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The incidence of complex regional pain syndrome: A population-based study

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Abstract

The complex regional pain syndrome (CRPS) is a painful disorder that can occur in an extremity after any type of injury, or even spontaneously. Data on the incidence of CRPS are scarce and mostly hospital based. Therefore the size of the problem and its burden on health care and society are unknown. The objective of the present study was to estimate the incidence of CRPS in the general population. A retrospective cohort study was conducted during 1996–2005 in the Integrated Primary Care Information (IPCI) project, a general practice research database with electronic patient record data from 600,000 patients throughout the Netherlands. Potential CRPS cases were identified by a sensitive search algorithm including synonyms and abbreviations for CRPS. Subsequently, cases were validated by electronic record review, supplemented with original specialist letters and information from an enquiry of general practitioners. The estimated overall incidence rate of CRPS was 26.2 per 100,000 person years (95% CI: 23.0–29.7). Females were affected at least three times more often than males (ratio: 3.4). The highest incidence occurred in females in the age category of 61–70 years. The upper extremity was affected more frequently than the lower extremity and a fracture was the most common precipitating event (44%). The observed incidence rate of CRPS is more as four times higher than the incidence rate observed in the only other population-based study, performed in Olmsted County, USA. Postmenopausal woman appeared to be at the highest risk for the development of CRPS.

Keywords: Complex regional pain syndrome; Dystrophy; Incidence; Epidemiology

1. Introduction

Complex regional pain syndrome (CRPS), formerly known as Sudecks dystrophy or reflex sympathetic dystrophy, is a painful disease with clinical features that include pain, sensory, sudo- and vasomotor disturbances, trophic changes and impaired motor function (Bruehl et al., 2002). The disease course varies from relatively mild and self-limiting to chronic disease with a high impact on daily functioning and quality of life (Galer et al., 2000). Usually, symptoms appear in one extremity after even a relatively mild trauma, for example a fracture, contusion or surgery, but symptoms have also been described after varicella zoster infection and myocardial infarction (Merritt, 2005). The diagnosis is based on the findings during the history and physical examination, for which several diagnostic criteria sets have been developed. The most well known are the IASP (International Association for the Study of Pain) criteria, that were

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established during a consensus meeting of experts in 1994 (Stanton-Hicks et al., 1995). The pathogenesis and etiology may involve both neurological and inflammatory disorders, but remain to be completely unraveled (Janig and Baron, 2004; Birklein, 2005).

Due to its complexity and broad spectrum of symptoms, CRPS patients are treated by physicians from different clinical backgrounds, including anesthesiologists, (orthopedic) surgeons, neurologists, rheumatologists and rehabilitation doctors. The incidence of CRPS has been studied retrospectively and prospectively in clinical settings after a certain precipitating event, most frequently after a distal radius fracture (Atkins et al., 1990; Veldman et al., 1993; Field and Atkins, 1997; Zollinger et al., 1999; Dijkstra et al., 2003). Sandroni and colleagues have been the only ones so far to assess the incidence of CRPS in the general population (Olmsted County, USA) and they reported an incidence rate of 5.46/100,000 person years (Sandroni et al., 2003).

In our study, the objective was to assess the incidence of CRPS in the general population in the Netherlands. Moreover, we classified cases according to different diagnostic criteria and described the precipitating events of CRPS.

2. Patients and methods

2.1. Setting

The Integrated Primary Care Information Project (IPCI) is a longitudinal observational database including electronic patient's records of more than 600,000 patients from more than 150 general practitioners (GPs). The patient population is representative of the Dutch population regarding age and sex (Lamberts et al., 1992; van der Lei et al., 1993).

In the Dutch Health Care System, all persons need to be registered with a GP who acts as a gatekeeper for further medical care. The electronic records store information on demographics, signs and symptoms (using the International Classification for Primary Care (ICPC) codes (a classification system for primary care (de Lusignan, 2005)) and narratives), diagnoses (using ICPC and narratives), clinical findings, specialist referrals, laboratory findings, hospitalizations, and drug prescriptions. Summaries of the hospital discharge letters and information and letters from specialists are entered in a free text format and hard copies of original letters can be provided upon request. To maximize completeness of the data, GPs who participate in the IPCI project are not allowed to use paper-based records. The system complies with the European Union guidelines on the use of medical data for medical research and has been proven valid for (pharmaco)-epidemiological studies (Vlug et al., 1999). The Scientific and Ethical Advisory Group of the IPCI project approved the study (Project No. 04/70).

