

PEYRONIE'S DISEASE

Treatment Trends and Cost Associated With Peyronie's Disease



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ABSTRACT

Introduction: Providers may use several treatment options for patients with Peyronie's disease; however, it is unclear whether practice patterns have evolved over recent years and if this has impacted cost.

Aims: To investigate trends in the treatment of Peyronie's disease over time and the associated costs using a national, commercial insurance claims database.

Methods: A retrospective cohort study was conducted using claims from the Truven MarketScan database from 2007 to 2018 for men with Peyronie's disease. Cost was estimated as either the sum of prescription oral or injectable treatment costs or as the single net cost associated with the operative procedure.

Main Outcome Measures: Frequency of use of various treatments for Peyronie's disease and associated costs were assessed as trends over the timeline by year.

Results: The estimated annual incidence of Peyronie's disease in this population rose from 61 to 77 per 100,000 patients over the included years, and the percent annual treatment rate rose from 17.8% to 26.2%. Colchicine was the most commonly prescribed oral agent in 2007 used in 22% of treated individuals; by 2018, pentoxifylline was the most common prescribed oral agent used in 33%. In 2007, 11% of treated patients received intralesional verapamil; however, by 2018, 24% received injectable collagenase, whereas <1% received intralesional verapamil. The mean annual, per-individual cost of Peyronie's disease treatment increased from \$1,531 in 2007 to \$10,339 in 2018. The cost increase was greatest for injectable therapies, which rose from \$811 per individual in 2007 to \$16,184 in 2018, a 19-fold increase.

Conclusions: Diagnosis and treatment of Peyronie's disease is increasing over time. Pentoxifylline has become the most common oral prescription, whereas injectable collagenase has become most common injection. The mean cost associated with Peyronie's disease treatment increased more than 5 times from 2007 to 2018 corresponding with Federal Drug Administration's approval of injectable collagenase. **Loftus CJ, Rajanahally S, Holt SK, et al. Treatment Trends and Cost Associated With Peyronie's Disease. Sex Med 2020;8:673–678.**

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Key Words: Healthcare Trends; Injectable Collagenase; Peyronie's Disease; Cost of Treatment

INTRODUCTION

The mechanistic cause of Peyronie's disease (PD) includes progressive fibrosis of the tunica albuginea of the corpora cavernosa. Plaque formation can result in penile deformity, sexual

disability, pain, and emotional distress. The true prevalence of PD is unclear, but studies report rates ranging from 0.4% to 3%.^{1–4} Higher rates have been identified in populations with certain conditions including erectile dysfunction, diabetes mellitus, prior pelvic surgery, and Dupuytren's contracture.^{5–8}

Treatment options for PD include oral drugs, injectable therapies, and surgery. While many oral agents have been used historically including pentoxifylline, colchicine, tamoxifen, vitamin E, and Potaba, there is limited evidence to suggest that these treatments are effective. Current American Urological Association (AUA) guidelines published in 2015 state that providers should not offer patients oral therapy with vitamin E, tamoxifen, procarbazine, or omega-3 fatty acids.⁹ Intralesional injections include interferon, verapamil, and collagenase clostridium histolyticum. Injectable collagenase was approved by the U.S Food and Drug

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Administration for PD treatment in December 2013, becoming the first and only pharmaceutical agent specifically approved for use in men with PD. Initial studies demonstrated patients had improvement in penile curvature and sexual function after several cycles of injections.^{10,11} Finally, surgical therapies include penile plication, excision or incision and grafting of Peyronie's plaque, and/or placement of a penile prosthesis.

Since the introduction of injectable collagenase, providers have grappled with the cost-to-benefit ratio of the expensive drug. The total cost of treatment for all cycles of collagenase injections may exceed \$25,000.¹² Despite these costs, it is unknown how widely this therapy has been used in the treatment of PD. The purpose of this study was to characterize temporal trends in the treatment of PD and their related costs using a large, commercial insurance claims database. Secondarily, we sought to determine whether introduction of collagenase resulted in changes in practice patterns.

