

2022 | A SUPERFICIAL SIDEROSIS PATIENT REGISTRY REPORT



# SUPERFICIAL SIDEROSIS

## THE PATIENT PERSPECTIVE

January 2023

# The Patient Perspective

## 2022 SUPERFICIAL SIDEROSIS PATIENT REGISTRY REPORT

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# INTRODUCTION

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The Superficial Siderosis Patient Registry connects our patient community from every corner of the world to a centralized data repository. Without the patient and caregiver's input, it becomes impossible to shape a research agenda to address the needs of those affected daily. Small population patient registries must prioritize the capability to collect patient data to provide real-world evidence for research planning while keeping pace with study development and multiple governments' regulatory needs.

The superficial siderosis patient community has met the challenge through their willingness to share their journey. Patient registry members contributed meaningful data in 2021 by supporting researcher requests for participation in their projects, allowing their data to help shape three research projects the Superficial Siderosis Research Alliance will sponsor, and allowing compiled statistics to be used with applications of funding opportunities. This willingness to contribute ensures that adequate participants will be available for clinical trials and observational studies.

Our knowledge and understanding of superficial siderosis are fluid and ever evolving. With three recognized subvariants of superficial siderosis, it remains crucial that clinicians are aware of the most recent data. In addition to symptom frequency, the 2022 Superficial Siderosis Patient Registry report focuses on patient member perspectives on real-world clinical care practices and overall satisfaction with their care plans.

# SUPERFICIAL SIDEROSIS SUBVARIANTS

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## BACKGROUND

### Infratentorial Superficial Siderosis, Type 1 (Classical) (iSS)

Infratentorial superficial siderosis, type 1 (classical) (iSS), or superficial siderosis of the central nervous system, is a profoundly disabling degenerative subvariant of superficial siderosis affecting the brain and spinal cord. iSS affects all races, ethnicities, and genders, with onset manifesting at any age. Persistent long-term hemorrhage into the subarachnoid space results in a neuro-toxic accumulation of free iron products on the brain and pia mater from circulating cerebrospinal fluid. This circulation distribution process may also result in hemosiderin deposition in the supratentorial region. Bergman glia and microglia cells in the cerebellar cortex function as conduits for iron entering the tissue, facilitating ferritin biosynthesis resulting in accumulation within the superficial layer of astrocytes, the gray matter of the brain, oligodendroglia, and sub-ependymal tissue.

Clinical features are related to sensorineural hearing loss, ataxia, and myelopathy with pyramidal signs. Characteristically, patients clinically manifest a diverse number of symptoms, including tinnitus, anosmia, nystagmus, diplopia, anisocoria, neurogenic bladder, constipation, urinary or fecal incontinence, decreased sensation during micturition or defecation, neuropathy, headache, hyperreflexia, cerebellar dysarthria, dysdiadochokinesia, autonomic nervous dysfunction, dysregulation of blood pressure and vessels, spasticity, myoclonus, seizure, gait/truncal ataxia, radicular pain, intracranial hypotension, cognitive impairment, mood and behavior changes, and dementia.

## INFRATENTORIAL SUPERFICIAL SIDEROSIS, TYPE 2 (SECONDARY)

Infratentorial superficial siderosis, type 2 (secondary), displays radiologically in an infratentorial region but is restricted to a single area extensively involving intracranial hemorrhage with only a thin rim of hemosiderin in adjacent areas. Iron and heme products are introduced from a major acute intracranial hemorrhagic event and are not distributed via cerebral spinal fluid circulation. Clinical features will be restricted to the affected region. For example, a patient may present with symptoms of gait/truncal ataxia or balance issues, but their hearing may never display any impairment beyond the normal aging process.

(Kharytaniuk N. et al, Practical Neurology 2022; 22:274-284)

## CORTICAL SUPERFICIAL SIDEROSIS (CSS)

Cortical superficial siderosis (cSS) radiologically presents only in the supratentorial region of the cerebrum, limited to cortical sulci favoring cerebral convexities of the cerebral hemispheres. It is most often associated with cerebral amyloid angiopathy (CAA), where rupture of amyloid-laden leptomenigeal arterioles results in subarachnoid bleeding over the cerebral convexities, resulting in subpial cortical hemosiderin. The etiology is primarily recognized as an age-related cerebral small vessel disorder.

Patients with Alzheimer's disease are nearly seven times more likely than other patients to radiologically display a serpentine pattern of cortical superficial siderosis (cSS) hemosiderin deposition across the brain's surface. (Zonneveld et al, Feb 25, 2014, Neurology)

