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Prevalence and Cost Analysis of Complex Regional Pain Syndrome (CRPS): A Role for Neurostimulation

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Abstract

OBJECTIVE—Diagnosis and treatment of complex regional pain syndrome (CRPS) is difficult. There is a paucity of data describing the cost burden associated with CRPS. The aim of this study was to assess the prevalence and healthcare utilization costs associated with CRPS.

METHODS—A retrospective longitudinal study was performed using the Truven MarketScan® database to identify patients with a new indexed diagnosis of CRPS (Type I, II, or both) from 2001 to 2012. We collected total, outpatient, and pain prescription costs 3-years prior to CRPS diagnosis (baseline), then at year of CRPS diagnosis and 8-year post-CRPS diagnosis. A longitudinal multivariate analysis was used to model the estimated total and pain prescription cost ratios comparing patients diagnosed before and after CRPS.

RESULTS—We included 35,316 patients with a new indexed diagnosis of CRPS (Type I: n=18,703, Type II: n=14,599, Both: n=2,014). Baseline characteristics were similar between the CRPS cohorts. Compared to 2- and 3-year baseline costs, 1-Year prior to diagnosis for all CRPS patients yielded the highest interquartile median [IQR] costs: total costs *$7,904[$3,469, $16,084];* outpatient costs *$6,706[$3,119, $12,715];* and pain prescription costs *$1,862[$147, $7,649]*. At the year of CRPS diagnosis, the median [IQR] costs were significantly higher than baseline costs: total costs *$8508[$3,943, $16,666]*; outpatient costs *$7251[$3.527, $13,568]*; and pain prescription costs *$2,077[$140, $8,856]*. Over the 8-year period after CRPS diagnosis, costs between all the years were similar, ranging from the highest (1-Year) to lowest (7-Years), $4845 to

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$3888. At CRPS diagnosed period, patients are expected to have a total cost 2.17-fold and prescription cost 2.56-fold of their baseline cost annually.

CONCLUSION—Our study demonstrates that there is a significant increase in cost and healthcare resource utilization one-year prior to and at diagnosis of CRPS. Furthermore, there is an increased annual cost post-diagnosis compared to baseline costs prior to diagnosis of CRPS.

Keywords

Complex Regional Pain Syndrome; CRPS; Neurostimulation; Cost; Healthcare Utilization; DRG Stimulator; SCS

INTRODUCTION

Complex regional pain syndrome (CRPS) Types I and II, also referred to as reflex sympathetic dystrophy or causalgia, respectfully, together represent a debilitating and uncommon pain diagnosis occurring in the distal extremities after trauma, surgery, or immobilization.[1] The pathophysiologic mechanism of CRPS differs from other pain syndromes in that it involves autonomic, sensory, motor, and vascular changes which manifest with allodynia, skin color and temperature changes, edema, and sensory and function loss.[2] The majority of CRPS cases are diagnosed clinically based on the presence of an inciting cause and clinical symptoms.[3] However, the diversity in presenting symptoms makes diagnosis difficult, often leading to misdiagnosis with other pain syndromes and subsequent delays in treatment, increasing both risk of progression to chronic disease and costs.[4]

Owing to the multiplicity of the underlying pathophysiologic mechanisms, treatment of CRPS is challenging and involves an interdisciplinary approach between physical therapists, psychotherapists, rheumatologists, anesthesiologists, and neurosurgeons.[3] Therapy involves pharmacologic management and often progresses to include interventional therapies including nerve blocks and neuromodulation, more commonly spinal cord stimulation (SCS).[5] While SCS is traditionally utilized after failure of conservative management, its efficacy of achieving pain relief in CRPS has been demonstrated across the literature.[6–15]

This multifaceted treatment approach as well as the difficulty in initial diagnosis contribute to the significant economic burden associated with CRPS, making it one of the most costly pain diagnoses.[16] An estimated 20–40% of patients remain refractory to both conservative therapy and SCS,[17] leading to additional excess consumption of healthcare resources. Recently, new neuromodulatory interventions such as dorsal root ganglion (DRG) stimulation have demonstrated efficacy in treating CRPS and have potential to reduce long-term costs associated with the syndrome.[17,18] However, despite the emergence of new interventional therapies and the demonstrated economic burden associated with CRPS, to date, no study has analyzed the trend of CRPS patients' resource consumption over time or quantified the current cost burden of CRPS to the United States healthcare system.

The use of large, nationwide databases that track overall healthcare outcomes and spending across various academic and community hospitals provides a unique view of the overall

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impact CRPS has on healthcare resources. In this large, retrospective study, we used patient data from the Truven MarketScan database to determine the overall short and long-term costs associated with CRPS. We postulate that the diagnosis of CRPS increases the overall medical-associated short- and long-term healthcare costs.

METHODS

Patients were retrospectively queried from the Truven Reuters MarketScan® database to identify patients with a new indexed diagnosis of CRPS (Type I, II, or both) from 2000 to 2012. Institutional Review Board approval was obtained prior to initiation of the study. The MarketScan database consists of patient-specific data on clinical utilization, including inpatient, outpatient, medication, and laboratory information from insurance enrollment and costs.

