

Healthcare Costs and Resource Use of Patients with Dupuytren Contracture Treated with Collagenase Clostridium Histolyticum or Fasciectomy: A Propensity Matching Analysis

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Objective: Studies examining differences in US healthcare resource utilization (HCRU) and associated healthcare costs between collagenase clostridium histolyticum (CCH) and fasciectomy for Dupuytren contracture (DC) are limited. This study evaluated US HCRU and direct healthcare cost for the treatment of DC in privately insured patients using insurance claims.

Methods: This retrospective observational cohort study analyzed data from large nationwide insurance claims databases; it included individuals diagnosed with DC between July 1, 2011, and June 30, 2017, who were adults at index date (date of first treatment: CCH or fasciectomy). Participants had continuous health plan coverage 24 months pre-index and 12 months post-index date. All-cause and DC-related HCRU and healthcare costs from the payers' perspective were compared between propensity score-matched cohorts. Generalized linear models assessed factors associated with all-cause total healthcare costs.

Results: Of 83,983 patients diagnosed with DC, 1932 adults receiving fasciectomy and 953 adults receiving CCH were included. The mean \pm standard deviation total all-cause healthcare cost was significantly lower with CCH than with fasciectomy (US\$11,897 \pm US\$14,633 versus US\$15,528 \pm US\$22,254, respectively; $P < 0.001$). After propensity score matching, 702 and 999 patients remained in the CCH and fasciectomy cohorts, respectively. In this analysis, all-cause and DC-related total costs were significantly lower in the CCH cohort versus the fasciectomy cohort (all-cause: US\$11,044 \pm US\$12,856 versus US\$12,912 \pm US\$19,237, respectively, $P = 0.02$; DC-specific: US\$3417 \pm US\$3671 versus US\$5800 \pm US\$4985, $P < 0.001$), mainly due to the lower frequency of outpatient visits. CCH treatment and the use of a consumer-driven healthcare plan were associated with lower healthcare costs.

Conclusion: Based on matched cohort data, adjusted 1-year healthcare costs for CCH-treated individuals were significantly lower compared with costs for fasciectomy-treated individuals.

Keywords: injection, surgery, insurance claims, retrospective database study

Plain Language Summary

- Dupuytren disease is characterized by thickening and shortening of the fibrous bands in the palm, ring finger, and little finger that may ultimately lead to permanent contracture of the fingers (Dupuytren contracture [DC])
- Dupuytren disease affects approximately 1% of adults in the United States, with a mean age at onset of approximately 60 years

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- There is a paucity of comparative information available on healthcare resource use and costs between collagenase clostridium histolyticum (CCH; minimally invasive treatment option) and fasciectomy (surgical treatment option) treatments for DC in the United States
- This retrospective study evaluated claims of privately insured US patients for healthcare costs and resource expenditures related to DC treatment between July 1, 2011, and June 30, 2017
- Propensity score matching (PSM) is a broadly used technique in retrospective claims studies that is performed to minimize potential selection bias due to confounding factors and to ensure unbiased comparison between the study cohorts
- After PSM, 702 and 999 patients remained in the CCH and fasciectomy cohorts, respectively; all-cause and DC-related total costs were significantly lower in the CCH cohort versus the fasciectomy cohort (all-cause: US\$11,044 ± US\$12,856 versus US\$12,912 ± US\$19,237, respectively, $P=0.02$; DC-specific: US\$3417 ± US\$3671 versus US\$5800 ± US\$4985, $P<0.001$), mainly due to fewer outpatient visits
- Based on propensity-matched cohort data, total healthcare costs for CCH-treated individuals were significantly lower compared with costs for fasciectomy-treated individuals

Introduction

Dupuytren disease is a fibrotic disorder characterized by thickening and shortening of the fibrous bands in the palm and fingers that may ultimately lead to permanent contracture of the fingers (Dupuytren contracture [DC]).^{1,2} Dupuytren disease most commonly involves the metacarpophalangeal and proximal interphalangeal joints of the ring and little fingers.^{1,2} This disease affects approximately 1% of adults in the United States,³ with a mean age at onset of approximately 60 years.² Although the etiology of Dupuytren disease is not clearly understood, several potential risk factors have been identified, including diabetes, smoking, and alcohol abuse.^{4–6}

