Systemic Sclerosis and Associated Interstitial Lung Disease in Ontario, Canada: An Examination of Prevalence and Survival Over 10 Years

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SHORT RUNNING HEAD:

SSc/SSc-ILD in Ontario

ABSTRACT

Objectives: Systemic sclerosis (SSc) is a rare autoimmune disease. Pulmonary complications of SSc are one of the leading causes of morbidity and mortality. The objective of this study was to determine prevalence and survival estimates of SSc and SSc-ILD in a Canadian province (Ontario) using administrative data over 10 years.

Methods: Using ICD-10-CA codes, adult patients diagnosed with SSc and SSc-ILD between April 1, 2008 and March 31, 2018 were identified from the National Ambulatory Care Reporting System (NACRS) and Discharge Abstract Database (DAD) administrative databases. SSc was identified first and ILD if present occurred after the SSc diagnosis. Prevalence estimates were determined for both SSc and SSc-ILD. For survival, Kaplan Meier survival curves were generated.

Results: At the start of fiscal year 2017/18 (final year of the cohort), there were 2,114 prevalent SSc cases for a cumulative prevalence of 19.1 per 100,000 persons and 257 prevalent cases of SSc-ILD, generating a prevalence of 2.32 cases per 100,000 persons. Mean age was 57 and 58 years with 84% and 80% females for SSc and SSc-ILD patients, respectively. One, 5 and 10 year survival rates respectively for the SSc group were 85.0%, 64.5% and 44.9%, and 77.1%, 44.4% and 22.0% for the SSc-ILD.

Conclusions: This study provides the first population-based estimates of SSc and SSc-ILD in Canada for prevalence and survival. Results confirm that the prevalence

estimates of SSc-ILD falls within the Canadian threshold of rare disease. It also demonstrates the poor survival in SSc especially when ILD is also present.

INTRODUCTION

Systemic sclerosis (SSc) is a rare and complex chronic connective tissue disease, characterized by immune dysregulation, microvascular damage and progressive fibrosis. Often there is severe organ involvement and increased risk of complications and rapid decline, leading to an unpredictable clinical course and a high disease burden. Estimates of the prevalence of SSc vary greatly depending on the methodology used for case ascertainment. (1) Diagnosis of SSc can be difficult due to its clinical heterogeneity and variety of organ manifestations. (2) In the European Union, SSc prevalence estimates range from 7.2 per 100,000 persons in Norway for the year 2009, to 33.9 per 100,000 persons in Italy in 2004. (3,4) In North America, one prevalence estimate of SSc in 2008 was 18.4 per 100,000 persons. (5) Thompson and colleagues examined a small population in Southwestern Ontario and estimated the prevalence to be 28 per 100,000 persons. (6)

The peak age onset of SSc is between 40 and 60 years, with women being four times more likely to develop the disease than men. (7) Results from studies conducted in 1999-2009 reported the mean age of SSc patients at diagnosis was 51.6 (±13.7) years and 47 years in the UK and Norway, respectively. (3,8) Similarly, a population-based cohort study conducted in the US reported a median age at diagnosis of 49.1 years. (9)

Interstitial lung disease (ILD) is a common manifestation of SSc associated with increased morbidity and mortality; however, few published estimates of the prevalence

and survival of SSc-ILD are available. Literature suggests that most patients with SSc have some evidence of lung disease including ILD and pulmonary hypertension. (8) ILD is among the leading causes of death related to SSc. Patients with SSc-ILD have a median survival of 5 to 8 years. (10,11) Estimates of SSc-ILD vary greatly; studies in Europe and North America respectively show 18.8% to 60.0% and 15.0% to 52.3% of SSc patients developing SSc-ILD. (9,12–14) The most recent Canadian estimates of SSc-ILD are based on the Canadian Scleroderma Research Group Registry (CSRG). (14) Steele et al. (2012) examined a sample of 1,168 adult SSc patients from the CSRG registry across 15 centres in Canada. SSc diagnosis was first confirmed by a rheumatologist in adult patients. To estimate the presence of ILD, an algorithm using clinical parameters was created to define SSc-ILD, which determined the prevalence of SSc-ILD to be 52%. (14) However, the findings represent a highly selected SSc patient population in the registry only referred to tertiary care centres, potentially subject to referral bias. A systematic literature review of SSc suggest that most severe organ complications including ILD occur at a frequency of 15%. (15)

