

## Real World Evidence in Italy in Patients with Interstitial Lung Disease (ILD)

Retrospective Observational Study from an Italian Administrative Database

Report 23/11/2023



**VALUE MESSAGES TO BE TESTED BY PRESENT EVIDENCE GENERATION**

In patients affected by **Systemic Sclerosis, Rheumatoid Arthritis**, Polymyositis and Dermatomyositis, Hypersensitivity Pneumonia, the objective of this project will be to analyze the **presence of pulmonary complications** through the use of specific healthcare services found within the current administrative flows. The results that will be obtained will be used in order to highlight the **need for monitoring in patients with pulmonary involvement** with the **aim of encouraging and supporting a multidisciplinary approach** that includes not only the rheumatologist but also the pulmonologist not only during the state of progression of the pathology.



**BACKGROUND**  
**OBJECTIVES**



**OBJECTIVES:**

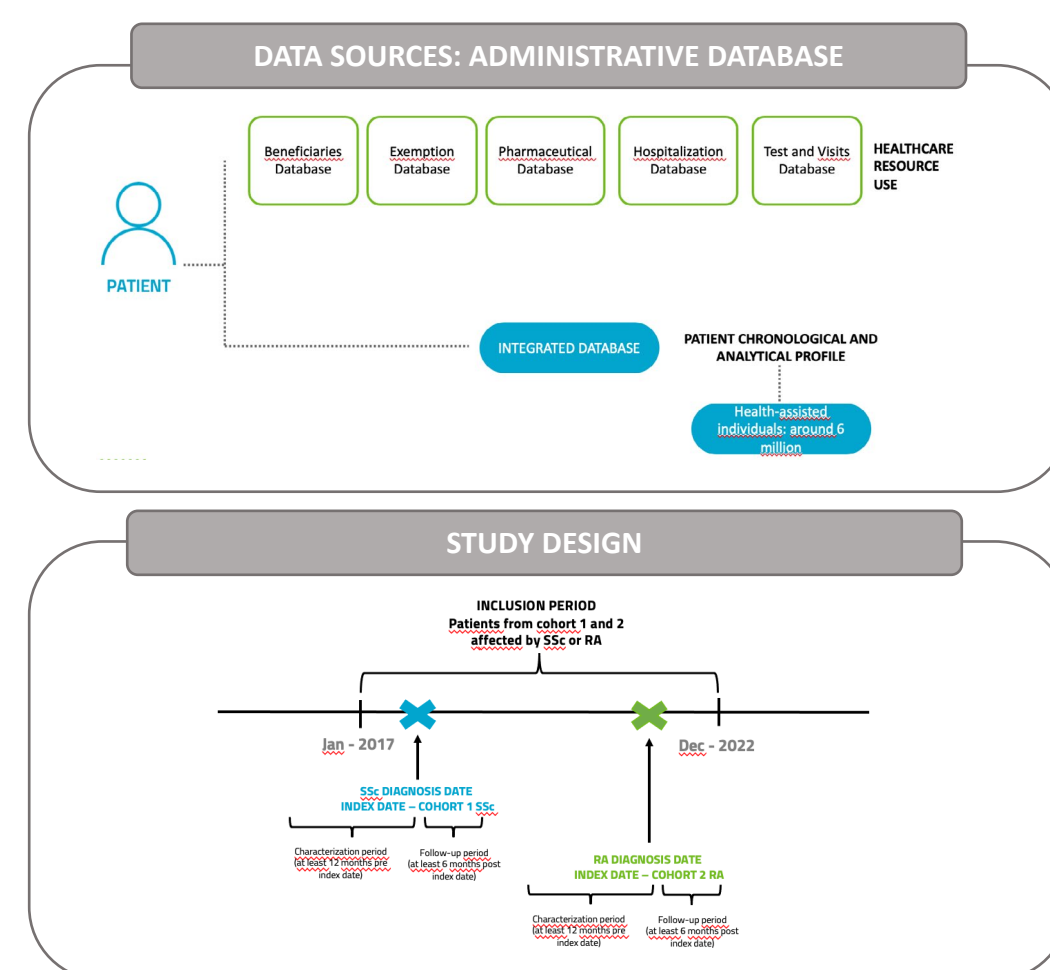
1. To analyze the diagnostic-therapeutic path and the **onset of healthcare services for the respiratory system** in patients affected by **Systemic Sclerosis, Rheumatoid Arthritis**, Polymyositis and Dermatomyositis, Hypersensitivity Pneumonia.
2. To analyze the **consumption of healthcare resources** (drugs, specialist visits, diagnostic tests and hospitalizations) for the respiratory system in patients affected by Systemic Sclerosis, Rheumatoid Arthritis, Polymyositis and Dermatomyositis, Hypersensitivity Pneumonia.

