Pain Medicine, 0(0), 2019, 1–11
doi: 10.1093/pm/pnz030
Original Research Article

Direct Health Care Cost and Work Incapacity Related to Complex Regional Pain Syndrome in Switzerland: A Retrospective Analysis from 2008 to 2015

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Funding sources: No funding was received for this study.

Conflicts of interest: The authors declare that they have no competing interests.

Abstract

Objective. First, to determine the number of accident-related complex regional pain syndrome (CRPS) cases from 2008 to 2015 and to identify factors associated with an increased risk for developing CRPS. Second, to analyze the duration of work incapacity and direct health care costs over follow-up periods of two and five years, respectively. **Design**. Retrospective data analysis. **Setting**. Database from the Statistical Service for the Swiss National Accident Insurances covering all accidents insured under the compulsory Swiss Accident Insurance Law. **Subjects**. Subjects were registered after an accident between 2008 and 2015. **Methods**. Cases were retrospectively retrieved from the Statistical Service for the Swiss National Accident Insurances. Cases were identified using the appropriate International Classification of Diseases, 10th Revision, codes. **Results**. CRPS accounted for 0.15% of all accident cases. Age, female gender (odds ratio [OR] = 1.53, 95% confidence interval [CI] = 1.47–1.60), and fracture of the forearm (OR = 38, 95% CI = 35–42) were related to an increased risk of developing CRPS. Over five years, one CRPS case accumulated average insurance costs of $86,900 USD and treatment costs of $23,300 USD. Insurance costs were 19 times and treatment costs 13 times the average costs of accidents without CPRS. Within the first two years after the accident, the number of days lost at work was 20 times higher in patients with CRPS (330 ± 7 days) than in patients without CRPS (16.1 ± 0.1 days). Two-thirds of all CRPS cases developed long-term work incapacity of more than 90 days. **Conclusion**. CRPS is a relatively rare condition but is associated with high direct health care costs and work incapacity.

Key Words: Complex Regional Pain Syndrome; Direct Health Care Costs; Work Incapacity

Introduction

Complex regional pain syndrome (CRPS) is a painful condition that usually appears on a distal extremity within six weeks after an initiating noxious event such as trauma or surgery [1]. Typically, signs and symptoms exceed the expected clinical course of the inciting event in magnitude and duration, often resulting in significant impairment of motor function. Clinical manifestations encompass a broad spectrum of signs and symptoms, including sensory, vasomotor, sudomotor, motor, and trophic changes [2]. Because of the broad spectrum of clinical manifestations, the diagnosis is often delayed and solely based on clinical signs and symptoms (Budapest criteria) [3]. Therapy is symptom based and includes a

variety of pharmacological, interventional, physiotherapeutic, occupational, and psychiatric treatment options.

CRPS represents a relatively rare disease and accounts for approximately 1.2% of chronic pain diagnoses in the United States [4]. The incidence ranges between 5.46 to 26.2 per 100,000 person-years, affecting mainly women in the age range of 46–70 years [5, 6]. Although many CRPS patients reach partial remission within three months after onset [7], numerous patients develop a chronic condition, with persisting complaints even after one year [8–11]. The patient burden in those patients suffering from the disease is high and is associated with substantial medical costs [12, 13]. CRPS is considered an expensive condition [14]. However, in the literature, limited data are available on health care costs associated with CRPS [15–17].

The aim of this study was twofold. First, we set out to determine the number of accident-related CRPS cases in Switzerland from 2008 to 2015 and to identify factors associated with an increased risk for developing CRPS in this population. Second, we aimed to calculate the direct health care costs and to analyze the duration of work incapacity over a five-year follow-up period after registration of the accident.

Methods

Data Source

Cases were retrospectively retrieved from the Statistical Service for the Swiss National Accident Insurances (SSUV) in Switzerland. The SSUV is an institution under the Federal Statistics Act and obligatorily receives data and information from all accident insurers. This registry covers all accidents insured under the compulsory Swiss Accident Insurance Law (UVG), at work as well as leisure time accidents, and is legally based on the Ordinance on Accident Insurance Statistics (VSUV). Since its inception in 1984, the core data set comprises approximately 700,000 accidents per year.

A representative sample of the cases in the database is linked to a medical diagnosis. This sample is stratified by a complete inventory of all cases leading to a disability pension and a 5% random sample of all other cases. The sampling procedure is described in more detail in the Appendix or in another publication (for German-speaking readers) [18]. Weighting or projection factors in the range from 1 to 20 are used to extrapolate the roughly 40,000 cases per year in the representative sample back to the core data set of 700,000 accidents per year.

The diagnoses were classified according to the International Classification of Diseases, 10th Revision (ICD-10), by a specialized coding team within SSUV. The main diagnosis of the cases was used, and cases with CRPS were identified by an additional M89.0 diagnosis code. Sociodemographic information on age (at the time of the accident) and gender was retrieved from the database as well. Acknowledged cases with registration years from 2008 to 2015 represented the base set for this study.

Direct Health Care Costs

Direct health care costs after accidents are fully covered by the accident insurers and included hospital care, medical procedures, medical specialist fees, ambulatory hospital care, general practice care, and paramedical care. Total insurance expenditures include health care and treatment costs, as well as allowances (for temporary incapacity to work) and pensions (for permanent incapacity to work).

After an accident, the costs often accumulate over an extended period of time. Financial reserves for pensions account for a substantial share of the total costs and are generally registered within five years after the accident. Therefore, we measured the health care and treatment costs as well as total insurance expenses over a five-year period after registration of the accident (2008–2010).