# REGISTRY ENROLLMENT

## 2022 Enrollment

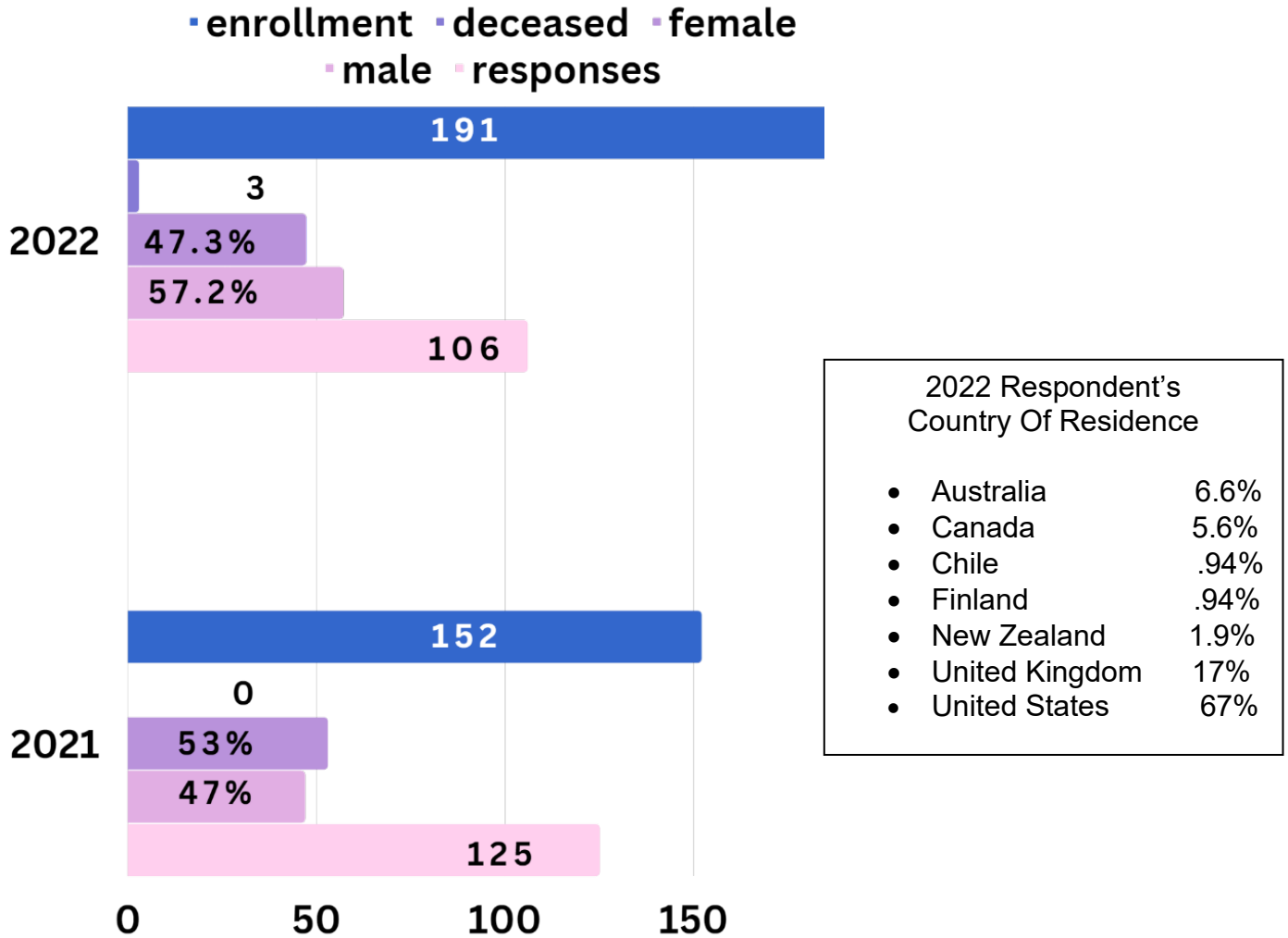


Figure 1 Enrollment and response statistics

# SYMPTOMS

## Preclinical Stage

Forty-nine registry members reported the date of the event responsible for initiating their superficial siderosis development in relation to becoming symptomatic. Four members reported their earliest symptoms presented within the same year.

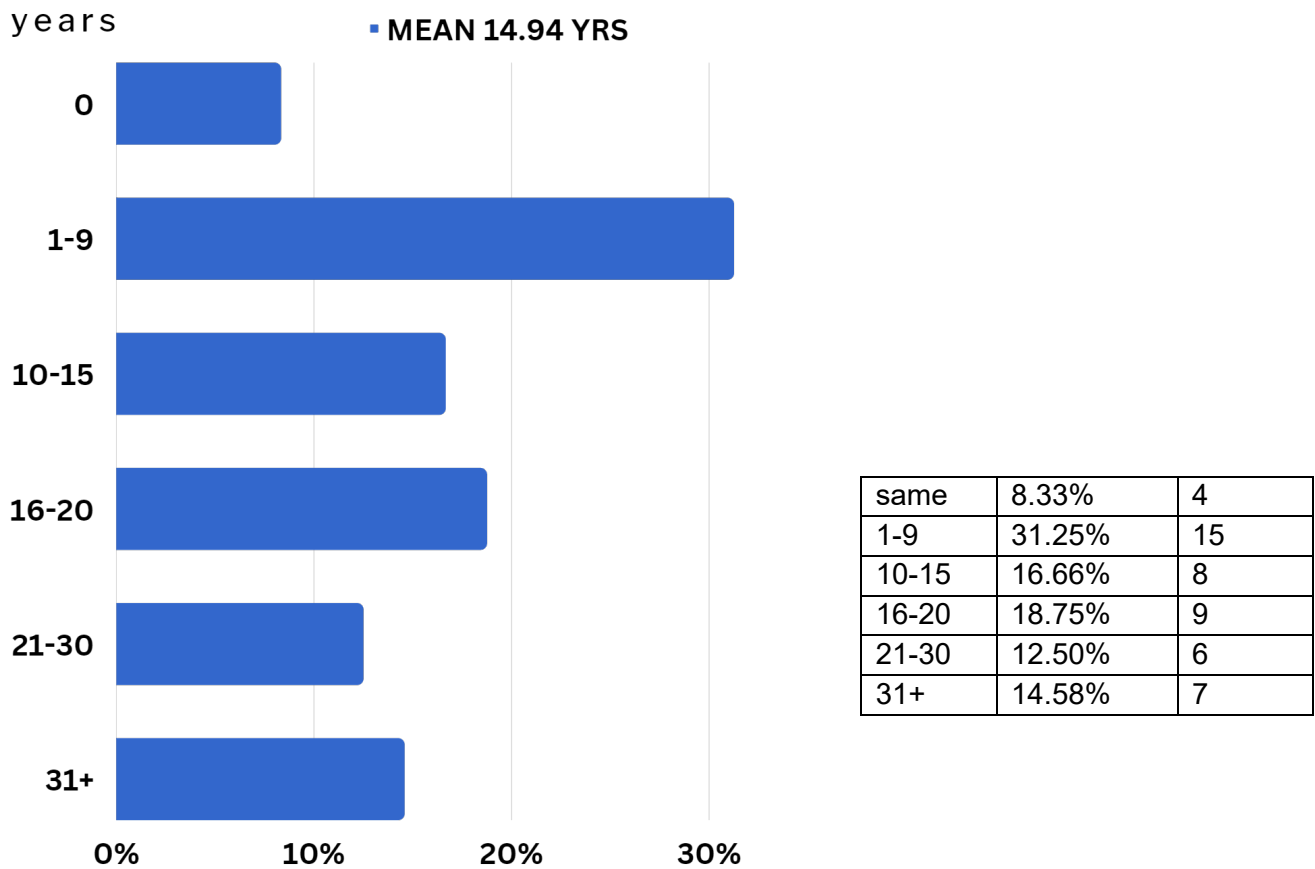
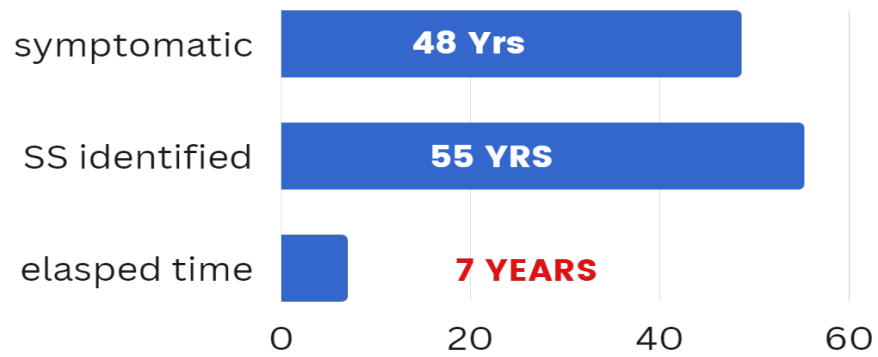