Diagnoses of SSc and subsequent SSc-ILD occur predominantly in women. (16) In another systematic review, the ratio of females to males diagnosed in Europe ranged from 4:1 to 12:1, and in North America, the ratio was about 8:1. They also found that the mean age at diagnosis of SSc-ILD was higher in older patients (61.8 years). Similarly, a recent US study reported the mean age at SSc-ILD diagnosis as 54 years. (17)

Ontario is the largest and most populated province in Canada with a population of 14.6 million. (18) All citizens have universal health care with respect to access to physician visits and hospitalizations. This large population with single payer reimbursement for healthcare makes it an excellent resource to determine the prevalence of rare diseases.

To date, no published study has generated population-based estimates of prevalence and survival SSc-ILD in Canada. The primary objective of this study is to determine prevalence and survival estimates of SSc and SSc-ILD in Ontario, Canada.

METHODS

Study Design

A non-interventional, retrospective population-based study was conducted with data from April 1, 2008 and March 31, 2018, in order to generate prevalence estimates using administrative hospital and ambulatory care data in Ontario. Patients were first identified as having SSc from the National Ambulatory Care Reporting System (NACRS) and the Discharge Abstract Database (DAD), using diagnosis codes from the International Classification of Diseases, version 10, adapted for Canada (ICD-10-CA): M34.X codes indicating SSc disease (M34, M34.0, M34.1, M34.2, M34.8, M34.9), followed by the ICD codes for ILD any of the following indicating pulmonary fibrosis: J84.1, J84.8, J84.9 or J99.1. A validation study of the CIHI-DAD conducted by the Institute for Clinical Evaluative Sciences (IC/ES) found that coding of data elements

occurs with a high degree of accuracy. The most responsible diagnosis tends to be coded well. (19)The majority of ICD codes in for SSc have been validated for use in hospital databases such as DAD and NACRS with the exception of M34.2 (Systemic Sclerosis induced by drugs and chemicals). We expanded on the validated codes M34.0, M34.1, M34.8 and M34.9 to include M34.2 as a plausible SSc diagnoses based on clinical input. (20) The ILD codes selected have been established for idiopathic pulmonary fibrosis (IPF). IPF is a subtype of ILD. Generally, IPF is classified under the J84 code, as a result we included all J 84 codes available based on the ICD-10 CA (J84.1, J84.8 and J84.9), which have been used in previous IPF studies. (21)The definition was expanded to include J.99.1 based on clinical input to suggest some patients with SSc may receive this diagnosis for ILD (J.99.1 Respiratory disorders in other connective tissue disorders). However, there is no consensus on a validated algorithm to define ILD in administrative data. (22)

In the primary analysis, the index date was defined as the date of SSc diagnosis for both SSc patients and SSc-ILD patients, with the ILD diagnosis occurring after the SSc diagnosis. Demographic and epidemiological information were examined. The study population included all alive Ontario adult residents (at least 18 years of age) with valid provincial health coverage; and had a date of last contact with the health care system in Ontario within the past 7 years (from the first day of each fiscal year) during this study period. Patients were excluded if they had an ILD diagnosis prior to the SSc diagnosis or if they had missing or incomplete information at the index date. Figure 1 shows the flow chart of included cases.

Data Sources

The Institute for Clinical Evaluative Sciences (ICES) collects population-level health information in order to generate real-world data available for research via a number of datasets. For this study, data from April 1, 2008 to March 31, 2018 was used to identify prevalent patients with SSc and SSc-ILD from two databases: the DAD and NACRS. The DAD includes administrative, clinical and demographic information on acute inpatient hospital discharges (including deaths, sign-outs and transfers). The NACRS database consists of emergency department visits and hospital-based ambulatory care such as day surgery and clinic visits.

Outcomes

The primary outcome in this study was to estimate the crude prevalence of SSc and SSc-ILD per 100,000 persons. Secondary outcomes included survival of both SSc and SSC-ILD patients over the 10 year study period, demographic and clinical characteristics.