2.2. Source population

The source population comprised all persons of all ages, with at least 1 year of valid history in the IPCI database during the study period (January 1996–June 2005). This meant that the practice had been contributing data to the IPCI database for at least 1 year and that the patient had been registered with the GP for at least 1 year. This 1-year period was required to have sufficient background information on all subjects. Follow-up started at the beginning of the study period or on the date that 1 year of valid history was available, whichever date was latest. Follow-up was terminated when the person transferred out of the practice, on the date of last data supply by the GP, death, diagnosis of CRPS or at the end of the study period, whichever came first.

Since additional data collection was required for validation of CRPS, the source population was restricted to all practices that were still active in the IPCI database in 2006 and provided additional information. For clarification of the data collection procedures see also Fig.1.

2.3. Case definition

Potential cases of CRPS were identified in the IPCI database using an extensive string search including an exhaustive list of synonyms and abbreviations for CRPS (for example complex regional pain syndrome, Sudecks dystrophy, reflex sympathetic dystrophy, posttraumatic dystrophy, CRPS, RSD, PTD, etc.), plus prescriptions of dimethyl sulfoxide (DMSO). In the Netherlands, DMSO is exclusively prescribed for CRPS. In a first validation step, performed by a medical doctor with clinical experience in CRPS, all potential cases were manually evaluated by reading the patient records in order to eliminate obvious non-cases and to classify possible cases as incident or prevalent. A possible case was defined as each patient for whom CRPS was suggested or diagnosed in the patient record. A possible case was considered incident when the first occurrence fell within the follow-up time of that person.

To further validate the diagnosis of CRPS in the incident possible cases, a short questionnaire was mailed to the GPs. The questionnaire was used to confirm whether the person, according to the GP's judgment, indeed suffered from CRPS and whether the patient had been seen and diagnosed by a specialist. Copies of all specialist letters were requested. Specialist letters usually provide information about history and physical examination of the patient. That information was used to verify the fulfillment of diagnostic criteria for CRPS according to the IASP criteria (Stanton-Hicks et al., 1995), the Bruehl criteria (Bruehl et al., 1999; Harden et al., 1999), and the Veldman criteria (Veldman et al., 1993) (see the legend of Table 1b for a description of the criteria sets). The choice for these sets of criteria was based on international acceptance of the IASP criteria, high specificity of the Bruehl criteria, and national acceptance of the Veldman criteria. These criteria sets differ from each other in the types and the number of symptoms and signs that have to be present in order to establish the diagnosis CRPS. The IASP criteria are regarded as very sensitive, whereas the Bruehl criteria have lower sensitivity, but are highly specific. The Veldman criteria are the only ones that theoretically allow a diagnosis of CRPS in the absence of pain.