Figure 2 Preclinical Stage

## Time to Diagnosis

Average reported time for accurate identification of superficial siderosis.



*Figure 3 Time to diagnosis*



## Which symptoms do you currently experience?

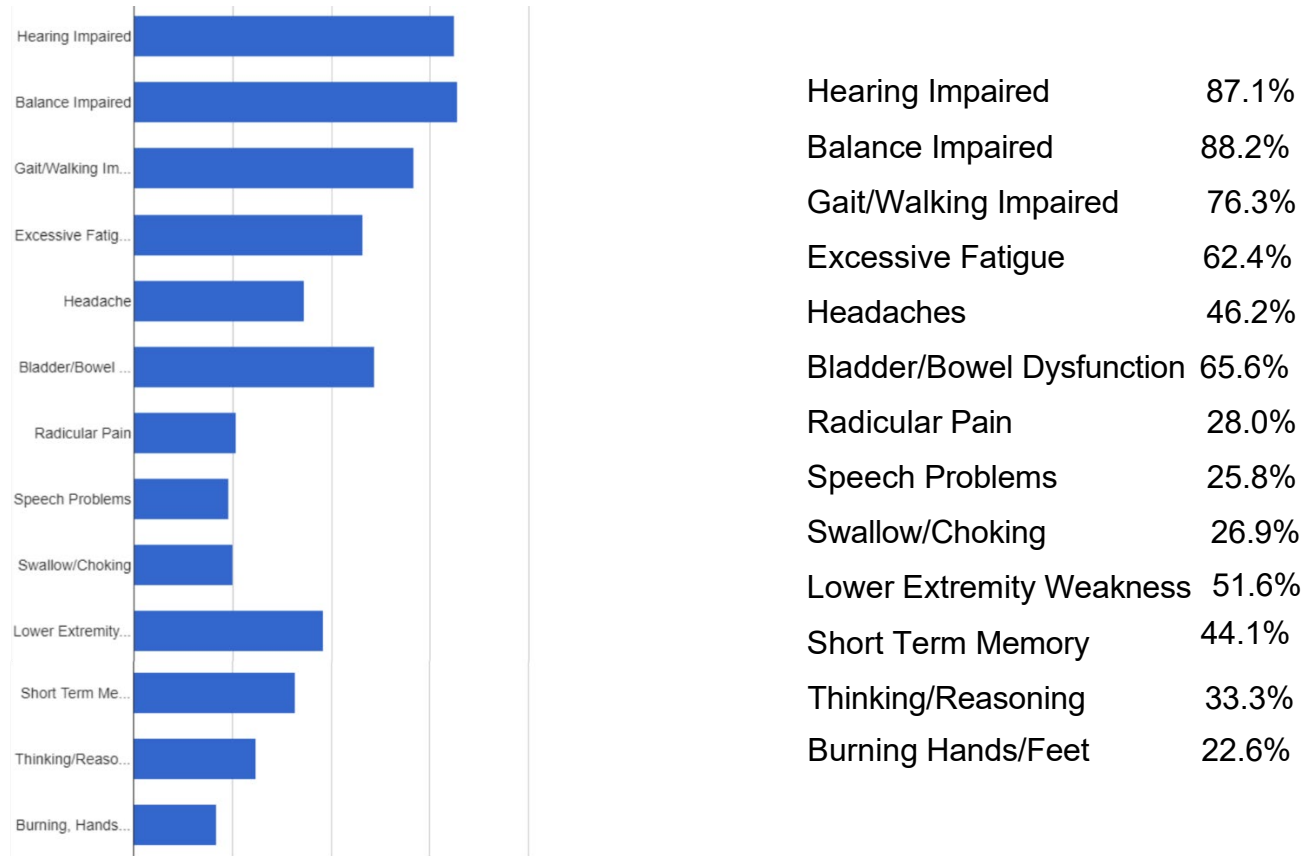


Figure 4 Reported symptoms

## How would you rate your daily level of fatigue?

Excessive fatigue is a prevalent topic among patients and caregivers in online support groups. Patients experiencing moderate symptom progression complain of constant feelings of exhaustion. In the profoundly disabling stage of progression, caregivers share narratives of patients routinely sleeping 12-18 hours daily.