Statistical Analyses

The results were reported at an aggregate level and tabulated, and all analyses were conducted by an ICES analyst, using the index date as the date of SSc diagnosis as the primary analysis. Descriptive statistics were used to evaluate the prevalence of the study cohorts. Patient and demographic characteristics were summarized for patients in the SSc and SSc-ILD cohorts by number and percentage for categorical variables (e.g. sex) and by mean and standard deviation for continuous variables (e.g. age). Cells with

a size of 5 or less were suppressed for privacy reasons and to reduce the chance of re-identification. (23)

Prevalence estimate calculation

Prevalence was calculated by dividing the number of patients with a SSc or SSc-ILD diagnosis by the total population drawn from the start of the fiscal year 2017/2018 to generate a cumulative prevalence estimate over 10 years. The SSc and SSc-ILD patient counts were generated at the start of the respective fiscal year. Prevalence estimates were stratified by factors such as age and gender.

Survival Analysis

Kaplan-Meier survival curves were generated for both the SSc and SSc-ILD cohorts, starting at date of diagnosis and continued to death (for those with the known date of death). Otherwise, patients still alive were censored.

Sensitivity analysis

A sensitivity analysis was conducted by changing the index date of SSc-ILD to ILD diagnosis date as index date (any of the 4 “J” diagnosis codes as outlined in Appendix 1). This served as a narrowing of the definition of SSc-ILD. Prevalence estimates of SSc-ILD were generated using this index date were determined.

Patient and Public Involvement

Due to the administrative nature of this study, all aspects of this research was conducted without patient involvement.

Ethics Review

This study was approved by Veritas Independent Review Board (IRB #16314).

RESULTS

Prevalent Population

Baseline Characteristics

For the primary analysis, over the 10-year study period (to 2017-18), there were 2,114 prevalent cases of SSc, and 257 prevalent cases of SSc-ILD identified. To be considered a prevalent case, patients had to be alive and have a positive diagnosis of SSc and/or SSc-ILD during the particular year. Table 1 outlines the baseline characteristics for the prevalent SSc and SSc-ILD cohorts, respectively. The mean age at the index date for patients with SSc was 57.4 years, and 84.2% were female. For patients with SSc-ILD, the mean age at index date was 57.9 years of age, and 80.2% were female.

The sensitivity analysis also identified 257 prevalent SSc-ILD patients over the 10-year study period using the diagnosis date of ILD (to 2017-18). The mean age at ILD index date was slightly higher, at 59.9 years, and 80.2% were female. Baseline characteristics of the sensitivity analysis can be found in Appendix 2.

Table 2 shows the number prevalent cases (by diagnosis year and cumulative) for both the SSc and SSc-ILD groups by fiscal year (2008/9-2017/18) of the study period. Table 3 shows the overall prevalence of SSc and SSc-ILD for the primary analysis by age groups and gender in both groups. Of the 2,114 prevalent SSc cases, the cumulative prevalence rate at the start of fiscal 2017-18 was found to be 19.1 per 100,000 persons. Patients aged 65+ had a higher cumulative prevalence (29.4 per 100,000 persons), and females had a higher overall prevalence (31.2 per 100,000 persons) compared with males (6.2 per 100,000 persons). Of the 257 SSc-ILD cases, cumulative prevalence at the start of fiscal 2017-18 was found to be 2.3 per 100,000 persons. Unlike SSc, SSc-ILD patients between the ages of 51 and 64 had the highest cumulative prevalence (4.2 per 100,000 persons). Females had a higher prevalence rate at the start of fiscal 2017 (3.6 per 100,000 persons) compared with males (1.0 per 100,000 persons).

For the sensitivity analysis, the cumulative prevalence at the start of fiscal 2017-18 was determined to be 2.3 cases per 100,000 persons. Patients aged 65+ had the highest cumulative prevalence (3.9 per 100,000 persons), and females had a higher prevalence of SSc-ILD at the start of fiscal 2017 (2.3 per 100,000 persons). Sensitivity analyses results can be found in Appendix 3.

Survival Results

Survival was calculated based on all identified cases during the 10 year study period. For SSc patients, there were 1,150 deaths (37.0%) in the population over the duration of the 10-year study period. The survival rates at one, five and ten years after diagnosis were 85.0%, 64.5% and 44.9%, respectively. Figure 2 presents the Kaplan Meier survival curve for SSc patients, along with the proportion of patients at risk, who died and who were censored.

