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Epidemiology and health outcomes of sarcoidosis in a universal health care population: a cohort study

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LF, MB, JF, MS and AG contributed to the conception and design of the performed research. LF, TT, and AG were involved in data analysis. All authors were responsible for data interpretation, drafting of the manuscript and approval of the final version.

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Take Home Message: The prevalence of sarcoidosis in Canada is increasing, with an estimated rate of 143 per 100,000 as of 2015. The burden of sarcoidosis is changing, with increasing incidence among men in recent years and decreasing disease rates in women.

Abstract

Sarcoidosis related mortality appears to be rising in North America, with increasing rates in women and the elderly. We aimed to estimate trends in sarcoidosis incidence, prevalence and mortality in Ontario, Canada.

We performed a cohort study using health administrative data from Ontario between 1996 and 2015. International Classification of Diseases and Ontario Health Insurance Plan codes were used for case detection. Three disease definitions were created; (1) sarcoidosis, >/=2 physician claims within 2 years; (2) chronic sarcoidosis, >/=5 physician claims within 3 years; (3) sarcoidosis with histology, >/=2 physician claims with a tissue biopsy performed between claims.

Overall, 18,550, 9199, and 3819 individuals with sarcoidosis, chronic sarcoidosis and sarcoidosis with histology were identified. The prevalence of sarcoidosis was 143 per 100,000 in 2015, increasing by 116% ($p<0.0001$) from 1996. The increase in age-adjusted prevalence was higher in men than women (136% versus 99%, $p<0.0001$). The incidence of sarcoidosis declined from 7.9 to 6.8 per 100,000 between 1996 and 2014 (15% decrease, $p=0.0009$). A 30.3% decrease in incidence was seen amongst females ($p<0.0001$), compared to a 5.5% increase in men ($p=0.47$). Age- and sex-adjusted mortality rates of patients with sarcoidosis rose from 1.15% to 1.47% between 1996 and 2015 (28% increase, $p=0.02$), with the overall trend being non-significant ($p=0.39$). Mortality rates in patients with chronic sarcoidosis increased significantly over the study period ($p=0.0008$).

The prevalence of sarcoidosis is rising in Ontario, with an apparent shifting trend in disease burden from women to men. Mortality is increasing in patients with chronic sarcoidosis.

Key words: sarcoidosis; epidemiology; mortality

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown cause.[1] The epidemiology of sarcoidosis has differed across studies, likely as a result of varied environmental factors, genetic susceptibility and study design.[1-3] Recent national database studies focused on the epidemiology of sarcoidosis in the United States have been insightful, but restricted to individuals with health insurance; this may misrepresent the epidemiology of sarcoidosis in the general population, as sarcoidosis is reportedly more common in African Americans, an ethnic group more likely to lack health insurance.[1,4,5] Research using complete population databases are needed for accurate disease estimates. Knowing the epidemiology and mortality trends of sarcoidosis is important to inform patients, health care providers and decision makers to allow adequate health care planning. Furthermore, little is known of the epidemiology of sarcoidosis in Canada.

There are over 14 million people living in Ontario with coverage under its universal health care system.[6] Using health administrative data, we aimed to estimate trends in prevalence, incidence and mortality of sarcoidosis in this large, complete Canadian population, a population reflective of many other areas of North America. Additional aims were to describe patient demographics and medication use of individuals with sarcoidosis over 65 years of age.

Methods

Data sources

We performed a population-based cohort study using health administrative data to estimate the incidence, prevalence and mortality of sarcoidosis in Ontario, Canada. Physician claim diagnoses, including both inpatient and outpatient claims by primary care physicians and specialists were obtained from the Ontario Health Insurance Plan (OHIP) records. OHIP covers all medical necessary services in the province of Ontario. The Canadian Institute of health Information Discharge Abstract Database was utilized to obtain information regarding hospital, day-unit and emergency department discharges. Demographic data, including patient deaths and date of entering/leaving the province were obtained from the Ontario Registered Persons Database. Medication prescription records for patients >/= 65 years of age were obtained from the Ontario Drug Benefit Program database. Data was linked on an individual level using encrypted health card numbers. Research ethics approval was obtained from Sunnybrook Health Sciences Centre Institutional Review Board in Toronto, Ontario, Canada.

Study design and participants

All adults, aged 18 to 105 living in Ontario between 1991 and 2015 were included. Those without a valid health card number, not present in the registered persons database, living outside of Ontario, or living in Ontario for less than 1 year were excluded. Sarcoidosis was identified using International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification (ICD-9)) codes from outpatient and hospitalization physician claims specific to sarcoidosis: (135 (sarcoidosis), and 3214 (sarcoid meningitis); ICD-10 sarcoidosis specific codes: D860 (lung), D861 (lymph nodes), D862 (lung and lymph

nodes), D863 (skin), D868 (other and combined sites), D869 (unspecified), G532 (cranial nerve palsies in sarcoidosis), M633 (myositis in sarcoidosis)); and a OHIP diagnostic code (135 (sarcoidosis)). The switch from ICD-9 to ICD-10 coding took place in Ontario in 2002.

Three sarcoidosis case definitions were created: sarcoidosis, chronic sarcoidosis, and sarcoidosis with histology. Sarcoidosis was defined as >/= 2 physician claims or hospitalizations for sarcoidosis, at least 2 weeks apart but within 2 years. This definition is similar to previously published epidemiologic studies.[4,7] A sarcoidosis disease definition requiring >/= 2 sarcoidosis-coded claims has been previously reported to identify 95% of patients with sarcoidosis in a well-characterized clinical cohort.[7] Patients with an increased number of physician claims for sarcoidosis specific codes were suspected to be more likely to have chronic sarcoidosis, given an ongoing need for medical evaluation. Chronic sarcoidosis was defined as >/=5 physician claims or hospitalizations for sarcoidosis, at least 2 weeks apart but within 3 years. Patients with sarcoidosis who underwent a tissue biopsy during their evaluation were felt to represent an important subgroup. Sarcoidosis with histology was defined as >/= 2 physician claims or hospitalizations for sarcoidosis plus the performance of a tissue biopsy. If there were multiple physician claims on the same day, only one was counted. Physician claims had to be separated by at least two weeks, and at least one of the sarcoidosis physician claims for sarcoidosis with histology cases had to occur after the tissue biopsy date. Tissue biopsy codes included: endobronchial ultrasound and biopsy (G050), transbronchial biopsy (E638,Z333), mediastinoscopy (Z329), lung biopsy (Z338,M137), lymph node biopsies (M138,Z405,Z411,Z406), liver biopsy (Z551), or skin biopsy (Z116, Z113). As we did not confirm with certainty that patients meeting the developed disease

definitions have the disease, the specific titles ascribed to the three case definitions (sarcoidosis, chronic sarcoidosis and sarcoidosis with histology) were applied for ease of description. The study investigators believed the case definitions to have face validity, given the ICD9/10 codes are specific to sarcoidosis, and repeated visits were required. The three sarcoidosis case definitions were also believed to have internal validity, allowing comparisons between disease subgroups. The first sarcoidosis physician claim date was labelled as the date of diagnosis. Given there is no cure for sarcoidosis, patients fulfilling any case definition remained part of our study population unless they left Ontario or died.