Dupuytren disease can severely impair hand function, resulting in difficulties with activities of daily living, reduced work productivity, and diminished quality of life.^{3,7,8} These functional impairments may be sufficiently severe to warrant treatment.⁹ Current treatment options for DC include surgical excision (fasciectomy) or transection (fasciotomy) of the fibrous cords, percutaneous needle aponeurotomy, and injection of collagenase clostridium histolyticum (CCH).¹⁰ CCH is a mixture of 2 types of collagenase (class I and class II) in a defined mass

ratio.¹¹ The 2 enzymes cleave collagen molecules at different sites, resulting in enzymatic disruption of collagen cords.^{10,12} CCH was approved in 2010 by the US Food and Drug Administration for the treatment of DC with a palpable cord in adults.¹² It is injected into the fibrous cord, and the treated joint is manipulated approximately 24–72 hours after injection if contracture persists to allow finger extension and cord rupture. The efficacy of CCH in the treatment of DC has been demonstrated in Phase 3, randomized, controlled trials, which have shown significant reductions in contractures and improvements in range of motion, compared with placebo.^{13,14} Besides, some studies conducted in the United States and Europe have reported that CCH treatment for DC is also associated with less use of healthcare resources and lower healthcare costs, compared with fasciectomy;^{15–20} however, few studies have examined differences in real-world healthcare resource utilization (HCRU) and associated healthcare costs with CCH versus fasciectomy for the treatment of DC in the United States. Hence, the objective of the current study was to analyze data from a large claims database to compare US HCRU and direct healthcare costs between CCH and fasciectomy for the treatment of DC in a privately insured population.

Materials and Methods

Data Source and Study Population

This was a retrospective observational cohort study conducted using data from the US IBM[®] MarketScan[®] Commercial Claims and Encounters Database. This database contains anonymized information on approximately 240 million patients from more than 300 employers and a wide range of health plans across all healthcare settings nationwide in the United States. The data collected include demographics, health insurance plan details, and individual HCRU and expenditures. Institutional review board or ethics committee approval was not required for this study because only anonymized data were used. All data used in this analysis are compliant with the specifications of the 1996 Health Insurance Portability and Accountability Act.

The current analysis included adults who had at least 1 administrative claim for DC (ie, an International Classification of Diseases 9th or 10th Revision [ICD-9/10] code 728.6 or M72.0) between July 1, 2011, and June 30, 2017. CCH-treated patients were identified by medication claims with a Healthcare Common Procedure

Coding System (HCPCS) code J0775 or a National Drug Code (NDC) 66887-0003-01; also, patients were required to have a Current Procedural Terminology (CPT) code claim for CCH injection into the palm (CPT code 20527) within 90 days after the medication claim. Patients undergoing fasciectomy were identified by CPT codes 26121, 26123, and 26125. The date of first treatment with CCH or fasciectomy for DC was defined as the index date. Patients were required to have had continuous health plan coverage for 24 months prior to the index date and 12 months after the index date (post-index period). Patients who were <18 years old on the index date, had a diagnosis of Peyronie's disease or had evidence of the use of a DC-associated treatment other than the index treatment (fasciotomy or needle aponeurotomy) during the study period were excluded from the analysis. To assess real-world healthcare costs during the 1-year course of the disease rather than a single-episode cost, patients were allowed to have additional treatments during the post-index period. Demographic characteristics (age, gender, geographic region, and type of insurance plan) were recorded at the index date, and comorbidities and risk factors were assessed over the 24 months preceding the index date.

