

## SARCOIDOSIS AND INCREASED RISK OF COMORBIDITIES AND MORTALITY IN SWEDEN

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**ABSTRACT.** *Introduction:* Sarcoidosis is a systemic inflammatory disorder, with an unclear etiology, involving granuloma formation that in most cases affects the lungs and intrathoracic lymph nodes. Sarcoidosis occurs in an acute or chronic form, each with different clinical presentation and prognosis. *Methods:* Case-control study of comorbidity and mortality in people diagnosed with sarcoidosis (ICD10 code D86) from 2007 through 2016 in Sweden. Controls were matched to cases (2:1) based on age, sex and county at the time of diagnosis. Data was collected from the Swedish National Patient Register and The Cause of Death Register. All men and women aged 20–65 years old who were diagnosed with sarcoidosis (D86, ICD10) during the years of study were included, resulting 7828 cases and 15656 controls. *Results:* Patients with sarcoidosis had increased mortality compared to matched controls (hazard ratio 1.88; 95% CI 1.56 – 2.26) and the Swedish general population (standardized mortality ratios 1.75; 95% CI 1.52 – 2.00). The sarcoid cases, compared to controls, also had a significantly greater number of inpatient visits within several different chapters of ICD10 e.g. cardiomyopathy, heart failure, pulmonary embolism and malignant neoplasm. *Conclusion:* Individuals with sarcoidosis are at higher risk of comorbidities and mortality than matched controls as well as the general population of Sweden. These findings are important knowledge for healthcare professionals who meet sarcoid patients, to encourage identification and treatment of comorbidities to reduce the risk of impaired quality of life and, eventually, premature death. (*Sarcoidosis Vasc Diffuse Lung Dis* 2020; 37 (2): 104–135)

**KEY WORDS:** Sarcoidosis, Case control, Comorbidity, Mortality

### INTRODUCTION

Sarcoidosis is a systemic inflammatory disorder involving granuloma formation that, in more than 90% of cases, affects the lungs and intrathoracic lymph nodes. Of all patients, 30–50% show extra pulmonary disease affecting, most commonly, the skin,

liver, eyes and peripheral lymph nodes. Sarcoidosis is diagnosed by biopsy of the affected organs. The etiology is unclear, but a genetic susceptibility to yet unidentified environmental factors is suggested (1). Most cases occur sporadically, but some are familial, and first-degree relatives of patients are at a higher risk of developing sarcoidosis than others (2). The annual incidence of sarcoidosis in Sweden is 11.5 per 100 000, among the highest worldwide (3).

Sarcoidosis occurs in an acute or chronic form, each with different clinical presentation and prognosis (1). Most deaths due to sarcoidosis are caused by advanced pulmonary fibrosis or involvement of the central nervous system or heart (4). Studies suggest increased coexistence of several immune-mediated

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and chronic inflammatory diseases with sarcoidosis (5, 6). Associations with hypertension, chronic obstructive pulmonary disease (COPD), thyroid diseases, and diabetes mellitus have also been identified (5-10).

Whether the risk of malignancy in sarcoidosis is increased or not has been debated. A meta-analysis including 16 original studies and more than 25,000 patients suggested a moderate, though significant, association between sarcoidosis and malignancy overall (11). Similar results were obtained in a study of hospitalized patients with sarcoidosis in Sweden (12).

Previous studies on mortality in sarcoidosis are largely based on data from death certificates (13-15). Inclusion in these mortality studies requires correct identification of a sarcoidosis case and declaration of sarcoidosis as cause of death on the death certificate. Since sarcoidosis can be a chronic disease affecting several organs there is a risk of misclassification and it may not be declared as the cause of death in patients with a clinically concealed disease. Moreover, patients who had sarcoidosis earlier in life that improved spontaneously would be excluded.

Mortality studies also have contradictory results, with some suggesting that mortality is up to twice as high among those with sarcoidosis compared to the general population while others propose that mortality is not increased in patients with sarcoidosis (16-18). Considering this, this study aimed to contribute with more information on the comorbidities and risk of mortality of sarcoidosis compared to matched controls and the Swedish general population.

## MATERIAL AND METHODS

In Sweden, all residents have equal access to publicly funded healthcare and residents have a unique personal identification number that can be used to link data across different nationwide registers. The National Board of Health and Welfare (NBHW) holds several registers, including the National Patient Register (NPR). Information on hospitalizations (inpatient register) and non-primary care outpatient visits (outpatient register) can be gathered from the NPR. Another register, The Cause of Death Register, provides the basis for official statistics on both main and contributory causes of death in Sweden. These registers have a high degree of coverage due to reporting obligations. The outpatient register was used to identify cases for the study population. The

Cause of Death Register provided information on date and cause of eventual death. Statistics Sweden is another Swedish authority accountable for many registers, including The Multi-Generation Register and The National Register of the Total Population, both used in this study to identify controls.

All data processing conducted to match data from the different registers was performed by the NBHW and Statistics Sweden and de-identified data recorded from 2005 – 2016 was received.

### *Study population*

The study population comprised of men and women aged 20 to 65 years (the typical working age in Sweden) diagnosed with sarcoidosis according to the outpatient register from January 1, 2005 through December 31, 2016. Sarcoidosis was defined according to the ICD10 code D86. Controls were matched to cases (2:1) based on age, sex and county at the time of diagnosis (Figure 1). The controls selected did not themselves have sarcoidosis, nor were they a first-degree relative of any case. The study population derived from a larger source of material that formed the basis of another study, thus neither the cases nor the controls are diagnosed with Ankylosing spondylitis-M45, Rheumatoid arthritis-M05 and -M06, Crohn's disease-K50 or Ulcerative colitis-K51. To include as many newly-diagnosed cases and as few re-visits as possible, a wash-out was performed over the years 2005-2006 to ensure that only newly-diagnosed cases was used in the statistical calculations.

To estimate comorbidities, information from the inpatient register about the main diagnoses provided on the first visit (date) after the date of the diagnosis of sarcoidosis in respective chapters of ICD10 was collected. Each individual can appear within several different chapters of the ICD10.

### *Statistical analysis*

Demographics are presented using descriptive statistics and is reported as number (n), percentage (%), and mean  $\pm$  standard deviation (SD). Using Cox regression, sarcoid cases were compared with their controls, and the results are presented as hazard ratios (HR) with 95% confidence intervals (CIs). Study subjects contributed person years from the date they received their sarcoidosis diagnosis to

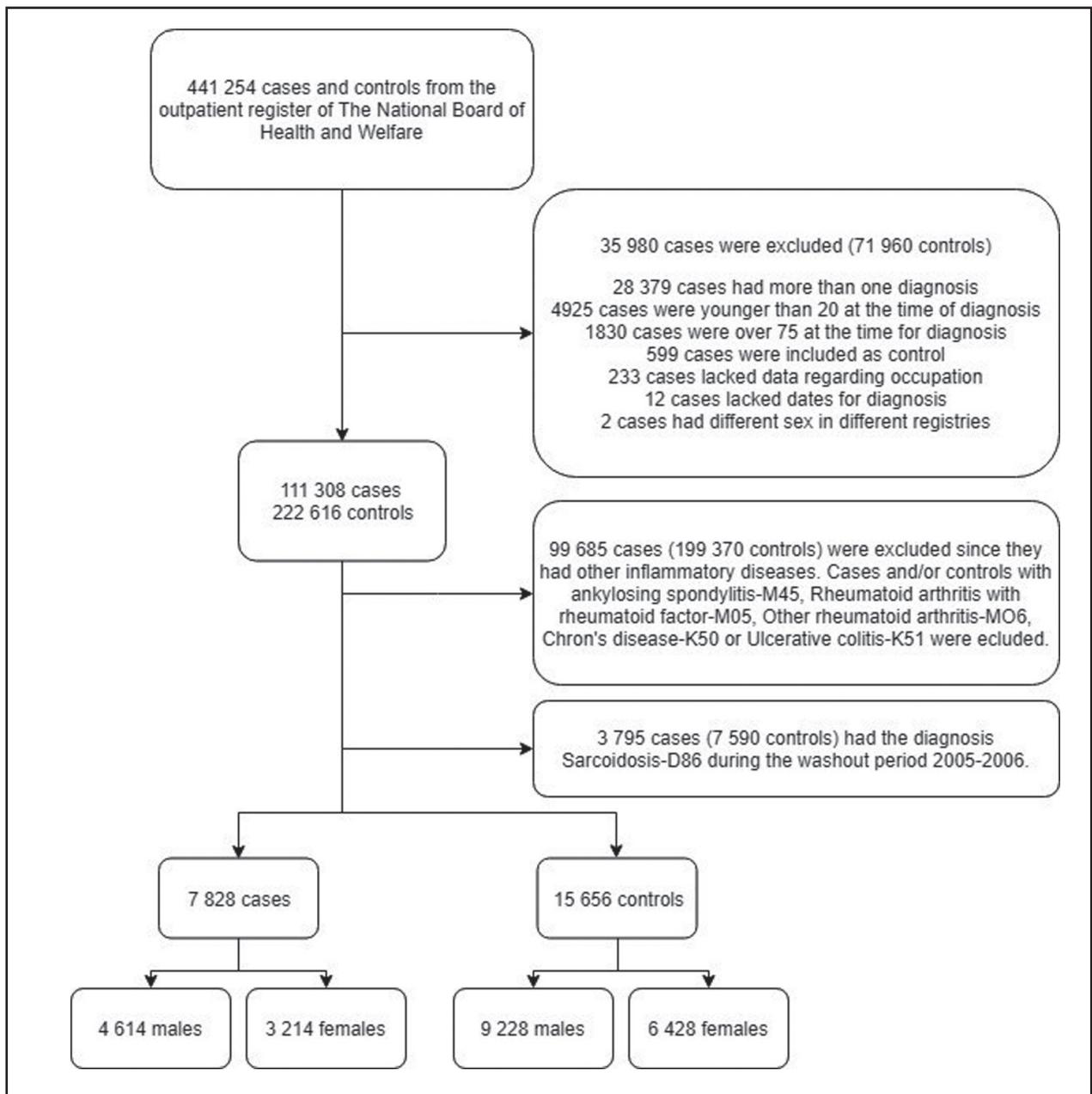


Fig. 1. Flow chart that visualizes inclusion and exclusion of the study population.

the date of event (that is, comorbidity and/or death), emigration or end of the study. Standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) were used to compare sarcoid cases and controls against the general population. With the general population in Sweden used as a reference, data was stratified according to sex, 5-year age

groups and 1-year calendar periods when calculating person-years at risk. Assuming a Poisson distribution of the observed numbers, SIRs and SMRs was calculated with 95% CIs. P-values less than 0.05 were considered statistically significant. All analyzes were made using STATA 14.0 (StataCorp LLC, TX; USA).

## Ethics

The Swedish Ethical Review Authority (Ref 2017/252) approved the study protocol.

## RESULTS

The study population consisted of 23,484 individuals in total, 7828 cases and 15,656 controls. The sex distribution was 58.9% males, 41.1% females. Deaths occurred in a total of 451 individuals, of which 218 (2.8%) were among the cases and 233 (1.5%) were among the controls. Further demographics are presented in Table 1.

### Comorbidity

#### Comparisons of cases and matched controls

The number of inpatient care visits by sarcoid patients, compared to controls, were significantly increased and were associated with diagnoses in most ICD10 chapters, as shown in Table 2. The most apparent increase among sarcoid patients were found in diseases of the blood and immune-mechanism (chapter III), HR 66.48 (95% CI 36.48 – 121.12), which most likely is due to sarcoidosis itself.