In particular, the following details were analyzed for each analysis cohort:

- The percentage of patients who perform specific healthcare services in the respiratory field.
- The characteristics of the patients who carry out these services.
- The time to onset of such performance.
- The direct costs borne by the NHS, connected to these services.

## METHODS

### DATA SOURCES – STUDY POPULATION AND STUDY DESIGN



#### STUDY POPULATION AND TIME PERIODS

##### INCLUSION AND EXCLUSION CRITERIA

- **INCLUSION CRITERIA Cohort 1 SSc:** Patients with a diagnosis of **SYSTEMIC SCLEROSIS (SSc)** identified by the presence of: at least one **hospitalization** discharge diagnosis at primary or secondary level for SSc (ICD-9-CM: 710.1); **OR** an **exemption** code for SSc (code: RM0120).
- **INCLUSION CRITERIA Cohort 2 RA:** Patients with a diagnosis of **RHEUMATOID ARTHRITIS (RA)** identified by the presence of: at least one **hospitalization** discharge diagnosis at primary or secondary level for RA (ICD-9-CM: 714); **OR** an **exemption** code for RA (code: 006).
- **EXCLUSION CRITERIA** Patients with Chronic obstructive pulmonary disease (COPD) (identified by the presence of: at least one hospitalization considering ICD-9-CM codes: 491, 493.2, 496 and/or presence of active exemption code 057) or **ASTHMA** (identified by the presence of: at least one prescription of ATC code R03DC and/or at least one hospitalization considering ICD-9-CM code 493 (excluded 493.2) and/or presence of active exemption code 007) before the index date were excluded.

##### TIME PERIODS

- **DATA AVAILABILITY:** from January 2009 to June 2023.
- **INCLUSION PERIOD:** from January 2017 to December 2022.
- **INDEX DATE:** the date of first matching with inclusion criteria.
- **CHARACTERIZATION PERIOD:** all available period, at least 12 months before index date (all patients had at least 1 year of data availability period before index date).
- **FOLLOW UP PERIOD:** all available period after index date (all patients had at least 6 months of data availability period after index date).

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**METHODS - IDENTIFICATION OF PULMONARY INVOLVEMENT**  
**LIST OF PROXIES/CODES USED AND COHORT OF ANALYSIS**

**IDENTIFICATION OF PULMONARY INVOLVEMENT**  
**LIST OF PROXIES AND CODES USED**

Among the patients included in the analysis, **THE IDENTIFICATION OF PULMONARY INVOLVEMENT WAS PROXIED** by the presence of the resource consumption mentioned in the table during the entire available follow-up period.