PATIENTS AND METHODS

The Truven Health MarketScan database contains information from more than 350 private sector, U.S. employer-based commercial health plans for more than 200 million patients. Enrollees are assigned unique, deidentified patient numbers that allow longitudinal inclusion across health plans over time. The health service records include patient demographics, service dates, International Classification of Diseases codes, current procedural terminology (CPT) codes, and outpatient pharmacy claims. In this study, only the core MarketScan database was used. MarketScan does not include demographic information such as race or socioeconomic status.

The database was queried from 2007 to 2018 for men between ages 18 and 64 years with PD based on International Classification of disease Ninth and Tenth revision, clinical modification (International Classification of Diseases 9 and 10) diagnostic codes (607.85 or N486). We assessed trends on a year-by-year basis. Patients who did not have continuous MarketScan enrollment for at least the entire year were excluded from analysis of that year. Prescription oral therapies were identified through outpatient pharmacy records using National Drug Code numbers to include pentoxifylline, colchicine, and tamoxifen prescribed for treatment of PD. The oral agents vitamin E, potassium aminobenzoate, coenzyme Q10, and omega 3 fatty acids were not included, as they do not have assigned National Drug Code numbers and are not recommended by AUA guidelines for treatment of PD. Injectable therapies included interferon alpha-2B, verapamil, and collagenase clostridium histolyticum. These treatments were identified both through outpatient pharmacy records and by J-codes specific to the injection drug type. Surgical therapies included penile plication, excision or incision of penile plaque with or without grafting, and penile prosthesis. Surgical interventions were identified by CPT codes and Healthcare Common Procedure Coding System codes. Specific details regarding CPT codes, Healthcare Common Procedure

Coding System codes, and J-codes can be found in [Appendix](#). When assessing changes in the frequency of specific treatment over time, analysis included the proportion of patients with a treatment of all those who received any treatment for that year.

Incidence of PD in this cohort was by dividing the number of patients with a new diagnosis of PD as the numerator by all male patients aged 18–64 who had continuous follow-up for that year as the denominator. Patients with a prior diagnosis of PD were excluded for these calculations.

Cost was determined separately for surgical and medical interventions. Surgical costs are represented as the procedure cost for that operation and do not include facility fees, anesthesia costs, or other potentially related costs of that visit/hospitalization. Costs for pharmacologic treatments were calculated as the sum of total cost of each drug treatment for that calendar year. Each calendar year was assessed separately so we did not assess total length of treatment, which may have extended across more than 1 year. All analyses were completed with SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Our search yielded 88,642 individual patients with a diagnosis PD from 2007 to 2018. Men from age group 55–64 years composed the largest proportion of individuals, accounting for 50.6% of all patients with PD ([Table 1](#)). Geographically, the south was most represented with 43.8% of men from this region. Preferred provider organization was the most common form of insurance (62.5%), whereas health maintenance organization was the second most common (10.8%).

The annual incidence of new PD diagnosis in this cohort rose from 61 to 77 per 100,000 patients over the included years, and the percent annual treatment rate rose from 17.8% to 26.2% ([Figure 1](#)). With respect to PD treatment, the percentage of patients prescribed oral agents from 2007 to 2018 nearly doubled from 5.5% to 10.8%, whereas the percentage of men undergoing surgical procedures decreased slightly from 4.7% in 2007 to 3.1% in 2018. Treatment with injectable therapies remained stable at 7–9% from 2007 to 2013 but rose sharply starting in 2014; in 2018, 14% of men with PD were treated with injections ([Figure 2A](#)).