Medication use was recorded in patients >/= 65 years old if received any time after a sarcoidosis diagnosis for any duration of use. Primary care and subspecialty visits were recorded if patients had at least one visit with an applicable physician after the date of sarcoidosis diagnosis. This way numerous visits to one physician or visits to more than one physician were captured.

Analysis

Analysis of disease trends were similar to that performed elsewhere.[8] The cumulative sarcoidosis prevalence was calculated from 1996 to 2015 by dividing the number of living patients meeting each sarcoidosis disease definitions at the end of each fiscal year by the provincial population for that year. To allow for the identification of existing cases, we reviewed patient data back to 1991, but began reporting prevalence rates as of 1996.

Incident sarcoidosis rates were calculated between 1996 and 2014 by dividing new sarcoidosis patients by the provincial population at risk for sarcoidosis (total population

subtract those previously diagnosed). We began reporting incidence rates as of 1996, allowing a washout period of 5 years. We did not present incident rates after 2014 given there was not enough time to meet case definitions.

All-cause mortality rates were calculated for patients with sarcoidosis between 1996 and 2015 by dividing total number of deaths per year among those with sarcoidosis by total number with sarcoidosis in the corresponding fiscal year.

Prevalence and incidence rates were standardized for age and sex using the 2015 population in Ontario. Mortality rates were standardized for age and sex using the 2015 sarcoidosis population. Relative percent changes for prevalence, incidence or mortality rates were calculated by dividing the rate of the most recent year by the rate of the earlier year. Percentage change in disease rates were compared between 1996 and 2015 between age and sex groups using the Cochran-Mantel Haenszel test. The Cochran-Armitage trend test was performed to assess for significance of trends over time. Rates between years were compared using Chi-squared testing and Fisher's exact test.

Results

In total, the number of patients between 1996 and 2015 meeting sarcoidosis, chronic sarcoidosis and sarcoidosis with histology definitions were 18550, 9199, and 3819, respectively. Descriptive statistics of sarcoidosis, chronic sarcoidosis and sarcoidosis with histology cohorts are shown in Table 1. Most patients with sarcoidosis were between 36 and 55 years of age at the time of diagnosis. Slightly more women were diagnosed with sarcoidosis than men. Prednisone, methotrexate and hydroxychloroquine were the most commonly prescribed treatments. Of specialists, pulmonologist were the most

commonly visited. Approximately 11% of sarcoidosis patients immigrated to Canada, with the most common countries of origin being India, Pakistan and Jamaica.

Comparisons between disease cohorts found patients with both chronic sarcoidosis and sarcoidosis with histology more commonly received prednisone, methotrexate, and azathioprine than patients with sarcoidosis. Those included in the sarcoidosis with histology cohort were more commonly male, of high-income quintile, and urban dwelling compared to the other sarcoidosis cohorts (Table 1).

The age and sex-standardized prevalence of sarcoidosis increased from 66 cases per 100,000 in 1996 to 143 cases per 100,000 in 2015. This represents a 116% relative increase ($p<0.0001$). The prevalence increase appeared to be continual across the study period (Figure 1A). Both men and women experienced an increase in age-standardized sarcoidosis prevalence between 1996 and 2015, but the increase was significantly higher in men (men 136% relative increase versus women 99%, $p<0.0001$). The largest growth in sarcoidosis prevalence rates was in the 36-45 age group ($p=0.001$) (Figure 2A).

The age and sex-standardized prevalence of chronic sarcoidosis increased from 36 cases per 100,000 in 1996 to 70 cases per 100,000 in 2015 ($p<0.0001$, for trend) (Figure E1). The age and sex-standardized prevalence of sarcoidosis with histology increased from 11 cases per 100,000 in 1996 to 30 cases per 100,000 in 2015 ($p<0.0001$, for trend) (Figure E1).

The age and sex-standardized incidence of sarcoidosis decreased from 7.9 cases per 100,000 adults in 1996 to 6.8 cases per 100,000 in 2014, representing a 15% relative decrease ($p=0.0009$) (Figure 1B). The trend of decreasing incidence was statistically significant ($p<0.0001$). A 30.3% relative decline in sarcoidosis incidence between 1996 and 2015 was seen in women ($p<0.0001$) compared to a 5.5% relative increase in men

(p=0.47). Across age groups, a significant relative decline in sarcoidosis incidence was seen in patients 26-35 and 36-45 years of age, estimated at 44.4% (p<0.0001) and 29.5% (p=0.001) respectively (Figure 2B).

The age and sex-standardized incidence of chronic sarcoidosis decreased from 4 cases per 100,000 in 1996 to 3.1 per 100,000 in 2013 (p<0.0001, for trend). The age and sex-standardized incidence of sarcoidosis with histology increased from 1.7 cases per 100,000 in 1996 to 1.8 per 100,000 in 2013 (p=0.73, for trend) (Figure E1).

Age and sex-standardized all-cause mortality in patients with sarcoidosis increased from 1.15% in 1996 to 1.47% in 2015, representing a 28% increase (p=0.02) (Figure 1C). The overall trend in mortality over the study period was not statistically significant (p=0.39). A 46% relative increase in mortality rate was seen in men with sarcoidosis between 1996 and 2015 (p=0.01), whereas in women the increase in mortality was 15% (p=0.32). Patients diagnosed with sarcoidosis at 46-55 (p=0.06) and ≥66 (p=0.08) years of age had the largest increase in mortality between 1996 and 2015 (Figure 2C).

In the chronic sarcoidosis cohort, age and sex-standardized mortality increased from 0.95% to 1.42% (p=0.0008, for trend). In the sarcoidosis with histology cohort, age and sex-standardized mortality decreased from 1.85% to 1.41% (p=0.04, for trend) (Figure E1).