International Classification of Diseases, Ninth Revision, [ICD-9] codes were used to select patients with a diagnosis of CRPS. The following codes were used for CRPS Type I: 337.20, 337.21, 337.22, and 337.29; and CRPS Type II: 354.4 and 355.71. We defined the index event as the first CRPS diagnosis of each patient in the database. Only patients with a minimum of one year of baseline data prior to index event and a minimum of 90 days follow-up data without requirement of continuous enrollment were included.

Baseline characteristics were collected for all patients including patient age, gender, race, employment status, and year of index event. Counts and percentages were reported for categorical variables. Mean and standard deviation (SD) were provided for continuous variables. Chi-square test was used for the group difference for categorical variables, and Kruskal–Wallis test was used for the group difference for the continuous variable. All analyses were aligned to the index event and all the annual costs were defined by date year in 365 days relative to the time of CRPS diagnosis. Cost data were collected for all patients up to three years prior to the first diagnosis of CRPS, as well as annual costs following the initial diagnosis up to eight years. Descriptive statistics were reported 3-years prior to CRPS diagnosis, at time of CRPS diagnosis, and 8-years post-diagnosis by median and 25 – 75% quantiles. Negative and extremely large values were removed by excluding the highest and lowest 1% of values to account for outliers. The data included pain prescriptions costs, outpatient costs, and total costs, which is the sum outpatient and inpatient costs.

A longitudinal analysis was used to model the value of log (cost) in each one year interval using a generalized estimating equations (GEE) model to account for the correlation of the same patient's cost in multiple years. Year was defined by date year in 365 days relative to the time of CRPS diagnosis. Baseline cost was defined as the total cost in the years that are 3 years and 2 years prior to CRPS diagnosis. Since HCRU already went up one year before CRPS diagnosis, we define a two-year interval, including one-year prior and one year after CRPS diagnosis, as the CRPS diagnosed period. And define post CRPS diagnosis year 2 up to post CRPS year 8 as post CRPS diagnosis period. Each model includes sex, insurance, age, employment status, prior Charlson score (comorbidity index), normalized calendar year, an indicator for CRPS diagnosed period, and an indicator for post-CRPS years, as the independent variables, among which sex, insurance, employment status, and indicator

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variables were evaluated as categorical variables. All the GEE models assumed an exchangeable correlation structure for patients with multiple years of data. All analyses and data processing were conducted using SAS software, V9.4, SAS Institute Inc., Cary, NC, USA.

RESULTS

From 2000 to 2012, we identified 35,316 patients with a new indexed diagnosis of CRPS (Type I: n=18,703, Type II: n=14,599, Both: n=2,014), who met all inclusion criteria. "Both" is defined as unspecified CRPS diagnosis or miscoding by the provider. The consort diagram is depicted in Figure 1. Baseline characteristics were similar between the cohorts, with the Type II patient population being older in age (years) than the other cohorts (Type I: 52.5±13.9, Type II: 57.0±14.4, Both: 49.6±12.8, Total: 54.2±14.2), Table 1. For all the cohorts, there were more females than males in each of the cohorts (Type I: 69.3%, Type II: 64.4%, Both: 71.4%, Total: 67.4%), with the majority of patients in each cohort have an active full-time employment status, Table 1. Commercial insurance was the most prevalent insurance status in each of the cohorts (Type I: 61.5%, Type II: 58.0%, Both: 68.3%, Total: 60.5%) and the patient cohort was composed of majority of patients diagnosed after 2008 (>50%), Table 1.

Annual Costs 3-Years Pre-CRPS Diagnosis and 8-Years Post-CRPS Diagnosis

Compared to 2- and 3-year baseline costs, 1-Year prior to diagnosis for all CRPS cohorts combined (n=35,316) yielded the highest median [IQR] costs: (1) total costs (*1-Year: $7,904 [$3,469, $16,084], 2-Year: $4,160 [$1,251, $10,227], 3-Year: $3,437 [$929, $8,808]*); (2) outpatient costs (*1-Year: $6,706 [$3,119, $12,715], 2-Year: $3,613 [$1,164, $8,203], 3-Year: $3,010 [$873, $7,180]*); and (3) pain prescription costs (*1-Year: $1,862 [$147, $7,649], 2-Year: $853 [$20, $5,207], 3-Year: $797 [$1, $5,045]*), Table 2, Figures 1–2.

At the year of CRPS diagnosis (n=35,316), the median [IQR] costs were significantly higher than baseline costs: (1) total costs (*$8508 [$3,943, $16,666]*); (2) outpatient costs (*$7251 [$3.527, $13,568]*); and (3) pain prescription costs (*$2,077 [$140, $8,856]*), Table 2, Figures 2–3.