The costs were calculated in Swiss Francs (CHF) and are presented in US dollars using the average exchange rate from 2008 to 2015 (1 CHF = $1,028 USD).

Work Incapacity

The duration of accident-related work incapacity (number of days lost from work) was determined from insurance expenditure data within the first two years after registering the accident. For the work incapacity, two years of follow-up was chosen because the majority of the patients return to work within the first two years after an accident. After more than two years, the likelihood of returning to work is negligible. Therefore, this analysis included cases that were registered from 2008 to 2014. Depending on the number of lost days at work, cases were grouped into "long-term cases" (>90 days) and "very long-term cases" (>360 days).

Data Analysis and Statistics

Characteristics of the sample were examined using descriptive statistics. Age distribution is reported as mean ± SD, gender or long-term cases as absolute number and percentage. For quantities like days lost and costs, mean values, standard errors, and medians and interquartile ranges (IQRs) were calculated and rounded according to the precision given by the standard error. The significance of differences between groups was tested with the *t* test, and costs were log-transformed for this. Cases with total health care expenditures of less than 100 CHF were omitted from the cost analysis.

The main diagnosis groups were formed in order to have a minimum of 80 cases per analyses subgroup. The diagnosis groups are summarized in the Appendix.

The probability of developing CRPS was analyzed through logistic regression. The input parameters age,

Table 1. Number of registered accidents with and without CRPS (raw cases, unweighted) and extrapolation for total of incidences (weighted for projection for all accidents)

	Total		Without CRPS		With CRPS	
	Unweighted	Extrapolated	Unweighted	Extrapolated	Unweighted	Extrapolated
Total	324,544	6,033,531	322,870	6,024,599	1,674	8,932
Year						
2008	40,877	731,052	40,541	729,842	336	1,210
2009	41,291	741,289	40,977	740,044	314	1,245
2010	41,405	751,093	41,117	749,836	288	1,257
2011	41,747	761,486	41,472	760,280	275	1,206
2012	40,857	753,680	40,660	752,514	197	1,166
2013	40,439	764,548	40,292	763,546	147	1,002
2014	39,061	758,895	39,002	758,209	59	686
2015	38,867	771,488	38,809	770,328	58	1,160
Main diagnosis						
Injury of muscle, fascia, and tendon at shoulder and upper arm level (S46)	7,300	89,532	7,219	89,280	81	252
Other injuries to the shoulder and upper arm (S4x)	19,819	366,132	19,743	365,885	76	247
Fracture of the forearm (S52)	4,005	65,090	3,757	63,816	248	1274
Fracture at wrist and hand level (S62)	7,436	138,859	7,297	138,017	139	842
Dislocation and sprain of joints and ligaments at wrist and hand level (S63)	11,345	213,847	11,205	213,232	140	615
Other injuries to the wrist, hand, and fingers (S6x)	46,941	912,410	46,752	911,366	189	1,044
Fracture of lower leg, including ankle (S82)	5,382	808,88	5,215	80,018	167	870
Dislocation and sprain of joints and ligaments of knee (S83)	20,302	373,493	20,230	372,946	72	547
Fracture of foot and toe (S92)	7,200	128,420	7,044	127,371	156	1,049
Dislocation and sprain of joints and ligaments at ankle, foot, and toe level (S93)	28,608	560,741	28,486	559,840	122	901
Other	166,206	3,104,119	165,922	3,102,828	284	1,291
Age category, y						
0–19	29,485	576,571	29,472	576,425	13	146
20–29	78,880	1,522,557	78,725	1,521,452	155	1,105
30–39	69,825	1,322,210	69,538	1,320,783	287	1,427
40–49	72,151	1,327,348	71,635	1,324,913	516	2,435
50–59	56,377	987,738	55,824	984,658	553	3,080
60–99	17,487	290,555	17,337	289,816	150	739
N/A	339	6,552	339	6,552		
Gender						
Male	218,365	4,012,703	217,419	4,008,223	946	4,480
Female	106,179	2,020,828	105,451	2,016,376	728	4,452
Subset						
2008–2014	285,677	5,262,043	284,061	5,254,271	1,616	7,772

CRPS = complex regional pain syndrome.

age^2 (for nonlinear relationships), year of registration, gender, and main diagnosis group were added stepwise to the model with a 0.05 significance level as the entry threshold.

To avoid offset effects, age was taken as the difference with respect to a reference age of 40 years for regression analysis. For the same reason, we used the year of registration 2010 as a zero reference point in regression calculations.

Differences in the percentage of long-term cases and very long-term cases due to CRPS were tested by a χ^2 test.

SAS 9.2 software was used for statistical analysis throughout the study, and a significance level of 0.05 was used.

Ethic Consideration

Data were anonymized by independent institutions (insurers) not involved in the project and separated in time and location. The database extraction did not include any personal identifiers (insurance number, name, date of birth, or address) and required no additional manipulation. The data did not contain names, addresses, social security numbers, or the like, and the information contained did not allow conclusions about the accident victims. The access is strictly restricted to scientific employees of the SSUV. Only aggregated information was issued by the SSUV. This study was submitted to the local ethics committee, which declared no objection (reference number 2018–00147).

Table 2. Age and gender of accident victims with and without CRPS.