HEALTHCARE SERVICES	ATC CODE	EXEMPTION CODE	PROCEDURE CODE	ICD-9-CM CODE
<b>TREATMENTS</b>				
prescription of pirfenidone	L04AX05	-	-	-
prescription of nintedanib	L01EX09	-	-	-
prescription of oxygen therapy	V03	-	-	-
prescription of drugs for obstructive airway diseases	R03	-	-	-
prescription of immunosuppressors	L04AC07, L04AA06, L01XC02, L01AA01, L04AA02	-	-	-
<b>DIAGNOSTIC PROCEDURES</b>				
chest radiograph	-	-	87.44.1	-
high-resolution computed tomography (HRCT)	-	-	87.41	-
diffusing capacity of the lungs for carbon monoxide test (DLCO)	-	-	89.38.3	-
Spirometry	-	-	89.37	-
<b>SPECIALISTIC VISITS</b>				
pneumological specialist visit	-	-	89.7, 89.01	-
<b>EXEMPTION FOR PATHOLOGY</b>				
exemption for interstitial lung diseases	-	RHG010	-	-
<b>HOSPITALIZATIONS</b>				
hospitalization for acute interstitial pneumonia	-	-	-	515
hospitalization for idiopathic pulmonary fibrosis	-	-	-	516.3
diseases of the respiratory system, emphysema, obstructive sleep apnea (OSA) *	-	-	-	460-519, 492, 327.23
<b>TRANSPLANT</b>				
lung transplant	-	-	33.5	V426

NOTE: \*To avoid the possibility to consider COVID related hospitalizations - diseases of the respiratory system, emphysema, obstructive sleep apnea (OSA) hospitalizations identified during 2020 - 2021 were not considered.



The presence of pulmonary involvement among all patients included in the analysis was evaluated. **ALL PATIENTS WERE STRATIFIED ACCORDING TO DIFFERENT LEVELS OF PULMONARY COMPROMISSION IDENTIFIED BY THE TYPE AND NUMBER OF RESOURCE CONSUMPTION** (during all period of follow-up available) **USED AS PROXY OF PULMONARY INVOLVEMENT.**

**Cohort 1 - Patients with SSc**

Among patients with at least 1 resource consumption selected as a "proxy of PULMONARY INVOLVEMENT", patients were categorized as:

- **CERTAIN cohort** if patients had  $\geq 3$  healthcare services or the presence of at least one prescription for pirfenidone, nintedanib or oxygen therapy.
- **POSSIBLE cohort** if patients had 2 healthcare services

**Cohort 2 - Patients with RA**

Among patients with at least 1 resource consumption selected as a "proxy of PULMONARY INVOLVEMENT", patients were categorized as:

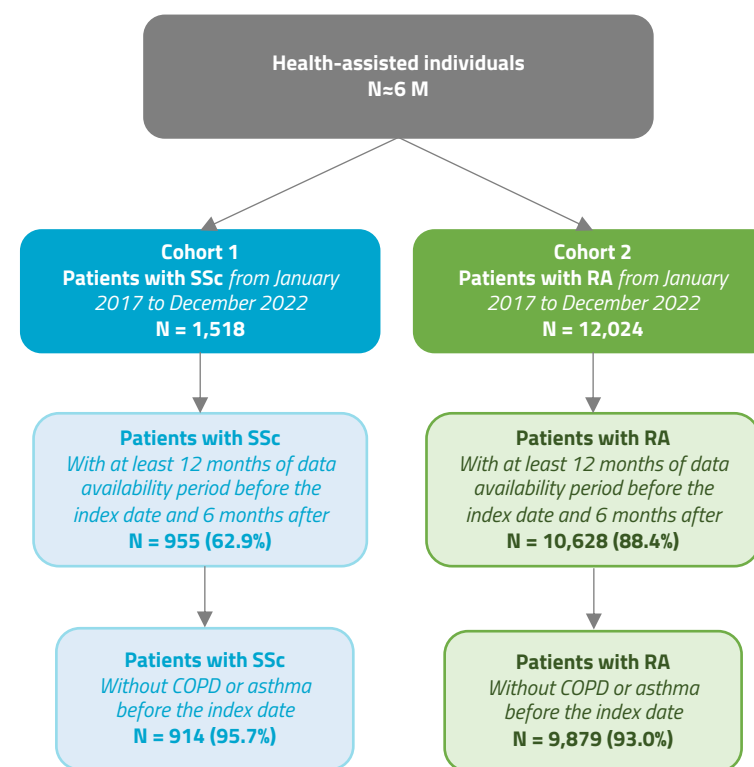
- **CERTAIN cohort** if patients had  $\geq 3$  healthcare services or the presence of at least one prescription for pirfenidone, nintedanib or oxygen therapy.
- **POSSIBLE cohort** if patients had 2 healthcare services.
- **AT RISK cohort** if patients had 1 healthcare services.