Discussion

Using a large, complete population, we estimated trends in prevalence, incidence, and mortality of sarcoidosis from 1996 to 2015 in Ontario, Canada. Our study represents a uniquely comprehensive report on the epidemiology of sarcoidosis in Canada and characterizes the epidemiology of sarcoidosis subpopulations (chronic sarcoidosis and

sarcoidosis with histology). Sarcoidosis appears to impact patients of all ages, socioeconomic status and ethnicity. However, the burden of sarcoidosis appears to be changing; we found the prevalence of sarcoidosis to be rising fastest in men, with higher disease incidence rates among men in recent years and declining incidence rates in women. Although age and sex-adjusted mortality rates in patients with sarcoidosis remained relatively stable during the study period, mortality increased significantly in patients with chronic sarcoidosis. These results serve to inform both clinicians and health policy makers of the current state and evolving trends of sarcoidosis disease epidemiology.

The Canadian healthcare system provides universal health coverage to all citizens, allowing for an inclusive and accurate representation of sarcoidosis epidemiology. Health administration studies performed in European countries with universal health care have shown similar sarcoidosis disease rates to those reported here. Applying similar case definitions, Arkema et al. reported a sarcoidosis prevalence in Sweden of 160 cases per 100,000 and incidence of 11.5 cases per 100,000 using health services data.[7] Although Sweden provides universal health coverage, only patients seen by specialists were captured, which may fail to identify patients with milder forms of disease managed by primary care physicians.[7] Our results comprise all types of physician visits (primary practitioners and specialists).

In certain parts of America, the prevalence of sarcoidosis has been reported to be on the rise.[9] Baughman et al. reported the prevalence of sarcoidosis in America as ~60 cases per 100,000 in 2013, substantially lower than that reported here.[4] Although they interrogated a database of >33 million individuals, only individuals with certain health insurance coverage were included in this study, which may underestimate sarcoidosis

prevalence. Historically, racial minorities are less likely to have health insurance, and have been reported to have higher rates of sarcoidosis.[4,5] We found the prevalence of sarcoidosis to be rising, despite a slight reduction in disease incidence over time. We suspect this is as a result of the low mortality rate compared to disease incidence, and few patients leaving the province over time.

More women than men were diagnosed with sarcoidosis in our cohort, though the difference between genders was smaller than previous studies.[10] The gap in disease prevalence between men and women appears to be closing, with higher sarcoidosis incidence rates among men in recent years and decreasing incidence among women. Although the reasons for these trends are unclear, one potential explanation is an increase in occupational exposures in men compared to women. Exposure to inorganic dusts and building materials has been associated with sarcoidosis.[11] Ontario's construction industry has increased by 50% since the year 2002, and employs nearly half a million Canadians with 87% of employees being male.[12] Further research focused on exploring risk factors for sarcoidosis in Ontario might help to better understand this disease trend.

A lower percentage of sarcoidosis with histology patients were women compared to the other disease cohorts. It is unclear why fewer women underwent a biopsy as part of their diagnostic evaluation. Previous studies have found a higher proportion of men with end-stage pulmonary fibrosis related to sarcoidosis, which may support this hypothesis.[13] Alternatively, gender inequalities in the performance of diagnostic procedures may exist. Women have reported higher unmet health care needs in Canada compared to men, despite a universal healthcare system.[14] Additional research is needed to investigate

whether these findings represent a true disparity in access to diagnostic testing or differences in disease presentation.

Sarcoidosis has been historically stated to develop predominantly in the second and third decade of life.[1] We found patients over 55 years of age at the time of diagnosis comprised less than 30% of sarcoidosis cases, with the majority of patients being in the third and fourth decade of life. Baughman et al. reported that over 50% of patients in their recent cohort were over 55 years of age at the time of diagnosis.[4] We speculate the higher proportion of sarcoidosis patients over age 50 in that study may be due to a shorter look back study time period (3 years); patients may have been diagnosed with sarcoidosis earlier in life, but if records were only examined within a short time-frame, prevalent cases may be inappropriately labelled as incident cases, falsely raising the age at diagnosis. We reviewed physician claims for 5-years prior to labelling incident cases, and reviewed a cohort spanning nearly 20 years, which we suspect allowed for a more accurate estimate of incidence trends. That said, we found the 56-65 year old age group to have the highest sarcoidosis incidence rates in recent years, with decreasing incidence rates in the younger age groups.

Of all the sarcoidosis patients we identified between 1996 and 2015, over 10% were immigrants to Canada. Between 2006 and 2011 the leading countries of origin of immigrants to Canada were the Philippines, China and India.[15] However, the countries of origin with the highest sarcoidosis prevalence were India, Pakistan, and Jamaica. The high frequency of cases from Southeast Asia was unexpected, as Southeast Asians are not reported to be an ethnic group with strong associations with sarcoidosis.[16] Immigrants make up 20.6% of the Canadian population and those living with sarcoidosis may have unique health care needs.[17]

Previous reports evaluating the mortality of sarcoidosis in America have described increasing mortality rates over time, with higher mortality in women with sarcoidosis compared to men.[18] We found mortality rates in patients with sarcoidosis to be relatively stable over time, with similar annual mortality rates between men and women. However, patients within the chronic sarcoidosis cohort experienced a significant increase in mortality rates during the study period. Further research focused specifically on this higher risk population is needed to evaluate for risk factors associated with adverse health outcomes.

Several limitations of this research warrant mentioning. Despite the use of ICD9/10 sarcoidosis specific diagnostic codes, it is possible that patients were mislabelled as having sarcoidosis when they did not. Patients with mild forms of sarcoidosis who do not present to healthcare professionals for medical care would also be underrepresented in this cohort. The presence of >/=2 sarcoidosis claims has been reported to capture the vast majority of sarcoidosis cases in a well-characterized cohort, though the specificity of this definition may be less optimal.[7] Ungprasert et al. reported a positive predictive value of 76.5% for >/=2 sarcoidosis claims for confirmed cases in a small American cohort. To improve upon this, we developed cohorts with >/=5 sarcoidosis claims and biopsy-associated claims in an effort to enhance specificity. While our chronic sarcoidosis definition is believed to have face validity, we cannot be certain that a higher number of physician claims and longer duration of follow-up equates to disease chronicity or activity, due to the limitations of health administrative data.

We were limited to reviewing medication use in patients >/= 65 year of age. Although we report the burden of sarcoidosis amongst Canadian immigrants, we were limited to data regarding country of origin as opposed to self-reported ethnicity. Other

important variables were not captured by the available databases, including pulmonary function testing, imaging and biopsy results.

