Trends in treatment of Peyronie’s disease in adult men in the United States from 2008 to 2017 – results from an encounter and claims database

Odinachi I. Moghalu, DO, MS¹, Rupam Das, MBA, MS¹,², Joshua Horns, PhD¹,², Alexander Campbell, MS¹,², James M. Hotaling, MD, MS, FECSM¹,³, Alexander W. Pastuszak, MD, PhD¹,³

¹Department of Surgery, Division of Urology, University of Utah Health Science Center, Salt Lake City, UT
²Surgical Population Analysis Research Core, University of Utah Health Science Center, Salt Lake City, UT
³Utah Center for Reproductive Medicine, Salt Lake City, UT

Abstract

Treatments for Peyronie’s Disease (PD) include oral medications, intrallesional injections and surgery. Collagenase Clostridium histolyticum (CCh) is the only FDA approved treatment for PD. We sought to examine current trends in treatment of PD across the United States. Using data in the MarketScan Database, we conducted a retrospective study of men with PD in the
United States. Cases were identified by ICD-9 and 10 codes, and treatments were identified using NDC and CPT codes. Treatment rates were analyzed using linear regression model, and a cox proportional hazard function test was performed for time-to-treatment analysis. About 27.8% of men with PD were treated within a year of diagnosis. Annual treatment rate increased from 23.2% to 35.4% and intralesional injection was the most used treatment. Over the study period, percentage of men receiving treatment with oral medication increased from 0.66% to 20.5%, while use of intralesional injection and surgery decreased. Increased odds of treatment were observed in men 45–54 years (odds ratio [OR] 1.35; 95% confidence interval [CI], 1.21–1.50; p=0) and in the southern region (OR 1.48; 95% CI, 1.39–1.56; p=0). Trends in treatment of PD have changed over time. Intralesional injection remains the most used treatment option for men with PD.

**Introduction**

Peyronie’s disease is a chronic and progressive penile abnormality characterized by fibrotic plaque formation in the tunica albuginea [1–4]. It is estimated to affect between 0.14% and 20% of adult men in the United States [5–8]. The mainstays of treatment for PD vary, ranging from observation to non-surgical and surgical approaches, aimed at addressing penile deformity, sexual function and overall quality of life and well-being. Over the last decade, the management of PD has seen some significant changes, following the Food and Drug Administration’s (FDA) approval of Collagenase Clostridium Histolyticum (CCh) in December 2013 [9]. In addition, new guidelines for diagnosing and treating PD were released in 2015 by the American Urological Association (AUA) [10]. Consensus recommendations suggest intralesional CCh in combination with penile modeling as the treatment for PD in men with stable PD, penile curvature >30° and <90° with intact erectile function [10, 11]. Many currently available non-surgical options, with the exception of CCh, have shown inconsistent or no beneficial results in several studies [12–16] yet, they continue to be used by clinicians [17–19]. Little is known about current treatment patterns and factors that influence access to healthcare services and utilization in men with PD. We sought to better understand this by using a large nation-wide insurance claims and encounters database to examine trends in treatment approaches for PD in the United States from 2010 to 2017.

**Materials and Methods**

**Study Design and Data Source**

Using data from the IBM MarketScan™ Commercial Claims and Encounters database, we conducted a retrospective review of men with a diagnosis of PD from January 1, 2008 to December 31, 2017. The MarketScan database contains de-identified longitudinal patient information and claims data on insured individuals in the United States [20, 21]. The database contains individual-level demographic information, insurance features, financial information, inpatient and outpatient medical information and outpatient prescription drug data, in addition to inpatient and outpatient claims, diagnosis and procedure codes. Institutional Review Board (IRB) approval was not required for this study due to the de-identified nature of the dataset.
Patient Selection and Cohort Assignment

The present study included all men age ≥18 years with at least one inpatient or outpatient claim of a PD diagnosis or one claim for intralesional injection for PD. Diagnosis and procedures were identified using the International Classification of Disease, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM (607.85) and ICD-10-CM (N48.6)) codes and Current Procedural Terminology (CPT, 54200) codes. Patients were required to have at least two years of continuous enrollment prior to their first PD diagnosis. Patients were censored after they dropped out of the MarketScan database.