NOTE: In the results section it is also mentioned among the patients included, **how many do not present resource consumption related to pulmonary involvement** during the entire available follow-up period.

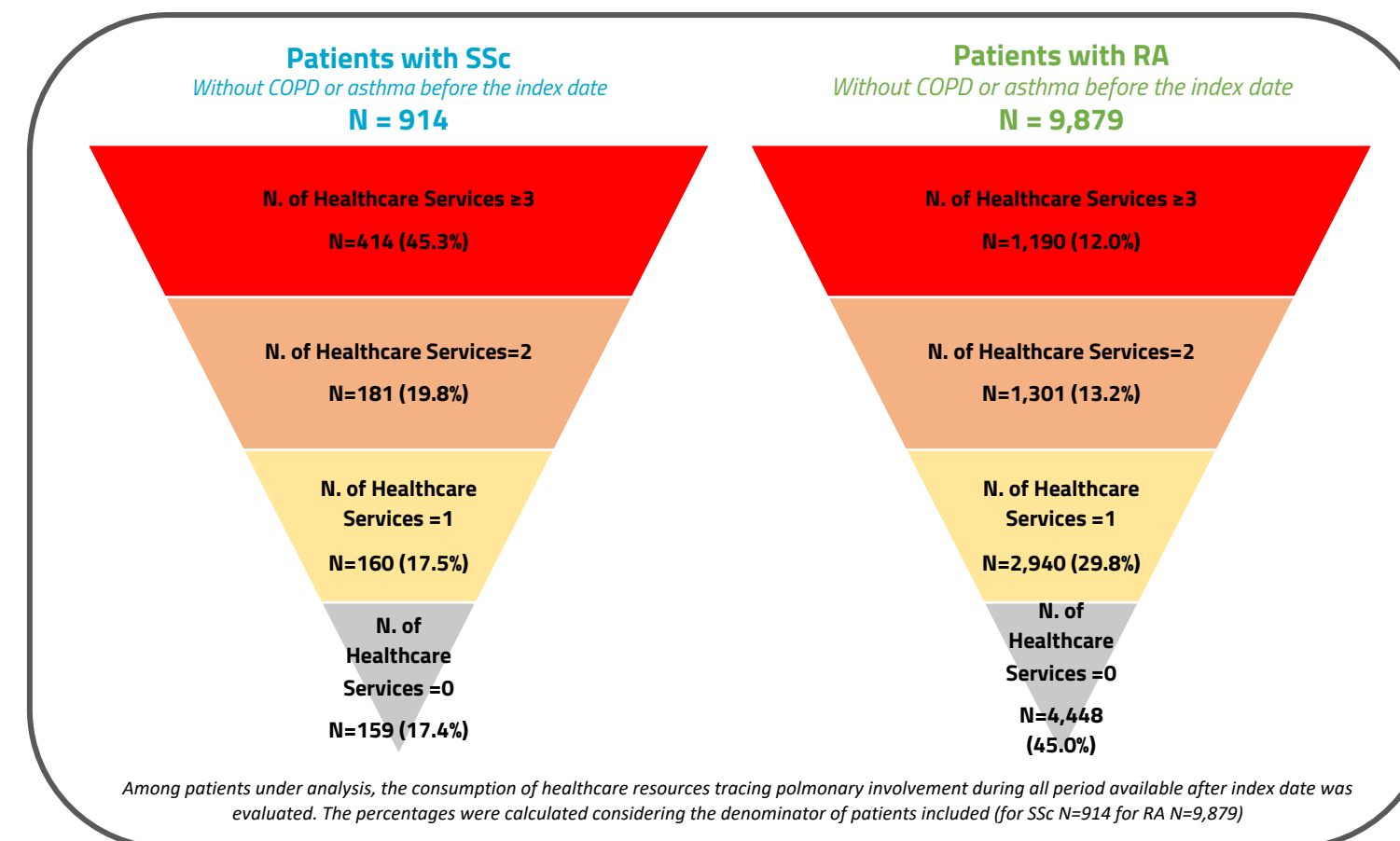
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**RESULTS –STUDY POPULATION\_ EVALUATION OF PULMONARY INVOLVEMENT**  
**SSc - RA IDENTIFICATION AND STRATIFICATION ACCORDING TO THE PRESENCE OF PULMONARY INVOLVEMENT**