Given the presented results were generated from a universal health care system, the reported patient outcomes may not be generalizable. Extrapolating the reported mortality trends to countries where health care access is limited may be flawed, as mortality rates may be higher in individuals without health insurance. However, we believe these results have external validity given the multiethnic cohort, which is similar to other North American populations.

Strengths of this research include the large, complete and heterogeneous population. We evaluated the epidemiology and mortality of three sarcoidosis cohorts, incorporating the performance of a tissue biopsy, which is often lacking in other health services research. We believe that the distribution of patients across disease cohorts is consistent with what is seen clinically, providing some degree of internal validity.

In conclusion, we report a large, population-based study of prevalence, incidence and mortality trends of sarcoidosis in Canada. The prevalence of sarcoidosis is rising, with an apparent shifting trend in disease burden from women to men. Mortality in patients suffering from chronic sarcoidosis is increasing. Additional research regarding risk factors for disease development and adverse health outcomes within the sarcoidosis population in Canada is needed to inform patients, health care providers and health policy experts.

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TABLE 1 Demographics and medication use in the prevalence cohorts of sarcoidosis, chronic sarcoidosis and sarcoidosis with histology from 1996 – 2015.

	Sarcoidosis	**Chronic sarcoidosis**	**Sarcoidosis with histology**
Age at diagnosis, median (IQR)			
Female	49 (18)	50 (18)	50 (18)
Male	45 (18)	45 (18)	45 (18)
Age at diagnosis, n (%)			
18-25	422 (2.3)	154 (1.7)	62 (1.6)
26-35	3083 (16.6)	1473 (16.0)	592 (15.5)
36-45	4855 (26.2)	2481 (27.0)	990 (25.9)
46-55	4713 (25.4)	2409 (26.2)	1039 (27.2)
56-65	3268 (17.6)	1687 (18.3)	715 (18.7)
>66	2209 (11.9)	995 (10.8)	421 (11.0)
Gender, n(%)			
Female	9856 (53.1)	4960 (53.9)	1942 (50.9)
Income Quintile, n (%)			
1 (lowest)	3567 (19.2)	1736 (18.8)	737 (19.3)
2	3604 (19.4)	1804 (19.6)	727 (19.0)
3	3720 (20.1)	1857 (20.2)	732 (19.2)
4	3702 (20.0)	1806 (19.6)	738 (19.3)
5 (highest)	3814 (20.1)	1934 (21.0)	866 (22.7)
Rural (vs Urban)	2562 (13.8)	1185 (12.9)	446 (11.7)
Physician type, n (%)			
Family Medicine	18339 (98.9)	9151 (99.5)	3785 (99.1)
Pulmonology	15805 (85.2)	8486 (92.2)	3517 (92.1)
Cardiology	14716 (79.3)	7753 (84.3)	3230 (84.6)
Dermatology	8053 (43.4)	4482 (57.8)	2103 (55.1)
Internal Medicine	13699 (73.8)	7216 (78.4)	2882 (75.5)
Neurology	6385 (34.4)	3571 (38.8)	1388 (36.3)
Ophthalmology	10904 (58.8)	6144 (66.8)	2442 (64.0)
Medications, n (%)			
Azathioprine	178 (2.4)	117 (3.1)	51 (3.6)
Biologics	19 (0.2)	9 (0.2)	<5 (0.4)
Hydroxychloroquine	315 (4.3)	210 (5.5)	88 (6.2)
Leflunamide	49 (0.7)	25 (0.7)	9 (0.6)
Methotrexate	344 (4.6)	243 (6.4)	100 (7.0)
Mycophenolate	66 (0.9)	44 (1.2)	25 (1.8)
Prednisone	2989 (40.3)	1800 (47.1)	640 (44.9)
Immigrants, n (%)	1867 (10.6)	921 (10.0)	420 (11.0)
Country of origin			
India	277 (1.5)	131 (1.4)	55 (1.4)
Pakistan	138 (0.7)	69 (0.8)	30 (0.8)

Jamaica	130 (0.7)	83 (0.9)	37 (1.0)
Other	1322 (7.1)	638 (6.9)	298 (7.8)
World region			
South Asia	586 (3.2)	291 (3.2)	121 (3.2)
Western Nations/Europe	399 (2.2)	188 (2.0)	84 (2.2)
Caribbean	258 (1.4)	149 (1.6)	26 (0.7)
Middle East/North Africa	214 (1.2)	111 (1.2)	56 (1.5)
Sub-Saharan Africa	168 (0.9)	84 (0.9)	39 (1.0)
Hispanic America	138 (0.7)	67 (0.7)	26 (0.7)
East Asia and Pacific	104 (0.6)	31 (0.3)	17 (0.4)

Definition of abbreviations: IQR=interquartile range

Physician type is expressed as the total number of patients in the corresponding cohort seen by each physician group. The denominator for sarcoidosis, chronic sarcoidosis and sarcoidosis with histology was 18550, 9199, is 3819 respectively. Patients could see more than one type of physician.

* Only included patients >65 years of age; 7419, 3823, 1423 total patients for sarcoidosis, chronic sarcoidosis and sarcoidosis with histology cohorts respectively.

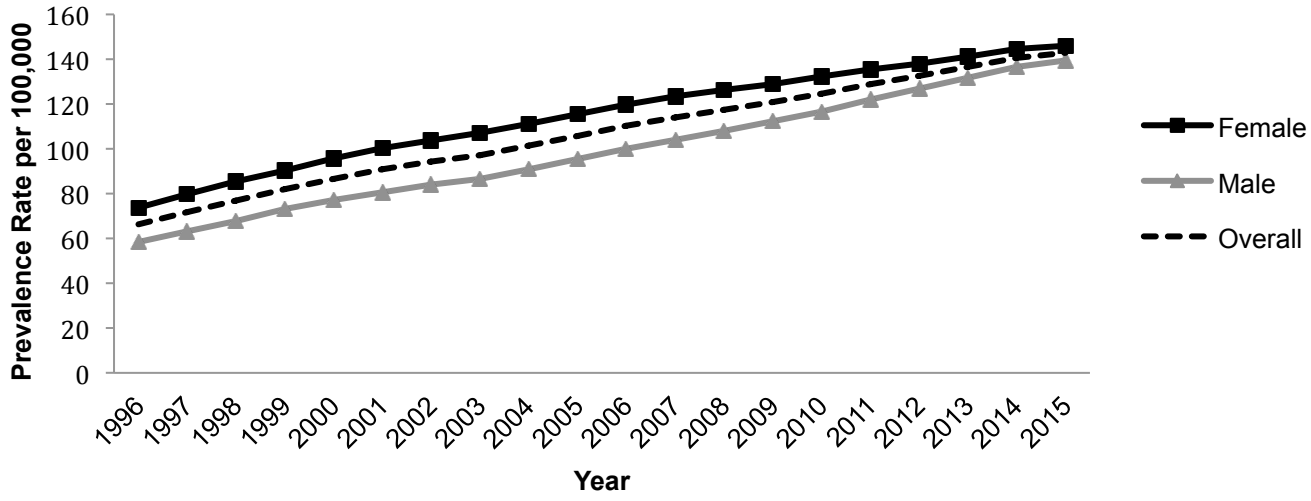
The “other” category for country of origin reflects a combination of 119 different countries with at least one individual diagnosed with sarcoidosis in the described cohorts.

