

# A Nationwide Survey of Pulmonary Sarcoidosis Clinics in the United States

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## Abstract

**Rationale:** Management of sarcoidosis patients with the potential for multi-organ involvement can be complex and require the expertise of multiple specialties.

**Objectives:** Our goal was to estimate the current number of clinics dedicated to the management of patients with sarcoidosis, and to evaluate what clinic structures and definitions currently exist.

**Methods:** A link to an online survey was emailed to Division Directors of Pulmonary and Critical Care Programs at academic medical centers in the United States. The survey email included 126 of the 142 U.S. academic pulmonary and critical care programs. The National Inpatient Sample database (2010) was used to identify yearly hospitalizations for sarcoidosis patients by state, as a surrogate indicator of prevalence of sarcoidosis across the United States.

**Measurements and main results:** A total of 40 (31.8%) Pulmonary Division Directors responded to the survey. Our survey results suggest a minority of academic medical centers have dedicated sarcoidosis clinics (40%), and that the existence of a dedicated sarcoidosis clinic is associated with the number of sarcoidosis patients seen annually. Only three centers (7.5%) reported having a multidisciplinary sarcoidosis clinic in which providers from different specialties see sarcoidosis patients concurrently. Multidisciplinary sarcoidosis clinics appeared to be located where hospitalization rates for sarcoidosis are higher.

**Conclusions:** A minority of academic medical centers has a dedicated sarcoidosis clinic, and the minority of dedicated sarcoidosis clinics used a concurrent multidisciplinary model. Additional research comparing patient populations, clinic organization and processes, as well as patient outcomes is needed to determine the optimal clinic structure for sarcoidosis. We assert that the sarcoidosis community should create a standard multidisciplinary model for evaluation, diagnosis, and treatment which could lead to more reliable conclusions and progress in treatment of sarcoidosis.

**Keywords:** Pulmonary sarcoidosis; Surrogate; Idiopathic pulmonary fibrosis; Bronchiolar epithelial cells; Cystic fibrosis

## Introduction

Sarcoidosis is a granulomatous disease of unknown etiology that can affect any organ. Management of sarcoidosis patients with the potential for multi-organ involvement can be complex and require the expertise of multiple specialties. The prevalence of sarcoidosis is increasing in the United States (US) [1], but the clinic structure and processes for providing efficient and optimal care to this complex outpatient population is unknown.

Prednisone for immunomodulation is the mainstay of therapy for sarcoidosis [2]. A previous study has shown that in bronchiolar epithelial cells in the Idiopathic Pulmonary Fibrosis (IPF) and sarcoidosis patients, the expression levels of cyclooxygenase 1 (COX1) and COX2 were significantly lower than in the healthy individuals [3]. To investigate the underlying mechanisms that associated with initiation and development of this disease, recent observations indicated that histone methyltransferases G9a and polycomb repressive complex 2 (PRC2) associated H3K9me2 and H3K27me3 play a critical role in the silencing of COX-2 in IPF [4]. In addition, as inhibition of DNA methyltransferases 1 (DNMT1) was also able to markedly reduce the levels of H3K9me2, H3K27me3, as long as DNA methylation at the COX-2 promoter is present, aberrant establishment of DNA methylation might also trigger the occurrence of this disorder. This hypothesis has been confirmed by a recent study, in which it has been shown that histone methyltransferases G9a is able to directly interact with DNA methyltransferases and is essential for the maintenance of DNA methylation at specific loci [5]. Taken together, to better understand the mechanisms that associated with this disorder, studies that focus on epigenetic regulation might create a novel direction as well as identify the novel therapeutic targets.

In April 2016, Senate Resolution 443 designated April 2016 as “National Sarcoidosis Awareness Month” and pointed out some timely facts about the disease. This includes “sarcoidosis patients are often left undertreated or misdiagnosed due to the diverse presentation of sarcoidosis; the lack of knowledge of sarcoidosis among some physicians, and the diagnosis of sarcoidosis through exclusions; the average time it takes to diagnose sarcoidosis is 7 years, and many sarcoidosis patients struggle to find knowledgeable physicians and emotional support resources relating to sarcoidosis; and treatment options for sarcoidosis are limited due in part to the lack of informative research and funding specific to sarcoidosis.” This nicely outlines the challenges in sarcoidosis care and research. Research funding for sarcoidosis has been lacking in the past, although this may improve through continued efforts by investigators and through collaboration with such organizations as the Foundation for Sarcoidosis Research and the Bernie Mac Foundation.