Healthcare Resource Utilization and Cost Outcomes

To examine the overall and DC-related economic burden, all-cause and DC-specific HCRU and costs were determined during the 1-year post-index period. All-cause resource utilization and costs were calculated based on any claims recorded downstream, while DC-specific resource utilization and costs were calculated based on claims with a diagnosis code for DC. Healthcare resource utilization was calculated based on events captured in specific claims (outpatient visits, inpatient admissions, and emergency department visits). Healthcare costs were calculated based on insurance plan payments for medical and pharmaceutical services provided. All treatment courses occurring during the 12-month follow-up period were included in the analyses and the respective costs of re-interventions were also evaluated if they occurred during the follow-up period.

Statistical Analysis

Demographic and clinical characteristics for the CCH and fasciectomy cohorts were analyzed using χ^2 tests for

categorical variables and independent *t*-tests for continuous variables. To minimize study selection bias, patients categorized into treatment cohorts were subjected to propensity score matching. A propensity score is a probability that a patient with certain demographic or baseline characteristics will be assigned to a particular treatment; propensity score matching in cohort studies allows one to balance treatment groups across measured covariates. The nearest neighbor matching algorithm²¹ was used to match patients treated with CCH to fasciectomy-treated patients in a 1:2 ratio.

Total all-cause costs were calculated by summing the adjudicated amounts paid by insurance for medical and pharmaceutical services during the post-index period. A generalized linear model with gamma log link distribution was used to analyze differences in total healthcare costs between the 2 cohorts, after adjustment for confounding variables. Confounding variables and effect modifiers that showed significant correlations with outcome or treatment choice were included in the base model. Variables were retained in the final model if statistically significant, and this model was used for cost adjustment. Statistical analyses were performed using the software package IBM® SPSS® Statistics for Windows, version 23.0 (IBM Corp, Armonk, NY). *P* values <0.05 were considered significant.

Results

Patient Characteristics

Between July 1, 2011, and June 30, 2017, 83,983 patients in the database had a diagnosis of DC, of whom 18,942 had ≥1 claim for CCH or fasciectomy and 2885 met all the inclusion criteria (CCH, *n*=953; fasciectomy, *n*=1932; [Figure 1](#)). In the unmatched sample, the characteristics of the CCH and fasciectomy cohorts were similar, except for a higher percentage of males in the CCH cohort and some differences in patient geographic distributions ([Table 1](#)). Most patients were Charlson Comorbidity Index weight group score 0 in the CCH (62.9%) and fasciectomy (59.1%) cohorts, and the percentage of patients with medical conditions that comprise the Charlson Comorbidity Index were generally similar between the 2 cohorts ([Supplementary Table](#)). Also, patients in the fasciectomy cohort had a higher frequency of trigger finger syndrome, carpal tunnel syndrome, and tobacco use disorder versus those in the CCH cohort ([Table 1](#)). After propensity score matching, 702 patients remained in the CCH cohort and