TABLE 2 Frequency of sarcoidosis subgroups as documented by ICD-9 and ICD-10 coding.

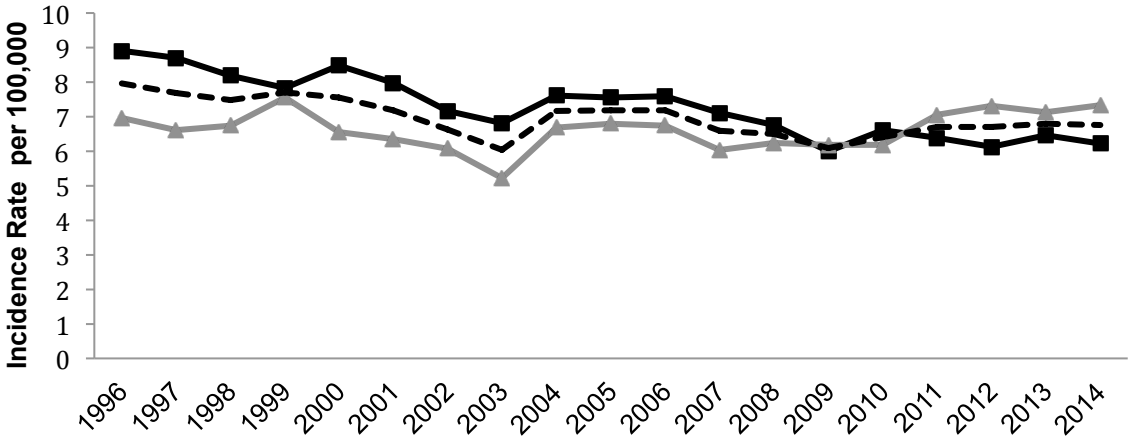
Sarcoidosis Subgroup	
1996-2001 (ICD-9 codes), n=6338	
Sarcoidosis	6318 (99.7)
Sarcoidosis meningitis	20 (0.3)
2002-2015 (ICD-10 codes), n=6681	
Pulmonary sarcoidosis	2368 (35.4)
Lymph node sarcoidosis	213 (3.2)
Pulmonary and lymph node sarcoidosis	188 (2.8)
Cutaneous sarcoidosis	82 (1.2)
Other / Combined sites	1015 (15.2)
Sarcoidosis unspecified	2896 (43.3)
Cranial nerve palsies in sarcoidosis	51 (0.8)
Myositis in sarcoidosis	7 (0.1)

From 1996 – 2001 and 2002 – 2015 a total of 6338 and 6681 hospitalization events occurred respectively. A single patient could contribute to more than one hospitalization and more than one ICD code could be applied to the same admission.

a)


Prevalence Rate per 100,000
160
140
120
100
80
60
40
20
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Year
Female
Male
Overall

b)


Incidence Rate per 100,000
10
9
8
7
6
5
4
3
2
1
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014

c)

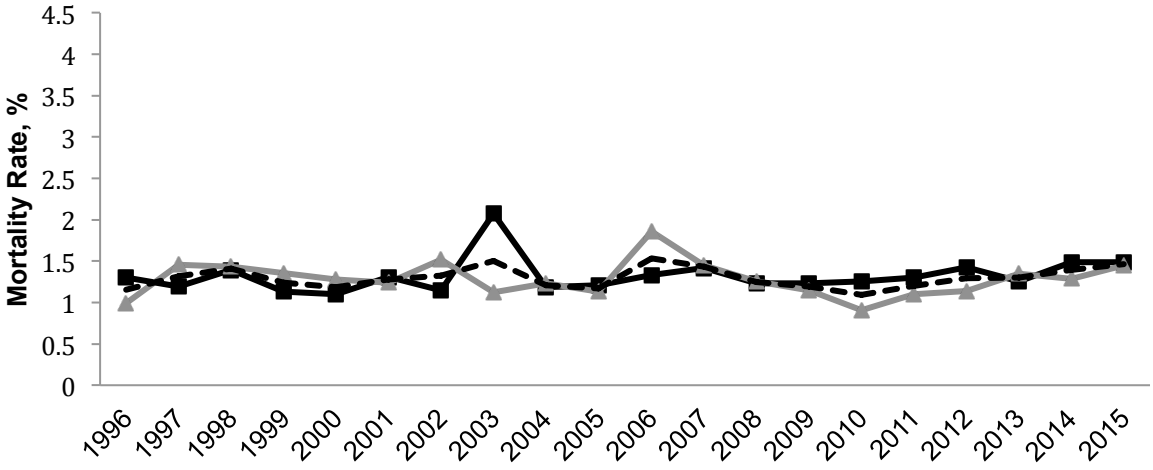
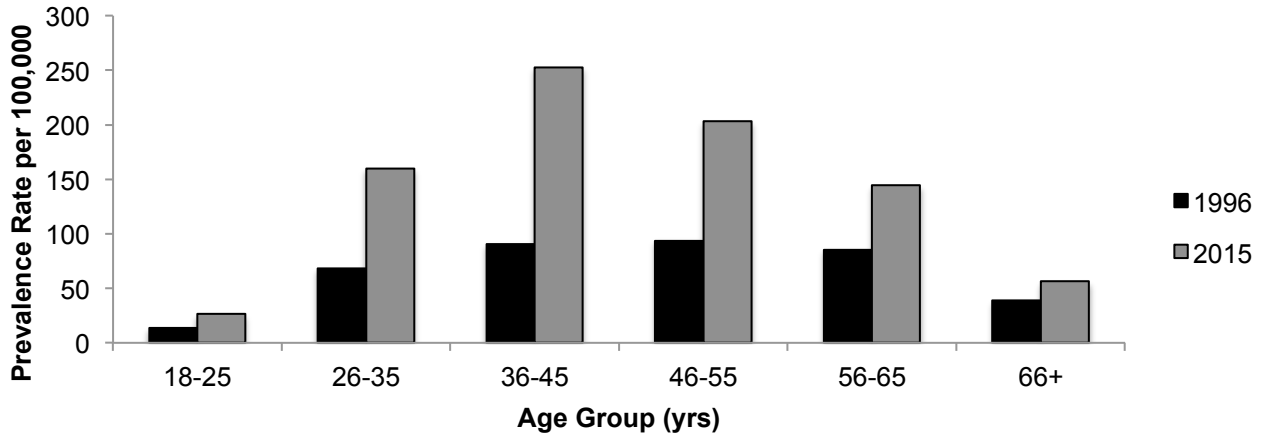
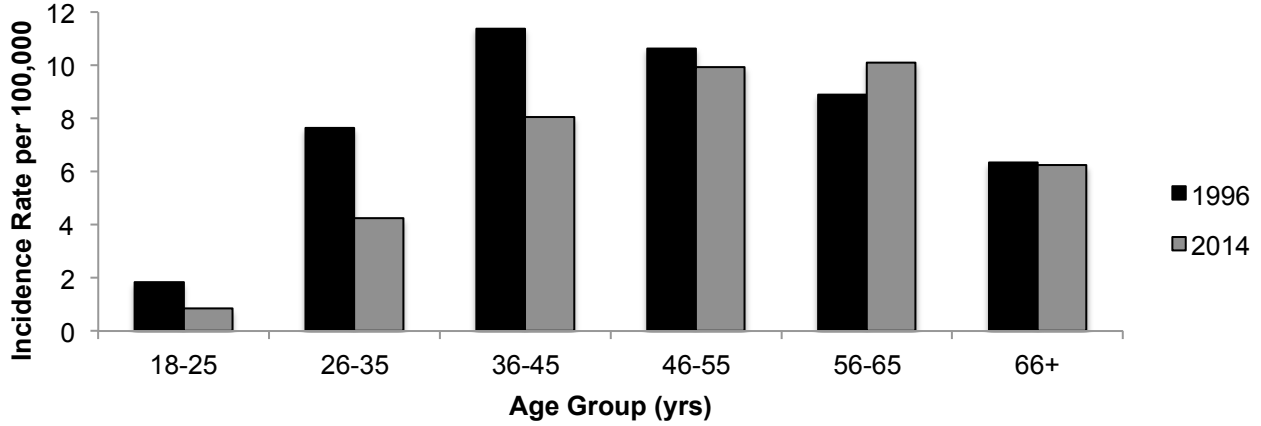