Among oral therapies, colchicine was the most commonly prescribed drug in 2007 (21.6% of all patients with PD who received treatment). By 2018, pentoxifylline was used in 32.9% of patients receiving any treatment, whereas colchicine decreased to 11.4%. ([Figure 2B](#)). In 2007, the most common injectable treatment was intralesional verapamil, used in 11.1% of patients who received any treatment. By 2018, 24.1% of treated patients received injectable collagenase, whereas only 0.8% received verapamil ([Figure 2C](#)). Over this time, use of interferon remained less than 1% for patients receiving any treatment. Penile plication was the most common surgical procedure from 2007 to 2018 and occurred in 12.8% of treated patients in 2007 and decreased to

Table 1. Demographics of individuals with a diagnosis of PD from 2007 to 2018

	# Of PD diagnoses	Percent of total (%)
Age at first PD coding		
18–24 y	1798	2.0
25–34 y	4300	4.9
35–44 y	9553	10.8
45–54 y	28,129	31.7
55–64 y	44,862	50.6
Total	88,642	100
Geographic region		
Northeast	14,494	16.4
North Central	18,433	20.8
South	38,804	43.8
West	14,946	16.9
Missing/unknown	1965	2.2
Total	88,642	100
Insurance type		
Comprehensive	2230	2.5
EPO	1379	1.6
HMO	9553	10.8
POS	6113	6.9
PPO	55,424	62.5
POS w/capitation	709	0.8
CDHP	5176	5.8
HDHP	3739	4.2
Missing/unknown	4319	4.9
Total	88,642	100

CDHP = consumer-driven health plan; EPO = Exclusive Provider Organization; HDHP = high deductible health plan; HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization.

8.8% of treated patients in 2018, whereas inflatable penile prosthesis was the second most common surgery, decreasing from 10.9% to 7.0% over the study period (Figure 2D).

Mean annual cost of PD treatment per individual increased from \$1531 in 2007 to \$10339 in 2018 (Figure 3). The cost of all treatment modalities rose over the study period, with injectable therapy having the highest increase. Mean oral therapy costs per individual increased from \$42 to \$175 (a 3-fold increase) and mean surgical therapy costs per individual increased from \$4255 to \$10,930 (a 1.6-fold increase). In 2007, the mean annual, per-individual cost of injectable therapies rose from \$811 in 2007 to \$16,184 in 2018, a 19-fold increase. For patients receiving injectable collagenase, the mean cost per patient rose from \$17,187 in 2014 to \$20,260 in 2018.

DISCUSSION

In this study, we aimed to characterize temporal trends in PD treatment and the costs associated with these treatments using a large, commercial insurance claims database. During the study period from 2007 to 2018, we found that the estimated annual

incidence of new PD diagnoses in our cohort nearly doubled from 61 to 71 patients per 100,000. It is unclear whether the trend of increased incidence in new PD diagnoses over time represents increased awareness among patients and providers, reflects increased direct to consumer marketing by pharmaceutical companies, or is a true representation of increased burden of disease. This annual incidence of PD diagnosis is higher than in other historical studies,¹ which is likely due to increased awareness of PD by physicians and patient's willingness to seek medical treatment for the condition. Our estimated incidence is not a true incidence calculation because we only included patients with private insurance and could only identify individuals seeking medical treatment. In this study, the majority of men with a diagnosis of PD did not obtain active treatment during the year in which they had a diagnosis, only 22.6% received any treatment overall. However, the rate of treatment increased over the time interval of the study (17.8–26.2%).

Interestingly, there was a shift in oral therapy prescription patterns for PD during the included time frame. In 2007, colchicine was the most commonly prescribed oral agent; however, by 2018, the rate of pentoxifylline prescription among treated patients was 4 times higher than that of colchicine (32.9% vs 8.5%). This transformation reflects pertinent urologic studies published during the study period. In 2010, 2 basic science articles were published with evidence that pentoxifylline attenuates collagen deposition and elastogenesis in tunica albuginea-derived fibroblasts.^{13,14} In the same year, a double-blind, placebo-controlled study comparing oral pentoxifylline with placebo in patients with early, chronic PD suggested significantly increased self-reported positive response and