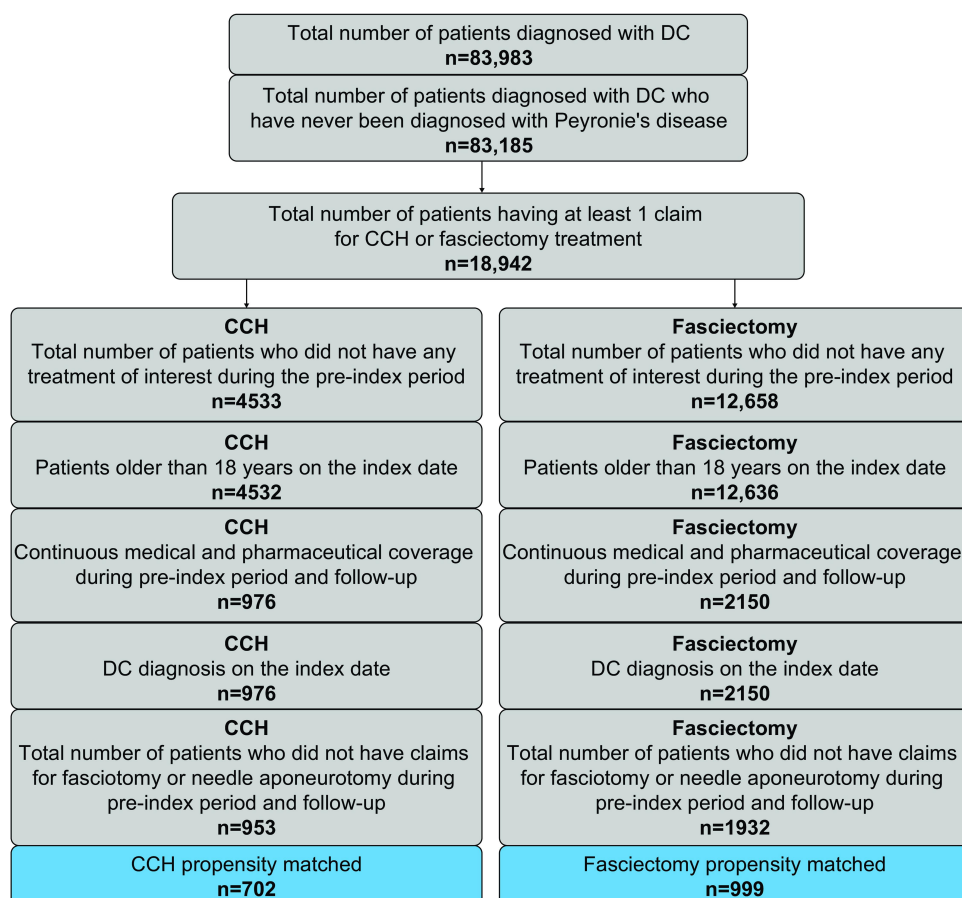


Figure 1 Study flow.

Abbreviations: CCH, collagenase clostridium histolyticum; DC, Dupuytren contracture.

999 remained in the fasciectomy cohort. Overall, the matched cohorts were well balanced across demographic and clinical characteristics.

Healthcare Costs and Resource Utilization

In the unmatched sample, the mean total all-cause healthcare cost was significantly lower with CCH versus fasciectomy (US\$11,897 ± US\$14,633 vs US\$15,528 ± US\$22,254, respectively; $P < 0.001$), mainly due to lower costs of outpatient care (Table 2). After matching, significant differences between CCH and fasciectomy were noted in several components of both all-cause (Figure 2A) and DC-related (Figure 2B) costs in the post-index period. Overall, all-cause and DC-related total costs were significantly lower in the CCH cohort than in the fasciectomy cohort (all-cause: US\$11,044 ± US\$12,856 vs US\$12,912 ± US\$19,237, respectively, $P = 0.02$; DC-specific: US\$3417 ± US\$3671 vs US\$5800 ± US\$4985, respectively, $P < 0.001$), despite the higher

prescription costs in the CCH cohort (US\$3600 ± US\$6164 vs US\$1806 ± US\$7114, $P < 0.001$). This difference was mainly driven by costs related to outpatient HCRU, as mean all-cause and DC-related outpatient visits were significantly lower in the CCH cohort compared with the fasciectomy cohort ($P \leq 0.001$; Table 3). No significant differences in hospitalization, emergency department visits, or outpatient medical prescriptions were found between the 2 treatment cohorts (Table 3).

Demographic and baseline clinical characteristics that correlated with outcome or treatment choice were age, gender, Charlson Comorbidity Index score, certain risk factors for DC, depression, some types of insurance, and geographic region (Table 1 and Supplementary Table). A generalized linear model was designed to identify key drivers of total healthcare costs in the matched cohorts. Factors independently associated with total all-cause healthcare costs were age, Charlson Comorbidity Index score, payer plan type, choice of treatment (CCH or fasciectomy), and the presence of depression or anxiety at