Mortality Rate, %
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015

FIGURE 1. Age-standardized prevalence a), incidence b) and mortality c) of patients with sarcoidosis in Ontario, Canada. Both prevalence and incidence rates are expressed in cases per 100,000. Mortality rates are expressed in percent of patients susceptible.

a)


Prevalence Rate per 100,000
300
250
200
150
100
50
0
18-25
26-35
36-45
46-55
56-65
66+
Age Group (yrs)
1996
2015

b)


Incidence Rate per 100,000
12
10
8
6
4
2
0
18-25
26-35
36-45
46-55
56-65
66+
Age Group (yrs)
1996
2014

c)

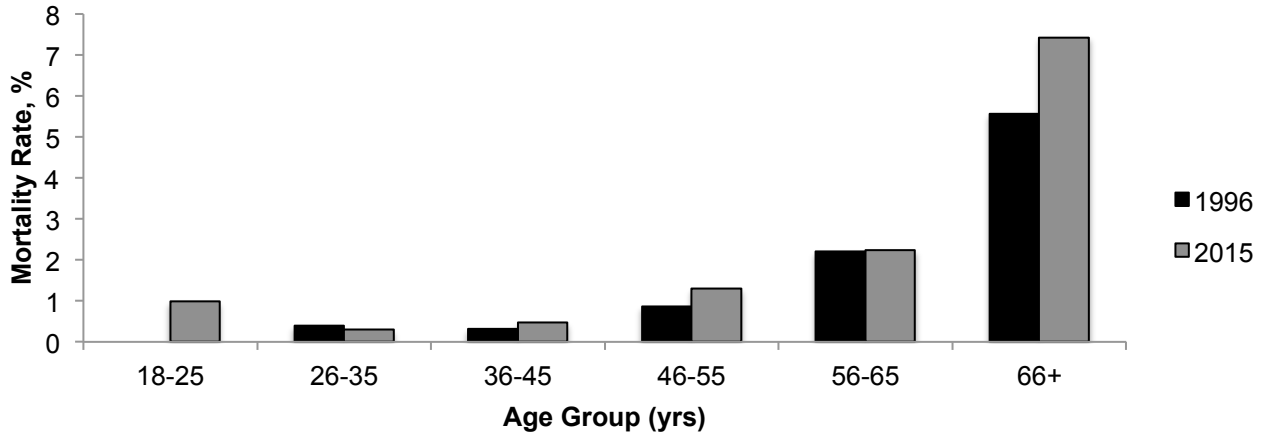

Mortality Rate, %
8
7
6
5
4
3
2
1
0
18-25
26-35
36-45
46-55
56-65
66+
Age Group (yrs)
1996
2015

FIGURE 2. Sex-standardized prevalence a), incidence b) and mortality c) of sarcoidosis by age group at the beginning and end of the study time period. Mortality is reported as the rate among individuals with sarcoidosis.