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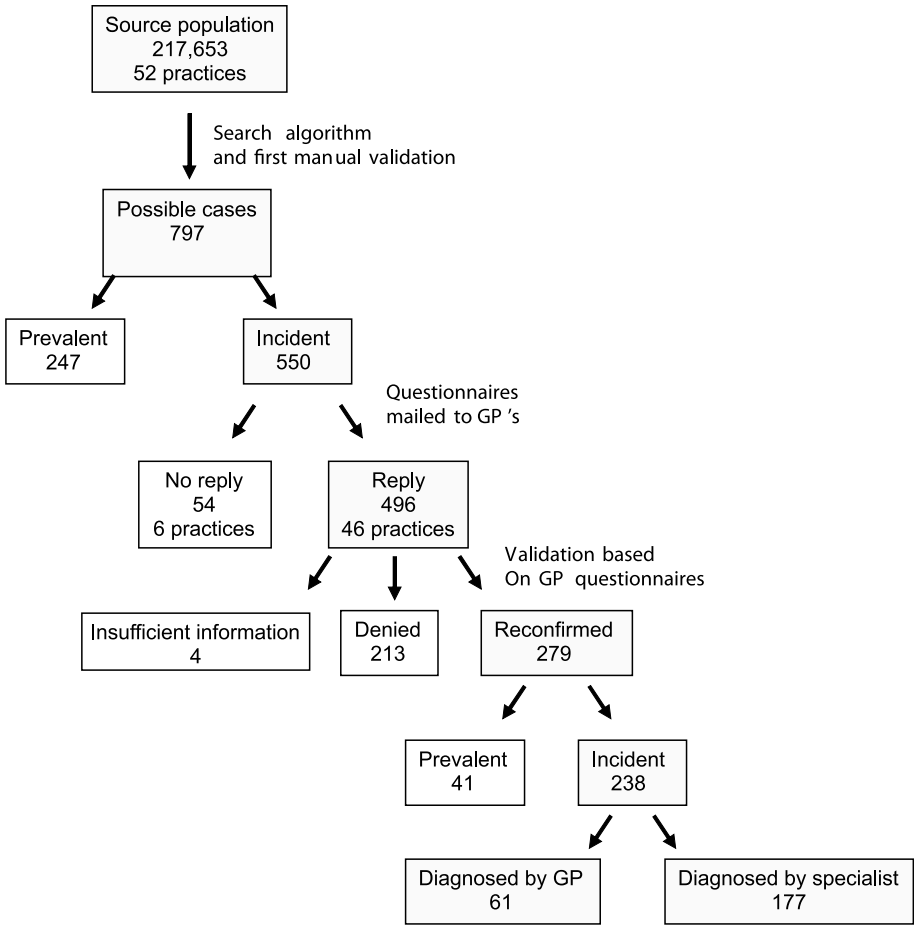

Fig. 1. Process of identification of CRPS cases in the Integrated Primary Care Information (IPCI) database.

The fulfillment of the diagnosis according to the different criteria sets was judged independently by two physicians who are familiar with CRPS. In case of discrepancies between their judgments, consensus was reached by discussion. Where pain and an increase of the symptoms after use of the affected limb (an obligatory feature according to the Veldman criteria) were not mentioned in the letters, it was reasonable to assume that they were present in most of the cases. Therefore, the criteria were first applied both in a strict sense, and subsequently without taking into account the presence of pain and increase after use of the affected limb.

Information on precipitating events and referrals were derived from the electronic medical records and the specialist letters.

2.4. Analysis

The incidence rate of CRPS was calculated by dividing the number of incident cases (as established by reconfirmation of the diagnosis) (numerator), by the total number of accrued person years in the population (denominator). Incidence rates (IR) were calculated per calendar year, sex, and age category. Calculations were stratified for CRPS following a fracture and CRPS following other precipitating events. 95% Confidence intervals were constructed around the rates based on the Poisson distribution.

In addition to the incidence rate based on the reconfirmed diagnoses, we also calculated an incidence rate based on cases that fulfilled the IASP criteria. However, the IASP criteria could only be applied in a subset of the specialist-diagnosed cases (for whom specialist letters with diagnostic information were available). Therefore, the percentage of fulfillment was extrapolated only within the specialist-diagnosed case group. Cases that were diagnosed by the GP alone were excluded from this analysis.

In order to be able to compare our results with the incidence found by Sandroni and colleagues, we calculated standardized morbidity ratios (SMR), using the method of indirect standardization on age and gender, as described by Rothman (Rothman, 1986).

Standard descriptive statistics were used to compare categorical variables (χ^2 test, univariate logistic regression), or means (Student's t-test). κ statistics were calculated to judge interrater agreement for the diagnostic criteria. The Statistical Package for Social Sciences (SPSS) 12.0 for Windows was used for all statistical tests.

3. Results

In the initial source population of 217,653 persons registered with at least 1 year of valid history at one

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of the 52 active practices in the IPCI database, 238 incident cases of CRPS could be identified after finalization of the validation process (Fig. 1). The response rate for the short questionnaires amongst GPs was 88%. Only the populations from the practices that responded were included in the source population for calculations of the IR. This source population comprised 190,902 persons from 46 practices, and concerned the mentioned 238 cases.