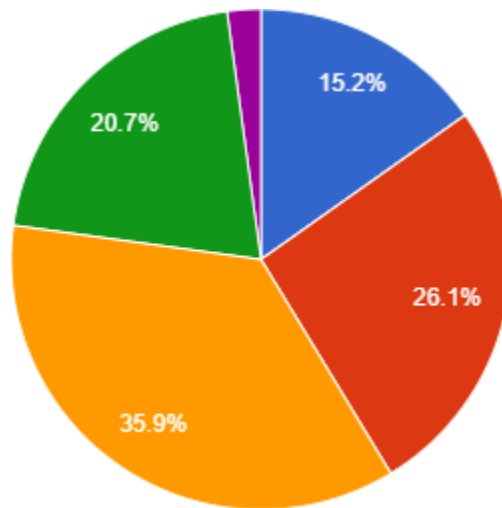


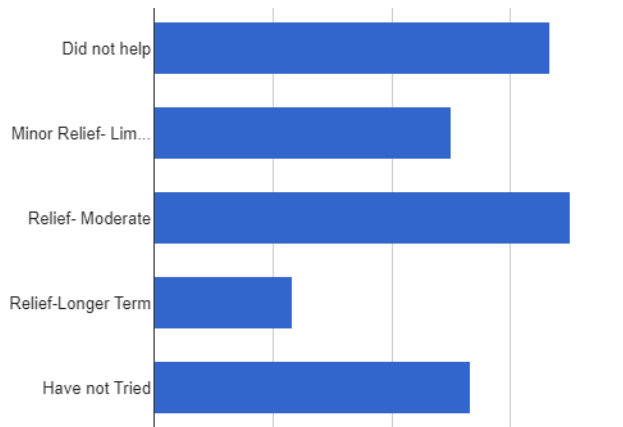
Figure 5 Quality of life – Fatigue

Fatigue does not interfere with activities of daily living	15.2%
Fatigue mildly interferes with activities of daily living	26.1%
Fatigue moderately interferes with activities of daily living	35.9%
Fatigue severely interferes with activities of daily living	20.7%
I am bed- or wheelchair-bound because of fatigue	2.2%

# PAIN RELIEF

Which pain relief methods have you tried, and how effective were they?

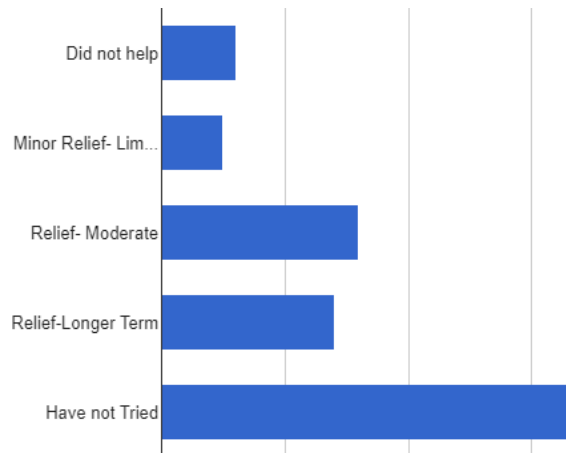
## OTC pain relievers



Did not help	25.6%
Minor Relief- Limited Time	19.2%
Relief- Moderate	26.9%
Relief-Longer Term	9.0%
Have not Tried	20.5%

Figure 6 OTC Pain Relievers

## Prescription pain medication



Did not help	7.1%
Minor Relief- Limited Time	0.0%
Relief- Moderate	5.7%
Relief-Longer Term	5.7%
Have not Tried	82.9%

Figure 7 Prescription Pain Relief

## Acupuncture

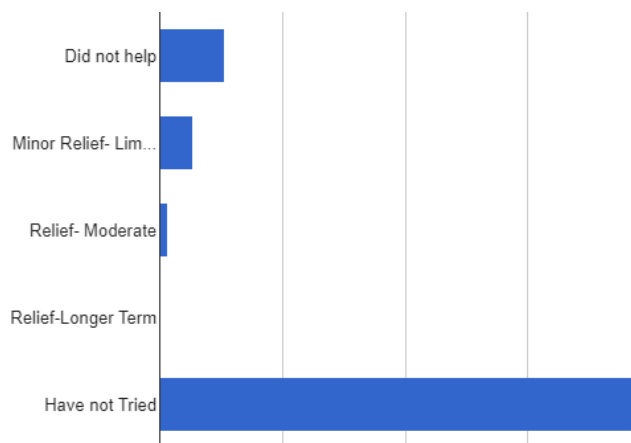


Figure 8 Acupuncture for Pain Relief

Did not help	11.4%
Minor Relief- Limited Time	5.7%
Relief- Moderate	1.4%
Relief-Longer Term	0.0%
Have not Tried	82.9%

## Meditation

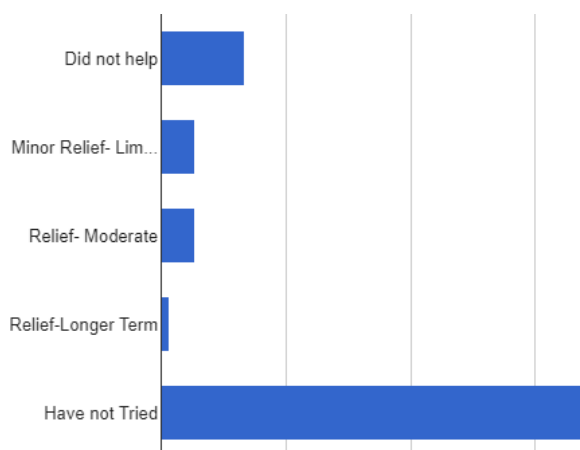


Figure 9 Meditation for Pain Relief

Did not help	14.3%
Minor Relief- Limited Time	5.7%
Relief- Moderate	5.7%
Relief-Longer Term	1.4%
Have not Tried	72.9%

