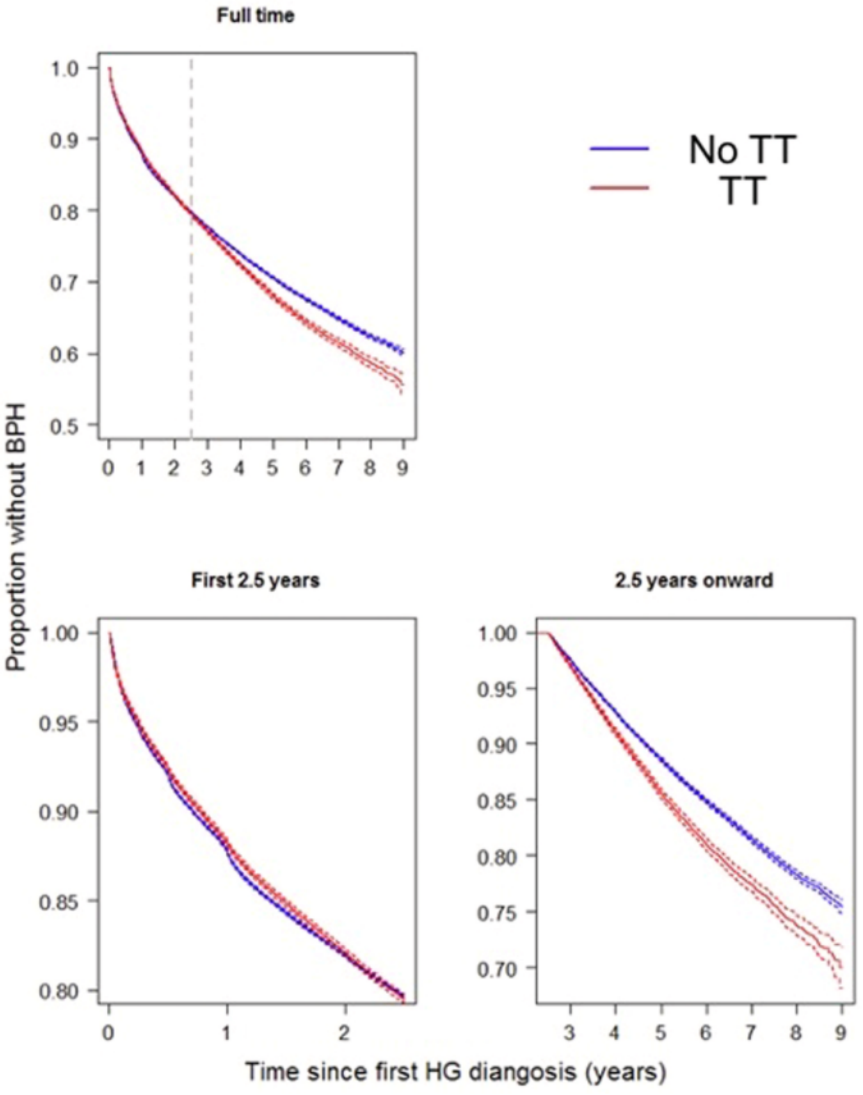


**Figure 1.** *Benign prostatic hyperplasia (BPH) survival:* Kaplan-Meier curves showing BPH-free survival for people with testosterone therapy (TT) (red) vs those without (blue). The first panel shows survival for the full timespan since hypogonadism (HG) diagnosis of BPH or dropout. Non-proportional hazards are evident between years 2 and 3 (region bracketed by gray bars). The second panel shows survival from the time of initial HG diagnosis up to 2.5 years; the third panel shows survival from 2.5 years to dropout. Dashed lines in all figures represented 95% confidence intervals.

long-term effects of TT on prostate health. In this study, our findings indicated that TT did not alter the risk of BPH interventions in hypogonadal males. This aligns with previous findings which indicated that TT does not significantly impact the need for BPH-related interventions.[9]

Hypogonadism affects 3%-7% of the male population before age 70 and up to 18% of males aged 70 years and above. Considering that prostate development and growth are partially dependent on the presence of androgens, high levels of testosterone and dihydrotestosterone were traditionally considered to be associated with the development of BPH and increased LUTS.[10] According to some guidelines, severe LUTS is a relative contraindication to starting TT in hypogonadal males.[11] However, the clinical effects of physiological or exogenous androgens on the development of BPH and LUTS is controversial, as recent longitudinal investigations, ranging from 6 months to 7 years, demonstrated that physiological levels of testosterone are not correlated with the development of BPH, increased prostate volume, and LUTS.[12] While some studies reported higher rates of prostate-related events in males who received TT, others have suggested that TT can indeed alleviate urinary symptoms in hypogonadal males with BPH.