	Age of Accident Victims, y					Percentage of Female Accident Victims		
	Without CRPS		With CRPS					
	Mean	SD	Mean	SD	*P*	Without CRPS	With CRPS	*P*
Total	37.6	13.3	45.5	11.8	<0.001	33.5	49.8	<0.001
Main diagnosis								
Injury of muscle, fascia, and tendon at shoulder and upper arm level (S46)	46.6	12.2	52.2	9.6	<0.001	22.9	30.6	<0.001
Other injuries to the shoulder and upper arm (S4x)	39.5	13.4	51.8	12.0	<0.001	31.3	54.7	<0.001
Fracture of the forearm (S52)	41.8	14.3	50.2	8.7	<0.001	47.8	70.4	<0.001
Fracture at wrist and hand level (S62)	36.1	13.4	46.2	13.2	<0.001	23.8	39.8	<0.001
Dislocation and sprain of joints and ligaments at wrist and hand level (S63)	36.3	13.5	43.9	10.5	<0.001	35.3	57.6	<0.001
Other injuries to the wrist, hand, and fingers (S6x)	36.5	13.1	43.9	12.7	<0.001	32.6	56.6	<0.001
Fracture of lower leg, including ankle (S82)	41.5	13.6	45.6	11.2	<0.001	39.8	39.0	<0.001
Dislocation and sprain of joints and ligaments of knee (S83)	38.8	12.9	42.9	10.0	<0.001	31.6	32.2	0.19
Fracture of foot and toe (S92)	39.4	13.0	48.6	9.4	<0.001	46.9	58.8	0.08
Dislocation and sprain of joints and ligaments at ankle, foot, and toe level (S93)	34.9	12.7	41.7	11.4	<0.001	38.6	53.3	<0.001
Other	37.7	13.2	41.3	12.9	<0.001	32.9	34.9	<0.001

CRPS = complex regional pain syndrome.

Table 3. Logistic regression estimates for risk of developing CRPS (multiple logistic regression model) and odds ratios*

	Estimate	SE	*P*	Standardized Estimate	OR (95% CI)
Parameter					
Intercept	–8.366	0.074	<0.0001	–	
Age	0.119	0.005	<0.0001	3.76	1.127 (1.117–1.137)
Age^2	–0.122	0.007	<0.0001	–2.31	0.885 (0.873–0.896)
Year of registration	–0.062	0.005	<0.0001	–0.34	0.940 (0.932–0.949)
Female gender	0.425	0.022	<0.0001	0.48	1.53 (1.47–1.6)
Main diagnosis					
Injury of muscle, fascia, and tendon at shoulder and upper arm level (S46)	–0.155	0.059	0.0084	–0.19	5.4 (4.7–6.1)
Other injuries to the shoulder and upper arm (S4x)	–1.418	0.059	<0.0001	–2.05	1.51 (1.32–1.73)
Fracture of the forearm (S52)	1.816	0.029	<0.0001	2.25	38.4 (35.5–41.6)
Fracture at wrist and hand level (S62)	0.953	0.034	<0.0001	1.23	16.2 (14.8–17.7)
Dislocation and sprain of joints and ligaments at wrist and hand level (S63)	0.147	0.039	0.0001	0.20	7.2 (6.6–8.0)
Other injuries to the wrist, hand, and fingers (S6x)	–0.771	0.031	<0.0001	–1.34	2.89 (2.66–3.14)
Fracture of lower leg, including ankle (S82)	1.257	0.033	<0.0001	1.57	21.9 (20.1–23.9)
Dislocation and sprain of joints and ligaments of knee (S83)	–0.618	0.041	<0.0001	–0.90	3.4 (3.0–3.7)
Fracture of foot and toe (S92)	1.023	0.031	<0.0001	1.32	17.4 (16.0–18.9)
Dislocation and sprain of joints and ligaments at ankle, foot, and toe level (S93)	–0.401	0.033	<0.0001	–0.62	4.2 (3.8–4.6)

CI = confidence interval; CRPS = complex regional pain syndrome; OR = odds ratio.

*The odds ratios are calculated as point estimates with a male 40-year-old accident victim with other main diagnoses as the reference point.

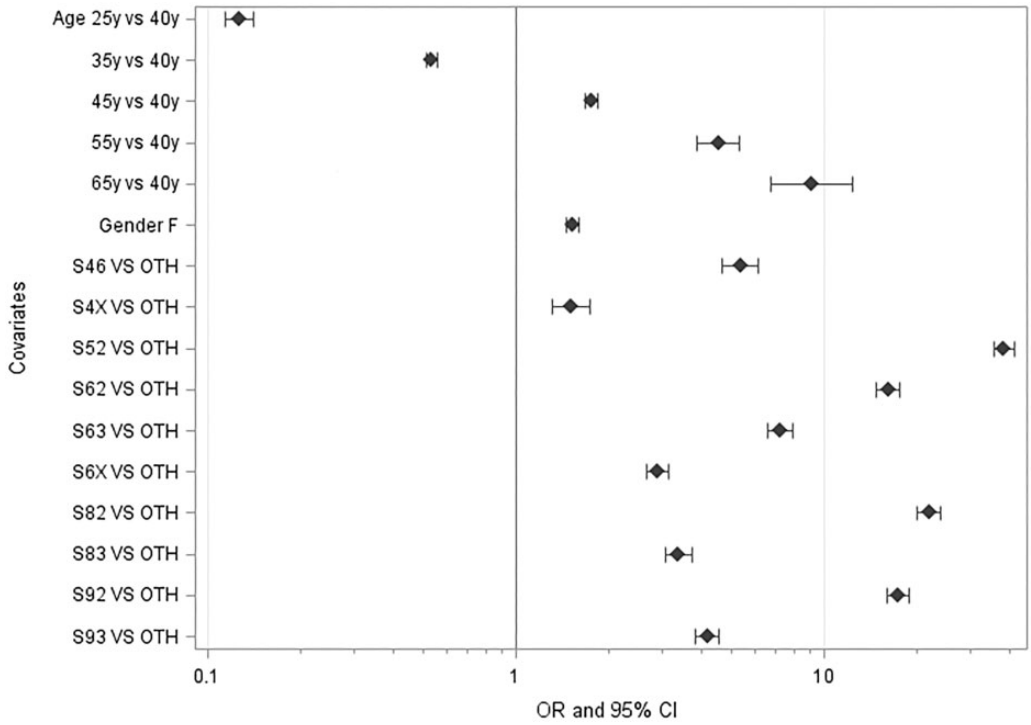

Figure 1. Odds ratios for developing a complex regional pain syndrome, with 95% confidence intervals.