For 95 (54%) of the 177 cases that were diagnosed by a specialist, letters with information on anamnesis and physical examination were available. Structured extraction of data (Table 1a) allowed for classification of the cases according to different CRPS criteria sets (Table 1b). Eighty-six percentage of these specialist-diagnosed cases fulfilled the strictly applied IASP criteria for CRPS. If pain and an increase in pain after use of the body part were assumed to be present (even if not mentioned in the letter), 93% of the cases fulfilled the IASP criteria, 47% the Bruehl criteria and 58% the Veldman criteria (Table 1b). The interrater agreement varied between the different criteria sets, with the lowest $\kappa = 0.43$ (moderate) for the IASP criteria with pain assumed to be present, and the highest $\kappa = 0.78$ (good) for the Veldman criteria. In the available specialist letters the presence or absence of vaso- and sudomotor and motor-trophic signs and symptoms was reported more frequently than the presence or absence of sensory and neurological signs and symptoms.

Characteristics of the cases are displayed in Table 2. The mean age at CRPS diagnosis was 52.7 ± 2.20 (range 7–90) years in the total group. The mean age for males was 51.1 ± 4.2 years and for females 53.0 ± 2.6 years. The age at diagnosis did not differ between males and females ($p = 0.404$). The most common precipitating event for CRPS was a fracture, followed by a contusion/sprain. In more than ten percent of the cases no precipitating event was reported or could be identified in the medical record. Upper extremities were more often affected than lower extremities (59.2% versus 39.1%, $p < 0.001$), whereas the right side and left side of the body were affected with the same frequency ($p = 0.464$). Patients who were diagnosed only by GPs were significantly older than patients who were also

Table 1a
Relevant characteristics in anamnesis and physical examination that were described in specialist letters regarding CRPS patients

Symptom/sign ($N = 95$)	Anamnesis (n, %)			Physical examination (n, %)		
	Present	Absent	Not mentioned	Present	Absent	Not mentioned
Sensory						
Spontaneous pain	81 (85.3)		14 (14.7)	37 (38.9)	1 (1.1)	57 (60.0)
Hyperesthesia	4 (4.2)		91 (95.8)	5 (5.3)	5 (5.3)	85 (89.5)
Hyperalgesia			95 (100)	2 (2.1)	3 (3.2)	90 (94.7)
Allodynia	9 (9.5)		86 (90.5)	11 (11.6)	4 (4.2)	80 (84.2)
Hyperpathy	2 (2.1)		93 (97.9)	6 (6.3)	4 (4.2)	85 (89.5)
Paraesthesias	9 (9.5)		86 (90.5)			
Hypoesthesia	4 (4.2)		91 (95.8)	8 (8.4)		87 (91.6)
Vasomotor						
Temperature asymm.	56 (58.9)	2 (2.1)	37 (41.1)	44 (46.3)	8 (9.2)	43 (45.3)
Color asymmetry	51 (52.6)	2 (2.1)	42 (44.2)	43 (45.3)	9 (9.5)	43 (45.3)
Sudomotor						
Swelling/edema	53 (55.8)		42 (44.2)	55 (57.9)	5 (5.3)	35 (36.8)
Sweating asymmetry	23 (24.2)	6 (6.3)	66 (69.5)	29 (30.5)	11 (11.5)	55 (57.9)
Motor-trophic						
Limited range of motion	20 (21.1)	2 (2.1)	73 (76.8)	51 (53.7)	3 (3.2)	41 (43.2)
Paresis	7 (7.4)		88 (92.6)	15 (15.8)	6 (6.3)	74 (77.9)
Dystonia	4 (4.2)		91 (95.8)	5 (5.3)		90 (94.7)
Altered hair growth	2 (2.1)	6 (6.3)	87 (91.5)	5 (5.3)	15 (15.7)	75 (78.9)
Altered nail growth	4 (4.4)	3 (3.2)	88 (92.6)	4 (4.3)	10 (10.5)	81 (85.3)
Skin atrophy			95 (100)	2 (2.1)		93 (97.9)
Neurologic						
Disturbed coordination	2 (2.1)		93 (97.9)	1 (1.1)	1 (1.1)	93 (97.9)
Tremor			95 (100)	1 (1.1)		94 (98.9)
Involuntary movements	1 (1.1)		94 (98.9)		1 (1.1)	94 (98.9)
Paralysis			95 (100)	1 (1.1)		94 (98.9)
Muscle atrophy			95 (100)	7 (7.4)	1 (1.1)	87 (91.6)
Various						
Increase of complaints after use	26 (27.4)		69 (72.6)			
Alternative diagnosis	6 (6.3)		89 (93.7)			