Over the 8-year period after CRPS diagnosis, costs between all the years were similar, ranging from the highest (1-Year) to lowest (7-Years), $4845 to $3888, respectively. The three years with the highest healthcare costs were 1-, 2-, and 4-Years post-CRPS diagnosis, with median [IQR]: (1) total costs (*1-Year: $4,845 [$1582, $11,432], 2-Year: $4,598 [$1,505, $11,083], 4-Year: $4,351 [$1296, $10,664]*); (2) outpatient costs (*1-Year: $4,212 [$1,465, $9,241], 2-Year: $4,028 [$1,383, $9,014], 4-Year: $3,742 [$1,184, $8,565]*); and (3) pain prescription costs (*1-Year: $1,488 [$37, $8,734], 2-Year: $1,644 [$38.0, $10,186], 4-Year: $1,307 [$18, $10,71]*), Table 2, Figure 2–3. Figure 4 is a depiction of the cumulative median total cost per patient illustrating an overall increasing cost overtime after CRPS diagnosis. Figure 5 is a depiction of the cumulative median pain prescription cost per patient illustrating an overall increasing cost overtime after CRPS diagnosis.

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Multivariate Longitudinal Regression GEE Model

Table 3 is the estimated total cost ratio comparing patients diagnosed before and after CRPS. At CRPS diagnosed period, patients are expected to have a total cost 2.17-fold of their baseline cost (117% increase) annually. Years after CRPS diagnosis period, patients' annual total cost are similar to their baseline cost.

Similarly, Table 4 is the estimated pain prescription cost-ratio comparing patients diagnosed before and after CRPS. In the CRPS diagnosed period, patients are expected to have a pain prescription cost 2.56-fold of their baseline cost (156% increase) annually. The years after CRPS diagnosis period, patients are expected to have a pain prescript cost 1.06-fold of their baseline cost (6% increase) annually.

DISCUSSION

Our study demonstrates that there is a significant increase in cost and healthcare resource utilization one-year prior to and at diagnosis of CRPS. Furthermore, there is an increased annual cost post-diagnosis compared to baseline costs prior to diagnosis of CRPS.

The significant healthcare economic burden associated with CRPS begins with diagnosis. CRPS has been estimated to account for approximately 1.2% of chronic pain diagnoses[4] and is known to occur in about 7% of patients after trauma or immobilization with a preponderance of diagnoses occurring in the distal upper limbs, adult females, and smokers.[1] Diagnosis is clinical based on the presence of an inciting cause, pain disproportionate to the inciting cause, and vasomotor or sudomotor skin changes in the area.[1] Interestingly, in a comparison of the diagnoses of chronic pain syndromes, Murphy et al. reported that CRPS patients on average carried an average of 7 coded pain diagnoses, a finding that surpassed the number of comorbid diagnoses in other chronic pain conditions and likely reflects initial difficulty in diagnosis and incidence of misdiagnosis associated with CRPS.[4] Similarly, this initial period of diagnosis, with associated testing and possibly even initiation of treatment for a misdiagnosis, could contribute to the increased costs seen 1-year prior to the initial diagnosis of CRPS in our cohort.

After establishing the diagnosis, the multidisciplinary approach to treating CRPS then adds significantly to its economic burden after diagnosis. Conservative medical management involves physical and occupational therapy and pharmacotherapy with NSAIDs, corticosteroids, topical DMSO, and gabapentin; however, many cases of CRPS refractory to this first-line therapy.[19] Intravenous drugs, namely ketamine, have demonstrated efficacy in treating CRPS, but systemic side effects and some physicians" inability to address these side effects limit the widespread applicability of these approaches.[19,20] Interventional approaches, including sympathetic and nerve blocks by anesthesiologists,[21] as well as surgical management with SCS implantation,[6–15] are pursued after failure of conservative medical management. Other surgical approaches include sympathectomy in patients who experienced benefit from sympathetic blockade,[22] and amputation can be pursued as a last line therapy.[23] However, CRPS patients often have refractory pain despite undergoing trials of both conservative and interventional options, leading to excess healthcare expenditures associated with failed therapies, increased use of pain medications even years after

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diagnosis, and hospitalizations for management of intractable pain and increased use of pain medications. In fact, in our study, CRPS patients on average spent more on pain medications 4 years after their diagnosis compared to the year of diagnosis. Based on healthcare expenditures alone, it is evident that more effective interventions to treat CRPS are necessary.[24]

Chronic pain syndromes as a whole impose one of the highest significant economic burdens on today's healthcare system, leading to an estimated annual economic burden of nearly $635 billion in the United States alone.[4,25] Due to difficulty in diagnosis, a need for multidisciplinary management, comorbid conditions, and eventual progression to chronicity, CRPS is one of the most costly pain syndromes.[26] The economic implications of CRPS extend beyond healthcare costs, as chronic pain often impedes CRPS patients' ability to work.[26] In fact, it has been estimated that only 40% of CRPS patients who previously worked will return to work after their diagnosis.[15] While recent economic analyses of total healthcare costs accrued by CRPS patients in the United States are lacking, Kemler et al. estimated the annual economic burden of CRPS to be 5,741 Euro per patient in the Netherlands in 1998.[26] While this analysis showed no significant difference in annual healthcare costs between CRPS confined to the hand versus the foot CRPS.[26] Our study demonstrated an overall increase in healthcare resources and cost with the diagnosis of CRPS.