In other multi-system diseases such as cystic fibrosis, evidenced-based clinic models have demonstrated improved disease management

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and outcomes, and this has been recognized for the past 18 years [6]. It is certainly possible that a similar clinic structure would be beneficial for patients with sarcoidosis. However, as an orphan disease, sarcoidosis lacks consistent definitions and practice patterns across institutions. Assessment of the current state of sarcoidosis clinics in the U.S. is necessary prior to development and testing of potential clinic models.

The goal of our study was to estimate the current number of pulmonary clinics dedicated to the management of patients with sarcoidosis, and to evaluate what clinic structures and definitions currently exist, and examine their geographic locations in relation to prevalence of the disease. We hypothesize that a minority of academic medical centers will have dedicated sarcoidosis clinics, and that various clinical models are in use. We are hopeful that this survey will lead to further collaboration and research resulting in the development of practice standards that will improve the outpatient care of patients with sarcoidosis.

## Methods

A link to an online survey was emailed to Division Directors of Pulmonary and Critical Care Programs at academic medical centers. The contacts were obtained from a list supplied by the American Thoracic Society that included 126 of the 142 U.S. academic pulmonary and critical care programs in the United States. Please see a copy of the survey (Table 1). Survey questions were focused on 3 areas: general characteristics, clinic organizational structure, academic and research endeavors. We also assessed the number of different subspecialists with a self-reported special interest in sarcoidosis. A dedicated sarcoidosis clinic is defined as a clinic where only sarcoidosis patients are seen. Multidisciplinary clinics are clinics that exhibit shared clinic space and close collaboration between multiple disciplines or specialties. Our statistical analysis concerned general descriptive statistics which were used to describe the prevalence and characteristics of sarcoidosis clinics. A p-value of <0.05 was considered statistically significant.

Accurate estimates for the geographic distribution of prevalence of sarcoidosis in the US are lacking. The National Inpatient Sample database (2010) was used to identify yearly hospitalizations for sarcoidosis patients by state, as a surrogate indicator of prevalence across the United States. The Nationwide Inpatient Sample is one of the databases comprising the Healthcare Cost and Utilization Project from the Agency for Health Care Research and Quality. It is the largest publicly available all-payer inpatient healthcare database in the United States and contains data on more than 7 million hospitalizations [7].

Question	Answer, n (%)		Total, n (%)
	Yes	No	
Does your division have a dedicated sarcoidosis clinic?	16 (40.0)	24 (60.0)	40 (100)
Is your division actively engaged in sarcoidosis research?	19 (47.5)	21 (52.5)	40 (100)
Are there other subspecialists at your medical center with a special interest in sarcoidosis?	22 (55.0)	18 (45.0)	40 (100)
Does your division have multidisciplinary sarcoidosis clinical conferences?	7 (17.5)	33 (82.5)	40 (100)
Features of Dedicated Sarcoidosis Clinics Do multiple providers see sarcoidosis patients concurrently?	3 (18.8)	13 (81.2)	16 (100)
Are there mid-level providers who see sarcoidosis patients?	7 (43.8)	9 (56.2)	16 (100)
Does your clinic have a dedicated nurse coordinator?	6 (37.5)	10 (62.5)	16 (100)

Table 1: Survey report.