Table 1 Baseline Demographic and Clinical Characteristics for Unmatched Cohorts

Parameter	CCH (n=953)	Fasciectomy (n =1932)	P-value
Age, y, mean (SD)	56.8 (5.6)	56.0 (6.5)	0.001
Age range, y	32–64	20–64	–
>50 years, n (%)	836 (87.7)	1611 (83.4)	0.002
Males, n (%)	782 (82.1)	1316 (68.1)	<0.001
Geographic region, n (%)			
Northeast	223 (23.4)	345 (17.9)	<0.001
North Central	184 (19.3)	473 (24.5)	0.002
South	373 (39.1)	732 (37.9)	0.52
West	171 (17.9)	368 (19.0)	0.47
Unknown	2 (0.2)	14 (0.7)	0.11
Payer type, n (%)			
Preferred provider organization	597 (62.6)	1143 (59.2)	0.07
Consumer-driven health plan	99 (10.4)	232 (12.0)	0.20
Health maintenance organization	80 (8.4)	182 (9.4)	0.37
Non-capitated point-of-service plan	69 (7.2)	114 (5.9)	0.16
High-deductible health plan	56 (5.9)	105 (5.4)	0.63
Other*	52 (5.5)	156 (8.1)	0.01
CCI score, mean (SD) [†]	0.72 (1.27)	0.84 (1.40)	0.02
DC-associated risk factor comorbid condition, n (%)			
Hypertension	402 (42.2)	877 (45.4)	0.10
Hyperlipidemia	390 (40.9)	857 (44.4)	0.08
Tobacco use disorder	73 (7.7)	208 (10.8)	0.008
Trigger finger syndrome	52 (5.5)	336 (17.4)	<0.001
Gout	39 (4.1)	75 (3.9)	0.78
Carpal tunnel syndrome	34 (3.6)	217 (11.2)	<0.001
Alcohol use	25 (2.6)	56 (2.9)	0.67
Complex regional pain syndrome	0 (0.0)	3 (0.2)	0.56
Epilepsy	5 (0.5)	16 (0.8)	0.49

Notes: *Comprehensive, exclusive provider organization, point-of-service with capitation, or unknown. [†]Comorbidities were assessed during the 24-month pre-index period.

Abbreviations: CCH, collagenase clostridium histolyticum; CCI, Charlson Comorbidity Index; DC, Dupuytren contracture.

baseline (Table 4). Treatment with CCH and the use of a consumer-driven healthcare plan were significant predictors of lower insurance company expenditures (ie, associated with lower costs). After adjustment for confounders, total healthcare costs remained significantly higher in the fasciectomy cohort than in the CCH cohort (US\$9987 vs US\$8934, respectively; $P<0.001$).

Discussion

Studies examining differences in real-world HCRU and associated healthcare costs with CCH versus fasciectomy for the treatment of DC in the United States are limited. The current study demonstrated that utilization of healthcare resources and associated costs, reflected in this study as payments made by insurance companies, are lower in adults who receive CCH as therapy for DC compared with

fasciectomy in the United States over a 1-year study period. The higher outpatient prescription costs in the CCH cohort were outweighed by the reduced total costs, mainly driven by fewer outpatient office visits.

Table 2 Mean (SD) All-Cause Healthcare Costs During the 12-Month Post-Index Period in Unmatched Cohorts

Cost, US \$, Mean (SD)	CCH (n=953)	Fasciectomy (n=1932)	P-value
Outpatient	6894 (9261)	10,601 (12,643)	<0.001
Outpatient prescription	3911 (6569)	2701 (7612)	<0.001
Inpatient	835 (6584)	1817 (12,812)	0.07
Emergency department	257 (1317)	409 (1628)	0.02
Total	11,897 (14,633)	15,528 (22,254)	<0.001

Abbreviation: CCH, collagenase clostridium histolyticum.