The American Urological Association and European Association of Urology guidelines acknowledged a lack of associations between TT in BPH patients and increased symptoms.[13,14] Nonetheless, European Association of Urology guidelines indicate that testosterone administration can increase prostate volume, especially during the first year of the treatment.[14]

**Table 2.** Model outputs for benign prostatic hyperplasia (BPH)-free survival.

| Variables | First 2.5 y | From 2.5 y to dropout |
|---|---|---|
| TT | 0.997 (0.985-1.01); $P = .662$ | 1.319 (1.28-1.358); $P < .001$ |
| Urban | 1.104 (1.087-1.12); $P < .001$ | 1.053 (1.017-1.09); $P = .003$ |
| Age | 1.056 (1.056-1.057); $P < .001$ | 1.049 (1.047-1.05); $P < .001$ |
| Diabetes mellitus | 1.007 (0.996-1.018); $P = .221$ | 1.013 (0.987-1.04); $P = .337$ |
| hyperlipidemia | 1.224 (1.206-1.242); $P < .001$ | 1.267 (1.218-1.318); $P < .001$ |
| Peripheral vascular diseases | 1.018 (0.998-1.04); $P = .084$ | 0.977 (0.934-1.022); $P = .314$ |
| Cardiovascular diseases | 1.048 (1.033-1.062); $P < .001$ | 1.049 (1.017-1.081); $P = .002$ |
| Hypertension | 1.047 (1.034-1.059); $P < .001$ | 1.108 (1.075-1.142); $P < .001$ |
| BMI: 30-40 | 1.07 (1.056-1.085); $P < .001$ | 1.027 (0.998-1.057); $P = .066$ |
| BMI: +40 | 0.877 (0.857-0.898); $P < .001$ | 0.941 (0.899-0.984); $P = .008$ |
| Smoking | 0.99 (0.978-1.003); $P = .131$ | 0.951 (0.924-0.979); $P = .001$ |
| Alcohol abuse | 0.88 (0.855-0.905); $P < .001$ | 0.919 (0.867-0.974); $P = .004$ |
| Drug abuse | 1.061 (1.036-1.087); $P < .001$ | 1.012 (0.962-1.066); $P = .64$ |
| Renal disease | 1.017 (1-1.034); $P = .046$ | 1.115 (1.076-1.155); $P < .001$ |
| Chronic pulmonary disease | 1.078 (1.066-1.091); $P < .001$ | 1.104 (1.075-1.134); $P < .001$ |
| Liver disease | 1.249 (1.229-1.27); $P < .001$ | 1.279 (1.237-1.323); $P < .001$ |
| Depression | 1.017 (1.004-1.03); $P = .011$ | 1.043 (1.013−1.075); $P = .005$ |
| Anxiety disorders | 1.065 (1.051-1.08); $P < .001$ | 1.122 (1.09-1.155); $P < .001$ |
| Bipolar disorders | 1.127 (1.082-1.174); $P < .001$ | 1.191 (1.097-1.294); $P < .001$ |
| Injury | 1.063 (1.05-1.075); $P < .001$ | 1.07 (1.043-1.097); $P < .001$ |
| Autoimmune disease | 1.164 (1.151-1.177); $P < .001$ | 1.184 (1.154-1.216); $P < .001$ |

TT, testosterone therapy. All results are in hazard ratios (with 95% confidence intervals and *P* values). Effect of TT relative to those without; effect of urban relative to rural; effect of age represents an increase of one year; effect of comorbidities relative to those without.

Most prospective trial studies have failed to demonstrate any association between TT and increased BPH incidence or LUTS severity.[12] Recent evidence from a large randomized trial demonstrated that the incidence of prostate-related events did not differ significantly between testosterone and placebo groups, with no notable differences in symptoms, medication use, or the need for interventions.[9] Additionally, evidence from a meta-analysis of 14 clinical trials involving 2029 participants indicated that TT does not significantly impact LUTS compared to placebo. The study found no statistically significant difference in the pooled changes in International Prostate Symptom Score between males receiving TT and those receiving placebo.[15] Our study's findings differ from those of several clinical trials that generally report no significant impact of TT on BPH or LUTS. Our study indicates a possible long-term association between TT and increased BPH diagnosis, this finding underscores the need for further research. This discrepancy may stem from the distinctive aspects of our research, particularly the large cohort size and extended follow-up duration.

Importantly, TT was not associated with an increased rate of interventions for BPH, which further supports previously reported findings that testosterone does not adversely affect BPH progression.[9] Instead, TT was associated with a longer time to intervention for BPH treatment, suggesting that while BPH may be diagnosed more frequently after prolonged TT, the need for clinical intervention is not accelerated. This finding underscores the need to distinguish between diagnosis and clinically significant disease requiring treatment.