SSc-ILD patients had lower survival rates and higher proportions at risk. There were 336 patients (63.7%) who died over the study period. The survival rates at one, five and ten years after diagnosis were 77.1%, 44.4% and 22.0%, respectively. Figure 3 presents the Kaplan Meier survival curve for SSc-ILD patients, along with the proportion of patients at risk, who died and who were censored.

DISCUSSION

This study represents the total population in Ontario, Canada which has universal healthcare access determining SSc and SSc-ILD prevalence and mortality.

There is a paucity of information on prevalence estimates for SSc and SSc-ILD that have been published globally. A systematic review conducted by Bergamasco and

colleagues examined the epidemiology of SSc and SSc-ILD including prevalence and survival from a number of studies in Europe and in North America. (16) They examined 39 studies from Europe and North America, and found a wide variation in Europe and North America the prevalence estimates for SSc that were reported (7.2 per to 33.9 per 100,000 persons and 13.5 to 44.3 per 100,000 persons, respectively). The investigators were only able to derive prevalence estimates for SSc-ILD from one study from Norway, where the estimated prevalence was found to be in the range of 1.7-4.2 per 100,000 persons. We found that the prevalence of SSc-ILD estimates from our study falls within this range (2.3 per 100,000 persons). The investigators also examined multiple sites in the United States and Canada. However, North American SSc-ILD prevalence results were not available. (16)

There are some Canadian studies that have previously reported on the prevalence in SSc and SSc-ILD. One of the first Canadian studies by Thompson and colleagues that explored prevalence in a small setting estimated prevalence of SSc to be 28 cases per 100,000 persons. (6) However, the authors acknowledge that the results are not truly reflective of the larger population, as results from two of the three communities that they examined did not reach statistical significance. Bernatsky and colleagues analyzed data (1989-2003) from Quebec to estimate prevalent SSc using physician billing and hospitalization information. (24) They found the overall prevalence in 2003 to be 44.3 per 100,000 persons also higher than our estimates. Similarly, a study from Alberta found that the SSc prevalence in 2007 using physician billing records and hospitalization data was 57.7 per 100,000 females, and 9.8 cases per 100,000 males.

(25). Another study from Canada reported that the sex ratio of SSc patients was 4.7 females to one male, where males had more dcSSc subset, more ILD and reduced survival. (26). These findings are similar to our current study with respect to the sex distribution of cases and reduced survival in SSc-ILD. Our study used data from outpatient hospital clinics and inpatients, and only considered ICD-10-CA diagnosis codes. It is likely that higher prevalence estimates determined in other Canadian studies captured more community cases of SSc in physician billing information.

In our study, the probability of survival for SSc patients was found to be lower/shorter than what has been previously reported. The systematic review conducted by Bergamasco and colleagues (16) found that in Europe, the survival of SSc patients at 5 and 10 years was between 83-84% and 65-73%, respectively, while in North America, 10-year survival ranged between 66-82%. A second systematic review and meta-analysis including 43 studies over years 1964 to 2005 conducted in 12 countries suggests 5 and 10 years SSc survival rates are 75% and 63% respectively. (27) In contrast, our study found lower survival estimates with 5 and 10 year survival of SSc at 65%, and 45% respectively. We believe that given our patient population is selected from inpatients and hospital-based outpatient clinics, they may have more severe SSc than patients in the studies that were included in the systematic reviews and meta-analysis.

Our study found that about 12.0% of patients diagnosed with SSc were further formally diagnosed as having SSc-ILD, and these patients had lower survival than overall SSc

cases. When compared to survival data from a single tertiary care centre in the US of whom only 24 had SSc-ILD and reported 100% survival at 1 year and 77% at 5 years, (28) our results showed lower survival. To put our SSc findings in context, at five years SSc-ILD survival rates are in line with a well-known cancer, specifically, multiple myeloma, has a similar 5 year survival rate as SSc-ILD (44%). (29)

Distribution by gender in our study was found to be in line with the expected distribution of approximately 80% women to 20% men affected by SSc and SSc-ILD, and aligned with reported distributions in other published studies. (7,8)

There are some notable strengths of the study. Our dataset is large and representative, as the denominator included the entire adult population of Ontario. Using administrative data from Ontario allows for population-level data to be examined without imputation and without extrapolation of results. SSc and SSc-ILD definitions derived using ICD-10 codes were validated by clinicians across both rheumatology and respirology that have extensive experience in treating and diagnosing SSc-ILD. Ten years of population data were included in order to ascertain stability of estimates. A sensitivity analysis was performed for defining SSc-ILD.