Apart from diseases of the blood and immune-mechanism (chapter III), the HRs were highest for: diseases of the eye and adnexa, HR 2.95 (95% CI 1.88 – 4.62); respiratory system, HR 2.76 (95% CI 2.22 – 3.45); and certain infectious and parasitic diseases, HR 2.49 (95% CI 1.84 – 3.38). Further significant increases in associated comorbidities stratified into ICD10 chapters are presented in Table 2. Further information about specific diseases are found in Supplementary Table 1 and 2.

In respiratory system several diagnoses has a higher rate than controls. There is an significant increase in pneumothorax (J93) HR 11.53 (95% CI 3.99 - 33.34), influenza and pneumonia (J09-J18) HR 2.98 (CI 2.41 – 3.68), chronic lower respiratory diseases (J40-J47) HR 2.53 (95% CI 1.66 – 3.85) and other respiratory diseases principally affecting the interstitium (J80-J84) HR 2.98 (95% CI 5.26 – 57.42) (see Supplement Files 2).

Compering cases and controls for diseases of the circulatory system there is an increased HR 1.40 (95% CI 1.21 – 1.63) for the whole chapter.

**Table 1.** Characteristics of Cases and Controls included in the Study.

	Cases (n = 7 828)	Controls* (n = 15 656)	Total (n = 23 484)
Males No. (%)	4 614 (58.9%)	9 228 (58.9%)	13 842
Females No. (%)	3 214 (41.1%)	6 428 (41.1%)	9 642
Age in males at inclusion, mean (SD), y	45 (10.7)	45 (10.7)	
Age in females at inclusion, mean (SD), y	47 (11.5)	47 (11.5)	
Deaths No. (%)	218 (2.8%)	233 (1.5%)	451 (1.9%)
Death due to sarcoidosis No. (%)	23 (10.6%)	0 (0.0%)	23 (5.1%)
Age at death event in males, mean (SD), y	55 (11.2)	59 (9.3)	
Age at death event in males, mean (SD), y	59 (9.0)	59 (8.6)	

\* Controls are matched 2:1 on age, sex and county at the time of diagnosis

Subgrouping in diagnosis yield pulmonary embolism (I26) HR 4.36 (95% CI 2.26 – 7.07), cardiomyopathy (I42) HR 5.13 (95% CI 2.37 – 11.08), paroxysmal tachycardia (I47) HR 3.27 (95% CI 2.28 – 4.68) and heart failure (I50) HR 3.27 (95% CI 2.28 – 4.68) and where in high rate and significant increased.

For cancer, there was an increase in malignant neoplasms of ill-defined, secondary and unspecified sites (C76–C80) HR 2.38 (95% CI 1.59 - 3.57) and malignant neoplasms of lymphoid, hematopoietic and related tissue (C81–C96) with HR 2.94 (95% CI 1.85 - 4.68).

A small but significant decrease in association of comorbidities in sarcoid cases, was also seen for mental and behavioral diseases (chapter V). However, when cases and controls were stratified by sex, the results are no longer significant.

#### Comparisons of cases and matched controls with the general population:

When comorbidities of the sarcoid cases and control groups are independently compared to those of the general population of Sweden, it appears that the sarcoid cases contacted the inpatient healthcare

Table 2: Numbers of Visits to Inpatient Care where Sarcoid Cases and Matched Controls are compared using Cox Regression.

Chapters of ICD 10			Number of visits cases (n) <sup>a</sup>	Number of visits controls (n) <sup>a</sup>	HR <sup>b</sup> (95% CI) <sup>c</sup>
Certain infectious and parasitic diseases	I	Total	93	75	2.49 (1.84 – 3.38)*
		Male	51	39	2.63 (1.73 – 3.99)*
		Female	42	36	2.34 (1.50 – 3.66)*
Neoplasms	II	Total	249	284	1.78 (1.50 – 2.10)*
		Male	133	102	2.64 (2.04 – 3.42)*
		Female	116	182	1.29 (1.02 – 1.62)*
Diseases of the blood and certain immune-mechanisms <sup>d</sup>	III	Total	357	11	66.48 (36.48 – 121.12)*
		Male	215	7	62.96 (29.66 – 133.66)*
		Female	142	4	72.61 (26.88 – 196.12)*
Endocrine, nutritional and metabolic disorders	IV	Total	108	107	2.03 (1.55 – 2.65)*
		Male	48	42	2.29 (1.52 – 3.47)*
		Female	60	65	1.86 (1.31 – 2.64)*
Mental and behavioural diseases	V	Total	91	236	0.77 (0.60 – 0.98)*
		Male	63	162	0.78 (0.58 – 1.04)
		Female	28	74	0.76 (0.49 – 1.17)
Diseases of the nervous system	VI	Total	108	94	2.31 (1.75 – 3.04)*
		Male	66	52	2.55 (1.77 – 3.67)*
		Female	42	42	2.01 (1.31 – 3.08)*
Diseases of the eye and adnexa	VII	Total	47	32	2.95 (1.88 – 4.62)*
		Male	25	18	2.78 (1.52 – 5.10)*
		Female	22	14	3.15 (1.61 – 6.16)*
Diseases of the ear and mastoid process	VIII	Total	22	44	1.00 (0.60 – 1.67)
		Male	11	24	0.92 (0.45 – 1.87)
		Female	11	20	1.10 (0.53 – 2.30)
Diseases of the circulatory system	IX	Total	283	407	1.40 (1.21 – 1.63)*
		Male	193	287	1.36 (1.13 – 1.63)*
		Female	90	120	1.51 (1.15 – 1.98)*
Diseases of the respiratory system	X	Total	186	136	2.76 (2.22 – 3.45)*
		Male	110	77	2.89 (2.16 – 3.86)*
		Female	76	59	2.61 (1.86 – 3.66)*
Diseases of the digestive system	XI	Total	221	352	1.26 (1.07 – 1.49)*
		Male	121	208	1.17 (0.93 – 1.46)*
		Female	100	144	1.40 (1.08 – 1.80)*
Diseases of the skin and subcutaneous tissue	XII	Total	27	23	2.35 (1.35 – 4.10)*
		Male	15	14	2.14 (1.04 – 4.44)*
		Female	12	9	2.67 (1.13 – 6.34)*

Chapters of ICD 10			Number of visits cases (n) <sup>a</sup>	Number of visits controls (n) <sup>a</sup>	HR <sup>b</sup> (95% CI) <sup>c</sup>
Diseases of the musculoskeletal system and connective tissue	XIII	Total	183	327	1.12 (0.94 – 1.34)
		Male	101	178	1.14 (0.89 – 1.45)
		Female	82	149	1.10 (0.84 – 1.44)
Diseases of the genitourinary system	XIV	Total	297	302	2.00 (1.70 – 2.34)*
		Male	143	151	1.91 (1.52 – 2.40)*
		Female	154	151	2.08 (1.66 – 2.61)*
Pregnancy, childbirth and the puerperium	XV	Total	280	584	0.96 (0.83 – 1.10)
		Female	280	584	0.95 (0.82 – 1.10)
Congenital malformations and chromosomal abnormalities	XVII	Total	2	10	0.40 (0.09 – 1.86)
		Male	1	6	0.33 (0.04 – 2.77)
		Female	1	4	0.50 (0.06 – 4.47)
Symptoms and abnormal findings <sup>e</sup>	XVIII	Total	368	375	1.99 (1.73 – 2.30)*
		Male	209	215	1.97 (1.63 – 2.39)*
		Female	159	160	2.02 (1.63 – 2.52)*
Injury, poisoning & certain other consequences of external causes	XIX	Total	200	362	1.11 (0.93 – 1.31)
		Male	133	232	1.15 (0.93 – 1.42)
		Female	67	133	1.03 (0.77 – 1.38)
Factors influencing health status <sup>f</sup>	XXI	Total	93	96	1.95 (1.46 – 2.59)*
		Male	41	45	1.82 (1.20 – 2.79)*
		Female	52	51	2.05 (1.39 – 3.02)*

<sup>a</sup> Each individual can appear several times in different chapters, <sup>b</sup> Hazard ratio, <sup>c</sup> 95% confidence interval, <sup>d</sup> Diseases of the blood and blood-forming organs and certain disorders involving the immune-mechanism, <sup>e</sup> Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified, <sup>f</sup> Factors influencing health status and contact with health services

clinic significantly more frequently than the general population (Figure 2). The controls, however, contacted the inpatient clinic less frequently than the general population.

### Mortality

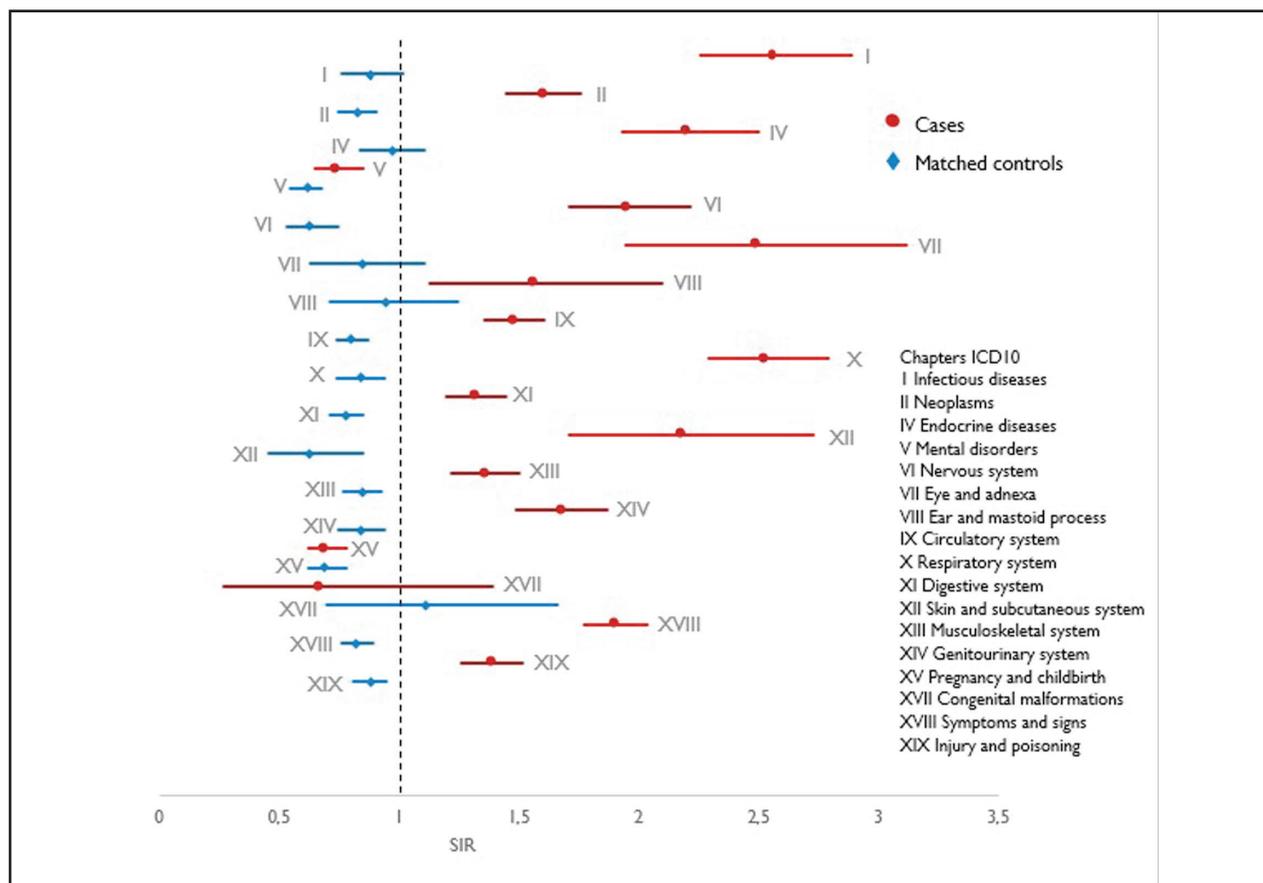
#### Comparison between cases and matched controls

Death occurred for 218 cases (2.8%) and for 233 (1.5%) controls. Mortality HR among sarcoid cases were 5.5 (95% CI 4.8 – 6.3) per 1000 person-years, and 2.9 (95% CI 2.6 – 3.3) per 1000 person-years in matched controls. The overall HR for mortality was 1.88 (95% CI 1.56 – 2.26) as seen in Table 3. Mortality caused by neoplasms (chapter II) was

significantly increased for sarcoid cases in both males and females. Increased mortality in males, but not in females, was seen for diseases of the circulatory system (chapter IX), respiratory system (chapter X) and external causes of mortality (chapter XX). Increased mortality HR was also seen for diseases of the blood and immune-mechanisms (chapter III) compared to controls, but this increase is probably due to the sarcoidosis-diagnosis itself.