While traditional management of CRPS begins with multiple trials of conservative management, based on these economic analyses, studies have suggested that neuromodulatory interventions should be considered sooner in the treatment algorithm to lower the high financial burden associated with CRPS.[13,16,26,27] Despite increase use of SCS as the next-line therapy for CRPS after failed conservative management, technical challenges limit the ability of SCS to reach pain in certain anatomic locations, especially the distal extremities.[18,28] For example, an estimated 10–20% of patients with CRPS, specifically those with pain confined to the distal extremities, can have pain refractory to both SCS and conservative management.[29] Furthermore, as the chronicity of the disease progresses, refractory CRPS patients tend to utilize increasing number of pain medications such that their total pain prescriptions costs continue to increase even years after initial diagnosis.[18]

DRG stimulation has recently gained attention as a potential alternative treatment for refractory CRPS, especially for cases with inadequate anatomic coverage by SCS.[18,28] DRG stimulation modulates the excitability of the primary sensory neurons that are dysregulated in CRPS through percutaneous implantation of electrodes in proximity to the ganglia implicated in the patient's distribution of pain.[18] This localization is thought to be one of the advantages of DRG stimulation over SCS, as the close proximity of the leads to target ganglia provides more targeted neurostimulation and limits lead migration.[17,18] The successful treatment of CRPS with DRG stimulation was first reported by Van Buyten et al., who showed that DRG stimulation achieved >50% pain relief in 8 subjects with CRPS.[18] This study also showed improvement in CRPS-induced edema and skin changes after DRG stimulation and found no postural variation in pain relief.[18] Moreover, in a prospective, randomized control trial comparing DRG stimulation and SCS for treatment of CRPS in 152

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patients, Deer et al. found that more patients experienced ≥50% pain relief and reported improved quality of life and psychological disposition after DRG compared to SCS.[17] Furthermore, this study also showed that DRG stimulation had less postural variation and off-target effects compared to SCS.[17] The efficacy of DRG stimulation in treating CRPS confined to the knee[30] and distal upper extremities[28] has also been described in case reports. While the number of studies demonstrating the efficacy of DRG stimulation is small, there is growing evidence that DRG stimulation may represent a viable option to treat refractory CRPS and lower the associated economic burden to the healthcare system.

Awareness of CRPS by clinicians has grown substantially in the past decade, reflected by our reported significant increase in total CRPS diagnoses made from 2001 to 2012. With this awareness, utilization of novel treatment options, especially neuromodulation with SCS, has led to significant pain relief in many CRPS patients. Clearly, current treatment options do achieve pain relief: while our cohort accumulated 2.17-fold total healthcare expenditures and 2.56-fold pain prescriptions in the diagnosis period, these multivariates significantly decreased to 1.01-fold and 1.06-fold, respectively, the years after diagnosis, which speaks to the success of some current treatments. However, we show that total costs as well as costs of pain prescriptions, medications, as well as inpatient and outpatient treatment continue to remain high up to 8 years after initial diagnosis despite these treatments, suggesting that there remains a role for novel interventions such as DRG to achieve better pain relief and reduce healthcare costs associated with CRPS. As utilization of these interventions grows, further economic analyses comparing healthcare utilization of CRPS patients undergoing conventional therapy, SCS, and DRG stimulation are necessary.

This study has limitations that have possible implications for its interpretation. First, the data were acquired retrospectively from a national database and limited by the data that were available. Therefore, we are limited to the judgment made by healthcare providers appropriately diagnosing patients with CRPS I and II, and cannot discern whether the diagnoses made are true or potentially inappropriate, which may have implications on our results. Second, baseline clinical states and other patient-related factors including the underlying etiology of CRPS could not be determined. Lastly, with most studies selecting patients using diagnosis and procedure codes, miscoding may be present. Despite these limitations, the comprehensive and inclusive nature of the MarketScan database provides us a useful trend. This study demonstrates that there is a significant increase in cost and healthcare resource utilization one-year prior to and at diagnosis of CRPS. Follow-up studies are required to delineate factors driving this difference in costs, and measures that may be taken to better diagnosis and treatment.

CONCLUSION

Our study demonstrates that there is a significant increase in cost and healthcare resource utilization one-year prior to and at diagnosis of CRPS. Furthermore, there is an increased annual cost post-diagnosis compared to baseline costs prior to diagnosis of CRPS. Further studies are necessary to understand the impact of DRG on cost differences between different treatment modalities, in hopes of reducing unnecessary health care expenditures for patients with CRPS.