Low testosterone levels are associated with decreased nitric oxide (NO) production and endothelial dysfunction.[16,17]

**Table 3.** Model outputs for intervention in benign prostatic hyperplasia (BPH) patients.

| Variables | Intervention |
|---|---|
| TT | 0.948 (0.892–1.007); $P = .081$ |
| Urban | 0.995 (0.927–1.068); $P = .89$ |
| Age | 1.044 (1.041–1.046); $P < .001$ |
| Diabetes mellitus | 1.013 (0.961–1.067); $P = .637$ |
| Hyperlipidemia | 0.858 (0.796–0.925); $P < .001$ |
| Peripheral vascular diseases | 0.812 (0.746–0.883); $P < .001$ |
| Cardiovascular diseases | 0.998 (0.94–1.06); $P = .955$ |
| Hypertension | 0.917 (0.864–0.974); $P = .005$ |
| BMI: 30-40 | 1.012 (0.951–1.078;) $P = .701$ |
| BMI: +40 | 0.976 (0.872–1.092); $P = .67$ |
| Smoking | 1.104 (1.042–1.169); $P = .001$ |
| Alcohol abuse | 1.029 (0.908–1.165); $P = .657$ |
| Drug abuse | 1.115 (1.005–1.237); $P = .04$ |
| Renal diseases | 1.138 (1.066–1.215); $P < .001$ |
| Chronic pulmonary disease | 1.05 (0.995–1.108); $P = .073$ |
| Liver disease | 1.087 (1.011–1.168); $P = .024$ |
| Depression | 1.095 (1.031–1.162); $P = .003$ |
| Anxiety disorders | 1.053 (0.989–1.121); $P = .109$ |
| Bipolar disorders | 1.094 (0.917–1.305); $P = .318$ |
| Injury | 1.004 (0.952–1.06); $P = .874$ |
| Autoimmune diseases | 1.042 (0.987–1.1); $P = .138$ |

All results are in hazard ratios (with 95% confidence intervals and *P* values). Effect of TT relative to those without; effect of urban relative to rural; effect of age represents an increase of one year; effect of comorbidities relative to those without.

Furthermore, NO synthase expression in prostate tissue is reduced in males with BPH compared to those with normal prostate and can lead to increased smooth muscle tone in prostate tissue.[18,19] Therefore, TT can potentially increase the NO production in prostate tissue, alleviate LUTS symptoms, and delay the need for BPH intervention. Also, studies have suggested that inflammation, ischemia, and chronic hypoxia in prostate tissue are associated with the development of BPH.[20,21] TT has been found to decrease prostatic inflammation in hypogonadal males with BPH.[22] Additionally, hypogonadal males were found to have an increased risk of developing depressive disorders and anxiety disorders.[23–25] Therefore, TT's positive benefits on the mood and general well-being of hypogonadal males can mitigate its negative effects on prostate growth in the short term.

The limitations of this study include the inherent constraints associated with the populations documented in the MarketScan database. Firstly, the reliance on administrative data and diagnosis codes may not accurately capture clinical diagnoses, leading to potential misclassification bias. Although we observed a 32% higher rate of BPH diagnosis after more than 2.5 years of TT, the clinical significance of this finding remains uncertain. This increase may reflect greater medical attention in patients with a higher burden of comorbid conditions, rather than being a direct effect of TT. All patients included were privately insured through generally large employers, thus representing only a subset of the U.S. population. This limits the generalizability of the findings to the broader population, including those without private or commercial health insurance, individuals who make out-of-pocket payments, and those covered by public health insurance plans such as Medicare and Medicaid. The lack of detailed clinical information, such as the severity of symptoms, duration of hypogonadism before treatment, and adherence to TT, also limits the depth of analysis. Moreover, the study is constrained by its observational nature, which cannot establish causality. While we adjusted for various confounding factors, unmeasured confounders may still influence the results. Overall, our study highlights a potential long-term between TT in hypogonadal males and an elevated risk of receiving a diagnosis of BPH. Conversely, we observed a longer duration before intervention in hypogonadal males diagnosed with BPH. Although TT has shown promise in managing hypogonadism and improving symptoms in this population, continued research efforts, including larger-scale studies with long-term follow-up, are necessary to understand the effects of TT on the incident and progression of BPH. Future research should endeavor to clarify and better understand the relationship between TT and BPH, exploring the impact of factors such as treatment duration, dosing regimens, and individual patient characteristics.

## CONCLUSION

In conclusion, TT in hypogonadal males was not associated with an increased need for BPH interventions, in alignment with recent large-scale studies. While TT was associated with a longer time to intervention for BPH, the increased risk of diagnosis after 2.5 years warrants further research to determine its clinical significance. Further work is needed to clarify the relationship between TT, BPH diagnosis, and disease progression.

## Disclosure

None.

## CRediT Authorship Contribution Statement

**Claudia M. Watkins:** Writing—review and editing, Writing—original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation. **James M. Hotaling:** Writing—review and editing, Writing—original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Joshua John Horns:** Writing—review and editing, Writing—original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Hojat Dehghanbanadaki:** Writing—review and editing, Writing—original draft, Visualization, Software, Resources, Project administration, Investigation, Data curation, Conceptualization. **Kiarad Fendereski:** Writing—review and editing, Writing—original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. KF conceptualized and designed the study, analyzed, and interpreted the data, drafted the initial manuscript, and critically reviewed and revised the manuscript. JJH, HD, and CMW designed the data collection instruments, collected data, carried out the initial analyses, and critically reviewed and revised the manuscript. JMH conceptualized and designed the study, coordinated, and supervised data collection, analyzed, and interpreted the data, and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## Declaration of Competing Interest

The authors declare that they have NO affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.urology.2024.11.006.

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