There are some limitations to the study. First, the databases capture diagnoses that are ambulatory and hospital based, and may not reflect community cases. They also provide limited clinical outcomes, and as the studies conducted in other provinces have shown, including billing and claims data may capture a wider population of patients.

(24,25) Despite the assumptions that were made to identify the patients with SSc and those with ILD, the prevalence and proportion with ILD align with other studies, adding face validity to the methods used in this study.

This study was conducted to provide estimates of the prevalence and survival of SSc and SSc-ILD to provide updated evidence to support the burden of SSc-ILD for clinicians, health system planning and costs to payers including approval for SSc-ILD treatments.

CONCLUSION

This analysis adds valuable information about prevalence estimates and survival in patients with SSc and SSc-ILD in Canada's largest province, and provides the first population based estimates using administrative data of SSc-ILD in Canada. The study suggests that SSc-ILD patients have a lower survival rate than SSc, and that survival continues to be poor for patients with SSc-ILD.

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Table 1: Baseline characteristics for prevalent SSc and SSc-ILD patients over the study period

SSc PATIENTS										
Variable	**2008-9 N=497**	**2009-10 N=823**	**2010-11 N=1,073**	**2011-12 N=1,239**	**2012-13 N=1,435**	**2013-14 N=1,590**	**2014-15 N=1,749**	**2015-16 N=1,909**	**2016-17 N=2,007**	**2017-18 N=2,114**
Age at index date										
Mean±SD	60.0±14.4	59.6±14.6	59.3±14.4	58.6±14.2	58.2±14.3	58.2±14.2	58.0±14.2	57.8±14.4	57.6±14.4	57.4±14.3
Median (IQR)	60(51-72)	60(50-71)	60(50-70)	59(49-69)	58(49-69)	59(49-68)	58(49-68)	58(48-68)	58(48-68)	58(48-67)
Age group, n (%)										
18-29	10(2.0%)	18(2.2%)	23(2.2%)	32(2.6%)	48(3.3%)	53(3.3%)	57(3.3%)	64(3.4%)	69(3.4%)	72(3.4%)
30-50	114(22.9%)	199(24.2%)	263(24.5%)	309(24.9%)	354(24.7%)	390(24.5%)	441(25.2%)	493(25.8%)	523(26.1%)	555(26.3%)
51-64	180(36.2%)	299(36.3%)	400(37.3%)	471(38.0%)	533(37.1%)	584(36.7%)	645(36.9%)	702(36.8%)	745(37.1%)	799(37.8%)
65+	193(38.8%)	307(37.3%)	387(36.1%)	427(34.5%)	500(34.8%)	563(35.4%)	606(34.7%)	650(34.1%)	670(33.4%)	688(32.5%)
Sex										
Female	412(82.9%)	698(84.8%)	914(85.2%)	1,060(85.5%)	1,215 (84.7%)	1,353(85.1%)	1,492(85.3%)	1,619(84.8%)	1,698(84.6%)	1,780(84.2%)
Male	85(17.1%)	125(15.2%)	159(14.8%)	179(14.5%)	220(15.3%)	237(14.9%)	257(14.7%)	290(15.2%)	309(15.4%)	334(15.8%)
SSc-ILD PATIENTS										
Variable	**2008-9 N=118**	**2009-10 N=178**	**2010-11 N=227**	**2011-12 N=262**	**2012-13 N=282**	**2013-14 N=288**	**2014-15 N=289**	**2015-16 N=296**	**2016-17 N=281**	**2017-18 N=257**
Time to ILD after SSc diagnosis (days)										
Mean±SD	964.5±981.5	974.4±961.9	987.3±910.5	971.8±886.9	975.7±870.8	958.3±861.8	935.0±866.2	865.0±855.3	798.7±846.8	732.2±840.1
Median (IQR)	629.5	735.5	810	844.5	848.5	801.5	771	611	511	390