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Table 1b
Classification of cases by different diagnostic criteria

Criteria ($N = 95$)	Strict n (%)	When the presence of pain was not taken into account n (%)	When the presence of increase of pain after use was not taken into account n (%)	κ
IASP[a] (Stanton-Hicks et al., 1995)	82 (86.3)	88 (92.6)	Not applicable	0.43–0.66 (moderate-good)
Bruehl[b] (Bruehl et al., 1999; Harden et al., 1999)	41 (43.2)	45 (47.4)	Not applicable	0.66–0.69 (good)
Veldman[c] (Veldman et al., 1993)	17 (17.8)	17 (17.8)	55 (57.9)	0.63–0.78 (good)

[a] IASP criteria: 1. Develops after an initiating noxious event (type 1) or after a nerve injury (type II). 2. Spontaneous pain or allodynia/hyperalgesia that is not limited to the territory of a single peripheral nerve and is disproportionate to the inciting event. 3. There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the inciting event. 4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

[b] Bruehl criteria: 1. Continuing pain which is disproportionate to any inciting event. 2. Must report at least one symptom (history) in each of the following categories. Must display at least one sign (physical examination) in two or more of the following categories. *Sensory*: hyperesthesia, hyperalgesia (to pinprick) and/or allodynia (to light touch). *Vasomotor*: temperature asymmetry and/or skin color changes and/or skin color asymmetry. *Sudomotor/edema*: edema and/or sweating changes and/or sweating asymmetry. *Motor/trophic*: decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).

[c] Veldman criteria: 1. Four or five of: unexplained diffuse pain; difference in skin color relative to other limb; diffuse edema; difference in skin temperature relative to other limb; limited active range of motion. 2. Occurrence or increase of above signs and symptoms after use. 3. Above signs are present in an area larger than the area of primary injury or operation and including the area distal to the primary injury.

Table 2
Characteristics of CRPS patients

	Total		By GP only		By specialist		p-value[*]
	N (238)	%	N (61)	%	N (177)	%	
Characteristics							
Mean age at onset (SD)	52.7 (17.31)		56.6 (19.63)		51.3 (16.27)		0.039
Female	184	77.3	52	85.2	132	74.6	0.086
CRPS II	7	2.9	1	1.6	6	3.4	0.485
Precipitating event							
None	25	10.8	8	13.1	17	9.6	0.941
Fracture	105	44.1	28	45.9	77	43.5	0.790
Sprain	42	17.6	13	21.3	29	16.4	0.953
Elective surgery	29	12.2	5	8.2	24	13.6	0.617
CTS	8	3.4	1	1.6	7	4.0	0.441
Dupytren	6	2.5	1	1.6	5	2.8	0.577
Tendon injury	13	5.5	2	3.3	11	6.2	0.484
Others	21	8.8	4	6.6	17	9.6	0.575
Unknown	3	1.3	1	1.6	2	1.1	
Localization at diagnosis							
Right side of the body	114	47.9	31	50.8	83	46.8	0.279
Left side of the body	115	48.3	26	42.6	89	50.2	0.154
Unknown	9	3.8	4	6.6	5	2.9	
Upper extremity	141	59.2	40	65.6	101	57.1	0.243
Lower extremity	93	39.1	19	32.2	74	41.8	0.141
Unknown	4	1.7	2	3.2	2	1.1	
Type of specialist to whom patient is referred (more than one possible)							
Anesthesiologist					87	49.7	
Rehabilitation doctor					52	29.4	
Orthopedic surgeon					49	27.7	
Surgeon					45	25.4	
Neurologist					19	10.7	
Rheumatologist					8	4.5	
Plastic surgeon					5	2.8	
Other					6	3.4	
Number of specialists seen							
1					105	59.3	
2					54	30.5	
3					14	7.9	
4					4	2.3	

[*] p-values are given for differences in characteristics between patients diagnosed by GPs alone and patients confirmed by a specialist.