External causes of mortality (chapter XX) includes accidents and intentional death. Of the sarcoid cases, 17 deaths were due to accidents and 10 were intentional. Of the controls, 12 died due to accidents, and 12 deaths were intentional.

Table 3 presents only the ICD10 chapters where at least five deaths among cases or controls



**Fig. 2.** Comparison of Comorbidities between Cases/Controls and the General Population. Every unique personal identification number was counted once a year, per chapter and county.

are declared. Seven deaths among the cases and six deaths among the controls were therefore not included in the table but are included in the analysis of total mortality.

#### *Comparison of cases and matched controls with the general population:*

Total overall mortality for sarcoid cases was greater than the general population, SMR 1.75 (95% CI 1.52-2.00). There was no significant difference in mortality between controls and the general population. Significantly more deaths were observed for sarcoid cases than for the general population due to neoplasms (chapters II), diseases of the respiratory system (chapter X) and external causes of mortality (chapter XX) as illustrated in Figure 3. These findings differ from the results of the comparison between sarcoid cases and matched controls, which

demonstrated a small increase in mortality caused by cardiovascular diseases, HR 1.64 (95% CI 1.08 – 2.48).

## DISCUSSION

In this longitudinal case-control study, the aim was to examine comorbidities and mortality in sarcoid patients in Sweden during the years 2007 – 2016. Increases in overall comorbidity and overall mortality in sarcoid patients compared to matched controls as well as the general population was observed during the observation period.

Sarcoid patients showed increased overall comorbidity compared to controls. Sarcoidosis is a systemic disease that manifests in several organs. Each organ manifestation has its own code in the ICD10, and these codes are found across several different chapters. Examples of codes include: G35-Cranial

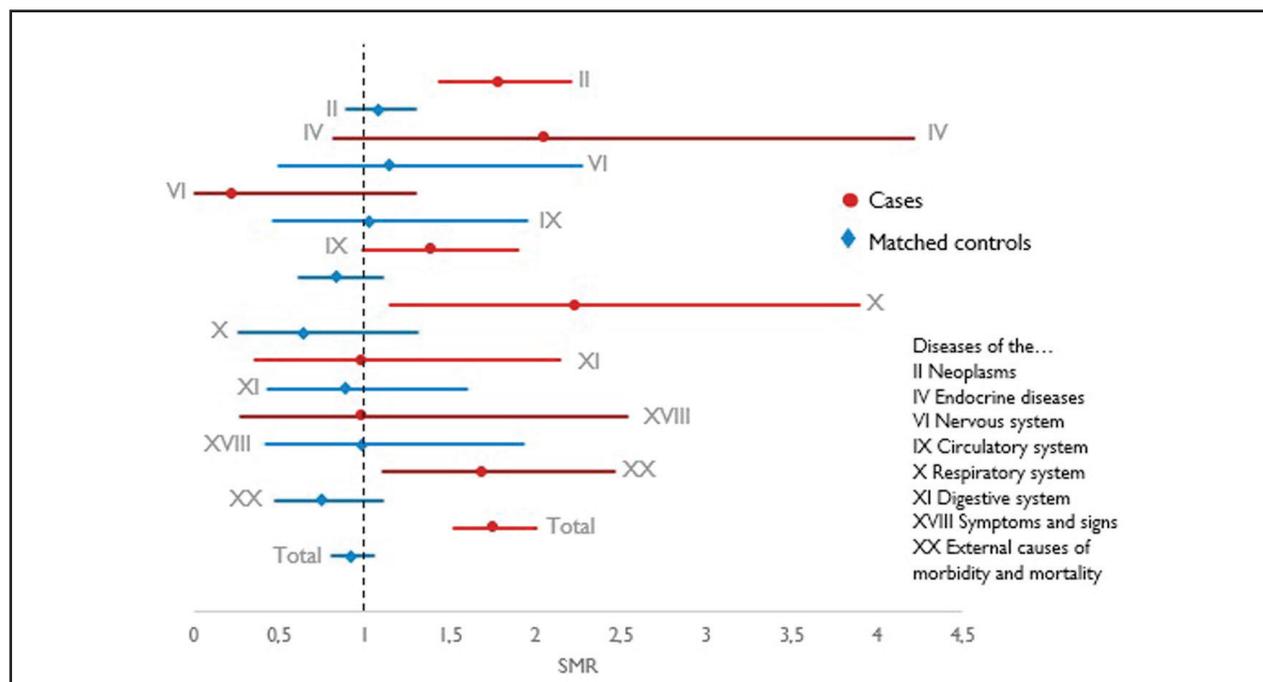
**Table 3.** Deaths in Sarcoid Cases and Matched Controls Compared using Cox Regression.

Chapters of ICD 10 <sup>a</sup>			Deaths cases (n)	Deaths controls (n)	HR <sup>b</sup> (95% CI) <sup>c</sup>
Total		Total	218	233	1.88 (1.56 – 2.26)*
		Male	131	149	1.76 (1.39 – 2.23)*
		Female	87	84	2.08 (1.54 – 2.81)*
Neoplasms	II	Total	90	110	1.64 (1.24 – 2.17)*
		Male	45	61	1.48 (1.00 – 2.17)
		Female	45	49	1.85 (1.23 – 2.77)*
Diseases of the blood and certain immune-mechanisms <sup>d</sup>	III	Total	24	1	48.15 (6.51 – 355.92)*
		Male	13	1	26.00 (3.40 – 198.75)*
		Female	11	0	-
Endocrine, nutritional and metabolic diseases	IV	Total	7	8	1.75 (0.64 – 4.84)
		Male	3	4	1.50 (0.34 – 6.71)
		Female	4	4	2.02 (0.50 – 8.06)
Diseases of the nervous system	VI	Total	1	9	0.22 (0.03 – 1.76)
		Male	0	7	-
		Female	1	2	1.01 (0.09 – 11.09)
Diseases of the circulatory system	IX	Total	40	49	1.64 (1.08 – 2.48)*
		Male	34	37	1.84 (1.15 – 2.93)*
		Female	6	12	1.00 (0.38 – 2.67)
Diseases of the respiratory system	X	Total	12	7	3.44 (1.36 – 8.74)*
		Male	7	4	3.50 (1.03 – 11.97)*
		Female	5	3	3.37 (0.81 – 14.12)
Diseases of the digestive system	XI	Total	6	11	1.09 (0.40 – 2.96)
		Male	2	5	0.80 (0.16 – 4.13)
		Female	4	6	1.34 (0.38 – 4.75)
Symptoms and abnormal findings <sup>e</sup>	XVIII	Total	4	8	1.00 (0.30 – 3.33)
		Male	1	7	0.29 (0.04 – 2.32)
		Female	3	1	6.00 (0.62 – 57.67)
External causes of morbidity and mortality	XX	Total	27	24	2.26 (1.30 – 3.91)*
		Male	22	19	2.32 (1.25 – 4.28)*
		Female	5	5	2.02 (0.58 – 6.98)

<sup>a</sup> Only chapters where at least 5 deaths are seen in either cases or the controls are reported, <sup>b</sup> Hazard ratio, <sup>c</sup> 95% confidence interval, <sup>d</sup> Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, <sup>e</sup> Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified

nerve disorders-, H22-Disorders of iris and ciliary body- and I41-Myocarditis in diseases classified elsewhere. In this study, observations of comorbidities are presented at the ICD10 chapter level instead of analyzing individual diagnoses. Therefore, it is not possible to specify which diagnoses are causing the increase.

As mentioned previously, a large meta-analysis suggested that the risk of malignancies increases slightly with sarcoidosis (11). In this study, malignancy was one of the most common reasons patients needed inpatient care, HR 1.78 (95% CI 1.50 – 2.10), which support this observation. Only cardiovascular diseases led to as many, and slightly more, inpatient



**Fig. 3.** Comparison of Mortality between Cases/Controls and the General Population. Every unique personal identification number was counted only once a year, per chapter and county. Only chapters with 5 or more deaths among cases or controls are included.

visits, but for these comorbidities, the difference between cases and controls was not as large, HR 1.40 (95% CI 1.21 – 1.63).

This study reveals increased mortality in sarcoid cases compared to controls, with death occurring in 2.8% of sarcoid cases and 1.5% of controls, HR 1.88 (95% CI 1.56–2.26). In previous studies, mortality rates have ranged between 9.4–14 per 1000 person-years (13, 14, 16). A recently-published Swedish study on mortality in sarcoid patients aged 18–85 years showed a mortality rate of 11 per 1000 person-years, while controls had a mortality rate of 6.7 per 1000 person-years (19). This study showed mortality rates of 5.5 (95% CI 4.8 – 6.3) per 1000 person-years among sarcoid cases and 2.9 (95% CI 2.6– 3.3) per 1000 person-years in matched controls. The lower mortality rate observed in this study might be due to the younger study population (aged 20–65 years), or to the somewhat healthier populations since neither the cases nor the controls suffered from ankylosing spondylitis, rheumatoid arthritis, Crohn’s disease or ulcerative colitis.

The ICD10 chapter associated with the highest increased risk of death was diseases of the blood

and immune-mechanism (*chapter III*), where the code for sarcoidosis diagnosis is found. Previously, sarcoidosis was reported to account for 24.7–58.8% of deaths occurring among sarcoid patients (14, 17). In this study, sarcoidosis was considered the cause of death in 10.6% of deaths among sarcoid patients. In Scandinavia, one third of sarcoid patients is affected by the acute form, Lofgren’s syndrome, rather than the chronic form. Lofgren’s syndrome is said to have a better prognosis. The cause of death among cases evaluated in this study may be affected by low reporting of sarcoidosis as the cause of death among patients, since patients may have suffered from Lofgren’s syndrome earlier in life and were considered recovered at the time of death. Another impact to mortality, as evaluated herein, is that the downstream consequences of the patients’ sarcoidosis were coded as the cause of death rather than the sarcoidosis diagnosis itself.