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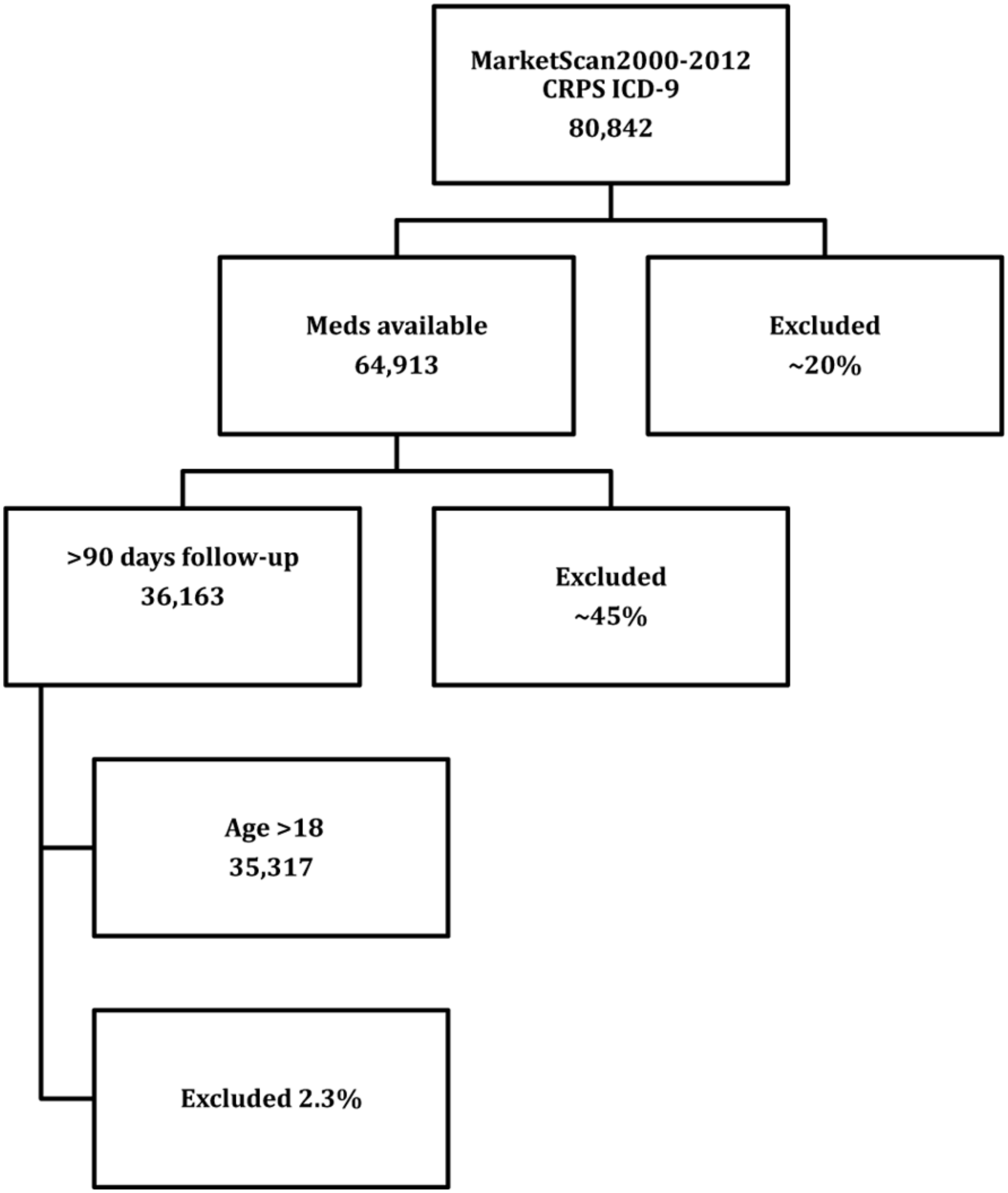

Figure 1.
Consort Diagram

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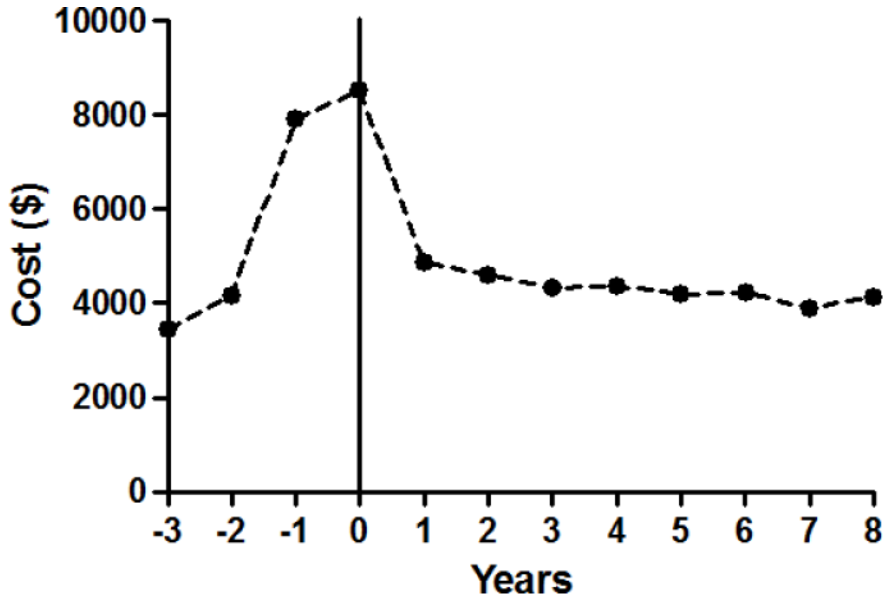