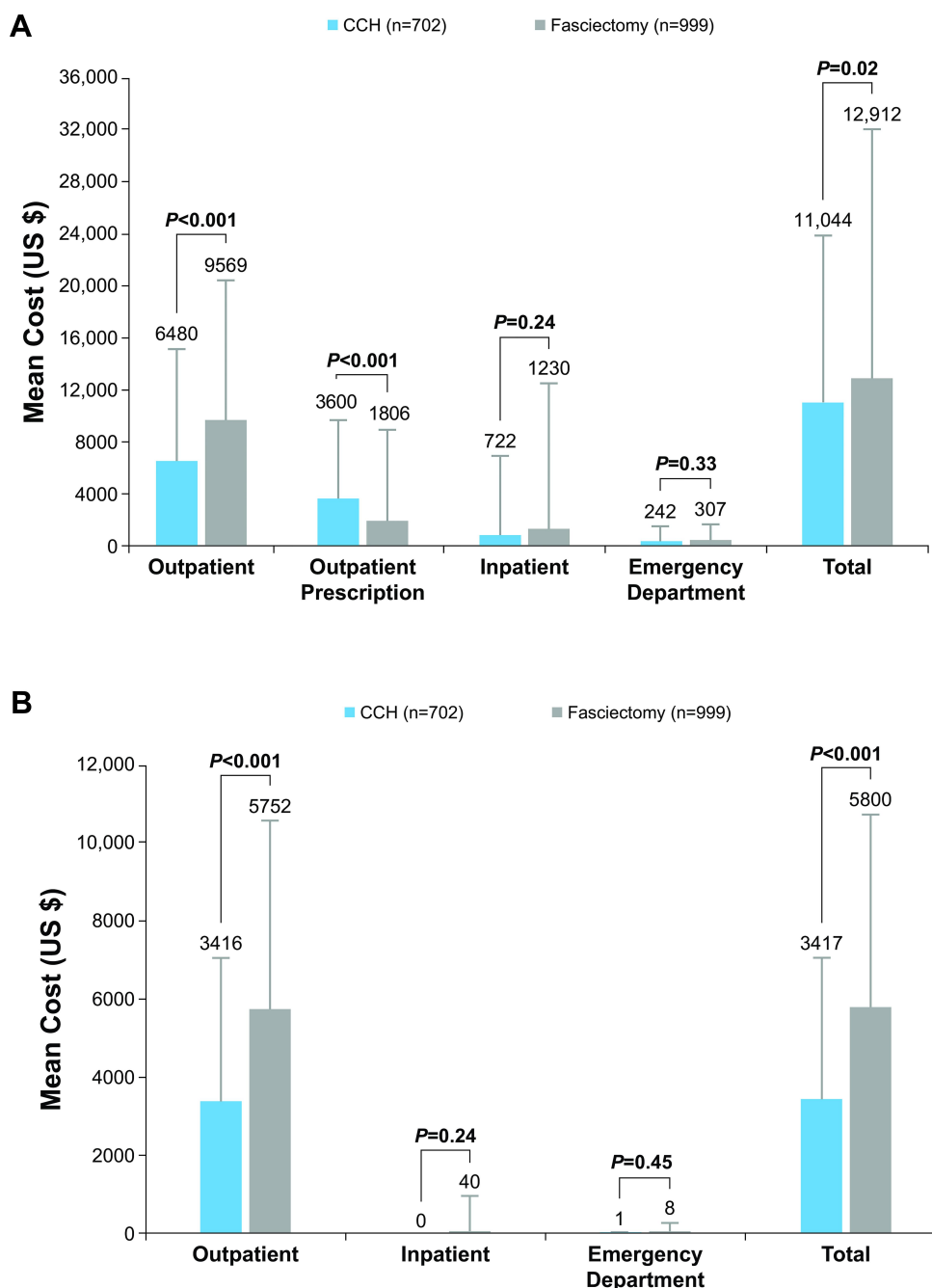


Figure 2 Mean (SD) all-cause (A) and DC-related (B) healthcare costs during the post-index period in the matched cohorts.
Abbreviations: CCH, collagenase clostridium histolyticum; DC, Dupuytren contracture.