PD Treatment

PD treatments were stratified into three categories: (a). Oral medication (Colchicine, Pentoxifylline, and Tamoxifen), (b). Intralesional Injection (CCh, Verapamil, Interferon alpha-2b (IFN α−2b) and Other) and (c) Surgery (penile plication, incision/excision of penile plaque, implantation of penile prosthesis). Treatment was assessed following PD diagnosis during the study period, defining use by at least one claim for each treatment. Oral medications were identified by their specific national drug (NDC) codes, while use of intralesional injection was confirmed by identifying a CPT code for penile injection (54200) alongside a drug J-code (CCh: J0775; Verapamil: J3940; IFN α−2b: J9214). CPT codes were used in identifying specific surgical procedures – (Plastic operation on penis: 54360; Incision/excision of penile plaque: 54110, 54111, 54112; Implantation of penile prosthesis: 54400, 54401, 54405). Treatments received before the index PD diagnosis were ignored. Diagnostic and treatment codes are listed in the appendix under Supplemental Table 1 and Table 2.

Statistical Analysis / Main Outcomes

Descriptive analyses were performed on the characteristics of patients with PD that received treatment within the first year of diagnosis. Patients were grouped by the initial treatment received during the first year following index diagnosis and were stratified by age group, region, population density (urban vs. rural), employment status, plan type for insurance coverage, place of service, provider network and year of diagnosis. Descriptive statistics were limited to patients with at least one year of follow up and patients were considered untreated if no treatment occurred during the first year. Continuous variables were expressed as mean (SD), while categorical variables were expressed as frequencies and percentages. SQL and R code used to generate and analyze data is available upon request.

Treatment Trends

To investigate how trends in treatment varied across the study period, we examined the total numbers of each treatment administered between 2010 and 2017 in patients with at least one year of follow-up data. Every treatment that a given patient received was counted. These totals were then divided by the number of PD patients enrolled each year and multiplied by 100 to give treatment rates in units of number of treatments/100 PD patients. Treatment rates were modelled using linear regression across years and since CCh was only approved in December 2013, linear model for its use was restricted to 2014 onward.
Time-to-Treatment

A cox proportional hazard function on time from PD diagnosis until first treatment was conducted to investigate how different patient and geographic factors influenced time-to-treatment. Patients were censored after they dropped out of the MarketScan database. Model cofactors included age-group, region, population density and plan type for insurance coverage. Resulting odds ratios are presented with 95% confidence intervals (CIs), relative to a defined intercept.

Results

An initial cohort of 921656 adult men with at least one record of PD diagnosis were identified between 2008–2017. Excluding men with less than 2-years of continuous enrollment prior to first PD diagnosis yielded a cohort of 38438 patients. A final cohort of 25901 patients were identified after applying 1-year follow-up criteria following diagnosis and were included in the treatment trend analysis (Figure 1).

A total of 7193 of the 25901 (27.8%) received at least one treatment for PD. Diagnosis of PD was most represented in age-group 55–64 years (46.2%), southern region (42.4%), urban community (85.5%), fully employed (47.2%), enrolled in preferred provider organization (PPO) insurance plan (59.1%). Baseline demographic characteristics can be found in Table 1. Annual percentage of men with PD that were treated increased from 23.3% in 2010 to 35.4% in 2016. Rates of oral medication use increased from 0.66% to 20.5%, while rates of intralesional injection (84.7% vs. 71.7%) and surgery (14.7% vs. 7.9%) decreased over the study period, Table 2.