Figure 2.
Annual Median Total Costs Prior and After CRPRS Diagnosis

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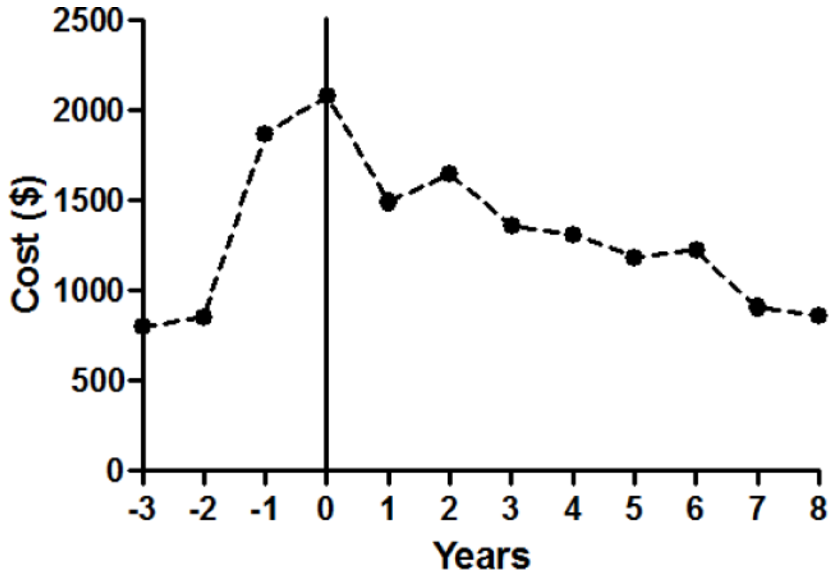

Figure 3.
Annual Median Pain Prescription Costs Prior and After CRPRS Diagnosis

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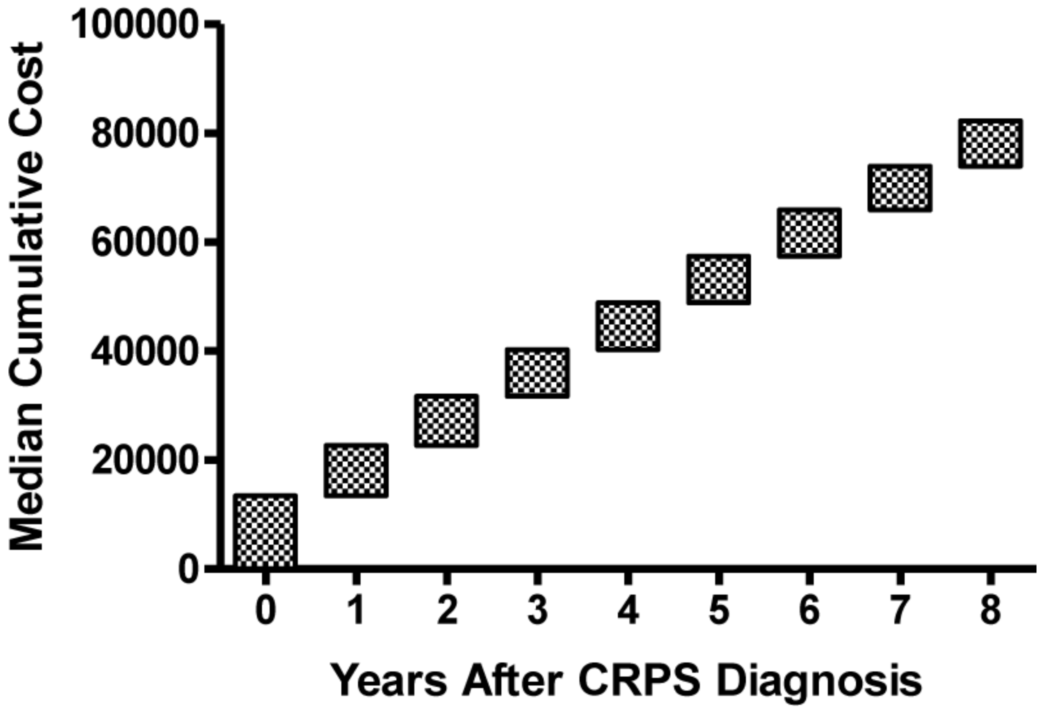