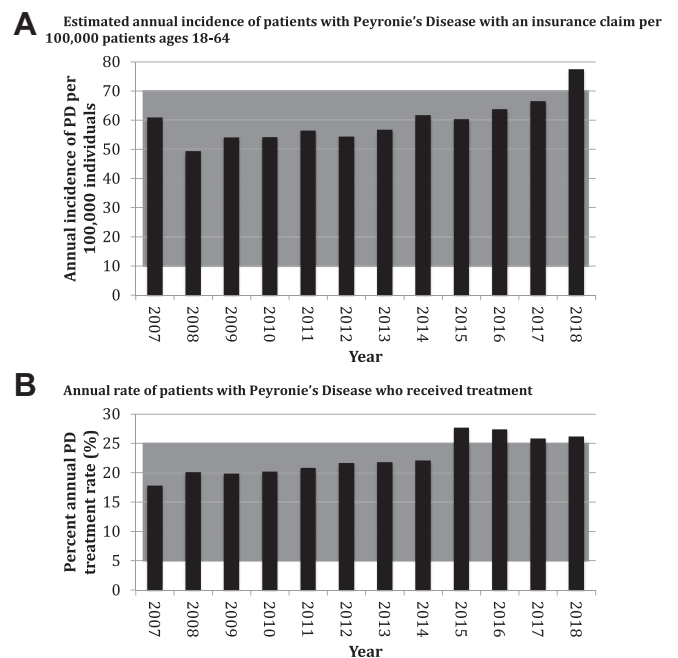


Figure 1. (A) Annual incidence of Peyronie's disease during each year of the study period. (B) Annual percentage of patients with Peyronie's disease who received treatment during the study period.

improvement in penile curvature, International Index of Erectile Function score, and mean peak systolic velocities in the pentoxifylline group.¹⁵ However, this article was retracted in 2015 owing to concerns over statistical analysis. In 2015, the AUA released its first guideline statements for the diagnosis and treatment of PD.⁹ These guidelines recommend against oral therapy for PD with vitamin E, tamoxifen, procabazine, omega-3 fatty acids, or a combination of vitamin E with L-carnitine. The panel reported that oral colchicine and pentoxifylline are possibly promising therapies for PD, but there was insufficient evidence to support even a conditional recommendation at that time. It remains to be seen how these guidelines will impact future clinical management of PD with oral agents.

During 2007 to 2018, the shift in injectable therapy from intralesional verapamil to collagenase was profound and directly parallels Food and Drug Administration approval of injectable collagenase for PD in December of 2013. In 2007, most of injections performed for PD were intralesional verapamil and were performed in 11.1% of treated patients. By 2018, almost all of injections were collagenase and were performed in 24.1% of treated patients. Approval of intralesional collagenase was based on the results of 2 double-blind, placebo-controlled clinical trials entitled the Investigation for Maximal Peyronie's Reduction Efficacy and Safety Studies I and II.¹¹ These studies reported mean percentage change of curvature of 33–35% in the treatment group, which was significantly greater than that of the control group. Subsequently, the 2015 AUA guidelines on PD provided a moderate recommendation that clinicians may administer intralesional collagenase in combination with modeling for the reduction of penile curvature in patients with

stable PD, curvature between 30° and 90°, and intact erectile function (with or without the use of medications).

These results demonstrate a striking increase in cost of therapy from 2007 to 2018; the average cost per patient for treatment of PD increased almost 6 times (\$1,531 to \$10,339 per patient). The timing of this cost escalation coincides with Food and Drug Administration approval of injectable collagenase and its introduction to the market at the end of 2013 (Figure 2D). These data suggest that the majority of this increase is attributable to the widespread use of injectable collagenase. The effect is visualized in Figure 3: cost of oral therapies remained low and relatively stable over the study period, cost of surgery steadily increased, and cost of injectable therapies surged 19 times starting in 2014. In comparison with 2007, cost of injectable therapies rose from a mean \$811 to \$16,184 per patient in 2018. The increase cannot be explained by healthcare inflation alone. In accordance with the U.S. Bureau of Labor Statistics, the estimated mean inflation rate was about 3% per year from 2007 to 2018 or an overall inflation of 38% in medical costs during this time.¹⁶

In this study, by 2018, the mean cost of treatment with injectable collagenase was substantially higher than surgery (\$20,260 vs \$10,930). A 2017 analysis describing penile plication vs intralesional collagenase for PD found that the cost, on average, associated with penile plication was approximately \$3000 vs \$25,000 for collagenase (average of 7 injections).¹² One-way sensitivity analyses demonstrated the total cost of collagenase would need to approach \$2500 to achieve equivalence to the plication pathway with no change in efficacy.