	(107-1632)	(118-1632)	(176-1609)	(181-1572)	(206-1572)	(222.5-1545)	(167-1494)	(144.5-1348)	(100-1246)	(68-1129)
Age at index date										
Mean±SD	59.1±13.3	57.8±13.1	57.8±12.7	58.4±12.5	59.0±12.3	58.9±12.3	58.4±11.9	58.5±12.4	58.1±12.2	57.9±12.2
Median(IQR)	59(52-69)	57(50-67)	58(49-67)	59(50-67)	60(51-68)	60(51-68)	59(51-67)	59(50-67.5)	59(50-67)	59(50-66)
Age group, n(%)										
18-29	*1-5	*1-5	*1 – 5	*1-5	*1-5	*1-5	*1-5	*1-5	0(0.00%)	0(0.0%)
30-50	*18-22	*42-46	*56 – 60	*62-66	*62 – 66	*61-65	*66-70	*71-75	74(26.33%)	65(25.3%)
51-64	55(46.6%)	77(43.3%)	100(44.1%)	112(42.7%)	119(42.2%)	122(42.4%)	127(43.9%)	124(41.9%)	122(43.4%)	117(45.5%)
65+	40(33.9%)	54(30.3%)	66(29.1%)	83(31.7%)	96(34.0%)	100(34.7%)	91(31.5%)	96(32.4%)	85(30.3%)	75(29.2%)
Sex										
Female	94(79.7%)	146(82.0%)	183(80.6%)	211(80.5%)	221(78.4%)	233(80.9%)	237(82.0%)	240(81.1%)	224(79.7%)	206(80.2%)
Male	24(20.3%)	32(18.0%)	44(19.4%)	51(19.5%)	61(21.6%)	55(19.1%)	52(18.0%)	56(18.9%)	57(20.3%)	51(19.8%)

SSc= Systemic Sclerosis; SSc-ILD= Systemic Sclerosis- Interstitial Lung Disease; SD= Standard Deviation; IQR= interquartile range

* Exact counts suppressed for privacy reasons

Table 2: Prevalent SSc and SSc-ILD cases

Fiscal Year	Prevalent SSc cases by diagnosis year	Cumulative prevalent cases of SSc*	Prevalent SSc-ILD cases by diagnosis year	Cumulative prevalent cases of SSc-ILD*
2008-9	497	497	118	118
2009-10	381	823	75	178
2010-11	334	1,073	70	227
2011-12	281	1,239	62	262
2012-13	290	1,435	50	282
2013-14	267	1,590	44	288
2014-15	271	1,749	39	289
2015-16	272	1,909	43	296
2016-17	257	2,007	38	281
2017-18	261	2,114	20	257

*Cumulative prevalence is the sum of patients that are alive with the indication at the start of that year who are recorded that year and were diagnosed in any of the eligible cohort years. For example, cumulative prevalent cases in 2010 (all patients alive on April 1, 2010 diagnosed in 2008-2010)

SSc= Systemic Sclerosis; SSc-ILD= Systemic Sclerosis- Interstitial Lung Disease

Table 3: Overall prevalence of SSc and SSc-ILD patients per 100,000 persons

Fiscal Year 2017/ 2018	SSc (N=2,114)	SSc-ILD (N=257)	% of SSc with ILD
Overall	19.1	2.3	12.0
Age group			
18-29	3.6	0.0	---
30-50	14.1	1.7	12.1
51-64	28.8	4.2	14.6
65+	29.4	3.2	10.9
Sex			
Female	31.2	3.6	11.5
Male	6.2	1.0	16.1

SSc= Systemic Sclerosis; SSc-ILD= Systemic Sclerosis- Interstitial Lung Disease;