**STUDY POPULATION**

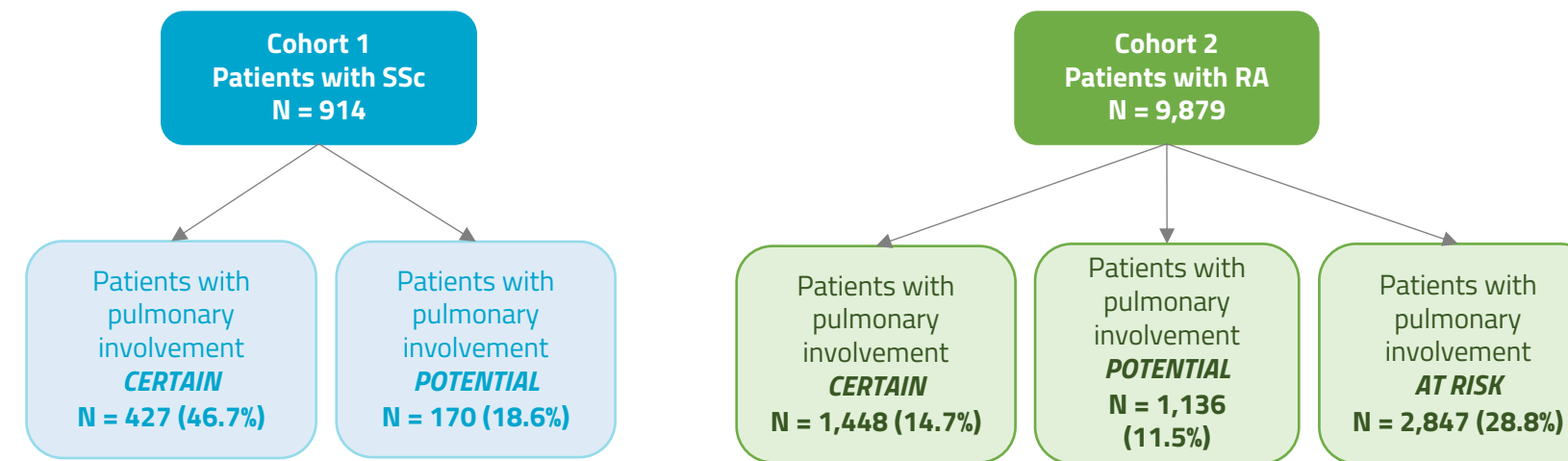


**PATIENTS STRATIFICATION ACCORDING TO DIFFERENT LEVEL OF PULMONARY INVOLVEMENT**



**RESULTS - PULMONARY INVOLVEMENT AMONG SSc AND RA PATIENTS**  
**STRATIFICATION OF PATIENTS ACCORDING TO DIFFERENT LEVEL OF PULMONARY INVOLVEMENT**

All patients affected by SSc and RA included in the analysis were stratified according to different levels of pulmonary compromise.  
 The different levels of pulmonary compromise were identified by the type and number of resource consumption (during all period of follow-up available) used as proxy of pulmonary involvement.



	Cohort 1 Patients with SSc			Cohort 2 Patients with RA			
	OVERALL* N = 755	CERTAIN N = 427	POTENTIAL N = 170	OVERALL* N = 5,431	CERTAIN N = 1,448	POTENTIAL N = 1,136	AT RISK N = 2,847
<b>Time from index date to onset of first healthcare resource in the respiratory field (months), mean (SD)</b>	9.2 (12.1)	<b>6.4 (9.2)</b>	<b>10.5 (12.3)</b>	10.9 (13.4)	<b>6.4 (10.0)</b>	<b>9.4 (11.8)</b>	<b>13.8 (14.7)</b>

\*Pts with at least one healthcare service.