Figure 4.
Cumulative Median Total Cost Per Patient Overtime Post-CRPS Diagnosis

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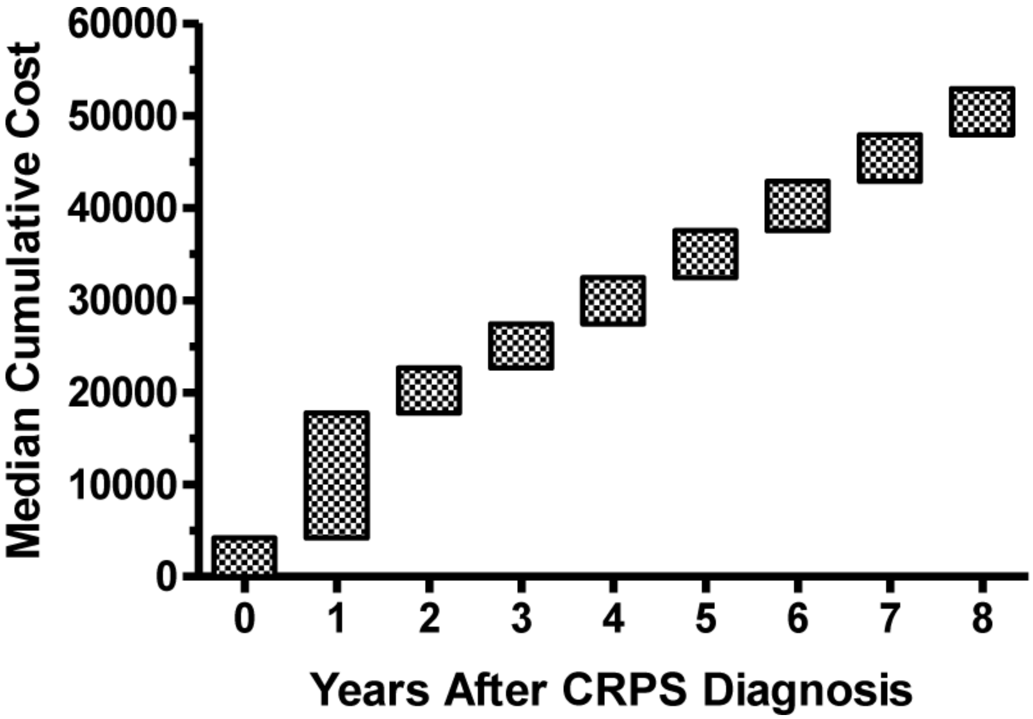

Figure 5.
Cumulative Median Pain Prescription Per Patient Overtime Post-CRPS Diagnosis

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Table 1

Patient Demographics and Years of Claims

Variable	Both (N=2014)	CRPSI (N=18703)	CRPSII (N=14599)	Total (N=35316)
Gender n(%)				
Male	577 (28.6%)	5733 (30.7%)	5197 (35.6%)	11507 (32.6%)
Female	1437 (71.4%)	12970 (69.3%)	9402 (64.4%)	23809 (67.4%)
Age (Year) at first diagnosis				
Mean (SD)	49.6 (12.8)	52.5 (13.9)	57.0 (14.4)	54.2 (14.2)
Employment Status				
Active Full Time	590 (29.3%)	4695 (25.1%)	3273 (22.4%)	8558 (24.2%)
Early Retiree	144 (7.1%)	1404 (7.5%)	1146 (7.8%)	2694 (7.6%)
Medicare Eligible Retiree	156 (7.7%)	2271 (12.1%)	2648 (18.1%)	5075 (14.4%)
Long Term Disability	39 (1.9%)	288 (1.5%)	92 (0.6%)	419 (1.2%)
Insurance Status				
Commercial Claims	1375 (68.3%)	11504 (61.5%)	8470 (58.0%)	21349 (60.5%)
Medicaid	425 (21.1%)	4132 (22.1%)	2310 (15.8%)	6867 (19.4%)
Medicare	214 (10.6%)	3067 (16.4%)	3819 (26.2%)	7100 (20.1%)
Diagnosis Year				
2001	50 (2.5%)	316 (1.7%)	151 (1.0%)	517 (1.5%)
2002	66 (3.3%)	596 (3.2%)	297 (2.0%)	959 (2.7%)
2003	127 (6.3%)	978 (5.2%)	595 (4.1%)	1700 (4.8%)
2004	125 (6.2%)	1480 (7.9%)	739 (5.1%)	2344 (6.6%)
2005	177 (8.8%)	1620 (8.7%)	1049 (7.2%)	2846 (8.1%)
2006	162 (8.0%)	1468 (7.8%)	1164 (8.0%)	2794 (7.9%)
2007	198 (9.8%)	1655 (8.8%)	1557 (10.7%)	3410 (9.7%)
2008	211 (10.5%)	1852 (9.9%)	1655 (11.3%)	3718 (10.5%)
2009	251 (12.5%)	2308 (12.3%)	2031 (13.9%)	4590 (13.0%)
2010	147 (7.3%)	1456 (7.8%)	1145 (7.8%)	2748 (7.8%)
2011	306 (15.2%)	2856 (15.3%)	2250 (15.4%)	5412 (15.3%)
2012	194 (9.6%)	2118 (11.3%)	1966 (13.5%)	4278 (12.1%)