The most frequently used treatment was intralesional injection, constituting 5612 (78.02%) of the initial treatment. Oral medication accounted for 824 (11.5%) treatments, while surgical management totaled 757 (10.5%) of initial treatments. Of the patients that were managed with intralesional injection, majority were treated with an unspecified medication that is not recommended by the AUA, that we classified as ‘other’ 5138 (91.6%). Amongst the AUA recommended intralesional injections, verapamil, 388 (6.91%) was the most commonly used. For those managed with an oral medication, pentoxifylline was the most used 814 (98.8%), and in men that were managed surgically, penile implant 444 (58.7%) was the most used surgical procedure. The overall median time to treatment from index diagnosis was 50 (6, 160) days. Median time to treatment was shortest in men who underwent penile implant 1.5 (0, 71.8) days and highest in those receiving tamoxifen 323 (323, 323) days. Breakdown of treatments are detailed in Table 3. Across the study period there was significant increase in the use of colchicine, pentoxifylline and unspecified intralesional injection, while a negative trend was observed in the use of intralesional IFN α−2b (Figure 2).

Patient characteristics were compared for those who had treatment versus those without any treatment. Patients between ages 45–54 years were most likely to undergo some form of treatment (odds ratio [OR] 1.35; 95% confidence interval [CI], 1.21–1.50; p=0). The geographic regions with significant association were the Midwest (OR 1.08; 95% CI, 1.01–1.15; p=0.029) and South (OR 1.48; 95% CI, 1.39–1.56; p=0), where men were more likely
to undergo treatment compared to those in the Northeast United States. Results of the cox proportional hazards model are presented in Table 4.

Discussion

Peyronie’s disease is a chronic condition with a complex symptomatology that may compromise quality of life if not properly managed. In this large cohort study, current treatment trends for PD in the U.S were investigated. Our findings suggest that approximately 28% of men with PD are treated on initial presentation. Prior to the present study, the most recent data on treatment trends is from a 2016 study by Sun, Li and Eisenberg, which found the percent of patients receiving treatment for PD on initial presentation ranged between 2.5% - 3.8% [22]. The higher rates observed in our study compared to the aforementioned study by Sun, Li and Eisenberg are likely due to including in our analysis men younger than 40 years old as well as using a larger database, thus, capturing more patients. Additionally, our study looked at some treatment options that are not recommended by the AUA for managing PD [10], but are still being used by clinicians [23].

When managing PD, there are several conservative and surgical treatment options available. Conservative therapies such as oral agents focus mainly on alleviating pain and preventing disease progression [24, 25]. Oral therapies such as Vitamin E, L-carnitine and para-aminobenzoates have been shown to have minimal to no demonstratable efficacy and are not recommended by the American Urological Association (AUA) as a suitable option for managing PD [26]. However, in a 2014 survey of urologists, 59% reported initiating therapy upon initial presentation, majority of them opting for oral agents [26]. The same trend is observed in our study where use of Colchicine and Pentoxifylline increased over the study period. Few studies and case reports have documented some efficacy of Pentoxifylline and colchicine as single agents or in combination with other medications [27, 28]. However, subsequent clinical trials have failed to show any real efficacy of these medications [29, 30], thus, neither are recommended by the AUA for treating PD [10].

Despite the decline in surgery and intraliesional injection, the annual percentage of patients receiving treatment for PD increased over the study period. This is likely due to increased use of oral medication, especially pentoxifylline. Following the approval of CCh by the FDA in 2013, there was a prominent increase in the use of CCh, despite an overall decline in use of intraliesional injections. CCh is the only FDA recommended treatment for PD and has been shown to be very effective in improving physical and psychological burdens of PD [15].

In our study, higher rates of treatment were observed amongst men living in the Southern region, even after controlling for the higher prevalence rates. The reason for this is not fully understood and further controlled studies will be required to better understand this. Furthermore, per the 2017 AUA census, practicing urologists in the South make up about 32.6% of all practicing urologists in the country, higher than any other regions [31], which could translate to lower patient to physician ration, thus, more patients are being seen without longer wait times.
Timing for PD treatment remains a topic of discussion among urologists. One issue surrounding timing is the efficacy of treatment in the active vs. chronic phases of PD [32]. Per the AUA guideline, intrallesional \textit{CCh} is recommended for stable disease, intact erectile function and penile curvature \textgreater 30° and \textless 90° [10], however, its efficacy and safety for use in active disease has been observed [33]. In a survey of practice patterns among urologists, the majority indicated that the optimal time for treatment with \textit{CCh} is more than 12 months after onset of symptoms and more than 3 months after plaque stabilization [26]. While the optimal time to treatment after PD diagnosis remains an open question, the present study shows that men aged 45–75 years, living in the Southern region of the United States and with a comprehensive insurance plan were factors associated with likelihood of receiving treatment. Patients with non-comprehensive insurance plans who were less likely to receive treatment may be due to problems relating lack of insurance coverage. However, due to variation in insurance coverage for PD across insurance providers, a definitive statement regarding differences in insurance coverage cannot be made. Furthermore, despite recommendations against oral agents such as vitamin E, some urologists opt for these as initial therapies, thus prolonging time to treatment using one of the recommended treatment options.