The ICD10 chapters associated with the highest number of deaths among sarcoid cases was neoplasms (90 deaths, 41.3%), cardiovascular diseases (40 deaths, 18.3%), external causes of mortality (27 deaths, 12.4%) and respiratory diseases (12 deaths,

5.5%). A study investigating sarcoidosis-related mortality in France, cardiovascular and respiratory diseases accounted for 16.8% and 7.5% of underlying causes of death while sarcoidosis was listed as a non-underlying cause of death, which is similar to the findings of this study (13). However, neoplasms accounted for 24.7% of the underlying cause of deaths which is clearly lower than the findings in this study (13).

Suicide is a cause of death included in external causes of mortality (chapter XX) and, in males, this chapter was associated with a significant increase in death compared to controls, HR 2.32 (95% CI 1.25 – 4.98). It has previously been reported that the prevalence of depression in patients with sarcoidosis may be up to 60% when a standardized protocol is used to identify depression (20). However, this study show no increased number of visits to inpatient care for mental and behavioural diseases (chapter V). One explanation for this finding might be that depression was under-diagnosed among the study cases. Another, possibly more likely explanation may be that mild to moderate depression is usually treated in primary care, but this study used data from the inpatient register only.

One limitation of this study was that it is not possible stratify sarcoid cases by level of severity of sarcoidosis or type of sarcoidosis (acute or chronic form). Another limitation, as this is a register study, there was no information on potential confounders such as smoking habits, however cases and controls are matched based on age, sex and geographical area and therefore one could assume the distribution of smokers and non-smokers to be similar in both groups. Furthermore, there was no information about medications, which also could be a confounder, as medications used to treat sarcoidosis can cause varying side effects. For instance Glucocorticoids, the first-line therapy, have numerous side effects that affect several different organ systems (21).

The strengths of this study is study is the large study population comprising 7828 cases and 15,656 matched controls, and cases and controls were also both compared to the general population. Moreover, Sweden maintains high-quality registers that cover the entire population, together with unique personal identification numbers that can link patient data across different nationwide registers, and therefore it was possible, with few exceptions, to include anyone

who was diagnosed with sarcoidosis in the years 2007–2016, and not just a selection.

In conclusion, individuals with sarcoidosis are at higher risk of comorbidities and mortality compared to matched controls as well as the general population. Thus healthcare professionals who meet sarcoid patients, should strive to identify and treat comorbidities to reduce the risk of impaired quality of life and, eventually, premature death among individuals with sarcoidosis.

Conflict of Interest: None

## REFERENCES

- Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Muller-Quernheim J. Sarcoidosis. *Lancet*. 2014;383(9923):1155–67. doi: 10.1016/S0140-6736(13)60680-7. PubMed PMID: 24090799.
- Rybicki BA, Iannuzzi MC, Frederick MM, Thompson BW, Rossmann MD, Bresnitz EA, et al. Familial aggregation of sarcoidosis. A case-control etiologic study of sarcoidosis (ACCESS). *Am J Respir Crit Care Med*. 2001;164(11):2085–91. Epub 2001/12/12. doi: 10.1164/ajrccm.164.11.2106001. PubMed PMID: 11739139.
- Arkema EV, Grunewald J, Kullberg S, Eklund A, Askling J. Sarcoidosis incidence and prevalence: a nationwide register-based assessment in Sweden. *Eur Respir J*. 2016. doi: 10.1183/13993003.00477-2016. PubMed PMID: 27471207.
- Costabel U, Hunninghake GW. ATS/ERS/WASOG statement on sarcoidosis. Sarcoidosis Statement Committee. American Thoracic Society. European Respiratory Society. World Association for Sarcoidosis and Other Granulomatous Disorders. *Eur Respir J*. 1999;14(4):735–7. Epub 1999/11/26. doi: 10.1034/j.1399-3003.1999.14d02.x. PubMed PMID: 10573213.
- Rajoriya N, Wotton CJ, Yeates DG, Travis SP, Goldacre MJ. Immune-mediated and chronic inflammatory disease in people with sarcoidosis: disease associations in a large UK database. *Postgrad Med J*. 2009;85(1003):233–7. Epub 2009/06/13. doi: 10.1136/pgmj.2008.067769. PubMed PMID: 19520873.
- Hu X, Carmona EM, Yi ES, Pellikka PA, Ryu J. Causes of death in patients with chronic sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2016;33(3):275–80. Epub 2016/10/21. PubMed PMID: 27758994.
- Pohle S, Baty F, Brutsche M. In-Hospital Disease Burden of Sarcoidosis in Switzerland from 2002 to 2012. *PLoS One*. 2016;11(3):e0151940. Epub 2016/03/18. doi: 10.1371/journal.pone.0151940. PubMed PMID: 26987059; PubMed Central PMCID: PMC4795542.
- Martusewicz-Boros MM, Boros PW, Wiatr E, Roszkowski-Sliz K. What comorbidities accompany sarcoidosis? A large cohort (n = 1779) patients analysis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2015;32(2):115–20. Epub 2015/08/19. PubMed PMID: 26278690.
- Westney GE, Habib S, Quarshie A. Comorbid illnesses and chest radiographic severity in African-American sarcoidosis patients. *Lung*. 2007;185(3):131–7. Epub 2007/03/27. doi: 10.1007/s00408-007-9008-z. PubMed PMID: 17384899.
- Brito-Zeron P, Acar-Denizli N, Siso-Almirall A, Bosch X, Hernandez F, Vilanova S, et al. The Burden of Comorbidity and Complexity in Sarcoidosis: Impact of Associated Chronic Diseases. *Lung*. 2018;196(2):239–48. Epub 2017/12/13. doi: 10.1007/s00408-017-0076-4. PubMed PMID: 29230534.

11. Bonifazi M, Bravi F, Gasparini S, La Vecchia C, Gabrielli A, Wells AU, et al. Sarcoidosis and cancer risk: systematic review and meta-analysis of observational studies. *Chest*. 2015;147(3):778–91. Epub 2014/10/24. doi: 10.1378/chest.14-1475. PubMed PMID: 25340385.
12. Ji J, Shu X, Li X, Sundquist K, Sundquist J, Hemminki K. Cancer risk in hospitalized sarcoidosis patients: a follow-up study in Sweden. *Ann Oncol*. 2009;20(6):1121–6. Epub 2009/02/13. doi: 10.1093/annonc/mdn767. PubMed PMID: 19211624.
13. Jamilloux Y, Maucort-Boulch D, Kerever S, Gerfaud-Valentin M, Broussole C, Eb M, et al. Sarcoidosis-related mortality in France: a multiple-cause-of-death analysis. *Eur Respir J*. 2016;48(6):1700–9. Epub 2016/09/24. doi: 10.1183/13993003.00457-2016. PubMed PMID: 27660516.
14. Swigris JJ, Olson AL, Huie TJ, Fernandez-Perez ER, Solomon J, Sprunger D, et al. Sarcoidosis-related mortality in the United States from 1988 to 2007. *Am J Respir Crit Care Med*. 2011;183(11):1524–30. Epub 2011/02/19. doi: 10.1164/rccm.201010-1679OC. PubMed PMID: 21330454; PubMed Central PMCID: PMC3137141.
15. Duncan ME, Goldacre MJ. Mortality trends for tuberculosis and sarcoidosis in English populations, 1979–2008. *Int J Tuberc Lung Dis*. 2012;16(1):38–42. Epub 2012/01/13. doi: 10.5588/ijtld.11.0077. PubMed PMID: 22236843.
16. Gribbin J, Hubbard RB, Le Jeune I, Smith CJ, West J, Tata LJ. Incidence and mortality of idiopathic pulmonary fibrosis and sarcoidosis in the UK. *Thorax*. 2006;61(11):980–5. Epub 2006/07/18. doi: 10.1136/thx.2006.062836. PubMed PMID: 16844727; PubMed Central PMCID: PMC2121155.
17. Tukey MH, Berman JS, Boggs DA, White LF, Rosenberg L, Cozier YC. Mortality among African American women with sarcoidosis: data from the Black Women's Health Study. *Sarcoidosis Vasc Diffuse Lung Dis*. 2013;30(2):128–33. Epub 2013/09/28. PubMed PMID: 24071884; PubMed Central PMCID: PMC3801105.
18. Viskum K, Vestbo J. Vital prognosis in intrathoracic sarcoidosis with special reference to pulmonary function and radiological stage. *Eur Respir J*. 1993;6(3):349–53. Epub 1993/03/01. PubMed PMID: 8472824.
19. Rossides M, Kullberg S, Askling J, Eklund A, Grunewald J, Arkeima EV. Sarcoidosis mortality in Sweden: a population-based cohort study. *Eur Respir J*. 2018;51(2). Epub 2018/02/23. doi: 10.1183/13993003.01815-2017. PubMed PMID: 29467203; PubMed Central PMCID: PMC5886843 erj.ersjournals.com.
20. Chang B, Steimel J, Moller DR, Baughman RP, Judson MA, Yeager H, Jr., et al. Depression in sarcoidosis. *Am J Respir Crit Care Med*. 2001;163(2):329–34. Epub 2001/02/17. doi: 10.1164/ajrccm.163.2.2004177. PubMed PMID: 11179101.
21. Oray M, Abu Samra K, Ebrahimiadib N, Meese H, Foster CS. Long-term side effects of glucocorticoids. *Expert Opin Drug Saf*. 2016;15(4):457–65. Epub 2016/01/21. doi: 10.1517/14740338.2016.1140743. PubMed PMID: 26789102.

**Supplement Table 1:** Visits to Inpatient Care for the all diseases found among Cases and Controls (ratio for cases/control is 1:2). Only one registration for each disease were counted, i.e. multiple visits due to the same disease are only counted as one.

Diagnosis	ICD 10	Cases	Control <sup>1</sup>
		number	
Other salmonella infections	A02	0	1
Other bacterial intestinal infections	A04	22	21
Other bacterial foodborne intoxications, not elsewhere classified	A05	1	0
Other protozoal intestinal diseases	A07	2	1
Viral and other specified intestinal infections	A08	16	2
Other gastroenteritis and colitis of infectious and unspecified origin	A09	39	22
Respiratory tuberculosis, bacteriologically and histologically confirmed	A15	3	3
Respiratory tuberculosis, not confirmed bacteriologically or histologically	A16	3	1
Tuberculosis of nervous system	A17	1	0
Tuberculosis of other organs	A18	3	0
Miliary tuberculosis	A19	1	0
Tularaemia	A21	0	1
Erysipeloid	A26	0	1
Infection due to other mycobacteria	A31	3	0
Streptococcal sepsis	A40	8	4
Other sepsis	A41	53	37
Erysipelas	A46	45	40
Other bacterial diseases, not elsewhere classified	A48	3	1
Bacterial infection of unspecified site	A49	20	13
Anogenital herpesviral [herpes simplex] infection	A60	1	1

