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 ratios1.75; 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)

Keywords: Sarcoidosis, Case control, Comorbidity, Mortality

Introduction

Sarcoidosis is a systemic inflammatory disorder involving granuloma formation that, in most 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 register. 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 -MO6, Crohn’s disease-K50 or Ulcerative colitis-K51. To include as many newly-diagnosed cases and as few revisit 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 ± 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
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).

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

Comparing 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.

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) | Number of visits controls (n) | HR (95% CI)          |
|----------------------------------------------------------|----------------------------|-------------------------------|----------------------|
| Certain infectious and parasitic diseases                |                            |                               |                      |
| 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                                                |                            |                               |                      |
| 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*     |                            |                               |                      |
| 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, nutrional and metabolic disorders             |                            |                               |                      |
| 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                          |                            |                               |                      |
| 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                           |                            |                               |                      |
| 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                           |                            |                               |                      |
| 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                  |                            |                               |                      |
| 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                       |                            |                               |                      |
| 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                       |                            |                               |                      |
| 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                         |                            |                               |                      |
| 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             |                            |                               |                      |
| 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

| Chapter Description                                      | Number of visits cases (n) | Number of visits controls (n) | HR (95% CI) |
|-----------------------------------------------------------|-----------------------------|-------------------------------|-------------|
| Diseases of the musculoskeletal system and connective tissue |                             |                               |             |
| 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                      |                             |                               |             |
| 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                  |                             |                               |             |
| Total                                                     | 280                         | 584                           | 0.96 (0.83 – 1.10) |
| Female                                                    | 280                         | 584                           | 0.95 (0.82 – 1.10) |
| Congenital malformations and chromosomal abnormalities    |                             |                               |             |
| 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                            |                             |                               |             |
| 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 |                 |                               |             |
| 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                          |                             |                               |             |
| 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) |

*Each individual can appear several times in different chapters,* ^1^ *Hazard ratio,* ^3^ *95% confidence interval,* ^4^ *Diseases of the blood and blood-forming organs and certain disorders involving the immune-mechanism,* ^5^ *Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified,* ^6^ *Factors influencing health status and contact with health services*

Clinical 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
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

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

| Chapters of ICD 10* | Deaths cases (n) | Deaths controls (n) | HRb (95% CI)c |
|--------------------|------------------|---------------------|----------------|
| 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       | 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* III | 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 | 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 | 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 | 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 | 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 | 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 XVIII | 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 | 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) |

*Only chapters where at least 5 deaths are seen in either cases or the controls are reported, b Hazard ratio, c 95% confidence interval, d Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, e Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
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,
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was possible, with few exceptions, to include anyone across different nationwide registers, and therefore it identification numbers that can link patient data the entire population, together with unique personal Sweden maintains high-quality registers that cover matched controls, and cases and controls were also study population comprising 7828 cases and 15,656 affect several different organ systems (21).

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

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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 |
|-----------|---------|-------|---------|
| **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 |
| **Tularemia** | A21 | 0 | 1 |
| **Erysipeloïd** | 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       |
| Diagnosis                                           | ICD 10 | Cases | Control |
|-----------------------------------------------------|--------|-------|---------|
| 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 |
|---------------------------------------------------------------------------|--------|-------|---------|
| 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 reticulo- | D76    | 2     | 0       |
| Imunodeficiency associated with other major defects                      | D82    | 1     | 1       |
| Common variable immunodeficiency                                         | D83    | 0     | 1       |
| Other immunodeficiencies                                                 | D84    | 1     | 0       |
| Sarcoïdosis                                                              | 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       |
| Diagnosis                                                        | ICD 10 | Cases | Control |
|-----------------------------------------------------------------|--------|-------|---------|
| 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     | 4       |
| 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       |
| Diagnosis                                                                 | ICD 10 | Cases | Control |
|--------------------------------------------------------------------------|--------|-------|---------|
| 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       |
| Diagnosis                                                                 | ICD 10 | Cases | Control |
|--------------------------------------------------------------------------|--------|-------|---------|
| 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     | 2       |
| 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      |
| Diagnosis                                      | ICD 10  | Cases | Control |
|-----------------------------------------------|---------|-------|---------|
| 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     | K56     | 28    | 43      |
| Diverticular disease of intestine             | K57     | 38    | 48      |
| Irritable bowel syndrome                      | K58     | 3     | 3       |
| Other functional intestinal disorders          | K59     | 29    | 17      |
| Abscess of anal and rectal regions            | K60     | 6     | 4       |
| Other diseases of anus and rectum             | K61     | 15    | 16      |
| Other diseases of intestine                   | K62     | 6     | 4       |
| 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  | 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       |
| Polyarthritis                                                   | 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       |
| Diagnosis                                                   | ICD 10 | Cases | Control |
|------------------------------------------------------------|--------|-------|---------|
| Ankylosing spondylitis                                     | M45    | 1     | 0       |
| Other inflammatory spondylopathies                         | M46    | 5     | 3       |
| Spondylitis                                                | 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       |
| Diagnosis                                                                 | ICD 10 | Cases | Control |
|-------------------------------------------------------------------------|--------|-------|---------|
| 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 antiparkinsonian 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       |
| Diagnosis                                                                 | ICD 10 | Cases | Control |
|---------------------------------------------------------------------------|--------|-------|---------|
| 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 healthcare               | 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 | J33 | 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