Management of PD aims to resolve symptoms including pain and penile curvature and to preserve erectile function. However, no single treatment approach is the universal standard of care [34]. Patient and disease characteristics such as extent of penile curvature, disease stability, extent of plaque calcification, patient desire for non-invasive vs. invasive management, and erectile function or dysfunction are used as guidelines for determining the best intervention [14, 35]. In men with PD, degree of curvature is an important factor influencing physical and psychosocial well-being [36]. In a recent study comparing treatment outcomes, surgical management of PD proved superior to intrallesional \textit{CCh} in correcting penile curvature, albeit with the risk of penile shortening and the risks associated with anesthesia [37]. The risk of penile shortening is lower with \textit{CCh} compared to surgery [37]. Although intrallesional \textit{CCh} is considered a less invasive management option, it still comes with the risk of a number of primarily self-limiting side effects including penile pain, bruising, hematoma [38] and corporal rupture [15]. In a recent study, the discontinuation rate of \textit{CCh} due to patient dissatisfaction and adverse effects was estimated at 10.7% [39]. Despite this, \textit{CCh} remains an effective treatment option for men who would like to avoid surgical management [15, 16]. When deciding on treatment for PD, balancing benefits and possible risks associated with the respective treatment options is the most important and complex issue for clinicians [19, 36–38, 40–44].

Studies based on commercial insurance claims, such as this, have important limitations and biases that may affect the generalizability of results to other populations. First, the people in our study are all employed with employee-sponsored insurance. Thus, the overall health and socio-economic status of this population may not be perfectly reflective of the United States as a whole. Second, only claims submitted to an insurance provider are included in MarketScan. Any medications or services paid for out-of-pocket or through a different payer will be unrecorded and not included in our analyses. Lastly, the level of detail recorded by insurers does not always allow for the identification of particular medications, making more-thorough analysis of medication type challenging.
Conclusion

This study investigates the current treatment trends for PD in the United States. Although physical and psychological stresses are associated with PD, only a small percentage of diagnosed men have their PD treated within a year of diagnosis with therapies that have shown some demonstratable efficacy. Patient factors such as age, geographic region and insurance type influence choice, timing of initial treatment and rate of overall treatment. Despite decline in surgical management of PD, since approval of CCh, there has been a significant increase in the proportion of men with PD who receive treatment, most especially with use of intraleisional injection. Each treatment modality has its own risk and benefit profile; thus, clinicians should engage in thoughtful counseling and discussion with patients. For optimal patient satisfaction and treatment effectiveness, patients must have realistic expectations regarding treatment effects and feasibility of adverse events.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1:
Diagram of patient and cohort selection
Figure 2:
Trends in treatment over time. Gray points/lines represent raw values. Red lines represent linear regression coefficients (solid lines indicate significant effect; dashed lines indicate non-significant effect). Linear regression for CCh injections include data from end of 2013 to 2017, following the approval of CCh by the FDA.
### Table 1:

**Baseline demographic and clinical characteristics**

| Patient Characteristics | Number (%) |
|-------------------------|------------|
| N (%)                   | 25901 (100) |
| **Received Treatment**  |            |
| Yes                     | 7193 (27.8) |
| No                      | 18708 (72.2) |
| **Age-group in years**  |            |
| 18–34                   | 1078 (4.16) |
| 35–44                   | 2234 (8.63) |
| 45–54                   | 7165 (27.7) |
| 55–64                   | 11953 (46.2) |
| 65–74                   | 2876 (11.1) |
| 75–84                   | 559 (2.16) |
| 85+                     | 36 (0.14) |
| **Geographic region**   |            |
| Northeast               | 4626 (17.9) |
| Midwest                 | 5617 (21.7) |
| South                   | 10975 (42.4) |
| West                    | 4654 (18.0) |
| Unknown                 | 29 (0.11) |
| **Population density**  |            |
| Urban                   | 22145 (85.5) |
| Rural                   | 3756 (14.5) |
| **Insurance plan**      |            |
| Comprehensive           | 2039 (7.87) |
| EPO                     | 361 (1.39) |
| HMO                     | 3064 (11.8) |
| POS                     | 1678 (6.48) |
| PPO                     | 15302 (59.1) |
### Patient Characteristics

| Characteristics          | Number (%) |
|--------------------------|------------|
| POS with capitation      | 162 (0.68) |
| CDHP                     | 1701 (6.57)|
| HDHP                     | 936 (3.61)|

### Employment status

| Status                  | Number (%) |
|-------------------------|------------|
| Full-time               | 12223 (47.2)|
| Part-time               | 191 (0.74)  |
| Early retiree           | 2258 (8.72)|
| Medicare eligible retiree | 2120 (8.19)|
| Retiree status unknown  | 508 (1.96)  |
| COBRA continue          | 42 (0.16)   |
| Long-term Disability    | 53 (0.20)   |
| Surviving spouse dependent | 24 (0.09)  |
| Employee Status Unknown | 8482 (32.8)|

### Place of service

| Type        | Number (%) |
|-------------|------------|
| Inpatient   | 118 (0.46) |
| Outpatient  | 25783 (99.5)|

### Provider In-Network

| Status   | Number (%) |
|----------|------------|
| Yes      | 20930 (80.8)|
| No       | 1843 (7.12) |
| Unknown  | 3128 (12.1) |

### Year of index diagnosis

| Year      | Number (%) |
|-----------|------------|
| 2010      | 5907 (15.1)|
| 2011      | 4317 (16.7)|
| 2012      | 3874 (15.0)|
| 2013      | 4071 (15.7)|
| 2014      | 3373 (13.0)|
| 2015      | 3335 (12.9)|
| 2016      | 3024 (11.7)|

EPO, exclusive provider organization; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; CDHP, consumer driven health plan; HDHP, high deductible health plan
### Table 2:

Annual PD treatment rate

| Year of index diagnosis | Men with PD receiving treatment, n (%) | % of men receiving Oral medication | % of men receiving Intrallesional Injection | % of men treated with Surgery | Total |
|-------------------------|----------------------------------------|-----------------------------------|------------------------------------------|-------------------------------|-------|
| 2010                    | 908 (23.2)                             | 6 (0.66)                          | 769 (84.5)                               | 133 (14.7)                   | 3907  |
| 2011                    | 1016 (23.5)                            | 28 (2.76)                         | 845 (83.2)                               | 143 (14.1)                   | 4317  |
| 2012                    | 967 (25)                               | 96 (9.93)                         | 767 (79.3)                               | 104 (10.8)                   | 3874  |
| 2013                    | 1085 (26.7)                            | 127 (11.7)                        | 836 (77.1)                               | 122 (11.2)                   | 4071  |
| 2014                    | 1041 (30.9)                            | 155 (14.9)                        | 806 (77.4)                               | 80 (7.68)                    | 3373  |
| 2015                    | 1106 (33.2)                            | 193 (17.5)                        | 822 (74.3)                               | 91 (8.23)                    | 3335  |
| 2016                    | 1070 (35.4)                            | 219 (20.5)                        | 767 (71.7)                               | 84 (7.85)                    | 3024  |
Table 3:

Demographic and clinical characteristics of treated patients

|                          | Oral Medication N = 824 (11.45) | Intralesional Injection N = 5612 (78.0) | Surgery N = 757 (10.52) |
|--------------------------|---------------------------------|----------------------------------------|-------------------------|
|                          | Colchicine | Pentoxifylline | Tamoxifen | Collagenase | Clostridium histolyticum | IFN α−2b | Verapamil | Other* | Plastic operation for angulation | Incision of penile plaque | Penile Implant | Total       |
| N (%)                    | 9 (0.125)  | 814 (11.32)  | 1 (0.014) | 80 (1.11)   | 6 (0.083)              | 388 (5.39) | 5138 (71.43) | 195 (2.70) | 118 (1.64)              | 444 (6.17)              | 7193 (100)     |
| Age-group in years       |            |              |           |             |                        |            |            |        |                       |                 |               |
| 18–34                    | 0          | 40           | 0         | 0           | 0                      | 11         | 158         | 11       | 6                      | 4                | 220            |
| 35–44                    | 0          | 80           | 0         | 1           | 0                      | 24         | 423         | 6        | 6                      | 21               | 561            |
| 45–54                    | 5          | 282          | 0         | 23          | 1                      | 113        | 1471        | 51       | 29                     | 82               | 2057           |
| 55–64                    | 2          | 364          | 0         | 45          | 4                      | 208        | 2437        | 105      | 65                     | 205              | 3435           |
| 65–74                    | 1          | 45           | 1         | 11          | 1                      | 26         | 559         | 17       | 11                     | 115              | 787            |
| 75–84                    | 1          | 8            | 0         | 0           | 0                      | 5          | 86          | 5        | 1                      | 17               | 118            |
| 85+                      | 0          | 0            | 0         | 0           | 0                      | 1          | 4           | 0        | 0                      | 0                | 5              |
| Geographic region        |            |              |           |             |                        |            |            |        |                       |                 |               |
| Northeast                | 2          | 76           | 1         | 22          | 1                      | 83         | 791         | 30       | 22                     | 75               | 1103           |
| Midwest                  | 0          | 147          | 0         | 16          | 3                      | 128        | 937         | 64       | 29                     | 93               | 1417           |
| South                    | 5          | 326          | 0         | 22          | 0                      | 133        | 2738        | 73       | 45                     | 216              | 3558           |
| West                     | 2          | 265          | 0         | 20          | 2                      | 44         | 669         | 28       | 21                     | 60               | 1111           |
| Unknown                  | 0          | 0            | 0         | 0           | 0                      | 3          | 0           | 1        | 0                      | 4                |                |
| Population density       |            |              |           |             |                        |            |            |        |                       |                 |               |
| Urban                    | 7          | 736          | 1         | 69          | 6                      | 344        | 4344        | 170      | 100                    | 381              | 6158           |
| Rural                    | 2          | 78           | 0         | 11          | 0                      | 44         | 794         | 25       | 18                     | 63               | 1035           |
| Insurance plan           |            |              |           |             |                        |            |            |        |                       |                 |               |
| Comprehensive            | 0          | 38           | 0         | 7           | 0                      | 39         | 392         | 21       | 13                     | 80               | 590            |
| Oral Medication N = 824 (11.45) | Intralesional Injection N = 5612 (78.0) | Surgery N = 757 (10.52) |
|----------------------------------|------------------------------------------|--------------------------|
|                                  | Colchicine | Pentoxifylline | Tamoxifen | Collagenase Clostridium histolyticum | IFN α-2b | Verapamil | Other* | Plastic operation for angulation | Incision of penile plaque | Penile Implant | Total |
| EPO                              | 0  | 7  | 0  | 1  | 0  | 4  | 62  | 3  | 1  | 9  | 87  |
| HMO                              | 0  | 140 | 0  | 8  | 2  | 41 | 503 | 18 | 19 | 36 | 767 |
| POS                              | 0  | 51  | 0  | 4  | 0  | 28 | 376 | 19 | 10 | 28 | 516 |
| PPO                              | 8  | 440 | 1  | 46 | 2  | 232 | 3160 | 113 | 59 | 241 | 4302 |
| POS with capitation              | 0  | 10  | 0  | 1  | 3  | 28 | 0   | 0  | 0  | 1  | 44  |
| CDHP                             | 1  | 73  | 0  | 9  | 0  | 18 | 357 | 8  | 8  | 29 | 503 |
| HDHP                             | 0  | 46  | 0  | 3  | 1  | 14 | 166 | 7  | 1  | 7  | 245 |