Diagnosis	ICD 10	Cases	Control'
Other predominantly sexually transmitted diseases, not elsewhere classified	A63	1	0
Other spirochaetal infections	A69	1	0
Tick-borne viral encephalitis	A84	1	1
Viral meningitis	A87	6	3
Dengue fever [classical dengue]	A90	0	1
Other viral haemorrhagic fevers, not elsewhere classified	A98	3	0
Herpesviral [herpes simplex] infections	B00	3	1
Varicella [chickenpox]	B01	1	0
Zoster [herpes zoster]	B02	6	4
Chronic viral hepatitis	B18	4	2
Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases	B20	2	0
Cytomegaloviral disease	B25	5	1
Infectious mononucleosis	B27	0	2
Viral infection of unspecified site	B34	26	8
Candidiasis	B37	4	4
Histoplasmosis	B39	1	0
Aspergillosis	B44	5	0
Plasmodium falciparum malaria	B50	1	1
Pneumocystosis	B59	4	1
Sequelae of tuberculosis	B90	1	0
Streptococcus and staphylococcus as the cause of diseases classified to other chapters	B95	0	2
Other specified bacterial agents as the cause of diseases classified to other chapters	B96	2	0
Other and unspecified infectious diseases	B99	11	12
Malignant neoplasm of base of tongue	C01	2	3
Malignant neoplasm of other and unspecified parts of tongue	C02	3	0
Malignant neoplasm of gum	C03	1	1
Malignant neoplasm of palate	C05	0	1
Malignant neoplasm of other and unspecified parts of mouth	C06	1	0
Malignant neoplasm of parotid gland	C07	0	2
Malignant neoplasm of other and unspecified major salivary glands	C08	1	0
Malignant neoplasm of tonsil	C09	4	2
Malignant neoplasm of oesophagus	C15	0	1
Malignant neoplasm of stomach	C16	0	4
Malignant neoplasm of small intestine	C17	1	0
Malignant neoplasm of colon	C18	22	15
Malignant neoplasm of rectum	C20	7	13
Malignant neoplasm of anus and anal canal	C21	1	0
Malignant neoplasm of liver and intrahepatic bile ducts	C22	2	6
Malignant neoplasm of other and unspecified parts of biliary tract	C24	0	4
Malignant neoplasm of pancreas	C25	4	5
Malignant neoplasm of nasal cavity and middle ear	C30	1	0
Malignant neoplasm of accessory sinuses	C31	1	0

Diagnosis	ICD 10	Cases	Control'
Malignant neoplasm of larynx	C32	1	0
Malignant neoplasm of bronchus and lung	C34	13	26
Malignant neoplasm of thymus	C37	1	1
Malignant neoplasm of bone and articular cartilage of limbs	C40	1	1
Malignant melanoma of skin	C43	8	9
Other malignant neoplasms of skin	C44	6	4
Mesothelioma	C45	2	0
Malignant neoplasm of retroperitoneum and peritoneum	C48	2	4
Malignant neoplasm of other connective and soft tissue	C49	3	4
Malignant neoplasm of breast	C50	22	66
Malignant neoplasm of cervix uteri	C53	4	4
Malignant neoplasm of corpus uteri	C54	6	13
Malignant neoplasm of ovary	C56	8	8
Malignant neoplasm of other and unspecified female genital organs	C57	1	1
Malignant neoplasm of penis	C60	2	0
Malignant neoplasm of prostate	C61	25	35
Malignant neoplasm of testis	C62	1	1
Malignant neoplasm of kidney, except renal pelvis	C64	8	9
Malignant neoplasm of renal pelvis	C65	0	3
Malignant neoplasm of ureter	C66	0	1
Malignant neoplasm of bladder	C67	7	20
Malignant neoplasm of eye and adnexa	C69	1	0
Malignant neoplasm of brain	C71	5	8
Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system	C72	1	0
Malignant neoplasm of thyroid gland	C73	5	2
Malignant neoplasm of adrenal gland	C74	1	0
Malignant neoplasm of other and ill-defined sites	C76	1	0
Secondary and unspecified malignant neoplasm of lymph nodes	C77	8	11
Secondary malignant neoplasm of respiratory and digestive organs	C78	23	20
Secondary malignant neoplasm of other and unspecified sites	C79	23	16
Malignant neoplasm, without specification of site	C80	4	0
Hodgkin lymphoma	C81	7	0
Follicular lymphoma	C82	0	1
Non-follicular lymphoma	C83	10	8
Mature T/NK-cell lymphomas	C84	4	1
Other and unspecified types of non-Hodgkin lymphoma	C85	14	6
Other specified types of T/NK-cell lymphoma	C86	3	0
Malignant immunoproliferative diseases	C88	2	2
Multiple myeloma and malignant plasma cell neoplasms	C90	4	11
Lymphoid leukaemia	C91	3	2
Myeloid leukaemia	C92	5	1
Monocytic leukaemia	C93	1	0

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Leukaemia of unspecified cell type	C95	0	1
Carcinoma in situ of other and unspecified digestive organs	D01	1	0
Carcinoma in situ of breast	D05	4	7
Carcinoma in situ of cervix uteri	D06	4	1
Carcinoma in situ of other and unspecified genital organs	D07	2	0
Benign neoplasm of mouth and pharynx	D10	0	1
Benign neoplasm of major salivary glands	D11	4	4
Benign neoplasm of colon, rectum, anus and anal canal	D12	4	7
Benign neoplasm of other and ill-defined parts of digestive system	D13	2	1
Benign neoplasm of middle ear and respiratory system	D14	9	1
Benign neoplasm of bone and articular cartilage	D16	1	2
Benign lipomatous neoplasm	D17	2	4
Haemangioma and lymphangioma, any site	D18	1	1
Benign neoplasm of soft tissue of retroperitoneum and peritoneum	D20	2	1
Other benign neoplasms of connective and other soft tissue	D21	2	3
Benign neoplasm of breast	D24	1	1
Leiomyoma of uterus	D25	18	46
Benign neoplasm of ovary	D27	5	11
Benign neoplasm of male genital organs	D29	1	0
Benign neoplasm of urinary organs	D30	1	0
Benign neoplasm of eye and adnexa	D31	3	0
Benign neoplasm of meninges	D32	8	6
Benign neoplasm of brain and other parts of central nervous system	D33	2	0
Benign neoplasm of thyroid gland	D34	1	3
Benign neoplasm of other and unspecified endocrine glands	D35	10	8
Benign neoplasm of other and unspecified sites	D36	3	0
Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	D37	20	15
Neoplasm of uncertain or unknown behaviour of middle ear and respiratory and intrathoracic organs	D38	79	5
Neoplasm of uncertain or unknown behaviour of female genital organs	D39	5	6
Neoplasm of uncertain or unknown behaviour of male genital organs	D40	3	0
Neoplasm of uncertain or unknown behaviour of urinary organs	D41	7	11
Neoplasm of uncertain or unknown behaviour of brain and central nervous system	D43	12	11
Neoplasm of uncertain or unknown behaviour of endocrine glands	D44	6	7
Myelodysplastic syndromes	D46	1	0
Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	D47	1	2
Neoplasm of uncertain or unknown behaviour of other and unspecified sites	D48	7	10
Iron deficiency anaemia	D50	17	8
Vitamin B12 deficiency anaemia	D51	0	1
Other nutritional anaemias	D53	0	1
Acquired haemolytic anaemia	D59	3	1

Diagnosis	ICD 10	Cases	Control <sup>1</sup>
Other aplastic anaemias	D61	1	1
Acute posthaemorrhagic anaemia	D62	1	2
Other anaemias	D64	14	20
Other coagulation defects	D68	3	1
Purpura and other haemorrhagic conditions	D69	4	3
Agranulocytosis	D70	14	3
Other disorders of white blood cells	D72	0	1
Diseases of spleen	D73	2	1
Other specified diseases with participation of lymphoreticular and reticulohistiocytic tissue	D76	2	0
Immunodeficiency associated with other major defects	D82	1	1
Common variable immunodeficiency	D83	0	1
Other immunodeficiencies	D84	1	0
Sarcoidosis	D86	526	0
Other hypothyroidism	E03	0	3
Other nontoxic goitre	E04	12	15
Thyrotoxicosis [hyperthyroidism]	E05	6	9
Thyroiditis	E06	1	1
Other disorders of thyroid	E07	0	1
Type 1 diabetes mellitus	E10	19	24
Type 2 diabetes mellitus	E11	51	36
Other specified diabetes mellitus	E13	2	0
Unspecified diabetes mellitus	E14	2	1
Nondiabetic hypoglycaemic coma	E15	0	1
Other disorders of pancreatic internal secretion	E16	2	3
Hyperparathyroidism and other disorders of parathyroid gland	E21	13	6
Hyperfunction of pituitary gland	E22	0	2
Hypofunction and other disorders of pituitary gland	E23	5	0
Other disorders of adrenal gland	E27	6	1
Other endocrine disorders	E34	1	0
Unspecified severe protein-energy malnutrition	E43	1	0
Unspecified protein-energy malnutrition	E46	3	1
Thiamine deficiency	E51	0	3
Localized adiposity	E65	7	4
Obesity	E66	84	79
Sequelae of hyperalimentation	E68	1	0
Lactose intolerance	E73	1	0
Disorders of sphingolipid metabolism and other lipid storage disorders	E75	0	1
Disorders of lipoprotein metabolism and other lipidaemias	E78	1	3
Disorders of mineral metabolism	E83	18	1
Volume depletion	E86	6	3
Other disorders of fluid, electrolyte and acid-base balance	E87	20	18
Postprocedural endocrine and metabolic disorders, not elsewhere classified	E89	0	2

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Dementia in other diseases classified elsewhere	F02	1	0
Unspecified dementia	F03	0	2
Delirium, not induced by alcohol and other psychoactive substances	F05	3	4
Other mental disorders due to brain damage and dysfunction and to physical disease	F06	3	2
Personality and behavioural disorders due to brain disease, damage and dysfunction	F07	0	2
Unspecified organic or symptomatic mental disorder	F09	1	1
Mental and behavioural disorders due to use of alcohol	F10	58	107
Mental and behavioural disorders due to use of opioids	F11	14	20
Mental and behavioural disorders due to use of cannabinoids	F12	1	2
Mental and behavioural disorders due to use of sedatives or hypnotics	F13	9	7
Mental and behavioural disorders due to use of cocaine	F14	1	1
Mental and behavioural disorders due to use of other stimulants, including caffeine	F15	6	4
Mental and behavioural disorders due to use of volatile solvents	F18	0	1
Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances	F19	22	32
Schizophrenia	F20	5	24
Persistent delusional disorders	F22	3	10
Acute and transient psychotic disorders	F23	4	8
Schizoaffective disorders	F25	3	7
Unspecified nonorganic psychosis	F29	3	12
Manic episode	F30	1	3
Bipolar affective disorder	F31	22	31
Depressive episode	F32	40	52
Recurrent depressive disorder	F33	18	27
Persistent mood [affective] disorders	F34	1	0
Unspecified mood [affective] disorder	F39	1	0
Other anxiety disorders	F41	43	40
Obsessive-compulsive disorder	F42	4	5
Reaction to severe stress, and adjustment disorders	F43	26	43
Dissociative [conversion] disorders	F44	4	3
Somatoform disorders	F45	5	0
Other neurotic disorders	F48	1	0
Eating disorders	F50	2	1
Nonorganic sleep disorders	F51	4	2
Specific personality disorders	F60	12	9
Mixed and other personality disorders	F61	0	1
Habit and impulse disorders	F63	1	0
Mild mental retardation	F70	1	3
Moderate mental retardation	F71	1	0
Unspecified mental retardation	F79	0	1
Pervasive developmental disorders	F84	3	4
Hyperkinetic disorders	F90	7	4