## Nerve Block Injections

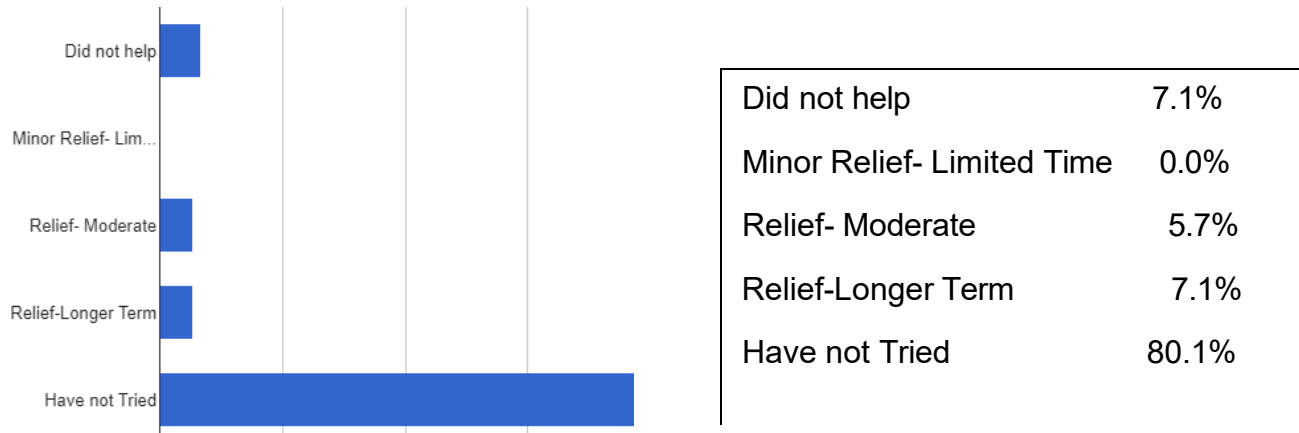


Figure 10 Nerve Blocks for Headache Pain

## MOBILITY, HEARING, MEMORY

### Which adaptive equipment do you use?

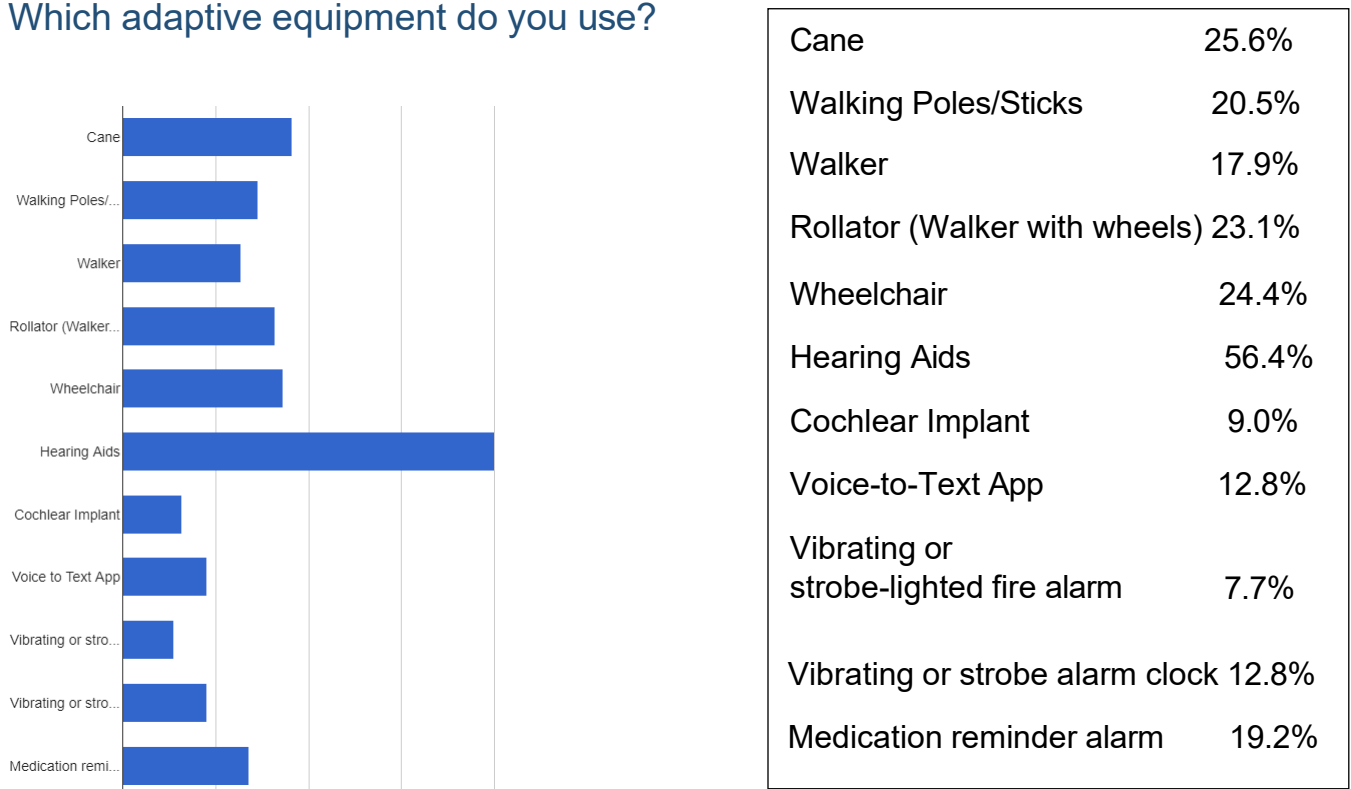


Figure 11 Assistive Aids and Devices

# QUALITY OF LIFE

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## Control

**On a scale of 0 -10, how much control do you feel you have over your life?**

0 = No control over my life → 10 = I have complete control over my life