| Year of index diagnosis          |                                   |                                   |                                   |
|----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| 2010                             | 0  | 6   | 0  | 0  | 2  | 61  | 706 | 38 | 27 | 68 | 908 |
| 2011                             | 0  | 28  | 0  | 0  | 2  | 65  | 778 | 37 | 30 | 76 | 1016 |
| 2012                             | 0  | 96  | 0  | 0  | 1  | 69  | 697 | 32 | 16 | 56 | 967 |
| 2013                             | 0  | 127 | 0  | 3  | 0  | 52  | 781 | 29 | 16 | 77 | 1085 |
| 2014                             | 0  | 154 | 1  | 25 | 1  | 56  | 724 | 24 | 8  | 48 | 1041 |
| 2015                             | 3  | 190 | 0  | 23 | 0  | 45  | 754 | 21 | 10 | 60 | 1106 |
| 2016                             | 6  | 213 | 0  | 29 | 0  | 40  | 698 | 14 | 11 | 59 | 1070 |

| Time-to-treatment in days        |                                   |                                   |                                   |
|----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Median (IQR)                     | 64 (0.171) | 15 (0.91) | 323 (323, 323) | 144.5 (74, 211) | 38.5 (17.5, 54.25) | 35 (6.75, 103.25) | 62 (12, 180.75) | 70 (11, 193) | 78 (9.25, 173.5) | 1.5 (0, 71.75) | 50 (6, 160) |

CCh, collagenase clostridium histolyticum; IFN α–2b, Interferon alpha-2b; SD, standard deviation; EPO, exclusive provider organization; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; CDHP, consumer driven health plan; HDHP, high deductible health plan. Other = intralesional injection other than verapamil, CCh and IFN α–2b.
Table 4:

Outputs of Cox proportional hazards model showing effect of age-group, region, population density and insurance plan on treatment. Age group effects are relative to 18–34, region effects are relative to Northeast, population density effects are relative to rural and insurance plan are relative to comprehensive plan.

| Patient Characteristics | Odds Ratio (OR) | 95% Confidence Interval (CI) | p-value |
|-------------------------|----------------|-----------------------------|---------|
| Age-group in years      |                |                             |         |
| 35–44                   | 1.11           | 0.98                        | 1.25    | 0.115 |
| 45–54                   | 1.35           | 1.21                        | 1.50    | 0 *   |
| 55–64                   | 1.32           | 1.19                        | 1.47    | 0 *   |
| 65–74                   | 1.28           | 1.13                        | 1.44    | 0 *   |
| 75–84                   | 1.03           | 0.87                        | 1.23    | 0.721 |
| 85+                     | 0.91           | 0.50                        | 1.65    | 0.747 |
| Geographic region       |                |                             |         |
| Midwest                 | 1.08           | 1.01                        | 1.15    | 0.029 *|
| South                   | 1.48           | 1.39                        | 1.56    | 0 *   |
| West                    | 1.01           | 0.94                        | 1.08    | 0.831 |
| Unknown                 | 0.63           | 0.30                        | 1.31    | 0.215 |
| Population density      |                |                             |         |
| Urban                   | 1.00           | 0.95                        | 1.06    | 0.959 |
| Insurance plan          |                |                             |         |
| EPO                     | 0.92           | 0.76                        | 1.1     | 0.348 |
| HMO                     | 0.86           | 0.79                        | 0.94    | 0.001 *|
| POS                     | 1.01           | 0.91                        | 1.12    | 0.87  |
| PPO                     | 0.92           | 0.86                        | 1.0     | 0.036 *|
| POS with capitation     | 0.96           | 0.76                        | 1.22    | 0.752 |
| CDHP                    | 0.99           | 0.90                        | 1.10    | 0.851 |
| HDHP                    | 0.87           | 0.76                        | 0.98    | 0.025 *|
* denoting showing statistical significance, \( p \leq 0.05 \). EPO, exclusive provider organization; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; CDHP, consumer driven health plan; HDHP, high deductible health plan.