CI = confidence interval; OR = odds ratio; OTH = other.

S46 Injury of muscle, fascia, and tendon at shoulder and upper arm level

S4x Other injuries to the shoulder and upper arm

S52 Fracture of forearm

S62 Fracture at wrist and hand level

S63 Dislocation and sprain of joints and ligaments at wrist and hand level

S6x Other injuries to the wrist, hand, and fingers

S82 Fracture of lower leg, including ankle

S83 Dislocation and sprain of joints and ligaments of knee

S92 Fracture of foot and toe, except ankle

S93 Dislocation and sprain of joints and ligaments at ankle, foot, and toe level

Other Other main diagnoses not mentioned above

Results

Incidence and Demographics

A total of 324,544 accidents were retrieved from the registry and extrapolated to just over 6 million accidents. Between 2008 and 2015, the number of CRPS cases was projected at 8,932 (or 0.15% of the accidents). The incidence of CRPS was stable or slightly decreasing (except for the year 2014). Among CRPS patients, fracture of the forearm (S52) represented the most frequent main diagnosis. Two-thirds of all accidents affected men, and the number of CRPS cases was equal for both sexes. For details, see Table 1.

Patients with CRPS were substantially older than patients without CRPS. Overall, women showed a significantly higher propensity to develop CRPS (Table 2).

Factors Associated with an Increased Risk for CRPS

Multivariate logistic regression revealed a strong correlation between developing CRPS and patient characteristics or trauma diagnosis. Besides age (point estimate for odds ratio [OR] = 1.13, 95% confidence interval [CI] = 1.12–1.14 at the age of 40 years), female gender seems to be a major risk factor (OR = 1.53, 95% CI = 1.47–1.60) for CRPS. Fracture of the forearm (S52) represented the diagnosis with the highest probability to develop CRPS

Table 4. Number of cases, insurance, and treatment costs for a five-year follow-up after registration

	No. of Cases Extrapolated		Insurance Costs, Mean ± SE, $ USD		Treatment Costs, Mean ± SE, $ USD	
	Without CRPS	With CRPS	Without CRPS	With CRPS	Without CRPS	With CRPS
Total (2008–2010)	2,114,516	3,552	4,640 ± 20	86,900 ± 2,800	1,820 ± 10	23,300 ± 600
Main diagnosis						
Injuries to the shoulder and upper arm (S4x, including S46)	159,180	123	9,700 ± 100	180,000 ± 18,000	3,230 ± 20	38,000 ± 3,000
Fracture of the forearm (S52)	23,452	366	12,900 ± 200	84,000 ± 6,000	5,010 ± 60	21,500 ± 1,100
Fracture at wrist and hand level (S62)	49,991	495	6,890 ± 80	58,000 ± 5,000	2,360 ± 20	15,300 ± 1,000
Dislocation and sprain of joints and ligaments at wrist and hand level (S63)	76,506	242	3,460 ± 70	128,000 ± 11,000	1,110 ± 10	32,000 ± 2,000
Other injuries to the wrist, hand, and fingers (S6x)	322,541	443	1,620 ± 20	66,000 ± 7,000	644 ± 4	13,500 ± 1,100
Fracture of lower leg, including ankle (S82)	27,257	352	24,200 ± 300	82,000 ± 7,000	11,000 ± 100	24,300 ± 1,500
Dislocation and sprain of joints and ligaments of knee (S83)	134,226	320	8,820 ± 60	55,000 ± 4,000	3,910 ± 20	20,200 ± 1,000
Fracture of foot and toe (S92)	41,407	418	6,600 ± 100	99,000 ± 9,000	2,210 ± 30	33,000± 3,000
Dislocation and sprain of joints and ligaments at ankle, foot, and toe level (S93)	195,556	279	2,400 ± 30	68,000 ± 7,000	1,030 ± 10	18,400 ± 1,400
Others	1,084,400	514	3,920 ± 40	117,000 ± 12,000	1,570 ± 10	29,000 ± 2,000

CRPS = complex regional pain syndrome.

(OR = 38, 95% CI = 35–42, with respect to the reference group). For details, refer to Table 3 and Figure 1.

Direct Health Care Costs

Over a five-year period after registration of the accident, the insurance companies spent on average $86,900 USD on insurance costs and $23,300 USD on treatment costs on a single CRPS case. These expenses were 19 times (insurance costs) and 13 times (treatment costs) as high as the costs of a case without CRPS.

The average insurance cost for a case with the same diagnosis and the presence of CRPS was three times (other injuries and sprain of joints and ligaments at wrist and hand level [S6x]) to 41 times (fracture at wrist and hand level [S62]) the cost of a case without CRPS.