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Conduct disorders	F91	1	0
Mental disorder, not otherwise specified	F99	3	0
Bacterial meningitis, not elsewhere classified	G00	0	1
Meningitis due to other and unspecified causes	G03	2	2
Encephalitis, myelitis and encephalomyelitis	G04	2	1
Encephalitis, myelitis and encephalomyelitis in diseases classified elsewhere	G05	1	0
Intracranial and intraspinal abscess and granuloma	G06	4	0
Hereditary ataxia	G11	1	0
Spinal muscular atrophy and related syndromes	G12	1	4
Parkinson disease	G20	2	3
Dystonia	G24	1	0
Other extrapyramidal and movement disorders	G25	5	2
Alzheimer disease	G30	0	2
Other degenerative diseases of nervous system, not elsewhere classified	G31	1	0
Multiple sclerosis	G35	7	11
Other demyelinating diseases of central nervous system	G37	3	1
Epilepsy	G40	27	34
Status epilepticus	G41	3	0
Migraine	G43	22	14
Other headache syndromes	G44	17	10
Transient cerebral ischaemic attacks and related syndromes	G45	44	40
Sleep disorders	G47	53	22
Disorders of trigeminal nerve	G50	5	2
Facial nerve disorders	G51	10	6
Nerve root and plexus disorders	G54	2	1
Mononeuropathies of upper limb	G56	3	3
Mononeuropathies of lower limb	G57	1	1
Hereditary and idiopathic neuropathy	G60	1	0
Inflammatory polyneuropathy	G61	5	6
Other polyneuropathies	G62	7	2
Polyneuropathy in diseases classified elsewhere	G63	0	1
Other disorders of peripheral nervous system	G64	1	0
Myasthenia gravis and other myoneural disorders	G70	0	1
Primary disorders of muscles	G71	2	1
Other myopathies	G72	1	2
Cerebral palsy	G80	0	1
Hemiplegia	G81	2	3
Paraplegia and tetraplegia	G82	5	1
Other paralytic syndromes	G83	2	3
Disorders of autonomic nervous system	G90	0	1
Hydrocephalus	G91	9	5
Other disorders of brain	G93	5	4

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Other diseases of spinal cord	G95	2	2
Other disorders of central nervous system	G96	2	1
Postprocedural disorders of nervous system, not elsewhere classified	G97	1	1
Other disorders of eyelid	H02	2	1
Disorders of lacrimal system	H04	6	1
Disorders of orbit	H05	2	2
Keratitis	H16	2	3
Other disorders of cornea	H18	1	3
Iridocyclitis	H20	1	0
Other cataract	H26	1	1
Chorioretinal inflammation	H30	2	0
Retinal detachments and breaks	H33	18	19
Retinal vascular occlusions	H34	1	3
Other retinal disorders	H35	15	4
Glaucoma	H40	9	0
Disorders of vitreous body	H43	5	6
Disorders of globe	H44	1	1
Optic neuritis	H46	2	0
Other disorders of optic [2nd] nerve and visual pathways	H47	2	0
Paralytic strabismus	H49	4	1
Other strabismus	H50	1	2
Other disorders of binocular movement	H51	0	1
Visual disturbances	H53	5	7
Visual impairment including blindness (binocular or monocular)	H54	1	0
Other disorders of eye and adnexa	H57	1	1
Otitis externa	H60	0	1
Other disorders of external ear	H61	2	0
Nonsuppurative otitis media	H65	0	1
Suppurative and unspecified otitis media	H66	4	3
Cholesteatoma of middle ear	H71	1	2
Perforation of tympanic membrane	H72	1	1
Other disorders of middle ear and mastoid	H74	1	0
Otosclerosis	H80	3	6
Disorders of vestibular function	H81	26	36
Conductive and sensorineural hearing loss	H90	2	2
Other hearing loss	H91	3	2
Rheumatic mitral valve diseases	I05	0	1
Essential (primary) hypertension	I10	18	28
Hypertensive heart disease	I11	2	1
Hypertensive renal disease	I12	1	0
Secondary hypertension	I15	5	0
Angina pectoris	I20	45	77

Diagnosis	ICD 10	Cases	Control
Acute myocardial infarction	I21	70	141
Subsequent myocardial infarction	I22	0	2
Certain current complications following acute myocardial infarction	I23	0	2
Other acute ischaemic heart diseases	I24	0	1
Chronic ischaemic heart disease	I25	18	28
Pulmonary embolism	I26	52	24
Other pulmonary heart diseases	I27	5	1
Acute pericarditis	I30	10	6
Other diseases of pericardium	I31	6	4
Pericarditis in diseases classified elsewhere	I32	1	0
Acute and subacute endocarditis	I33	4	4
Nonrheumatic mitral valve disorders	I34	2	5
Nonrheumatic aortic valve disorders	I35	6	13
Pulmonary valve disorders	I37	0	1
Endocarditis, valve unspecified	I38	2	4
Acute myocarditis	I40	3	8
Cardiomyopathy	I42	23	9
Cardiomyopathy in diseases classified elsewhere	I43	1	0
Atrioventricular and left bundle-branch block	I44	38	17
Other conduction disorders	I45	8	2
Cardiac arrest	I46	4	6
Paroxysmal tachycardia	I47	42	24
Atrial fibrillation and flutter	I48	91	95
Other cardiac arrhythmias	I49	41	17
Heart failure	I50	78	48
Complications and ill-defined descriptions of heart disease	I51	2	1
Other heart disorders in diseases classified elsewhere	I52	3	0
Subarachnoid haemorrhage	I60	4	4
Intracerebral haemorrhage	I61	5	14
Other nontraumatic intracranial haemorrhage	I62	6	4
Cerebral infarction	I63	51	82
Stroke, not specified as haemorrhage or infarction	I64	2	2
Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction	I65	3	7
Other cerebrovascular diseases	I67	8	3
Sequelae of cerebrovascular disease	I69	5	10
Atherosclerosis	I70	8	18
Aortic aneurysm and dissection	I71	8	12
Other aneurysm and dissection	I72	3	4
Other peripheral vascular diseases	I73	4	2
Arterial embolism and thrombosis	I74	4	3
Other disorders of arteries and arterioles	I77	6	0
Phlebitis and thrombophlebitis	I80	18	5

Diagnosis	ICD 10	Cases	Control'
Portal vein thrombosis	I81	1	1
Other venous embolism and thrombosis	I82	2	2
Varicose veins of lower extremities	I83	6	3
Oesophageal varices	I85	2	6
Varicose veins of other sites	I86	0	2
Other disorders of veins	I87	1	1
Nonspecific lymphadenitis	I88	3	1
Other noninfective disorders of lymphatic vessels and lymph nodes	I89	1	4
Hypotension	I95	9	8
Postprocedural disorders of circulatory system, not elsewhere classified	I97	1	0
Other and unspecified disorders of circulatory system	I99	0	1
Acute nasopharyngitis [common cold]	J00	1	0
Acute sinusitis	J01	14	3
Acute pharyngitis	J02	6	3
Acute tonsillitis	J03	9	11
Acute laryngitis and tracheitis	J04	4	1
Acute obstructive laryngitis [croup] and epiglottitis	J05	0	1
Acute upper respiratory infections of multiple and unspecified sites	J06	29	7
Influenza due to certain identified influenza virus	J09	6	4
Influenza due to other identified influenza virus	J10	10	11
Influenza, virus not identified	J11	2	3
Viral pneumonia, not elsewhere classified	J12	2	0
Pneumonia due to Streptococcus pneumoniae	J13	20	16
Pneumonia due to Haemophilus influenzae	J14	20	7
Bacterial pneumonia, not elsewhere classified	J15	74	65
Pneumonia due to other infectious organisms, not elsewhere classified	J16	1	0
Pneumonia, organism unspecified	J18	128	68
Acute bronchitis	J20	12	15
Unspecified acute lower respiratory infection	J22	6	2
Vasomotor and allergic rhinitis	J30	1	0
Chronic sinusitis	J32	9	4
Nasal polyp	J33	6	4
Other disorders of nose and nasal sinuses	J34	2	5
Chronic diseases of tonsils and adenoids	J35	8	9
Peritonsillar abscess	J36	2	8
Chronic laryngitis and laryngotracheitis	J37	1	1
Diseases of vocal cords and larynx, not elsewhere classified	J38	5	2
Other diseases of upper respiratory tract	J39	2	3
Bronchitis, not specified as acute or chronic	J40	4	2
Simple and mucopurulent chronic bronchitis	J41	1	0
Unspecified chronic bronchitis	J42	2	1

Diagnosis	ICD 10	Cases	Control
Emphysema	J43	1	0
Other chronic obstructive pulmonary disease	J44	24	27
Asthma	J45	14	9
Status asthmaticus	J46	4	4
Bronchiectasis	J47	3	1
Coalworker pneumoconiosis	J60	1	0
Respiratory conditions due to inhalation of chemicals, gases, fumes and vapours	J68	2	0
Pneumonitis due to solids and liquids	J69	5	7
Respiratory conditions due to other external agents	J70	0	1
Adult respiratory distress syndrome	J80	2	0
Pulmonary oedema	J81	4	2
Other interstitial pulmonary diseases	J84	20	1
Abscess of lung and mediastinum	J85	6	1
Pyothorax	J86	3	2
Pleural effusion, not elsewhere classified	J90	19	16
Pneumothorax	J93	23	4
Postprocedural respiratory disorders, not elsewhere classified	J95	1	0
Respiratory failure, not elsewhere classified	J96	23	8
Other respiratory disorders	J98	15	1
Diseases of pulp and periapical tissues	K04	4	1
Gingivitis and periodontal diseases	K05	2	0
Dentofacial anomalies [including malocclusion]	K07	1	2
Other disorders of teeth and supporting structures	K08	1	0
Other diseases of jaws	K10	0	2
Diseases of salivary glands	K11	5	5
Stomatitis and related lesions	K12	1	3
Other diseases of lip and oral mucosa	K13	1	1
Oesophagitis	K20	3	8
Gastro-oesophageal reflux disease	K21	12	6
Other diseases of oesophagus	K22	5	8
Gastric ulcer	K25	5	14
Duodenal ulcer	K26	5	13
Peptic ulcer, site unspecified	K27	0	1
Gastrojejunal ulcer	K28	0	1
Gastritis and duodenitis	K29	13	17
Functional dyspepsia	K30	8	6
Other diseases of stomach and duodenum	K31	6	3
Acute appendicitis	K35	50	67
Other appendicitis	K36	3	2
Unspecified appendicitis	K37	8	11
Other diseases of appendix	K38	2	0
Inguinal hernia	K40	15	16

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Femoral hernia	K41	1	0
Umbilical hernia	K42	10	8
Ventral hernia	K43	22	29
Diaphragmatic hernia	K44	4	4
Other abdominal hernia	K45	4	5
Unspecified abdominal hernia	K46	3	0
Crohn disease [regional enteritis]	K50	1	2
Ulcerative colitis	K51	1	2
Other noninfective gastroenteritis and colitis	K52	18	10
Vascular disorders of intestine	K55	3	3
Paralytic ileus and intestinal obstruction without hernia	K56	28	43
Diverticular disease of intestine	K57	38	48
Irritable bowel syndrome	K58	3	3
Other functional intestinal disorders	K59	29	17
Fissure and fistula of anal and rectal regions	K60	3	6
Abscess of anal and rectal regions	K61	15	16
Other diseases of anus and rectum	K62	6	4
Other diseases of intestine	K63	5	5
Haemorrhoids and perianal venous thrombosis	K64	3	6
Peritonitis	K65	6	3
Alcoholic liver disease	K70	3	9
Toxic liver disease	K71	1	1
Hepatic failure, not elsewhere classified	K72	2	9
Chronic hepatitis, not elsewhere classified	K73	1	0
Fibrosis and cirrhosis of liver	K74	5	5
Other inflammatory liver diseases	K75	2	3
Other diseases of liver	K76	6	4
Cholelithiasis	K80	115	110
Cholecystitis	K81	15	19
Other diseases of gallbladder	K82	1	1
Other diseases of biliary tract	K83	7	8
Acute pancreatitis	K85	33	26
Other diseases of pancreas	K86	4	6
Intestinal malabsorption	K90	1	1
Postprocedural disorders of digestive system, not elsewhere classified	K91	4	1
Other diseases of digestive system	K92	17	29
Cutaneous abscess, furuncle and carbuncle	L02	12	12
Cellulitis	L03	9	11
Acute lymphadenitis	L04	1	0
Pilonidal cyst	L05	3	1
Other local infections of skin and subcutaneous tissue	L08	10	7
Atopic dermatitis	L20	1	0