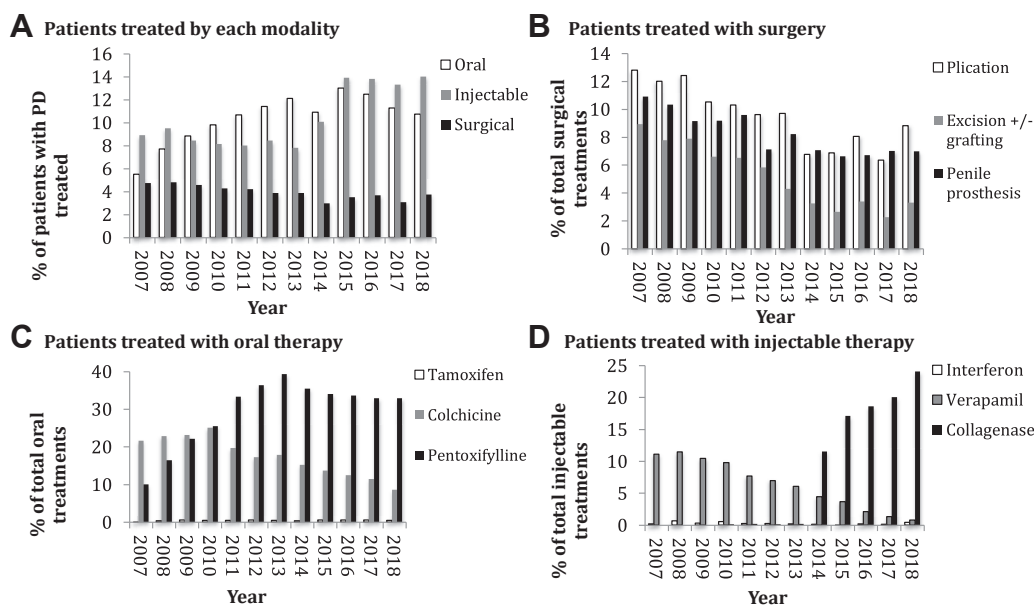


Figure 2. Temporal trends in treatment modalities. (A) Percentage of patients treated with oral, injectable, and surgical therapy by year. (B) Percentage of patients treated with each surgical type by year. (C) Percentage of patients treated with each oral therapy type by year. (D) Percentage of patients treated with each injectable therapy type by year.