These findings are consistent with results of another US claims database analysis, covering February 1, 2010, through December 31, 2011, in which patients with DC treated with CCH incurred significantly lower total healthcare costs and used fewer healthcare resources than patients undergoing fasciectomy.¹⁵ However, in that study, when analyzing the adjusted difference between DC-specific pre-index and post-index costs, no significant

differences were observed between cohorts.¹⁵ By contrast, in the current study, both all-cause and DC-specific total costs were significantly lower with CCH than with fasciectomy. However, direct comparison between these 2 studies is limited by the different outcomes assessed (ie, total and DC-specific healthcare costs over the post-index period in the current study versus differences between pre-index and post-index DC-specific costs in the prior study).

Table 3 Healthcare Resource Utilization During the 12-Month Post-Index Period in the Matched Cohorts

Parameter	CCH (n=702)	Fasciectomy (n=999)	P-value
Outpatient medical prescriptions, mean (SD)	16.8 (17.7)	18.3 (20.1)	0.11
Outpatient services, mean (SD)			
All-cause outpatient visits	14.4 (12.1)	16.9 (13.6)	<0.001
DC-related outpatient visits	4.8 (4.4)	5.7 (7.4)	0.001
Outpatient visits per patient with service	14.4 (12.1)	16.9 (13.6)	<0.001
Inpatient services			
Patients hospitalized, n (%)	16 (2.3)	39 (3.9)	0.06
All-cause hospitalizations, mean (SD)	0.03 (0.22)	0.05 (0.26)	0.08
Duration of hospitalization, days, mean (SD)	0.08 (0.73)	0.16 (1.0)	0.09
DC-related hospitalizations, mean (SD)	0.0 (0.04)	0.0 (0.02)	0.78
Duration of hospitalization, days, mean (SD)	0.0 (0.04)	0.0 (0.05)	0.78
Hospitalizations per patient, mean (SD)	1.2 (0.8)	1.3 (0.5)	0.97
Duration of hospitalization per hospitalized patient, days, mean (SD)	3.7 (3.3)	4.1 (3.4)	0.74
Emergency department visits			
Patients with emergency department visits, n (%)	77 (11.0)	112 (11.2)	0.88
All-cause emergency department visits, mean (SD)	0.2 (0.6)	0.2 (0.5)	0.92
DC-related emergency department visits, mean (SD)	0.0 (0.04)	0.0 (0.04)	0.80
Emergency department visits per urgently admitted patient, mean (SD)	1.5 (1.2)	1.4 (0.8)	0.69

Abbreviations: CCH, collagenase clostridium histolyticum; DC, Dupuytren contracture.

In another US claims database analysis, covering January 1, 2012, through June 30, 2016, fasciectomy for the treatment of DC was associated with a significantly higher total cost of care versus CCH treatment during the first 90 days post-treatment, with outpatient surgical visits as the main cost driver of this difference.²⁰

Table 4 Key Drivers of Total All-Cause Healthcare Costs in Matched Cohorts

Parameter	Adjusted Odds Ratio (95% CI)	P-value
CCH versus fasciectomy	0.90 (0.82–0.94)	<0.001
Age of patient (continuous)	1.01	<0.001
CCI score*		
Weight sum 1	1.22 (1.11–1.35)	<0.001
Weight sum 2	1.35 (1.22–1.35)	<0.001
Weight sum 3	2.01 (1.65–2.46)	<0.001
Weight sum ≥4	2.72 (2.01–3.29)	<0.001
Depression or anxiety diagnosis	1.35 (1.22–1.49)	<0.001
Type of insurance plan†		
Consumer-driven health plan	0.82 (0.74–0.94)	0.002
HMO	1.11 (1.01–1.35)	0.03
Non-capitated point-of-service plan	1.22 (1.02–1.35)	0.02

Notes: *Reference: sum of weights = 0. †Reference: preferred provider organization.

Abbreviations: CCH, collagenase clostridium histolyticum; CCI, Charlson Comorbidity Index; HMO, health maintenance organization.