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referred to and diagnosed by a specialist ($p = 0.039$). Anesthesiologists were the most frequently involved specialists and usually one type of specialist was seen by the patient.

The incidence rate of CRPS in the Netherlands was 26.2 per 100,000 person years (95% CI: 23.0–29.7) (Table 3). The standardized morbidity ratio (SMR) was calculated as 4.2, meaning that, after standardization for age and gender to the source population of Sandroni and colleagues, we found a 4.2 times higher incidence rate than described in their study. If only specialist confirmed cases were considered, the incidence rate was 19.5 per 100,000 person years (95% CI: 16.8–22.5). The incidence rate based on specialist-diagnosed cases that fulfilled the IASP criteria was 16.8 per 100,000 person years (95% CI: 14.7–19.2). The SMR compared to the results of Sandroni was 2.7.

Gender-specific incidence rates, based on the reconfirmed diagnoses, for females and males were 40.4 (95% CI: 34.8–46.8) and 11.9 (95% CI: 9.0–15.4) per 100,000 person years, respectively. The incidence of CRPS was more than threefold higher in females than in males (RR: 3.4, 95% CI: 2.9–3.9). The incidence rate of CRPS did not change significantly over time between 1996 and 2005 (Fig. 2). The confidence intervals in 1996 and 2005 were relatively wide due to the low number of person-years by left censoring in 1996 (early stage of the IPCI database) and a high degree of right censoring in 2005 (data available only until June). The incidence varied profoundly with age, the highest incidence rate was observed in the group 61–70 years of age (Fig.3). The age and sex distribution pattern was similar in a subgroup including only the cases with another precipitating event than a fracture.

4. Discussion

In this study, we demonstrated that the population-based incidence of CRPS in the Netherlands is 26.2 per 100,000 person-years, with a peak incidence at 61–70 years of age. Fracture was the most common precipitating event accounting for 44% of the CRPS cases. The upper extremities were more often affected than the lower extremities with no preference for either left or right side. A wide variety of specialists was involved in the diagnosis and treatment of CRPS patients.

The incidence rate in this study is more than four times higher than the population-based incidence rate that was reported by Sandroni and colleagues in Olmsted County (Sandroni et al., 2003). The difference sustained even after standardization (IR: 22.8 per 100,000 person-years) and when we included only specialist-diagnosed cases in our calculations (IR: 19.0 per 100,000 person-years). Possibly, differences in population characteristics such as ethnicity, socio-economic factors and incidence of fractures can explain the observed difference. More likely, however, it is secondary to the difference in case definitions and validation.

Table 3
Incidence of CRPS according to calendar year and age category

	Males			Females			Total		
	Cases	PY at risk	IR per 100,000 PY	Cases	PY at risk	IR per 100,000 PY	Cases	PY at risk	IR per 100,000 PY
Year									
1996	2	11,874	16.8	8	12,484	64.1	10	24,358	41.1
1997	0	19,800	0.0	9	20,663	43.6	9	40,464	22.2
1998	1	30,296	3.3	8	31,231	25.6	9	61,528	14.6
1999	2	50,098	3.9	16	50,335	31.8	18	100,433	17.9
2000	12	60,441	19.9	24	60,619	39.6	36	121,060	29.7
2001	8	61,394	13.0	29	61,529	47.1	37	122,923	30.1
2002	12	66,799	18.0	28	66,888	41.9	40	133,687	29.9
2003	10	70,710	14.1	23	70,679	32.6	33	141,390	23.3
2004	6	64,790	9.3	31	64,524	48.0	37	129,314	28.6
2005	1	17,220	5.8	8	17,063	46.9	9	34,283	26.3
Age group									
<10	1	51,252	2.0	1	49,182	2.0	2	100,434	2.0
10–19	1	56,063	1.8	8	53,639	14.9	9	109,702	8.2
20–29	4	64,319	6.2	17	60,723	28.0	21	125,042	16.8
30–39	7	77,401	9.0	20	72,058	27.7	27	149,459	18.1
40–49	11	70,805	15.5	19	69,640	27.2	30	140,445	21.4
50–59	15	61,482	24.4	43	59,597	72.1	58	77,760	47.9
60–69	12	38,206	31.4	48	39,554	121.3	60	75,377	77.2
70–79	3	24,582	12.2	19	32,695	58.1	22	57,277	38.4
>80	0	9,313	0.0	9	18,931	47.5	9	28,245	31.9
Total	54	453,425	**11.9 (9.0–15.4)**	184	456,018	**40.4 (34.8–46.8)**	238	909,443	**26.2 (23.0–29.7)**