The average treatment costs for a case with CRPS were two times (other injuries of the wrist, hand, and fingers [S6x]) to 21 times (fracture at wrist and hand level [S62]) the costs of a case without a CRPS. For details see Table 4 and Figures 2 and 3.

Work Incapacity

Within the first two years after registration of the accident, the number of lost days at work was 20 times higher in patients with CRPS (mean ± SD = 330 ± 7 days) than in patients without CRPS (mean ± SD = 16.1 ± 0.1 days) independent of the diagnosis. For all diagnosis groups, the proportion of long-term absence was substantially higher in the CRPS group. In particular, patients developing CRPS after injuries of the upper limb revealed the highest number of lost days (diagnosis codes S46 [681 ± 45 days] and S63 [mean ± SD = 526 ± 30 days]). Sixty-eight percent of all CRPS cases developed a long-term absence (>90 days), and a quarter of these cases accounted for a very long-term absence (>360 days). For details, refer to Table 5.

Discussion

Main Findings

The results of this study show that CRPS is a relatively rare condition but represents a high economic burden on the health care system. From 2008 to 2015, CRPS accounted for 0.15% of all accident cases covered by the compulsory accident insurance in Switzerland. Factors associated with an increased risk to develop CRPS were age, female gender, and fracture of the forearm. Over a five-year follow-up, the average insurance cost for a case with the same diagnosis was 19 times higher if CRPS was present. There was an increase in treatment costs by factors of 2–20 for cases with CRPS compared with cases without CRPS. Within the first two years after registration of the accident, the number of lost days at work was 20 times higher in patients with CRPS than in patients without CRPS. Two-thirds of all CRPS cases developed a long-term absence of more than 90 days.

Results in the Light of the Literature

Similar to our study, two population-based studies found that CRPS represents a rare condition, mostly affecting middle-aged women and typically occurring after a fracture of the forearm [5, 6]. The high proportion of male

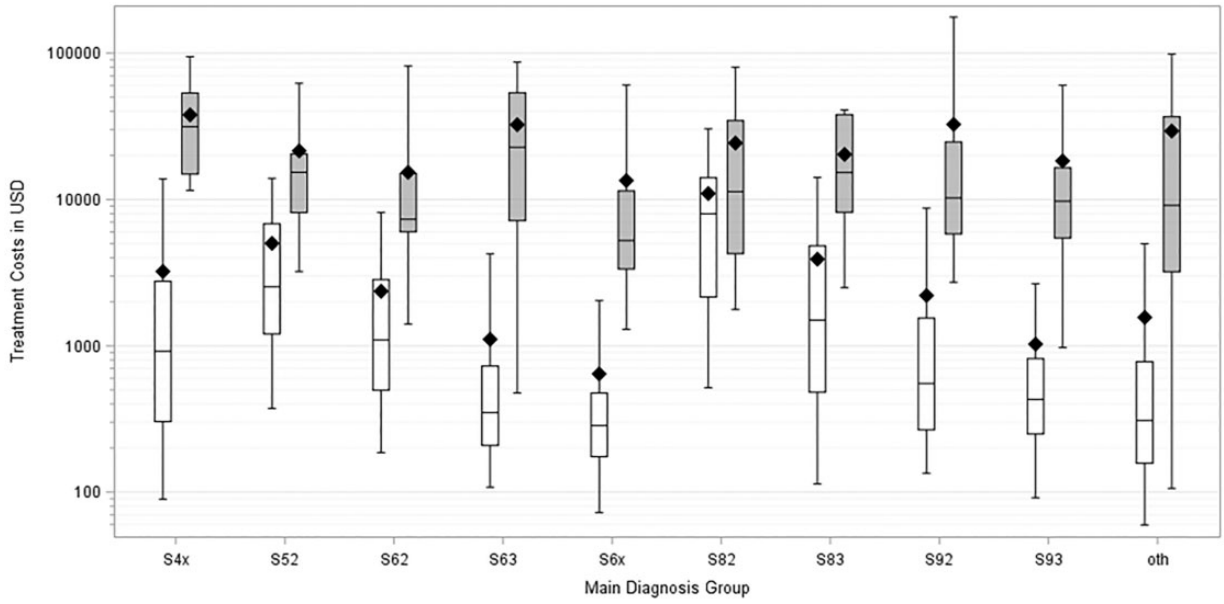

Figure 2. Treatment cost of accidents of registration years 2008–2011 after five-year follow-up. Mean values (diamonds) and median with quartiles (box) and 5% and 95% percentiles (whiskers) are shown for cases with (gray) and without (white) complex regional pain syndrome.

S46	Injury of muscle, fascia, and tendon at shoulder and upper arm level
S4x	Other injuries to the shoulder and upper arm
S52	Fracture of forearm
S62	Fracture at wrist and hand level
S63	Dislocation and sprain of joints and ligaments at wrist and hand level
S6x	Other injuries to the wrist, hand, and fingers
S82	Fracture of lower leg, including ankle
S83	Dislocation and sprain of joints and ligaments of knee
S92	Fracture of foot and toe, except ankle
S93	Dislocation and sprain of joints and ligaments at ankle, foot, and toe level
Other	Other main diagnoses not mentioned above

accident victims in our study is most likely due to the higher proportion of male employees in the Swiss workforce covered by the compulsory health insurance (www.unfallstatistik.ch). Whereas Sandroni et al. [6] found a high resolution rate, our study showed the significant impact of CRPS on direct health care costs and patients' likelihood to return to work. We explain this discrepancy primarily by using different case definitions and diagnostic criteria. The study of Sandroni and colleagues retrospectively applied the International Association for the Study of Pain criteria to information from electronic medical records. We also used a retrospective approach, but the diagnosis was based on the appropriate ICD-10 code (M89.0) from a national registry including all accidents insured under the compulsory Swiss Accident Insurance Law. Moreover, potential differences in population characteristics (e.g., ethnicity, incidence of accidents) might also contribute to this inconsistency.