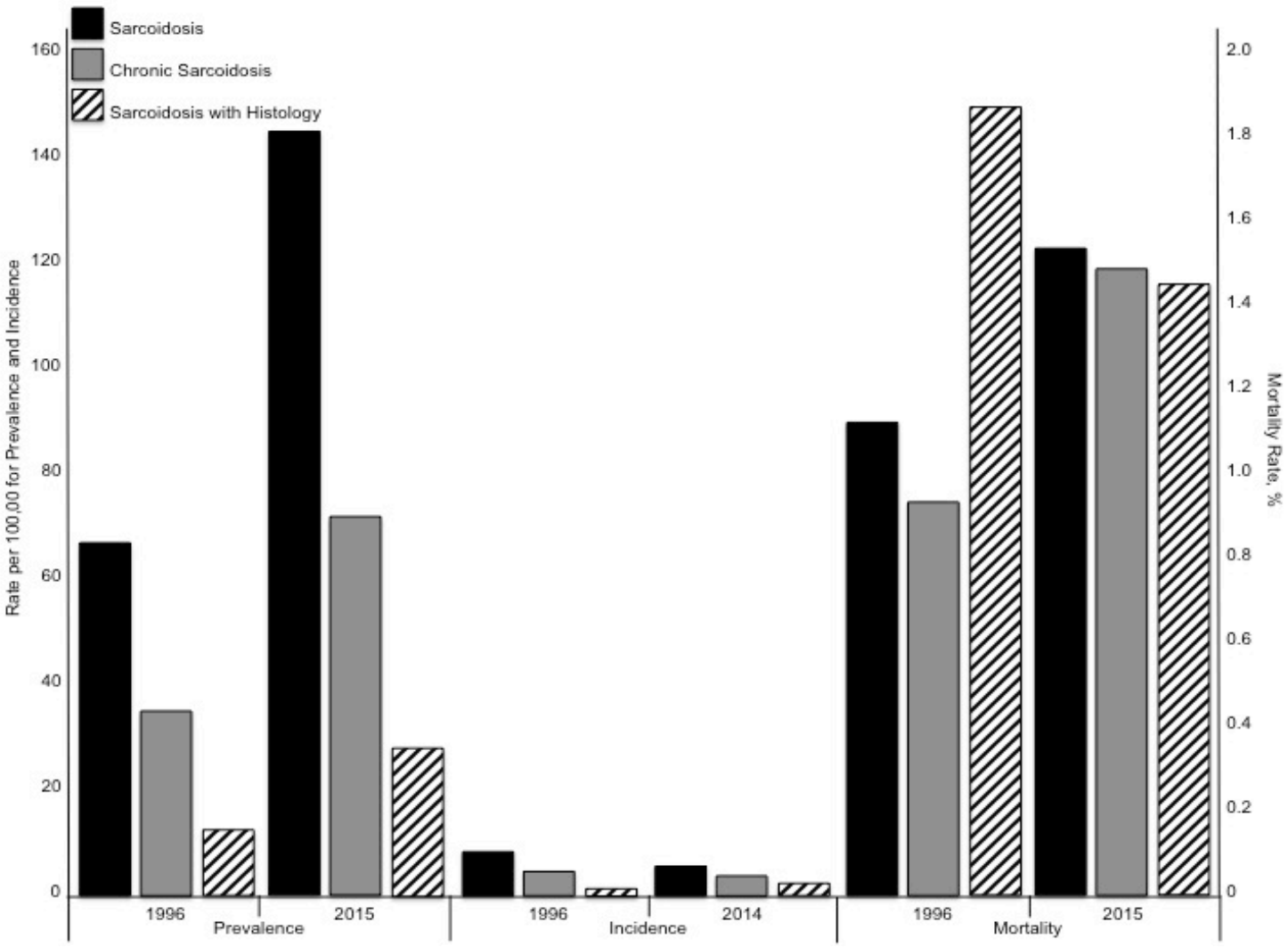
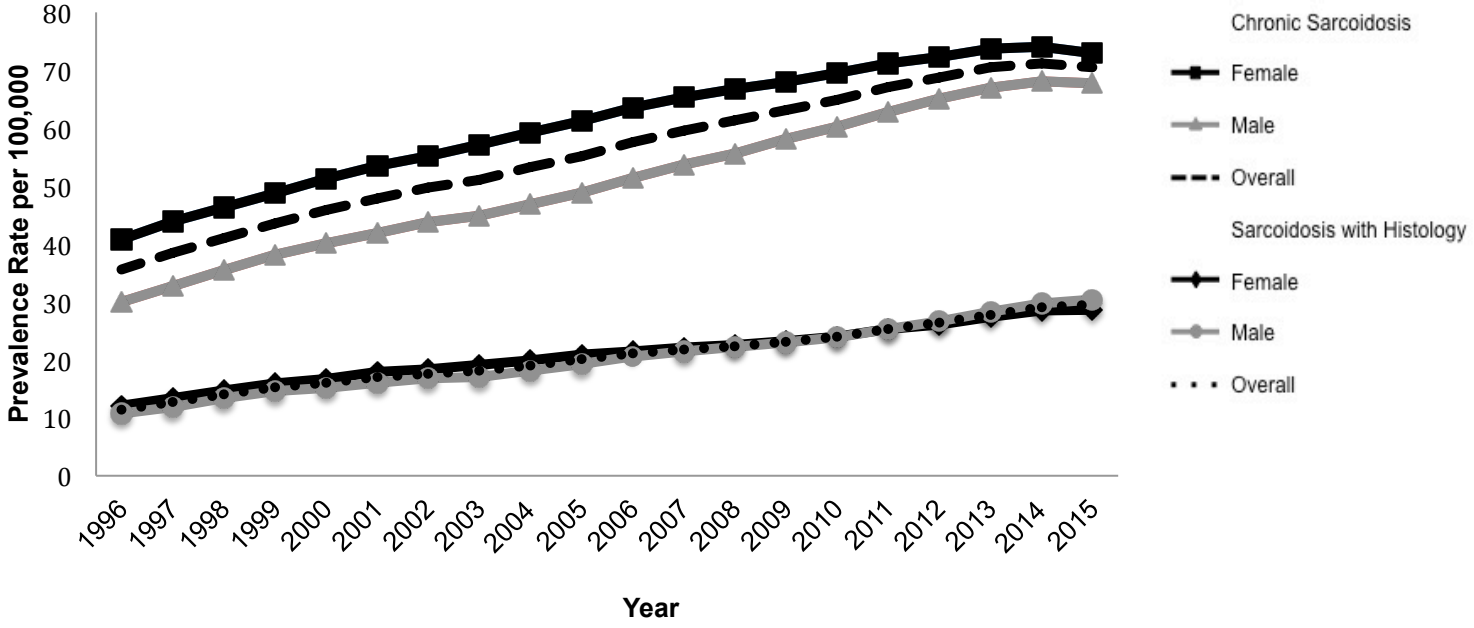
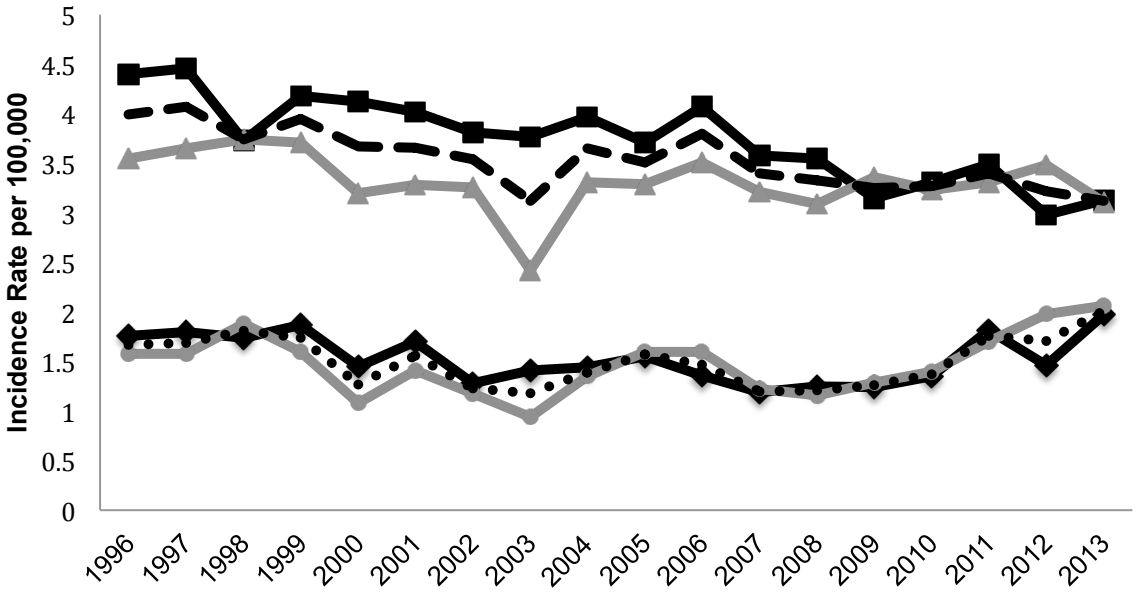