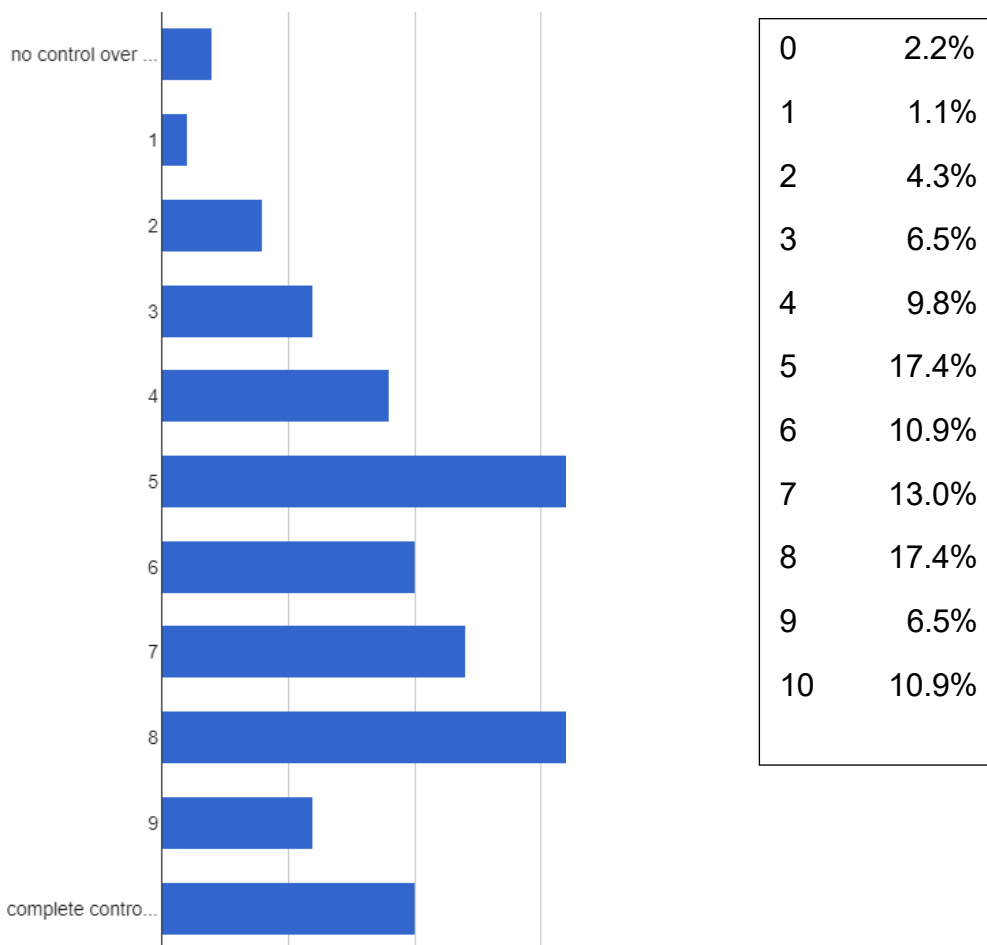


Figure 12 Quality of Life - Control

## Quality

**On a scale from 0 to 10, how would you rate or describe your life?**

0 = utterly meaningless and without purpose → 10 = very purposeful and meaningful

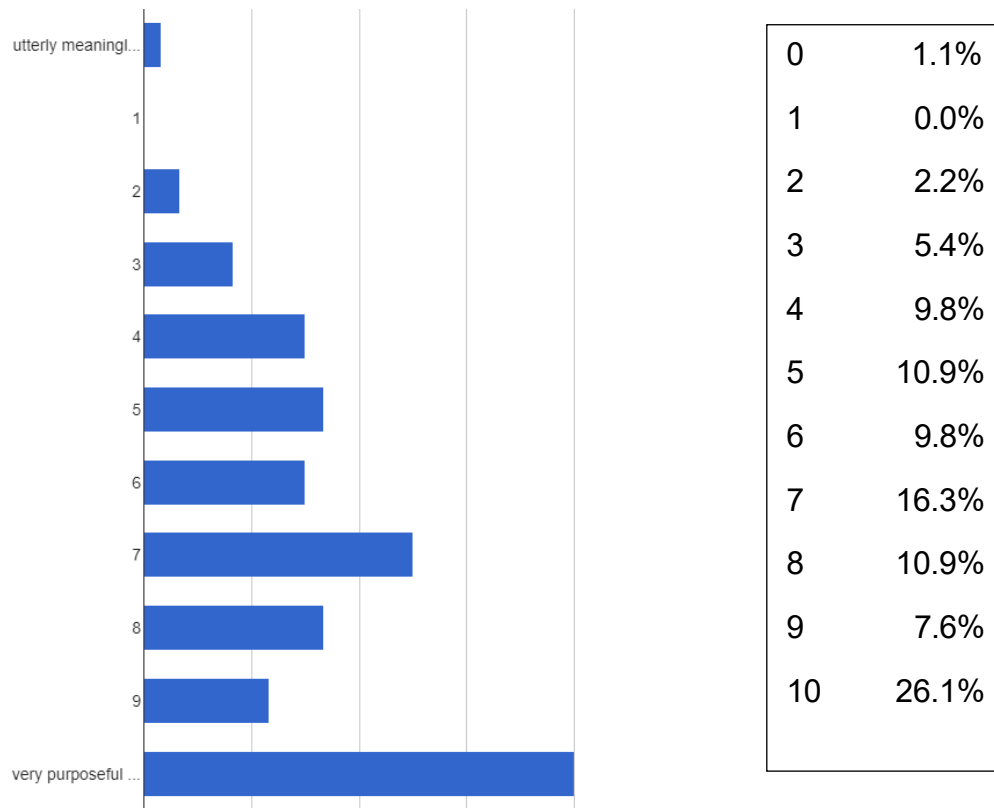


Figure 13 Quality of Life

# CLINICAL CARE SATISFACTION

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## Patient Assessment of Care for Chronic Conditions