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Table 2

Annual Costs 3-Years Pre-CRPS Diagnosis and 8-Years Post-CRPS Diagnosis

Variable-Median [IQR]	Total Costs	Outpatient Costs	Pain Prescription Costs
3 Years Prior (n=23,771)	3437 [929, 8808]	3010 [873, 7180]	797 [1, 5045]
2 Years Prior (n=34,680)	4160 [1251, 10227]	3613 [1164, 8203]	853 [20, 5207]
1 Year Prior (n=35,235)	7904 [3469, 16084]	6706 [3119, 12715]	1862 [147, 7649]
Diagnosis Year (n=35,316)	8508 [3943, 16666]	7251 [3527, 13568]	2077 [140, 8856]
1 Year (n=26501)	4845 [1582, 11432]	4212 [1465, 9241]	1488 [37, 8734]
2 Years (n=18089)	4598 [1505, 11083]	4028 [1383, 9014]	1644 [38, 10186]
3 Years (n=13488)	4324 [1313, 10545]	3756 [1214, 8747]	1357 [15, 10072]
4 Years (n=9393)	4351 [1296, 10664]	3742 [1184, 8565]	1307 [18, 10711]
5 years (n=6629)	4175 [1301, 10647]	3637 [1173, 8386]	1182 [0, 11031]
6 Years (n=4445)	4205 [1252, 10385]	3608 [1133, 8521]	1222 [0, 11287]
7 Years (n=2926)	3888 [1038, 9887]	3354 [923, 7839]	904 [0, 10237]
8 Years (n=1712)	4132 [1171, 9787]	3429 [1032, 7969]	857 [0, 10262]

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Table 3

Multivariate regression on Total Cost

Covariate	Level	Cost- Ratio	95% Confidence Interval	P-value
CRPS Diagnosis Period	Yes	2.17	(2.15, 2.20)	<.001*
	No	Reference		
Year After CRPS Diagnosis	Yes	1.01	(0.99, 1.03)	0.356*
	No	Reference		
Age in Decade Year		0.98	(0.97, 0.99)	<.001*
Gender of Patient	Female	1.19	(1.17, 1.22)	<.001*
	Male	Reference		
Insurance Source of Claims	Medicare	0.87	(0.84, 0.89)	<.001*
	Medicaid	0.58	(0.56, 0.60)	<.001*
	Commercial	Reference		
Employment Status	Long Term Disability	1.33	(1.22, 1.45)	<.001*
	Other	0.99	(0.96, 1.01)	0.340
	Retiree/Medicare Eligible Retiree	1.00	(0.98, 1.03)	0.763
	FT/PT	Reference		
Prior Charlson comorbidity score		1.21	(1.20, 1.21)	<.001*
Calendar Year		1.03	(1.02, 1.03)	<.001*

*** Full Time/Part Time: 1-Active Full Time 2-Active Part Time or Seasonal

Retiree/Medicare Eligible: 3-Early Retiree 4-Medicare Eligible Retiree 5-Retiree (status unknown)

Disabled: 7-Long Term Disability

Other: 6-COBRA Continue 8-Surviving Spouse/Depend 9-Other/Unknown

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Table 4

Multivariate regression on Pain Prescription Costs

Covariate	Level	Cost- Ratio	95% Confidence Interval	P-value
CRPS Diagnosis Period	Yes	2.56	(2.51, 2.62)	<.001*
	No	Reference		
Year After CRPS Diagnosis	Yes	1.06	(1.02, 1.10)	0.008*
	No	Reference		
Age in Decade Year		0.79	(0.77, 0.81)	<.001*
Gender of Patient	Female	1.46	(1.37, 1.56)	<.001*
	Male	Reference		
Insurance Source of Claims	Medicare	1.23	(1.14, 1.34)	<.001*
	Medicaid	0.41	(0.37, 0.44)	<.001*
	Commercial	Reference		
Employment Status	Long Term Disability	2.58	(2.14, 3.12)	<.001*
	Other	0.50	(0.46, 0.53)	<.001*
	Retiree/Medicare Eligible/Disabled	1.76	(1.63, 1.91)	<.001*
	FT/PT	Reference		
Prior Charlson comorbidity score		1.11	(1.09, 1.13)	<.001*
Calendar Year		0.91	(0.90, 0.92)	<.001*

*** Full Time/Part Time: 1-Active Full Time 2-Active Part Time or Seasonal

Retiree/Medicare Eligible: 3-Early Retiree 4-Medicare Eligible Retiree 5-Retiree (status unknown)

Disabled: 7-Long Term Disability

Other: 6-COBRA Continue 8-Surviving Spouse/Depend 9-Other/Unknown