FIGURE 3 Epidemiology and mortality of sarcoidosis, chronic sarcoidosis and sarcoidosis with histology cohorts at the beginning and end of the study time period.

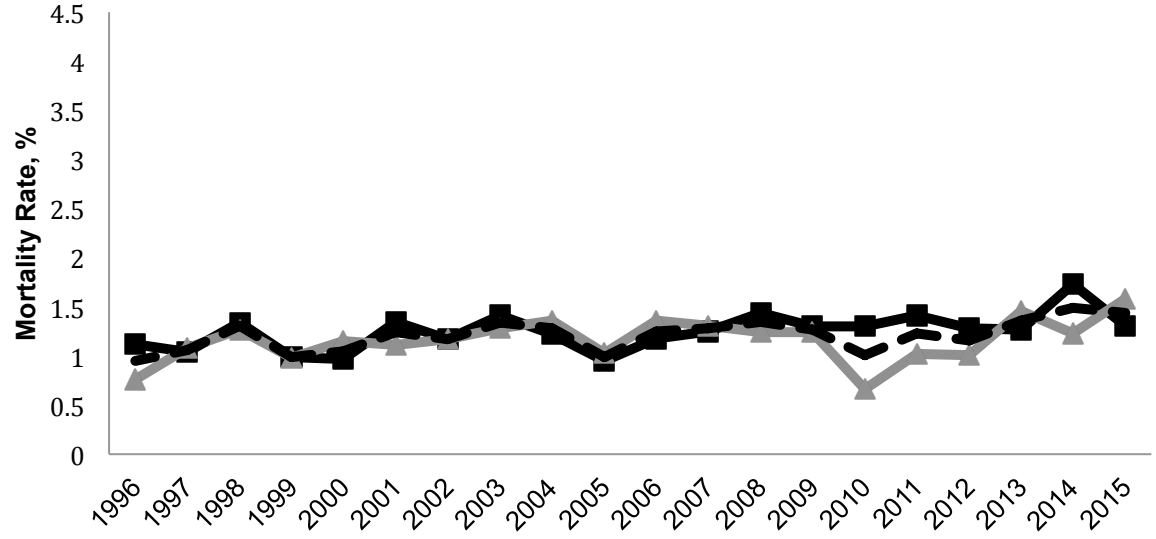
a)


Prevalence Rate per 100,000
80
70
60
50
40
30
20
10
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Year
Chronic Sarcoidosis
Female
Male
Overall
Sarcoidosis with Histology
Female
Male
Overall

b)


Incidence Rate per 100,000
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013

c)



d)

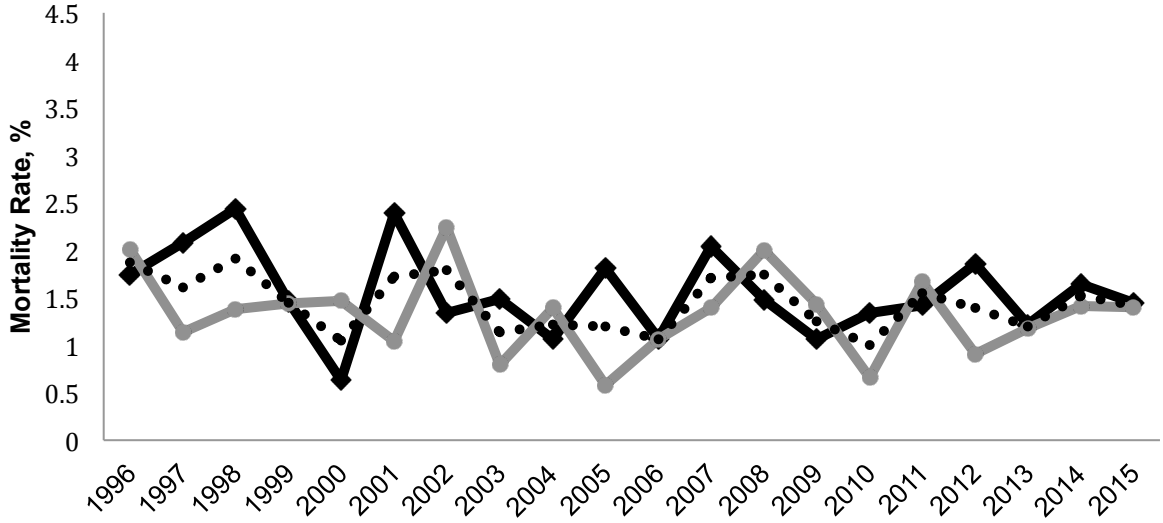


FIGURE E1 Age-standardized prevalence a), incidence b) and mortality c), d) of chronic sarcoidosis and sarcoidosis with histology patients in Ontario. Panels c) and d) represent mortality rates for the chronic sarcoidosis and sarcoidosis with histology cohorts respectively.