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**RESULTS – BASELINE CHARACTERISTICS**  
**DEMOGRAPHIC AND CLINICAL CHARACTERISTICS**

Table show the demographic (age at index date and gender distribution) and clinical characteristics (in terms of Charlson Index) evaluated at index date.

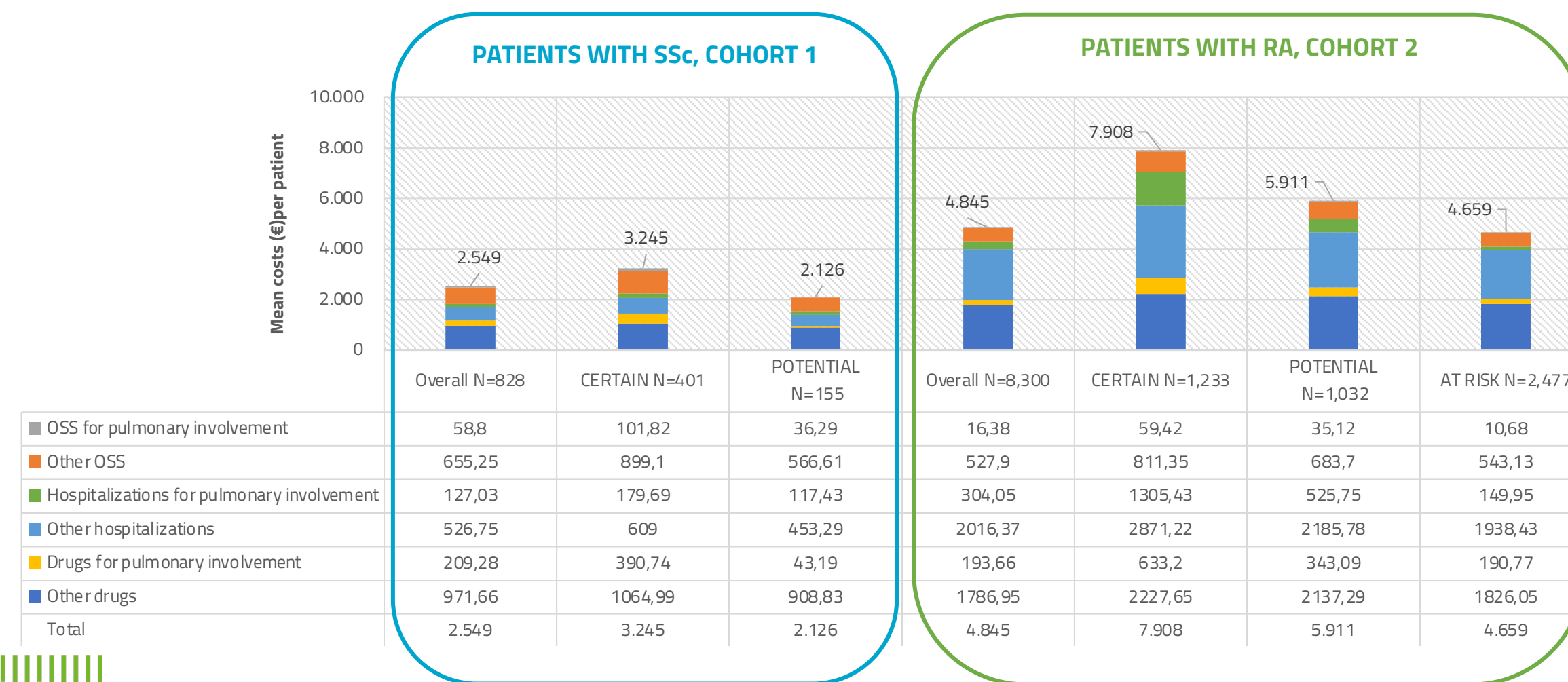
The detail related each cohort of analysis was mentioned.