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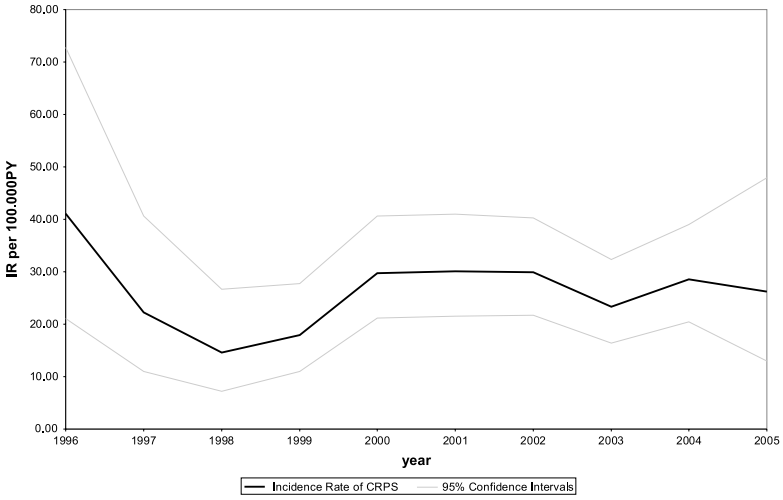

Fig. 2. Incidence rates of CRPS in the Netherlands according to calendar year, with upper and lower 95% confidence lines.

The study of Sandroni and colleagues used the IASP criteria, which were applied retrospectively to information from electronic medical records. We also used a retrospective approach and used both electronic medical records as well as information from GP questionnaires and specialist letters for the diagnosis. In contrast to Sandroni we did not require that all cases should fulfill diagnostic criteria; we retained all cases on the basis of a reconfirmed diagnosis of CRPS by the GP or specialist.

Criteria sets were also applied on a subset for which detailed diagnostic data were available, but were used merely to see differences in criteria sets. However, an incidence rate based on the strictly applied IASP criteria (IR: 16.8 per 100,000 person years), as done in the Sandroni study, was calculated and was still almost three times higher in our study as the incidence rate found in Olmsted County (SMR = 2.7). Remarkable is, that in our subset of specialist-diagnosed cases 86% fulfilled the IASP criteria, compared to 19% of the cases in the Sandroni study. The supposedly high rate of incorrectness of the CRPS diagnosis (81%) in the Sandroni study has been questioned by others before (Bennett and Harden, 2003), and suggests that the retrospective application of the IASP criteria to information on electronic charts might have been overly strict. The IASP criteria are considered highly sensitive and incidence rates based on this should be comparable with incidence rates based on specialist's diagnoses.

The highest incidence rate in our study was observed in the age group of 61–70 years and the mean age at diagnosis was 52.7 years. This age peak is higher than is generally expected and observed in some non-population-based investigations (Veldman et al., 1993). However, other clinical studies show high average ages of the