FIGURE 1: FLOW CHART OF SSc AND SSc-ILD INCLUDED CASES

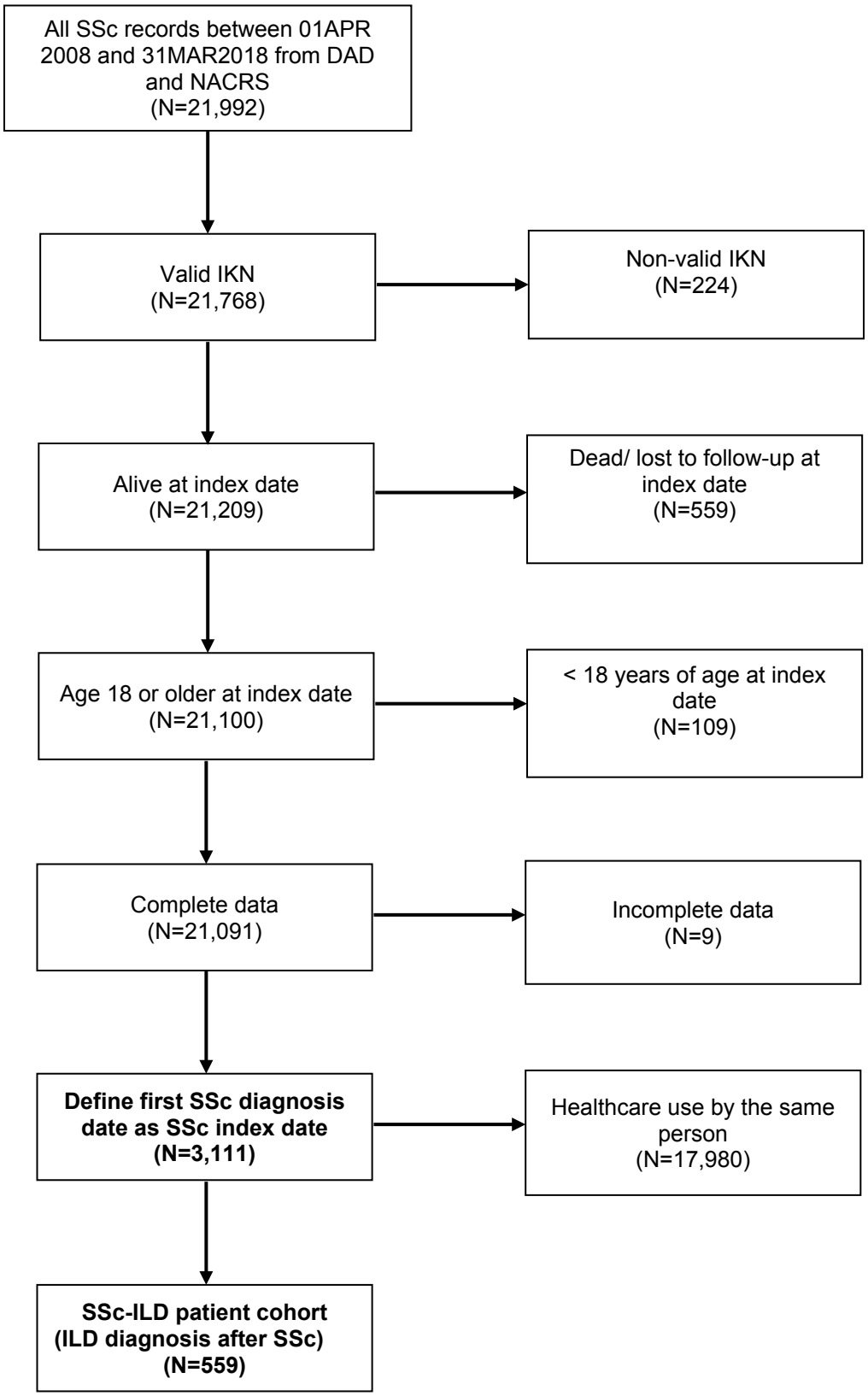
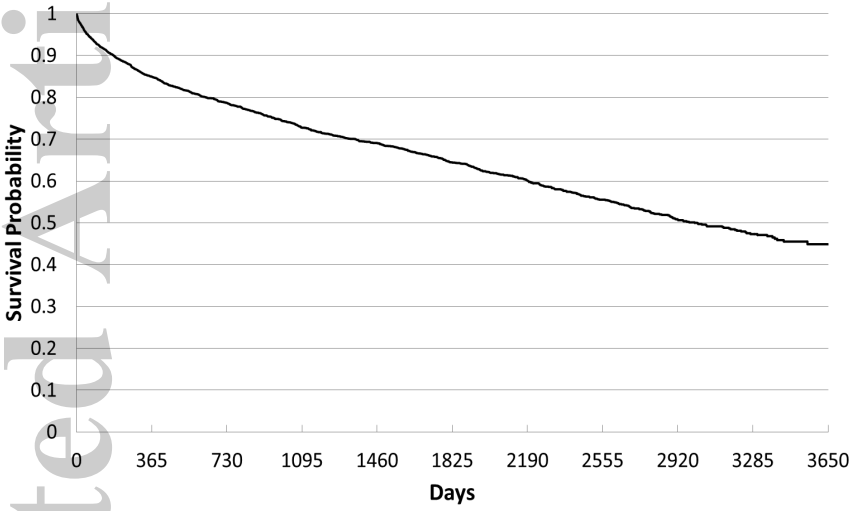
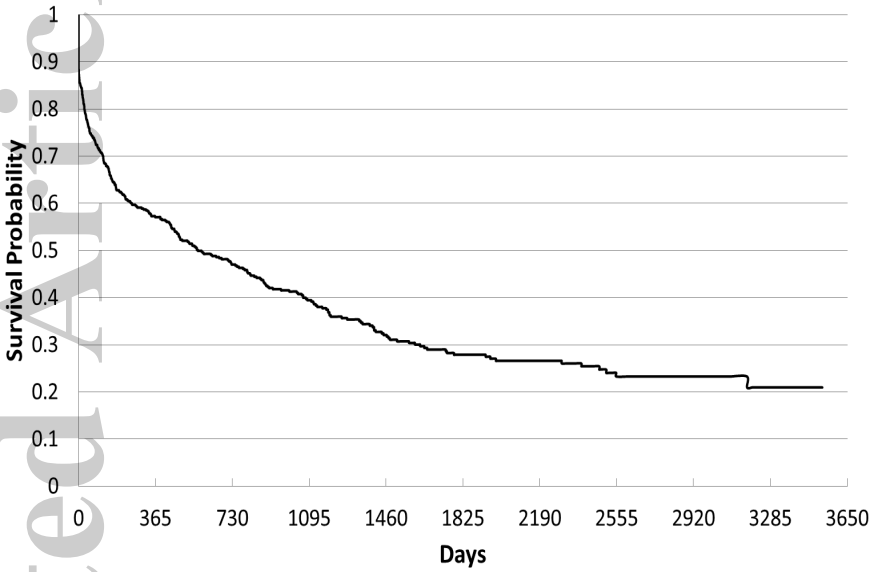