## Results

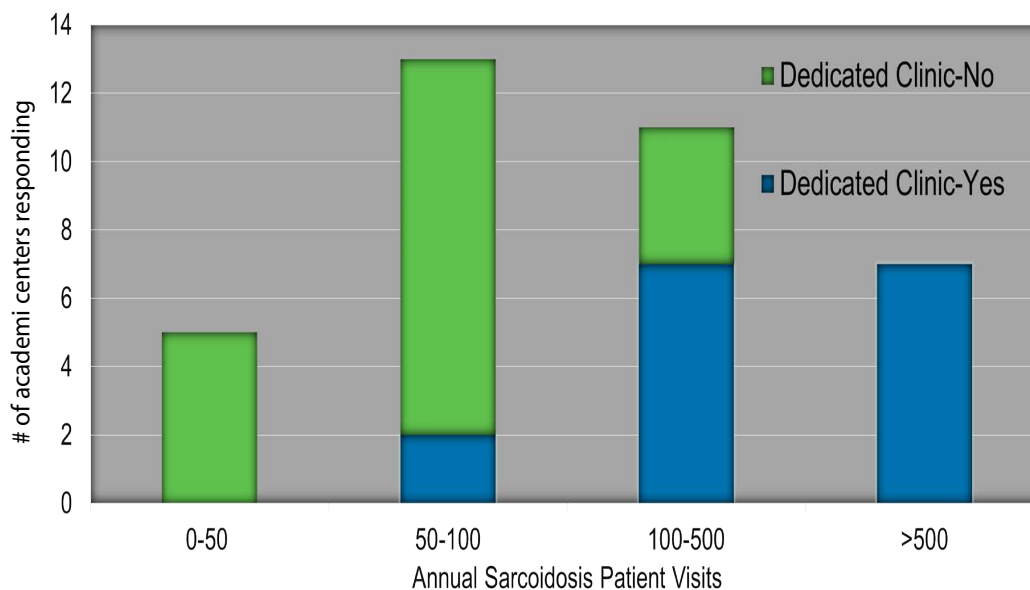
A total of 40 (31.8%) Pulmonary Division Directors responded to the survey. All centers reported that their division provided outpatient care for sarcoidosis patients. The majority of academic centers (47.5%) reported less than 100 annual sarcoidosis patient visits, with 30% reporting between 100-500 visits and 17.5% reporting greater than 500 visits (Figure 1). Centers with clinics dedicated to the treatment of sarcoidosis patients were in the minority (sixteen centers or 40%), however all centers with greater than 500 patient visits had a dedicated sarcoidosis clinic. While 54.3% of centers had non-pulmonary subspecialists interested in sarcoidosis, centers with a dedicated sarcoidosis clinic were significantly more likely to have subspecialty physicians with a special interest in sarcoidosis compared to centers without dedicated clinics (76.9% versus 40.9%, p<0.05). Rheumatologists were the most commonly reported subspecialty (11 centers), followed by cardiology, ophthalmology, neurology, and dermatology [7,8]. None of the centers without a dedicated sarcoidosis clinic reported plans to start a sarcoidosis clinic in the next year.

In regards to clinic structure for dedicated sarcoidosis clinics, only three centers (7.5%) reported having a multidisciplinary sarcoidosis clinic in which providers from different specialties see sarcoidosis patients concurrently. These were staffed by pulmonologists and rheumatologists in all three clinics, with cardiologists participating in two. Mid-level providers were involved in 43.8% of dedicated sarcoidosis clinics, and 37.5% of clinics had dedicated nurse coordinators (31.3% had both nurse coordinators and mid-level practitioners). Academic endeavors varied greatly. Active sarcoidosis research was reported by 47.4% of centers, but only 18.4% had multidisciplinary sarcoidosis clinical conferences. Centers with dedicated sarcoidosis clinics were significantly more likely to be engaged in research (87.5% versus 18.2%, p<0.05) and have multidisciplinary sarcoidosis clinical conferences (37.5% versus 4.6%, p<0.05).