	Cohort 1 Patients with SSc			Cohort 2 Patients with RA			
	OVERALL N = 914	CERTAIN N = 427	POTENTIAL N = 170	OVERALL N = 9,879	CERTAIN N = 1,448	POTENTIAL N = 1,136	AT RISK N = 2,847
<b>Age at index date, mean (SD)</b>	57.7 (14.3)	58.7 (13.7)	58.0 (12.5)	59.1 (18.8)	67.4 (13.9)	61.4 (16.5)	57.5 (19.3)
< 18 years, n (%)	6 (0.7)	<4	0 (0.0)	533 (5.4)	13 (0.9)	33 (2.9)	181 (6.4)
18-39 years, n (%)	84 (9.2)	39 (9.1)	10 (5.9)	718 (7.3)	26 (1.8)	58 (5.1)	240 (8.4)
40-59 years, n (%)	390 (42.7)	167 (39.1)	85 (50.0)	3,225 (32.6)	343 (23.7)	371 (32.7)	954 (33.5)
60-79 years, n (%)	404 (44.2)	208 (48.7)	71 (41.8)	4,253 (43.1)	784 (54.1)	548 (48.2)	1,191 (41.8)
≥80 years, n (%)	30 (3.3)	12 (2.8)	4 (2.4)	1,150 (11.6)	282 (19.5)	126 (11.1)	281 (9.9)
<b>Male (n, %)</b>	93 (10.2)	49 (11.5)	9 (5.3)	2,658 (26.9)	441 (30.5)	310 (27.3)	696 (24.4)
<b>Charlson index, mean (SD)</b>	0.3 (0.7)	0.3 (0.6)	0.4 (1.0)	0.6 (1.0)	1.0 (1.3)	0.8 (1.1)	0.5 (1.0)
Charlson index = 0, n (%)	683 (74.7)	297 (69.6)	127 (74.7)	6,344 (64.2)	609 (42.1)	592 (52.1)	1837 (64.5)
Charlson index = 1, n (%)	198 (21.7)	114 (26.7)	33 (19.4)	2,367 (24.0)	505 (34.9)	355 (31.3)	686 (24.1)
Charlson index ≥ 2, n (%)	33 (3.6)	16 (3.7)	10 (5.9)	1,168 (11.8)	334 (23.1)	189 (16.6)	324 (11.4)
<b>Follow-up (years), mean (SD)</b>	3.6 (1.5)	3.9 (1.3)	3.6 (1.5)	3.0 (1.6)	3.3 (1.6)	3.6 (1.5)	3.1 (1.6)





**RESULTS-HEALTHCARE DIRECT COSTS**  
**HEALTHCARE COSTS, DURING FIRST YEAR OF FOLLOW UP (DEATHS AND OUTLIERS EXCLUDED)**



*Note: Mean annual costs related to the healthcare resource were reported in Euros; outliers values (those 3X standard deviation over the mean value) were excluded.*

## MAIN RESULTS TAKE HOME MESSAGES

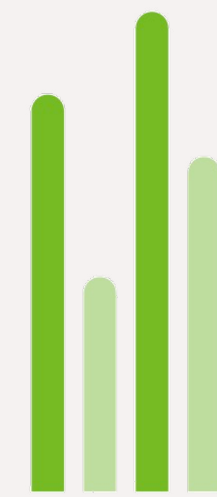
The main objective of this project was to analyze the presence of pulmonary complications through the use of specific healthcare services found within the current administrative flows. The results could be used in order to highlight **the need for monitoring in patients with pulmonary involvement with the aim of encouraging and supporting a multidisciplinary approach that includes not only the rheumatologist but also the pulmonologist** not only during the state of progression of the pathology.

The **usage of administrative databases** could allow to increase knowledge on pulmonary complications among SSc and RA patients, that could be helpful to inform health decision making.