FIGURE 2: KAPLAN MEIER SURVIVAL CURVE AND RISK TABLES OF SSc PATIENTS



Year (days)	At risk, n(%)	Death, n(%)	Censor, n(%)
0	3111(100.0%)	0(0.0%)	0(0.0%)
1 (365)	2419(77.8%)	453(14.6%)	239(7.7%)
2 (730)	2051(65.9%)	625(20.1%)	435(14.0%)
3 (1,095)	1699(54.6%)	771(24.8%)	641(20.6%)
4 (1,460)	1420(45.6%)	852(27.4%)	839(27.0%)
5 (1,825)	1146(36.8%)	941(30.3%)	1024(32.9%)
6 (2,190)	884(28.4%)	1012(32.5%)	1215(39.1%)
7 (2,555)	664(21.3%)	1073(34.5%)	1374(44.2%)
8 (2,920)	424(13.6%)	1121(36.0%)	1566(50.3%)
9 (3,285)	214(6.9%)	1143(36.7%)	1754(56.4%)
10 (3,650)	*1 - 5	1150(37.0%)	1956(62.9%)

FIGURE 3: KAPLAN MEIER SURVIVAL CURVE AND RISK TABLES OF SSc-ILD PATIENTS



Year (days)	At risk, n(%)	Death, n(%)	Censor, n(%)
0	559(100.0%)	0(0.0%)	0(0.0%)
1 (365)	417(74.6%)	126(22.5%)	16(2.9%)
2 (730)	335(60.0%)	192(34.3%)	32(5.7%)
3 (1,095)	275(49.2%)	232(41.5%)	52(9.3%)
4 (1,460)	224(40.1%)	261(46.7%)	74(13.2%)
5 (1,825)	184(32.9%)	287(51.3%)	88(15.8%)
6 (2,190)	139(24.9%)	311(55.6%)	109(19.5%)
7 (2,555)	108(19.3%)	329(58.9%)	122(21.8%)
8 (2,920)	58(10.4%)	350(62.6%)	151(27.0%)
9 (3,285)	30(5.4%)	355(63.5%)	174(31.1%)
10 (3,650)	0(0.00%)	356(63.7%)	203(36.3%)