Similar findings have been reported in studies from Europe. The mean cost of treatment for DC was substantially lower (~30–50%) with CCH versus fasciectomy in Spain.^{16,22} The cost savings ranged from 29% (CCH compared with fasciectomy with no subsequent physical therapy) to 51.5% (CCH compared with fasciectomy requiring subsequent hospitalization and physical therapy).¹⁶ Finally, cost savings in Australia were notably higher—reaching up to 64%—when treating DC with CCH instead of with fasciectomy.²³ During the 12-month post-index period in the current study, DC-related costs for CCH treatment were 41% less than costs for fasciectomy. While healthcare costs and utilization can vary substantially across countries and clinical settings, this study confirms significant 1-year US insurance company cost savings for DC treatment with CCH compared with fasciectomy. On the other hand, a single-surgeon retrospective review found that time horizon may play a significant role when comparing the costs of treatment for DC.²⁴ This study observed somewhat lower initial treatment window costs for CCH-treated patients (US \$4189) than fasciectomy-treated patients (US\$5291). However, when observed for 5 years, cumulative costs for CCH versus fasciectomy were similar (US\$5952 vs US\$5507). Statistical significance of the results was not reported in the study, thereby preventing our ability to

draw a conclusion about the cost difference between the cohorts.²⁴ The difference in the results of this study compared to ours stems from a multitude of factors. The Leafblad et al study was a one-institution, single-surgeon study versus the national level commercial data collection utilized in our study. Also, Leafblad et al performed the study in a substantially smaller cohort of patients (n=350) with quite different baseline characteristics, such as older age, and possibly different clinical stage of the disease compared to the patients included in our study's cohorts.

Strengths and Limitations

Strengths of the current study include the large data set, which can be considered representative of the privately-insured US patient population, and the use of propensity score matching, which is an established technique for balancing observational study cohorts.²¹ Limitations include the nature of the retrospective claims data that were collected primarily for administrative purposes, including a higher possibility of human error than in prospectively planned research. Although the claims underwent a rigorous data-cleaning process before the analysis was conducted, claims with negative monetary amounts or duplicate claims may remain in the dataset, leading to potential information bias. Also, the database used did not capture information on the severity of DC or the number of affected digit(s); thus, it was not possible to assess the effectiveness of treatment in terms of hand function. Although the observation period of the current study was longer than that of previously published studies assessing the health-economic burden of DC, the 1-year duration might be relatively short to capture the clinical course of the disease and/or recurrence. Also, treatment-related adverse events were not recorded. However, healthcare resource usage as assessed in this study reflects real-world treatment effectiveness, and thus, may serve as an indirect measure of the benefit-risk ratio of the different treatments. A further limitation is that while the incidence of DC increases with age,²⁵ the study comprised only privately insured patients <65 years of age. At 65 years, patients are eligible for Medicare insurance. Thus, the results of this study might not be generalizable to the Medicare-covered US population.

When interpreting the study results, it is important to note that the prescription claims database did not include information on the diagnosis, thus preventing an accurate assessment of DC-related prescription costs. However, the

study was primarily designed to assess all-cause costs in DC. Also, the cost of CCH injection was included in DC-specific outpatient and inpatient costs claimed by the HCPCS, along with DC diagnosis codes (Figure 2B).

Conclusion

Findings from this retrospective claims study suggest that treatment of DC with CCH is associated with lower healthcare costs, as reflected by payer spending, and less usage of healthcare resources than fasciectomy. Future studies should assess the costs associated with productivity loss, as well as the impact of different treatments on work productivity.

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Disclosure

Vladimir Zah, Djurdja Vukicevic, and Martina Imro are employees of ZRx Outcomes Research Inc. (institution founded by Endo Pharmaceuticals to conduct the present analysis), and have received grants from Endo Pharmaceuticals Inc. Jovana Pelivanovic and Simona Tatovic were employed by ZRx Outcomes Research Inc. at the time of the study. Jane Ruby was employed by Endo Pharmaceuticals Inc. at the time of the study. David Hurley is an employee of Endo Pharmaceuticals Inc. The authors report no other potential conflicts of interest for this work.

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