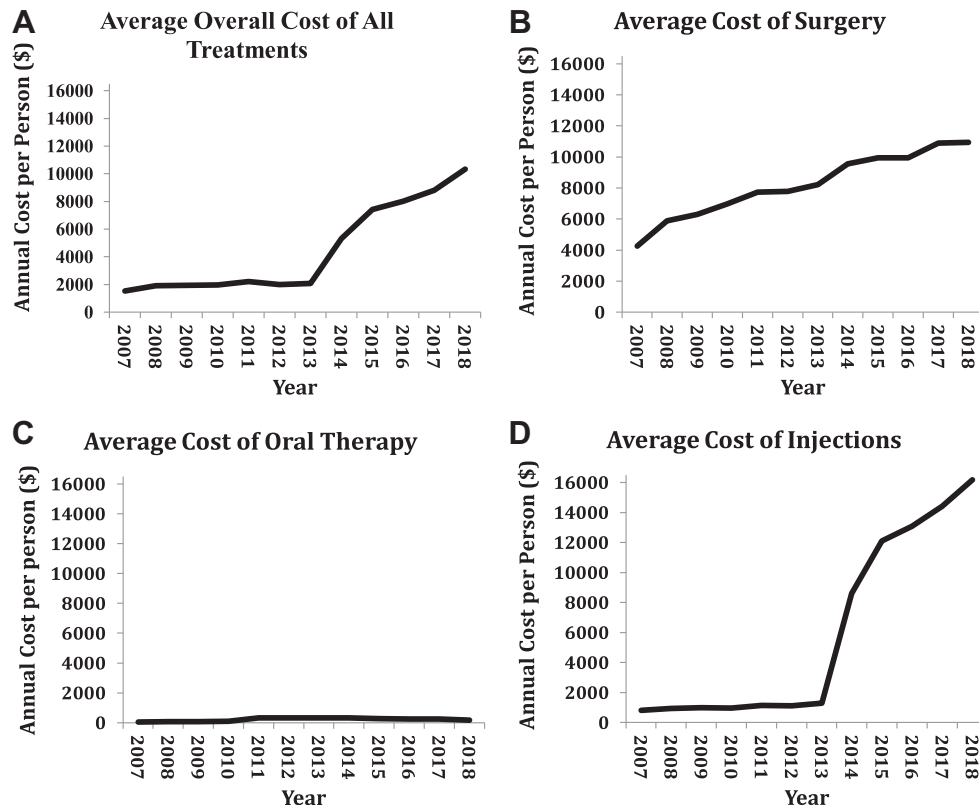


Figure 3. Temporal trends in treatment cost of PD. (A) Mean cost of all treatments (surgery, oral therapy, and injections) by year. (B) Mean cost of surgical therapy treatment by year. (C) Mean cost of oral therapy by year. (D) Mean cost of injectable therapy by year.

It remains to be seen whether the increased expenditure is justified by clinical outcomes over longer periods of time. A recent retrospective, multi-institutional study consisting of 918 patients across 5 institutions found a 30% improvement from baseline curvature and a 9% complication rate.¹⁷ Although studies demonstrate that a significant proportion of men undergoing injectable collagenase therapy exhibit benefit, this therapy does not eliminate curvature and there are no long-term data (greater than 5 years) on outcomes and patient satisfaction. Furthermore, the treatment has well-documented complications and associated adverse events including hematoma, pain, and swelling. It will be critical for future studies to assess long-term outcomes so that practitioners may fully counsel patients on both the financial and therapeutic effects of injectable collagenase.

There are several strengths of our study, including its large sample size, longitudinal nature of the database, and finite treatments with established CPT and International Classification of Diseases codes, which allow consistent data collection across years. Limitations include inability to control for coding bias/coding errors and changes in coding over the study period. This study focused on trends on treatment and cost of treatment for PD, so we did not assess outcomes for these patients. We anticipate that future studies will help determine whether the

large increases in costs to patients and the medical system are justified with improved patient outcomes and patient satisfaction. The population of patients used in this study was limited by the database. As a result, there may be limited generalizability as that subjects in our cohort are all commercially insured individuals younger than the age of 65 years. The use of claims-based data also limited our ability to understand the details of each patient's disease. We also were not able to assess trends for non-prescription medications such as vitamin D. Furthermore, MarketScan does not provide demographic information in race or socioeconomic status, so we were unable to analyze subgroups of patients.

CONCLUSIONS

The proportion of patients with a PD diagnosis who received treatment increased during the time period of this study. Pentoxifylline replaced colchicine as the most common prescription oral agent, whereas injectable collagenase replaced verapamil as the most common injectable therapy. Surgical interventions remained stable. The mean cost per patient associated with PD treatment rose more than 5 times from 2007 to 2018 with a timing that corresponds with the Federal Drug Administration's approval of injectable collagenase. Furthermore, longer-term studies are

needed to assess if the clinical outcomes for patients treated with injectable collagenase justify the high costs of the treatment.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.esxm.2020.08.003>.