### **PACIC - 20**

The registry asked patients to complete the ***Patient Assessment of Care for Chronic Conditions (PACIC-20)*** to understand better how our SS community views its current clinical care. One hundred three registry members participated, and 91 submitted a survey with all questions answered for an 88% response rate.

The assessment consists of 20 questions, with responses assigned a numerical score. The survey was scored by totaling participant responses across all 20 items and then dividing the result by 20, the number of items in the scale for each study completed. The mean 2022 PACIC score was 2.1 across all respondents.

Assessment Range 1= lowest and 5= highest

Response choices:

- a) None of the Time +1
- b) A Little of the Time +2
- c) Some of the Time +3
- d) Most of the time +4
- e) Always +5



<b>N=91</b>	NONE OF THE TIME (+1)	LITTLE OF THE TIME (+2)	SOME OF THE TIME (+3)	MOST OF THE TIME (+4)	ALWAYS (+5)	MEAN
<b>1. Asked for my ideas when we made a treatment plan</b>	28.6%	22.0%	15.4%	18.7%	15.4%	2.7
<b>2. Given choices about treatment to think about</b>	31.9%	19.8%	17.6%	14.3%	16.5%	2.6
<b>3. Asked to talk about any problems with my medicines or their effects</b>	31.9%	11.0%	17.6%	19.8%	19.8%	2.8
<b>4. Given a written list of things I should do to improve my health</b>	62.6%	13.2%	8.8%	8.8%	6.6%	1.8
<b>5. Satisfied that my care was well organized</b>	27.5%	18.7%	23.1%	16.5%	14.3%	2.7
<b>6. Shown how what I did to take care of myself influenced my condition</b>	52.7%	13.2%	13.2%	13.2%	7.7%	2.1
<b>7. Asked to talk about my goals in caring for my condition</b>	59.3%	15.4%	8.8%	11.0%	5.5%	1.9
<b>8. Helped to set specific goals to improve my eating or exercise</b>	57.1%	14.3%	13.2%	9.9%	5.5%	1.9
<b>9. Given a copy of my treatment plan</b>	58.2%	12.1%	4.4%	8.8%	16.5%	2.1
<b>10. Encouraged to go to a specific group or class to help me cope with my chronic condition</b>	69.2%	9.9%	9.9%	5.5%	5.5%	1.7
<b>11. Asked questions, either directly or on a survey, about my health habits</b>	41.8%	16.5%	23.1%	12.1%	6.6%	2.3
<b>12. Sure that my doctor or nurse thought about my values, beliefs, and traditions when they recommended treatments to me</b>	42.9%	8.8%	18.7%	13.2%	16.5%	2.5
<b>13. Helped to make a treatment plan that I could carry out in my daily life</b>	47.3%	12.1%	17.6%	13.2%	9.9%	2.3
<b>14. Helped to plan ahead so I could take care of my condition even in hard times</b>	60.4%	14.3%	9.9%	9.9%	5.5%	1.9
<b>15. Asked how my chronic condition affects my life</b>	32.5%	17.6%	25.3%	14.3%	7.7%	2.4
<b>16. Contacted after a visit to see how things were going</b>	45.9%	22.0%	11.0%	13.2%	4.4%	2.0
<b>17. Encouraged to attend programs in the community that could help me</b>	84.6%	6.6%	3.3%	3.3%	2.2%	1.3
<b>18. Referred to a dietitian, health educator, or counselor</b>	77.8%	7.8%	6.7%	5.6%	2.2%	1.5
<b>19. Told how my visits with other types of doctors, like an eye doctor or other specialist, helped my treatment</b>	53.8%	15.4%	13.2%	9.9%	7.7%	2.0
<b>20. Asked how my visits with other doctors were going</b>	49.5%	22.0%	9.9%	8.8%	9.9%	2.1

# PATIENT RESEARCH PARTICIPATION

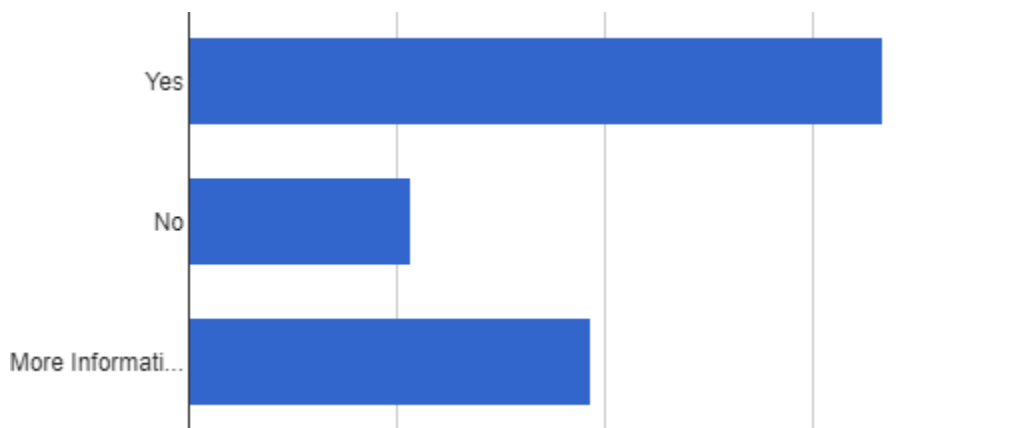
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Ninety-five registry members answered a participation interest poll covering five research project areas. Response totals demonstrate that an adequate number of participants will be available for enrollment.