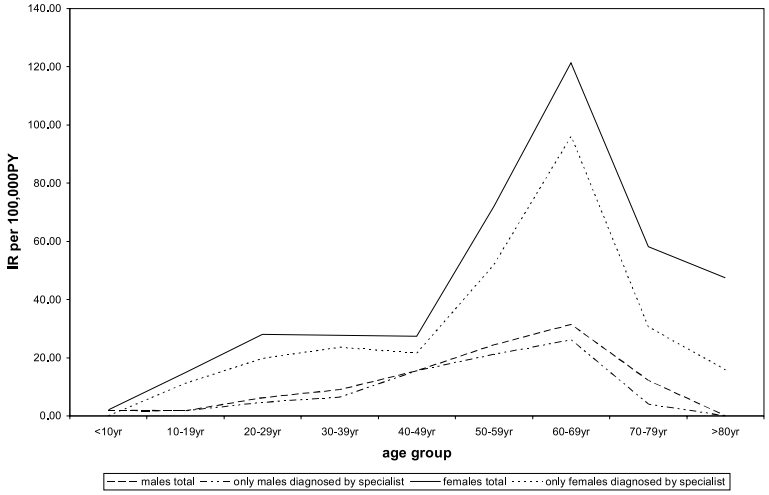

Fig. 3. Incidence rates of CRPS in the Netherlands according to age group and by level of confirmation (diagnosed only by specialist or all diagnosed).

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included CRPS patients, in line with our observation (Atkins et al., 1990; Field and Atkins, 1997; Zollinger et al., 1999). It could be suggested that the increasing incidence of CRPS with age is due to a higher occurrence of fractures at older age. However, the same age distribution pattern was observed in the group of patients with another precipitating event than a fracture. From our findings, it can be concluded that the majority of the CRPS cases in females occur in the postmenopausal stage of life. This was noted before by Zollinger and colleagues (Zollinger et al., 1999). The age and sex distribution pattern suggests that hormonal etiological factors may be involved in the pathogenesis of CRPS.

Noteworthy is that less than half of the CRPS cases have a fracture as precipitating event, similar to the observations of Sandroni and colleagues. Fracture is often regarded as the primary precipitating event and the incidence of CRPS after a fracture has been studied prospectively (Veldman et al., 1993; Dijkstra et al., 2003). Hence, other precipitating events, such as surgery and tendon rupture, may be worthwhile including in prospective research. Additional findings of interest were the fact that patients who were diagnosed only by the GP without referral to a specialist tended to be older.

Limitations in our study are related to the absence of a gold standard for the diagnosis of CRPS. As observed in the specialist letters, physicians focused on vaso- and sudomotor and motor-trophic signs, whereas the presence or absence of sensory and neurological symptoms was not frequently reported. van de Beek and colleagues have stated that general dissatisfaction with the available criteria has resulted in the use of personally favoured criteria (van de Beek et al., 2002). As a consequence of this, descriptions of the patients differ and lack detail, which has complicated uniform classification of the cases in our study. However, if detailed information for the application of diagnostic criteria would have been available as in a prospective study, the choice for one specific criteria set for validation of the diagnosis above the others would also have been disputable, since none of them is definitely superior (van de Beek et al., 2002). For this reason we decided that the most reliable incidence rate calculations would be based on reconfirmed clinical diagnoses. However, the problems regarding case definition that were encountered during our study emphasize again the need for validated and well-documented diagnostic criteria, that can be applied more in primary and secondary care and in prospective and retrospective studies.

Despite the above described, we do not believe that the inability to uniformly classify all patients has resulted in an overestimation of the incidence rate. We sought reconfirmation of all cases and allowed GPs to reconsider whether an initial diagnosis actually was correct. In addition, almost three-quarters of the patients were referred to a medical specialist who reconfirmed the diagnosis as well, after exclusion of alternative diagnoses. The actual incidence rates varied with the choice to base the validation of the CRPS diagnosis on GP or specialist confirmed cases. However, the pattern of the incidence rate (sex and age distribution) was similar for both groups. On the contrary, we consider it more likely that our incidence rates are an underestimation of the reality. Although we have used a sensitive search algorithm for identification of the CRPS cases, we might have missed cases that had symptoms but were not diagnosed as such in the medical record because of unfamiliarity of the GP with the syndrome and its nomenclature. Mainly the relative mild and self-limiting cases of CRPS might not always have been recorded as such in the medical journal and were therefore not included in our calculations.

In conclusion, we estimated an incidence of CRPS in the general population of the Netherlands of 26.2 per 100,000 person-years, which is much higher than previously described. Postmenopausal women appeared to be at an increased risk for the development of the disease. Uniform use of more generally accepted diagnostic criteria would improve the quality of epidemiological and clinical studies concerning CRPS in the future.

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