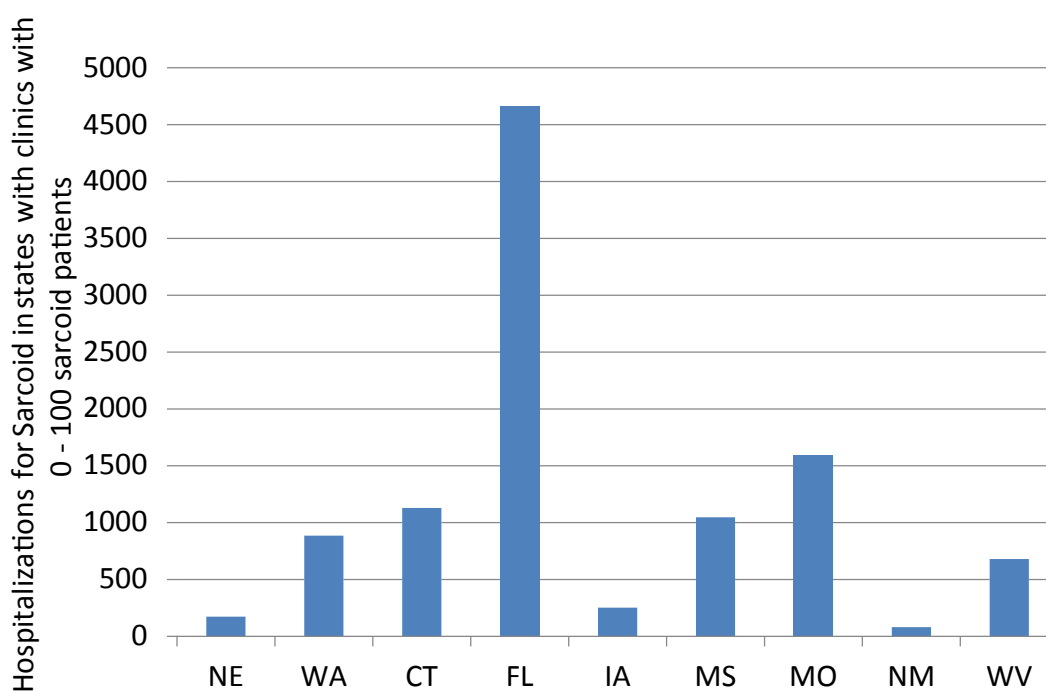
The prevalence of sarcoidosis varies based on location in the United States [8]. Geographic variation in the prevalence of sarcoidosis could impact the development of sarcoidosis clinics. We compared clinics with 0-100 reported sarcoid patient encounters per clinic reported (9 states) to clinics with >500 reported patients encounters per clinic reported (7 states), to rates of hospitalization for sarcoidosis patients per state based on the National Inpatient Sample database (Figure 2) [7]. Recall that clinics with >500 reported sarcoid patient visits were multidisciplinary clinics. Clinics with 0-100 sarcoid patients per clinic had 1,167 yearly hospitalizations for sarcoidosis per state. If you remove the one outlier (FL) from our data set, which was possibly present due to under-reporting, 730 yearly sarcoid hospitalizations per state were noted. This is compared to 3,436 yearly hospitalizations per state in the 7 states that reported clinics with >500 patients per clinic (Figure 3).

## Discussion

Our survey results suggest a minority of academic medical centers have dedicated sarcoidosis clinics, and that the existence of a dedicated sarcoidosis clinic is associated with the number of sarcoidosis patients seen annually. These larger clinics are located where the rates of hospitalization for sarcoidosis are higher in the United States. It may be reasonable to conclude that a dedicated clinic can help treat a larger number of patients in a more efficient manner. We are unable to determine from our results whether dedicated sarcoidosis clinic at centers with >500 annual sarcoidosis patients preceded or resulted from the large sarcoidosis patient population. However, the high frequency of involvement in sarcoidosis research suggests high patient volume may be a result of patients seeking these centers for their experience in sarcoidosis care and novel treatment options.



**Figure 1:** Number of Dedicated Sarcoidosis Clinics by Annual Patient Visits. Academic centers reporting between 100-500 patient visits and greater than 500 patient visits were more likely to offer a dedicated sarcoidosis clinic. However, the majority of centers reported less than 100 annual sarcoidosis patient visits.



**Figure 2:** States with clinics that saw fewer patients had less sarcoid hospitalizations (outlier FL).

As an orphan disease there is variability in sarcoidosis practice patterns between centers, and this is also evidence in the organizational structure of dedicated sarcoidosis clinics. The minority of dedicated sarcoidosis clinics used a concurrent multidisciplinary model. As sarcoidosis is a systemic disease that can affect any organ system (pulmonary, skin, and eye among the most common) [9], it is somewhat intuitive that a multispecialty clinic model could improve patient experience and outcomes. As supported by our study, rheumatology clearly plays an important role in the multidisciplinary management of sarcoidosis [10]. The most common other subspecialties

other than pulmonary that are involved in the currently existing multispecialty clinics include those associated with the more common disease manifestations (dermatology and ophthalmology) and the manifestations that can be life threatening (cardiology and neurology) [11]. These data suggest that development of a multidisciplinary model should include these specialties. We assert that the sarcoidosis clinical and scientific community needs to move forward and create a standard multidisciplinary model for evaluation, diagnosis, and treatment that could lead to more reliable conclusions and progress in sarcoidosis through collaboration and data sharing. Such models