### MAIN RESULTS:

- Among around 6 million health-assisted individuals 1,518 patients with SSc and 12,024 patients with RA were identified in the database from Jan 2017 to Dec 2022. Only patients With at least 12 months of data availability period before the index date and 6 months after and without COPD or asthma before the index date were included.
- **Considering SSc cohort:** 17.4% had no healthcare resources related to pulmonary involvement; 17.5% and 19.8% had 1 and 2 healthcare resources related to pulmonary involvement, respectively; approximately half of SSc patients (45.3%) had 3 or healthcare resources related to pulmonary involvement; **Among SSc patients, about 47% AND 18% of patients were defined as CERTAIN and POTENTIAL PULMONARY INVOLVEMENT, respectively.**
- **Considering RA cohort:** 45% had no healthcare resources related to pulmonary involvement; 29.8% and 13.2% had 1 and 2 healthcare resources related to pulmonary involvement, respectively; approximately 12% had 3 or healthcare resources related to pulmonary involvement; **Among RA patients, about 15% of patients were defined as CERTAIN, while 12% AND 29% of patients were defined as POTENTIAL and AT RISK PULMONARY INVOLVEMENT, respectively.**
- For both analysis cohorts, a shorter time between time from index date to onset of first healthcare resource in the respiratory field was observed for the cohort of patients with certain pulmonary involvement compared to the other patient cohorts. While regarding the cost analysis, again for the certain cohort, an average cost evaluated in the first 12 months of follow-up was observed to be higher than for the other patient cohorts.





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### **Delitti in materia di violazione del diritto d'autore (Art. 25-novies, D.Lgs. n. 231/2001) [articolo aggiunto dalla L. n. 99/2009]**

- Messa a disposizione del pubblico, in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta, o di parte di essa (art. 171, legge n.633/1941 comma 1 lett. a) bis)
- Reati di cui al punto precedente commessi su opere altrui non destinate alla pubblicazione qualora ne risulti offeso l'onore o la reputazione (art. 171, legge n.633/1941 comma 3)
- Abusiva duplicazione, per trarne profitto, di programmi per elaboratore; importazione, distribuzione, vendita o detenzione a scopo commerciale o imprenditoriale o concessione in locazione di programmi contenuti in supporti non contrassegnati dalla SIAE; predisposizione di mezzi per rimuovere o eludere i dispositivi di protezione di programmi per elaboratori (art. 171-bis legge n.633/1941 comma 1)
- Riproduzione, trasferimento su altro supporto, distribuzione, comunicazione, presentazione o dimostrazione in pubblico, del contenuto di una banca dati; estrazione o reimpiego della banca dati; distribuzione, vendita o concessione in locazione di banche di dati (art. 171-bis legge n.633/1941 comma 2)
- Abusiva duplicazione, riproduzione, trasmissione o diffusione in pubblico con qualsiasi procedimento, in tutto o in parte, di opere dell'ingegno destinate al circuito televisivo, cinematografico, della vendita o del noleggio di dischi, nastri o supporti analoghi o ogni altro supporto contenente fonogrammi o videogrammi di opere musicali, cinematografiche o audiovisive assimilate o sequenze di immagini in movimento; opere letterarie, drammatiche, scientifiche o didattiche, musicali o drammatico musicali, multimediali, anche se inserite in opere collettive o composite o banche dati; riproduzione, duplicazione, trasmissione o diffusione abusiva, vendita o commercio, cessione a qualsiasi titolo o importazione abusiva di oltre cinquanta copie o esemplari di opere tutelate dal diritto d'autore e da diritti connessi; immissione in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta dal diritto d'autore, o parte di essa (art. 171-ter legge n.633/1941)
- Mancata comunicazione alla SIAE dei dati di identificazione dei supporti non soggetti al contrassegno o falsa dichiarazione (art. 171-septies legge n.633/1941)
- Fraudolenta produzione, vendita, importazione, promozione, installazione, modifica, utilizzo per uso pubblico e privato di apparati o parti di apparati atti alla decodificazione di trasmissioni audiovisive ad accesso condizionato effettuate via etere, via satellite, via cavo, in forma sia analogica sia digitale (art. 171-octies legge n.633/1941).

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