In 2014, Bean et al. examined the outcome of CRPS in a systematic review [8]. Whereas the three prospective studies indicated a favorable outcome with a high recovery rate within six to 13 months, the 12 retrospective studies documented lasting impairment in many patients. The authors explained this discrepancy by the highly heterogeneous results, with ratings as low as 22% and as high as 90% for those who continue to have symptoms at long-term follow-up.

To date, limited data on CRPS-related direct health care costs and work incapacity are available from the literature. Due to the different health systems, a direct comparison with our results is only possible to a limited extent. Our cost analysis suggests an exacerbation of costs and work incapacity in the presence of CRPS, which is in line with previous reports. A retrospective database analysis was mainly based on commercial insurance data in the United States and included 35,316

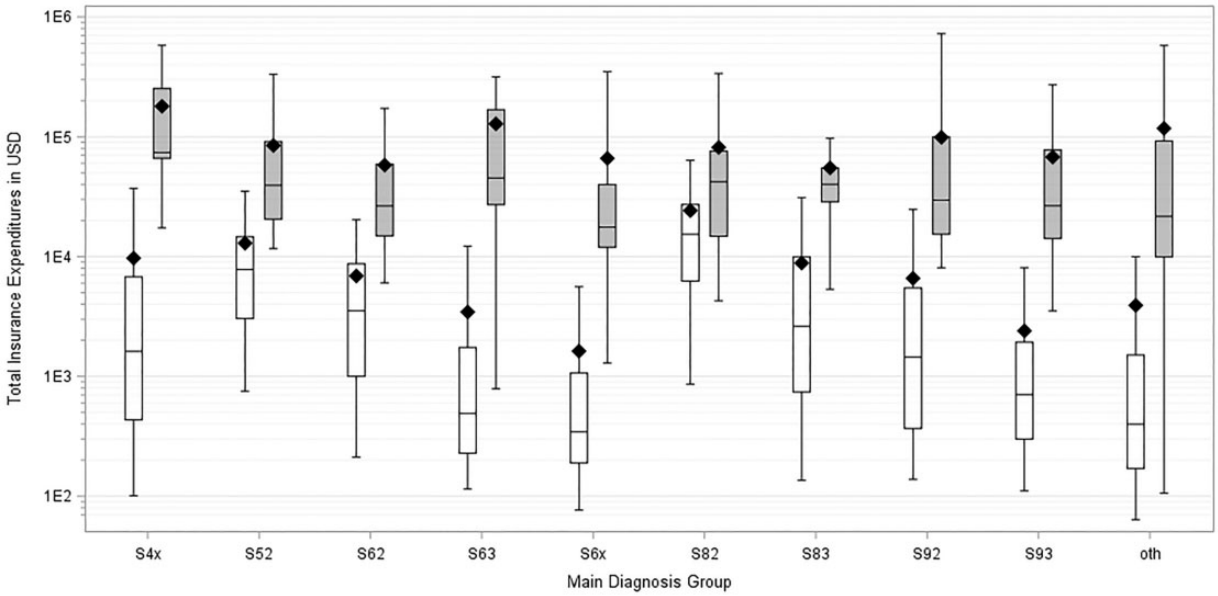

Figure 3. Total insurance expenditures per case of accidents of registration years 2008–2011 after five-year follow-up. Mean values (diamonds) and median with quartiles (box) and 5% and 95% percentiles (whiskers) are shown for cases with (gray) and without (white) complex regional pain syndrome.

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Other	Other main diagnoses not mentioned above

patients or 25% of employed workers with a new diagnosis of CRPS. Over an eight-year period, the annual costs ranged between $3,888 USD and $4,845 USD per case, and the median total cumulative cost after eight years ranged from $12,037 USD to $43,026 USD [15]. Kemler et al. determined that CRPS patients receiving conventional medical management (without spinal cord stimulation) accrued costs of £79,775 British pounds over a period of 15 years [17]. In another study, the same author calculated annual routine costs at baseline of €5,741 euros in 1998 [16]. The data of this study cover almost half of the country's population. Therefore, the results of our study further expand the knowledge on the working population and suggest that once CRPS is diagnosed, more than 60% will develop a long-term absence (>90 days) and 25% a very long-term absence (>360 days).

Previous studies have also confirmed our findings that CRPS is often associated with a significant work loss. In Turkey, almost one-third of patients with CRPS do not return to work [12]. In a retrospective chart review of 134 CRPS patients from the United States, over half of all patients were involved in worker compensation claims [19]. However, to the best of our knowledge, our study compares for the first time the work incapacity between patients with and without CRPS.