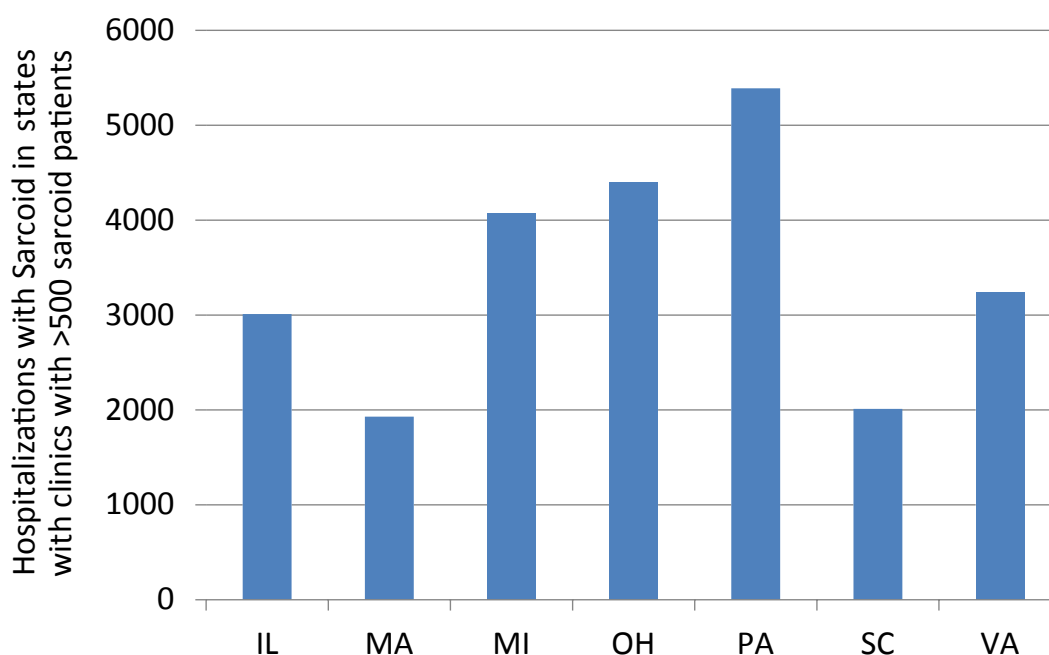


Figure 3: States with clinics that saw more patients had more sarcoid hospitalizations.

have proven to improve outcomes in other diseases, including cystic fibrosis [6].

Achieving such a goal is not without barriers. Cost and time issues are certainly concerns when developing multidisciplinary clinics. Non-physician participation in multidisciplinary clinics is another intriguing possibility. Pharmacists participating in the outpatient care of high risk patients have improved outcomes [12]. At our institution, we have discussed the addition of physical therapy, dietary and pharmacy to our multidisciplinary team. No randomized trials regarding multidisciplinary care programs exist. Legally and economically, the framework for establishing multidisciplinary care clinics is unclear, and a reimbursement formula based on individual practitioner interactions is problematic [13]. Medical liability in the multidisciplinary approach has also been questioned [14].

Sarcoidosis patients are often on one or more immune-modulating therapies which lead itself to the need for close care coordination. Multiple referrals to different specialties and disciplines are often necessary. Mid-level providers and dedicated nurse coordinators were involved in the minority of clinics [31.3% had both nurse coordinators and mid-level practioners]. Increasing participation of mid-level providers and nurse coordinators may improve clinical care for sarcoidosis patients.

The limitations of our study are those commonly associated with survey research and include nonresponse and self-selection bias. Our response rate was 31.8%, and this rate is similar to that reported in other surveys [15]. Other Divisions within the academic medical centers were not surveyed.

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