Diagnosis	ICD 10	Cases	Control'
Dermatitis due to substances taken internally	L27	5	0
Pruritus	L29	1	0
Other dermatitis	L30	1	3
Psoriasis	L40	7	0
Urticaria	L50	5	7
Erythema multiforme	L51	1	0
Erythema nodosum	L52	1	0
Other erythematous conditions	L53	1	1
Other follicular disorders	L73	1	0
Decubitus ulcer and pressure area	L89	4	2
Atrophic disorders of skin	L90	2	0
Vasculitis limited to skin, not elsewhere classified	L95	1	0
Ulcer of lower limb, not elsewhere classified	L97	10	1
Other disorders of skin and subcutaneous tissue, not elsewhere classified	L98	6	3
Pyogenic arthritis	M00	7	15
Reactive arthropathies	M02	3	2
Postinfective and reactive arthropathies in diseases classified elsewhere	M03	1	0
Other rheumatoid arthritis	M06	0	1
Gout	M10	6	5
Other crystal arthropathies	M11	1	2
Other arthritis	M13	6	6
Arthropathies in other diseases classified elsewhere	M14	1	0
Polyarthrosis	M15	1	0
Coxarthrosis [arthrosis of hip]	M16	48	81
Gonarthrosis [arthrosis of knee]	M17	56	65
Arthrosis of first carpometacarpal joint	M18	5	6
Other arthrosis	M19	17	23
Acquired deformities of fingers and toes	M20	4	2
Other acquired deformities of limbs	M21	3	9
Disorders of patella	M22	1	1
Internal derangement of knee	M23	2	8
Other specific joint derangements	M24	8	17
Other joint disorders, not elsewhere classified	M25	3	4
Polyarteritis nodosa and related conditions	M30	1	1
Other necrotizing vasculopathies	M31	5	4
Systemic lupus erythematosus	M32	3	3
Dermatopolymyositis	M33	2	0
Systemic sclerosis	M34	1	0
Other systemic involvement of connective tissue	M35	5	4
Kyphosis and lordosis	M40	1	1
Scoliosis	M41	1	0
Other deforming dorsopathies	M43	4	8

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Ankylosing spondylitis	M45	1	0
Other inflammatory spondylopathies	M46	5	3
Spondylosis	M47	1	7
Other spondylopathies	M48	36	47
Cervical disc disorders	M50	15	7
Other intervertebral disc disorders	M51	33	42
Other dorsopathies, not elsewhere classified	M53	2	4
Dorsalgia	M54	58	54
Myositis	M60	0	2
Other disorders of muscle	M62	5	4
Synovitis and tenosynovitis	M65	3	6
Spontaneous rupture of synovium and tendon	M66	1	0
Soft tissue disorders related to use, overuse and pressure	M70	4	5
Other bursopathies	M71	1	0
Fibroblastic disorders	M72	4	5
Shoulder lesions	M75	13	19
Enthesopathies of lower limb, excluding foot	M76	2	2
Other enthesopathies	M77	3	2
Other soft tissue disorders, not elsewhere classified	M79	40	43
Osteoporosis with pathological fracture	M80	0	1
Disorders of continuity of bone	M84	5	11
Other disorders of bone density and structure	M85	1	0
Osteomyelitis	M86	6	5
Osteonecrosis	M87	7	8
Other disorders of cartilage	M94	1	0
Other acquired deformities of musculoskeletal system and connective tissue	M95	0	1
Postprocedural musculoskeletal disorders, not elsewhere classified	M96	1	4
Biomechanical lesions, not elsewhere classified	M99	7	7
Acute nephritic syndrome	N00	1	0
Chronic nephritic syndrome	N03	4	3
Nephrotic syndrome	N04	2	3
Unspecified nephritic syndrome	N05	1	1
Acute tubulo-interstitial nephritis	N10	30	45
Chronic tubulo-interstitial nephritis	N11	0	1
Tubulo-interstitial nephritis, not specified as acute or chronic	N12	3	1
Obstructive and reflux uropathy	N13	22	13
Other renal tubulo-interstitial diseases	N15	1	0
Acute renal failure	N17	18	18
Chronic kidney disease	N18	31	20
Unspecified kidney failure	N19	3	3
Calculus of kidney and ureter	N20	66	48
Calculus of lower urinary tract	N21	7	1

Diagnosis	ICD 10	Cases	Control'
Disorders resulting from impaired renal tubular function	N25	1	0
Other disorders of kidney and ureter, not elsewhere classified	N28	1	4
Cystitis	N30	9	9
Neuromuscular dysfunction of bladder, not elsewhere classified	N31	0	3
Other disorders of bladder	N32	3	1
Urethral stricture	N35	5	2
Other disorders of urethra	N36	0	2
Other disorders of urinary system	N39	53	58
Hyperplasia of prostate	N40	11	26
Hydrocele and spermatocele	N43	1	0
Torsion of testis	N44	1	0
Orchitis and epididymitis	N45	4	7
Redundant prepuce, phimosis and paraphimosis	N47	1	0
Other disorders of penis	N48	0	1
Inflammatory disorders of male genital organs, not elsewhere classified	N49	1	1
Hypertrophy of breast	N62	5	5
Salpingitis and oophoritis	N70	2	7
Inflammatory disease of uterus, except cervix	N71	2	1
Other female pelvic inflammatory diseases	N73	0	1
Diseases of Bartholin gland	N75	1	1
Other inflammation of vagina and vulva	N76	0	1
Endometriosis	N80	6	12
Female genital prolapse	N81	19	22
Fistulae involving female genital tract	N82	1	1
Noninflammatory disorders of ovary, fallopian tube and broad ligament	N83	7	6
Polyp of female genital tract	N84	2	1
Other noninflammatory disorders of uterus, except cervix	N85	2	1
Dysplasia of cervix uteri	N87	3	4
Other noninflammatory disorders of cervix uteri	N88	0	1
Other noninflammatory disorders of vagina	N89	3	0
Other noninflammatory disorders of vulva and perineum	N90	0	1
Excessive, frequent and irregular menstruation	N92	15	17
Pain and other conditions associated with female genital organs and menstrual cycle	N94	2	1
Menopausal and other perimenopausal disorders	N95	4	2
Postprocedural disorders of genitourinary system, not elsewhere classified	N99	2	3
Ectopic pregnancy	O00	6	10
Other abnormal products of conception	O02	3	11
Spontaneous abortion	O03	9	12
Medical abortion	O04	0	1
Complications following abortion and ectopic and molar pregnancy	O08	1	0
Pre-existing hypertension complicating pregnancy, childbirth and the puerperium	O10	1	0
Gestational [pregnancy-induced] hypertension	O13	3	5

Diagnosis	ICD 10	Cases	Control'
Pre-eclampsia	O14	3	5
Haemorrhage in early pregnancy	O20	3	0
Excessive vomiting in pregnancy	O21	5	7
Venous complications and haemorrhoids in pregnancy	O22	1	1
Infections of genitourinary tract in pregnancy	O23	2	1
Diabetes mellitus in pregnancy	O24	2	1
Maternal care for other conditions predominantly related to pregnancy	O26	5	8
Multiple gestation	O30	1	0
Maternal care for known or suspected malpresentation of fetus	O32	0	4
Maternal care for other known or suspected fetal problems	O36	0	3
Placenta praevia	O44	0	1
Antepartum haemorrhage, not elsewhere classified	O46	1	5
False labour	O47	10	20
Failed induction of labour	O61	1	0
Postpartum haemorrhage	O72	1	1
Other complications of labour and delivery, not elsewhere classified	O75	0	1
Single spontaneous delivery	O80	201	431
Single delivery by forceps and vacuum extractor	O81	18	42
Single delivery by caesarean section	O82	63	120
Other assisted single delivery	O83	0	1
Multiple delivery	O84	3	10
Puerperal sepsis	O85	1	5
Other puerperal infections	O86	3	2
Obstetric embolism	O88	1	0
Complications of anaesthesia during the puerperium	O89	1	0
Complications of the puerperium, not elsewhere classified	O90	0	1
Infections of breast associated with childbirth	O91	3	4
Other disorders of breast and lactation associated with childbirth	O92	1	1
Maternal infectious and parasitic diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium	O98	1	1
Other maternal diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium	O99	12	7
Congenital hydrocephalus	Q03	0	1
Spina bifida	Q05	1	0
Other congenital malformations of nervous system	Q07	0	1
Other congenital malformations of eye	Q15	0	1
Other congenital malformations of face and neck	Q18	1	4
Congenital malformations of cardiac septa	Q21	1	3
Congenital malformations of aortic and mitral valves	Q23	0	1
Other congenital malformations of circulatory system	Q28	1	1
Congenital malformations of oesophagus	Q39	1	0
Other congenital malformations of intestine	Q43	0	1

Diagnosis	ICD 10	Cases	Control'
Congenital malformations of gallbladder, bile ducts and liver	Q44	0	1
Cystic kidney disease	Q61	1	2
Congenital ichthyosis	Q80	0	1
Other congenital malformations of skin	Q82	0	1
Congenital malformations of breast	Q83	1	1
Phakomatoses, not elsewhere classified	Q85	0	3
Congenital malformation syndromes due to known exogenous causes, not elsewhere classified	Q86	0	1
Other specified congenital malformation syndromes affecting multiple systems	Q87	0	1
Abnormalities of heart beat	R00	24	24
Haemorrhage from respiratory passages	R04	12	6
Cough	R05	9	1
Abnormalities of breathing	R06	66	26
Pain in throat and chest	R07	175	197
Other symptoms and signs involving the circulatory and respiratory systems	R09	1	5
Abdominal and pelvic pain	R10	129	107
Nausea and vomiting	R11	32	15
Dysphagia	R13	6	6
Faecal incontinence	R15	0	1
Hepatomegaly and splenomegaly, not elsewhere classified	R16	4	0
Unspecified jaundice	R17	3	4
Ascites	R18	5	4
Other symptoms and signs involving the digestive system and abdomen	R19	6	3
Disturbances of skin sensation	R20	25	23
Rash and other nonspecific skin eruption	R21	0	1
Localized swelling, mass and lump of skin and subcutaneous tissue	R22	3	5
Other skin changes	R23	0	1
Abnormal involuntary movements	R25	4	2
Abnormalities of gait and mobility	R26	2	3
Other lack of coordination	R27	1	0
Other symptoms and signs involving the nervous and musculoskeletal systems	R29	6	6
Pain associated with micturition	R30	2	0
Unspecified haematuria	R31	6	4
Unspecified urinary incontinence	R32	0	1
Retention of urine	R33	1	7
Polyuria	R35	2	0
Other symptoms and signs involving the urinary system	R39	1	0
Somnolence, stupor and coma	R40	7	6
Other symptoms and signs involving cognitive functions and awareness	R41	13	9
Dizziness and giddiness	R42	56	68
Other symptoms and signs involving general sensations and perceptions	R44	0	2
Symptoms and signs involving emotional state	R45	1	0
Speech disturbances, not elsewhere classified	R47	0	2