Strengths and Limitations

In Switzerland, it is compulsory for every citizen to procure health insurance, and it is mandatory for the insurer to report all accident cases to the SSUV national database. Therefore, the major strength of this study is the analysis of a comprehensive and complete data set of accident cases in Switzerland. The SSUV registry covers the accidents of approximately 4 million employees (almost half of the country's

Table 5. Cases between 2008 and 2014 with and without CRPS by main diagnosis, with the number of cases, the number of days lost, and the percentage of long-term (>90 days) and very long-term (>360 days) cases

	No. of Cases Extrapolated		Work Loss, Mean ± SE, d		Percentage of Long-term Cases		Percentage of Very Long-term Cases	
	Without CRPS	With CRPS	Without CRPS	With CRPS	Without CRPS	With CRPS	Without CRPS	With CRPS
Total 2008–2014	5,254,271	7,772	16.1 ± 0.1	330 ± 7	3.8	68.3	0.6	27.0
Main diagnosis								
Injury of muscle, fascia, and tendon at shoulder and upper arm level (S46)	76,998	192	103.8 ± 1.2	681 ± 45	28.9	100.0	5.8	75.0
Other injuries to the shoulder and upper arm (S4x)	319,221	227	23.7 ± 0.2	470 ± 53	5.9	73.1	0.7	40.5
Fracture of the forearm (S52)	54,895	1,094	57.7 ± 0.7	426 ± 20	15.2	73.9	1.7	29.4
Fracture at wrist and hand level (S62)	120,272	742	34.8 ± 0.3	232 ± 13	6.9	64.3	0.7	15.6
Dislocation and sprain of joints and ligaments at wrist and hand level (S63)	187,832	555	15.6 ± 0.3	526 ± 30	3.1	78.0	0.5	39.5
Other injuries to the wrist, hand, and fingers (S6x)	797,412	944	7.0 ± 0.1	288 ± 19	1.1	65.0	0.1	24.7
Fracture of lower leg, including ankle (S82)	70,415	770	89.3 ± 0.8	274 ± 19	28.1	78.3	3.1	29.0
Dislocation and sprain of joints and ligaments of knee (S83)	323,899	507	33.7 ± 0.2	208 ± 14	9.5	60.2	1.0	10.8
Fracture of foot and toe (S92)	109,489	909	29.8 ± 0.4	368 ± 20	6.8	71.2	0.7	24.8
Dislocation and sprain of joints and ligaments at ankle, foot, and toe level (S93)	489,858	741	11.0 ± 0.1	241 ± 18	1.8	53.8	0.2	21.9
Other	2,703,980	1,091	10.4 ± 0.1	324 ± 19	2.3	60.6	0.5	28.3

A χ^2 test showed significant differences of these percentages with $P < 0.0001$ for all categories.
CRPS = complex regional pain syndrome; oth = other diagnosis.

population). Therefore, our study represents a representative and important sample of the adult working population in Switzerland.

Our study has several limitations. First, as the diagnosis was made by physicians not necessarily specialized in pain or CRPS and the data were acquired retrospectively from an anonymized national database, we were not able to verify the diagnosis of CRPS and the correct coding by the insurer. Second, the setup of the database did not allow us to determine the overall cost of a specific case over more than five years. Third, as the database involved anonymized health-related data, we were not able to analyze any patient or clinical characteristics. Fourth, the diagnosis groups are unrefined and may contain heterogeneous subgroups, which may not be evenly distributed in the CRPS and non-CRPS branches, but the order of magnitude of the observed effects makes it seem unlikely that these differences are entirely due to details of the diagnoses. Lastly, the results of our study are limited to CRPS after an initiating traumatic event and do not include patients with spontaneous onset. Nevertheless, trauma-related CRPS is by far the most common type of CRPS, with only 3–11% of patients reporting spontaneous onset [20].

Implication for Practice

Whereas many patients recover within six to 13 months [8], this study showed the tremendous impact of the disease on work incapacity and the direct health care costs in the working population. Clinicians and insurers should be aware that CRPS is a relatively rare but costly condition and is associated with significant work incapacity.

Implications for Research

Future research should aim at getting a better understanding of the underlying mechanism of CRPS and deriving effective prophylactic and therapeutic measures for this condition. In addition, the available therapies should be assessed for their cost-effectiveness to avoid unnecessary and costly therapies. The associated treatment costs and the impact of work incapacity shown in this study emphasize the relevance of this disease. As long as the causal factors for the initiation and maintaining of CRPS remain unclear, subgroups of patients who respond to a specific treatment should be identified. For example, a network meta-analysis showed that patients with early CRPS responded better to bisphosphonates than patients with persisting symptoms [21]. However, it remains unclear how this treatment effect translates into

clinically important improvement or return to work; this should be further assessed.

Conclusion

CRPS is a relatively rare condition, but it is associated with high direct health care costs and work incapacity.

Acknowledgments

The authors would like to thank Christian Streng for preparing the figures for this publication.