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Fever of other and unknown origin	R50	50	32
Headache	R51	39	40
Pain, not elsewhere classified	R52	22	12
Malaise and fatigue	R53	5	15
Syncope and collapse	R55	72	71
Convulsions, not elsewhere classified	R56	26	33
Shock, not elsewhere classified	R57	2	1
Haemorrhage, not elsewhere classified	R58	0	2
Enlarged lymph nodes	R59	55	1
Oedema, not elsewhere classified	R60	10	4
Symptoms and signs concerning food and fluid intake	R63	4	4
Cachexia	R64	1	0
Unknown and unspecified causes of morbidity	R69	0	1
Elevated erythrocyte sedimentation rate and abnormality of plasma viscosity	R70	2	0
Elevated blood glucose level	R73	7	4
Abnormal serum enzyme levels	R74	2	3
Other abnormal findings of blood chemistry	R79	3	2
Isolated proteinuria	R80	0	1
Abnormal findings on diagnostic imaging of central nervous system	R90	2	1
Abnormal findings on diagnostic imaging of lung	R91	31	7
Abnormal findings on diagnostic imaging of other body structures	R93	5	4
Abnormal results of function studies	R94	6	0
Superficial injury of head	S00	7	8
Open wound of head	S01	4	9
Fracture of skull and facial bones	S02	14	12
Dislocation, sprain and strain of joints and ligaments of head	S03	1	0
Injury of eye and orbit	S05	0	1
Intracranial injury	S06	36	42
Other and unspecified injuries of head	S09	2	0
Superficial injury of neck	S10	1	3
Open wound of neck	S11	1	0
Fracture of neck	S12	4	7
Dislocation, sprain and strain of joints and ligaments at neck level	S13	4	1
Injury of nerves and spinal cord at neck level	S14	0	2
Crushing injury of neck	S17	0	1
Traumatic amputation at neck level	S18	1	0
Superficial injury of thorax	S20	8	3
Fracture of rib(s), sternum and thoracic spine	S22	14	26
Dislocation, sprain and strain of joints and ligaments of thorax	S23	0	1
Injury of nerves and spinal cord at thorax level	S24	0	1
Injury of heart	S26	1	0
Injury of other and unspecified intrathoracic organs	S27	6	8

Diagnosis	ICD 10	Cases	Control'
Superficial injury of abdomen, lower back and pelvis	S30	3	6
Open wound of abdomen, lower back and pelvis	S31	1	1
Fracture of lumbar spine and pelvis	S32	6	16
Dislocation, sprain and strain of joints and ligaments of lumbar spine and pelvis	S33	0	2
Injury of intra-abdominal organs	S36	0	1
Injury of urinary and pelvic organs	S37	2	2
Superficial injury of shoulder and upper arm	S40	2	1
Open wound of shoulder and upper arm	S41	2	0
Fracture of shoulder and upper arm	S42	29	46
Dislocation, sprain and strain of joints and ligaments of shoulder girdle	S43	3	3
Injury of muscle and tendon at shoulder and upper arm level	S46	5	9
Open wound of forearm	S51	2	1
Fracture of forearm	S52	16	26
Dislocation, sprain and strain of joints and ligaments of elbow	S53	1	4
Injury of nerves at forearm level	S54	1	1
Superficial injury of wrist and hand	S60	0	3
Open wound of wrist and hand	S61	4	3
Fracture at wrist and hand level	S62	7	13
Dislocation, sprain and strain of joints and ligaments at wrist and hand level	S63	2	3
Injury of nerves at wrist and hand level	S64	2	1
Injury of muscle and tendon at wrist and hand level	S66	5	8
Traumatic amputation of wrist and hand	S68	2	2
Superficial injury of hip and thigh	S70	4	3
Open wound of hip and thigh	S71	0	1
Fracture of femur	S72	28	28
Dislocation, sprain and strain of joint and ligaments of hip	S73	1	0
Injury of muscle and tendon at hip and thigh level	S76	7	6
Superficial injury of lower leg	S80	3	3
Open wound of lower leg	S81	2	1
Fracture of lower leg, including ankle	S82	54	81
Dislocation, sprain and strain of joints and ligaments of knee	S83	4	7
Injury of nerves at lower leg level	S84	1	0
Injury of blood vessels at lower leg level	S85	1	0
Injury of muscle and tendon at lower leg level	S86	2	9
Superficial injury of ankle and foot	S90	0	2
Open wound of ankle and foot	S91	0	2
Fracture of foot, except ankle	S92	6	6
Dislocation, sprain and strain of joints and ligaments at ankle and foot level	S93	3	1
Injury of muscle and tendon at ankle and foot level	S96	1	0
Superficial injuries involving multiple body regions	T00	1	0
Fractures involving multiple body regions	T02	0	1
Crushing injuries involving multiple body regions	T04	0	1

Diagnosis	ICD 10	Cases	Control'
Unspecified multiple injuries	T07	0	1
Injury of unspecified body region	T14	2	2
Foreign body in respiratory tract	T17	3	0
Foreign body in alimentary tract	T18	4	8
Foreign body in genitourinary tract	T19	0	2
Burn and corrosion of head and neck	T20	0	3
Burn and corrosion of trunk	T21	1	0
Burn and corrosion of wrist and hand	T23	1	0
Burn and corrosion of ankle and foot	T25	0	2
Burn and corrosion of respiratory tract	T27	0	1
Burns classified according to extent of body surface involved	T31	0	2
Frostbite involving multiple body regions and unspecified frostbite	T35	0	1
Poisoning by hormones and their synthetic substitutes and antagonists, not elsewhere classified	T38	0	1
Poisoning by nonopioid analgesics, antipyretics and antirheumatics	T39	1	1
Poisoning by narcotics and psychodysleptics [hallucinogens]	T40	3	2
Poisoning by antiepileptic, sedative-hypnotic and antiparkinsonism drugs	T42	6	6
Poisoning by psychotropic drugs, not elsewhere classified	T43	2	1
Poisoning by agents primarily affecting the cardiovascular system	T46	0	1
Poisoning by diuretics and other and unspecified drugs, medicaments and biological substances	T50	28	40
Toxic effect of alcohol	T51	6	6
Toxic effect of organic solvents	T52	0	1
Toxic effect of carbon monoxide	T58	1	0
Toxic effect of other gases, fumes and vapours	T59	3	2
Toxic effect of contact with venomous animals	T63	2	4
Toxic effect of other and unspecified substances	T65	0	3
Unspecified effects of radiation	T66	1	0
Effects of heat and light	T67	1	0
Asphyxiation	T71	0	2
Effects of other external causes	T75	0	1
Adverse effects, not elsewhere classified	T78	16	20
Certain early complications of trauma, not elsewhere classified	T79	5	5
Complications following infusion, transfusion and therapeutic injection	T80	0	2
Complications of procedures, not elsewhere classified	T81	74	70
Complications of cardiac and vascular prosthetic devices, implants and grafts	T82	6	8
Complications of genitourinary prosthetic devices, implants and grafts	T83	7	6
Complications of internal orthopaedic prosthetic devices, implants and grafts	T84	22	23
Complications of other internal prosthetic devices, implants and grafts	T85	8	4
Failure and rejection of transplanted organs and tissues	T86	4	3
Complications peculiar to reattachment and amputation	T87	1	0
Other complications of surgical and medical care, not elsewhere classified	T88	16	8
Sequelae of injuries of neck and trunk	T91	2	0
Sequelae of injuries of upper limb	T92	5	8

<b>Diagnosis</b>	<b>ICD 10</b>	<b>Cases</b>	<b>Control'</b>
Sequelae of injuries of lower limb	T93	1	2
Sequelae of injuries involving multiple and unspecified body regions	T94	1	0
Sequelae of burns, corrosions and frostbite	T95	0	1
General examination and investigation of persons without complaint and reported diagnosis	Z00	3	13
Other special examinations and investigations of persons without complaint or reported diagnosis	Z01	4	2
Medical observation and evaluation for suspected diseases and conditions	Z03	112	95
Examination and observation for other reasons	Z04	6	10
Follow-up examination after treatment for malignant neoplasms	Z08	3	2
Follow-up examination after treatment for conditions other than malignant neoplasms	Z09	7	2
Special screening examination for other diseases and disorders	Z13	1	0
Carrier of infectious disease	Z22	1	0
Need for other prophylactic measures	Z29	4	3
Contraceptive management	Z30	1	2
Pregnancy examination and test	Z32	1	0
Supervision of normal pregnancy	Z34	2	4
Supervision of high-risk pregnancy	Z35	1	2
Outcome of delivery	Z37	0	1
Postpartum care and examination	Z39	2	7
Prophylactic surgery	Z40	2	2
Procedures for purposes other than remedying health state	Z41	4	3
Follow-up care involving plastic surgery	Z42	16	15
Attention to artificial openings	Z43	6	5
Fitting and adjustment of external prosthetic device	Z44	1	0
Adjustment and management of implanted device	Z45	15	6
Fitting and adjustment of other devices	Z46	3	2
Other orthopaedic follow-up care	Z47	10	8
Other surgical follow-up care	Z48	27	39
Care involving dialysis	Z49	3	6
Care involving use of rehabilitation procedures	Z50	2	0
Other medical care	Z51	52	36
Donors of organs and tissues	Z52	1	2
Persons encountering health services for specific procedures, not carried out	Z53	6	4
Problems related to social environment	Z60	0	2
Other problems related to primary support group, including family circumstances	Z63	1	0
Persons encountering health services for other counselling and medical advice, not elsewhere classified	Z71	3	3
Problems related to medical facilities and other health care	Z75	2	1
Persons encountering health services in other circumstances	Z76	0	1
Family history of malignant neoplasm	Z80	1	0
Personal history of malignant neoplasm	Z85	4	5
Personal history of certain other diseases	Z86	1	0

Diagnosis	ICD 10	Cases	Control'
Personal history of other diseases and conditions	Z87	2	0
Acquired absence of limb	Z89	1	0
Personal history of risk-factors, not elsewhere classified	Z91	1	0
Personal history of medical treatment	Z92	1	0
Artificial opening status	Z93	0	2
Transplanted organ and tissue status	Z94	17	1
Presence of cardiac and vascular implants and grafts	Z95	4	2
Presence of other functional implants	Z96	1	0
Other postsurgical states	Z98	4	1

Two matched controls for each case

**Supplement Table 2.** Numbers of Visits to Inpatient Care for the major diseases found, where Sarcoid Cases and Matched Controls are compared using Cox Regression.

Diagnosis	ICD10	Case events	Case rate	Controls events	Controls rate	HR	CI
Malignant neoplasms of ill-defined, other secondary and unspecified sites	C76-C80	51	1.29	43	0.54	2.38	1.59 - 3.57
Malignant neoplasms of lymphoid, hematopoietic and related tissue	C81-C96	44	1.12	30	0.38	2.94	1.85 - 4.68
Pulmonary embolism	I26	52	1.32	24	0.30	4.36	2.69 - 7.07
Cardiomyopathy	I42	23	0.58	9	0.11	5.13	2.37 - 11.08
Paroxysmal tachycardia	I47	42	1.07	24	0.30	3.51	2.13 - 5.80
Heart failure	I50	78	1.99	48	0.61	3.27	2.28 - 4.68
Pneumothorax	J93	23	0.58	4	0.05	11.53	3.99 - 33.34
Influenza and pneumonia	J09-J18	215	5.54	146	1.86	2.98	2.41 - 3.68
Chronic lower respiratory diseases	J40-J47	49	1.25	39	0.49	2.53	1.66 - 3.85
Other respiratory diseases principally affecting the interstitium	J80-J84	26	0.66	3	0.04	17.38	5.26 - 57.42