References

1. Merskey H, Bogduk N. Classification of Chronic Pain: Description of Chronic Pain Syndrome and Definitions of Pain Terms. 2nd ed. Seattle: IASP Press; 1994.
2. Harden R, Bruehl S. Diagnostic criteria: The statistical derivation of the four criterion factors. In: Wilson P, Stanton-Hicks M, RN Harden R, eds. CRPS: Current Diagnosis and Therapy. Seattle, WA: IASP Press; 2005:45–58.
3. Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med 2007;8(4):326–31.
4. Murphy KR, Han JL, Yang S, et al. Prevalence of specific types of pain diagnoses in a sample of United States adults. Pain Phys 2017;20(2):E257–E68.
5. de Mos M, de Bruijn AG, Huygen FJ, et al. The incidence of complex regional pain syndrome: A population-based study. Pain 2007;129(1–2):12–20.
6. Sandroni P, Benrud-Larson LM, McClelland RL, Low PA. Complex regional pain syndrome type I: Incidence and prevalence in Olmsted County, a population-based study. Pain 2003;103(1–2): 199–207.
7. Brunner F, Bachmann LM, Perez R, Marinus J, Wertli MM. Painful swelling after a noxious event and the development of complex regional pain syndrome 1: A one-year prospective study. Eur J Pain 2017;21(9): 1611–7.
8. Bean DJ, Johnson MH, Kydd RR. The outcome of complex regional pain syndrome type 1: A systematic review. J Pain 2014;15(7):677–90.
9. Beerthuizen A, Stronks DL, van't Spijker A, et al. Demographic and medical parameters in the development of complex regional pain syndrome type 1 (CRPS1): Prospective study on 596 patients with a fracture. Pain 2012;153(6):1187–92.
10. de Mos M, Huygen FJ, van der Hoeven-Borgman M, et al. Outcome of the complex regional pain syndrome. Clin J Pain 2009;25(7):590–7.
11. Veldman PH, Reynen HM, Arntz IE, Goris RJ. Signs and symptoms of reflex sympathetic dystrophy: Prospective study of 829 patients. Lancet 1993;342 (8878):1012–6.
12. Duman I, Dincer U, Taskaynatan MA, et al. Reflex sympathetic dystrophy: A retrospective epidemiological study of 168 patients. Clin Rheumatol 2007;26 (9):1433–7.
13. Schwartzman RJ, Erwin KL, Alexander GM. The natural history of complex regional pain syndrome. Clin J Pain 2009;25(4):273–80.
14. Goebel A. Complex regional pain syndrome in adults. Rheumatology (Oxford) 2011;50(10):1739–50.
15. Elsamadicy AA, Yang S, Sergesketter AR, et al. Prevalence and cost analysis of complex regional pain syndrome (CRPS): A role for neuromodulation. Neuromodulation 2017;21(5):423–30.
16. Kemler MA, Furnee CA. Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy. Neurology 2002;59(8):1203–9.
17. Kemler MA, Raphael JH, Bentley A, Taylor RS. The cost-effectiveness of spinal cord stimulation for complex regional pain syndrome. Value Health 2010;13 (6):735–42.
18. Scholz-Odermatt S. Die UVG-Medizinstatistik im Internet. Medizinische Mitteilungen 2008;79: 124–34.
19. Allen G, Galer BS, Schwartz L. Epidemiology of complex regional pain syndrome: A retrospective chart review of 134 patients. Pain 1999;80(3):539–44.
20. de Rooij AM, Perez RS, Huygen FJ, et al. Spontaneous onset of complex regional pain syndrome. Eur J Pain 2009;14(5):510–3.
21. Wertli MM, Kessels AG, Perez RS, Bachmann LM, Brunner F. Rational pain management in complex regional pain syndrome 1 (CRPS 1)–a network meta-analysis. Pain Med 2014;15(9):1575–89.

Appendix: SAMPLING Procedure and Extrapolation Method

Basic Set of the Registry

The registry of the Statistical Service for Swiss National Accident Insurance (SSUV) covers all accidents insured under the compulsory Swiss Accident Insurance Law. It comprises approximately 700,000 accidents per year.

Variables

The database contains selected variables with administrative data (like the date of the accident, age and gender of the victim, economic branch of the employer, daily allowances and costs) for all cases of the basic set.

Additional structured data (like activity at the time of the accident, involved items, course of the accident events, and diagnoses for injuries and health consequences) are obtained by a dedicated team of coding personnel. Coding is done based on the case files.

Sampling Procedure for Additional Structured Variables

For financial reasons, obtaining all this additional information for the complete data set is not feasible. Therefore, the statistics are based on a representative sample of the accidents. This sampling method consists of two strata:

Stratum A: Because of their substantial financial impact, all cases with pensions and all occupational disease cases are fully covered. These only account for about 2% of the cases but include more than half of all costs.

Stratum B: From the rest of the cases, a random sample is selected with a given probability that corresponds to the desired sample set. Since 1993, the sampling rate has been set at 5%, which means that every 20th accident is included in the statistic.

Extrapolation of the Cases

To extrapolate the results from the sample, the cases were multiplied by the reciprocal of the sample rate (the extrapolation factor). Since 1993, the cases of the sample have been weighted by a factor of 20. The pensions and occupational diseases are weighted by a factor of 1.

For example, when 420 sample cases from stratum B and 53 pension cases from stratum A are available for a given type of accident, they are extrapolated to $(420 \times 20) + (53 \times 1) = 8{,}453$ cases.

It is important to note, that this number represents an unbiased estimate, and the precision of the estimation is based on a random sample, which introduces additional variance. The precision of the results from the 5% sample depends on the size N of the estimated number of cases. With an increasing number of cases, the results are more precise. The relative estimation error or the mean deviation of the projected sample results from the full set is approximately proportional to $1/\sqrt{N}$.

Extrapolation of the Costs

Estimation of quantities, for example, average costs per case, is possible in an unbiased way too. Extrapolation of the costs takes place by multiplication with the corresponding weights.

For example, for six cases from the stratum B, a 5% sample with a costs per case of USD \$2,000 and one pension case from stratum A with costs of USD \$200,000 will result in an extrapolated total of

$(6 \times 2{,}000 \times 20) + (200{,}000 \times 1) = 440{,}000$ USD.

The extrapolated number of cases here would be $(6 \times 20 + 1) = 121$ cases. The average cost is $440{,}000/(6 \times 20 + 1) = 3{,}636$ USD.

Scattering of the observed quantities leads to an estimation error (standard error), depending on standard deviation and sample size. These errors have to be calculated for each stratum separately, and then be combined according to the error propagation rules in order to calculate the standard error of the estimate.

As the sample size increases, a more precise estimate of the average cost is possible. The precision of estimations can often be improved by combining several years.