Response choices were:

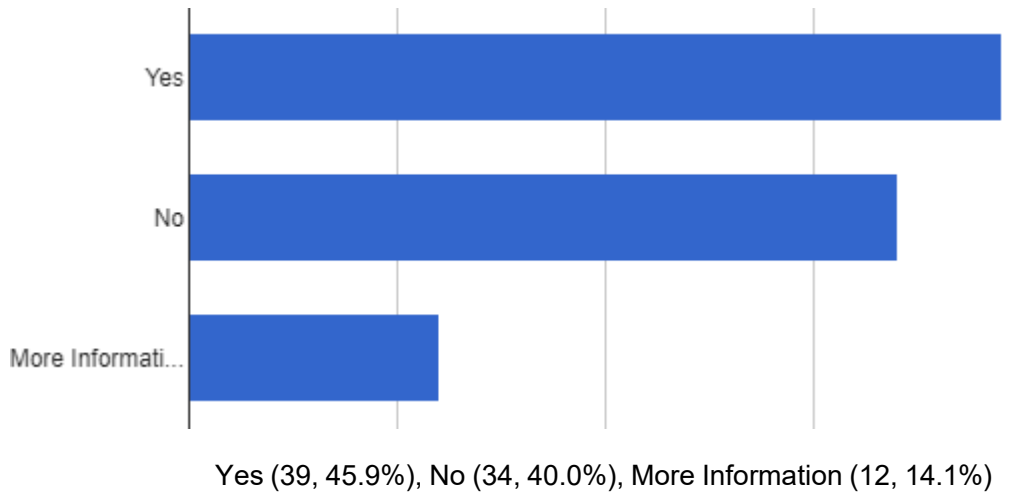
- a. Yes - Interested in participation
- b. No - Not interested in participation
- c. More Information

## Natural History Study

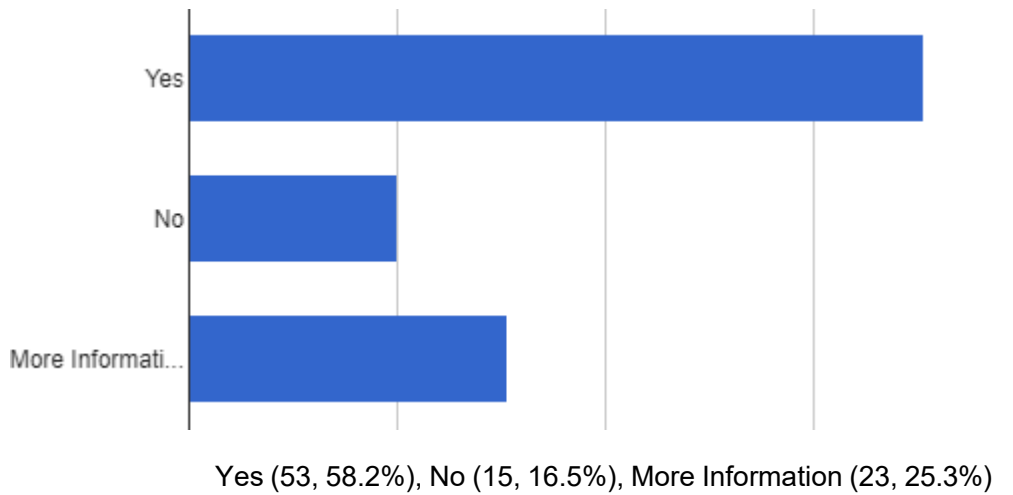


Yes (50, 52.6%), No (16, 16.8%), More Information (29, 30.5%)

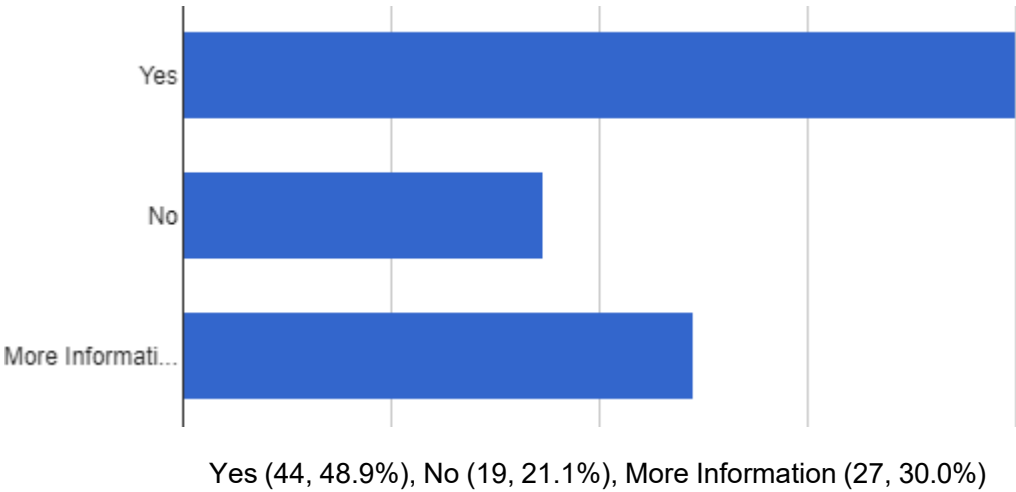
## Double Blind Placebo Controlled Deferiprone Clinical Trial



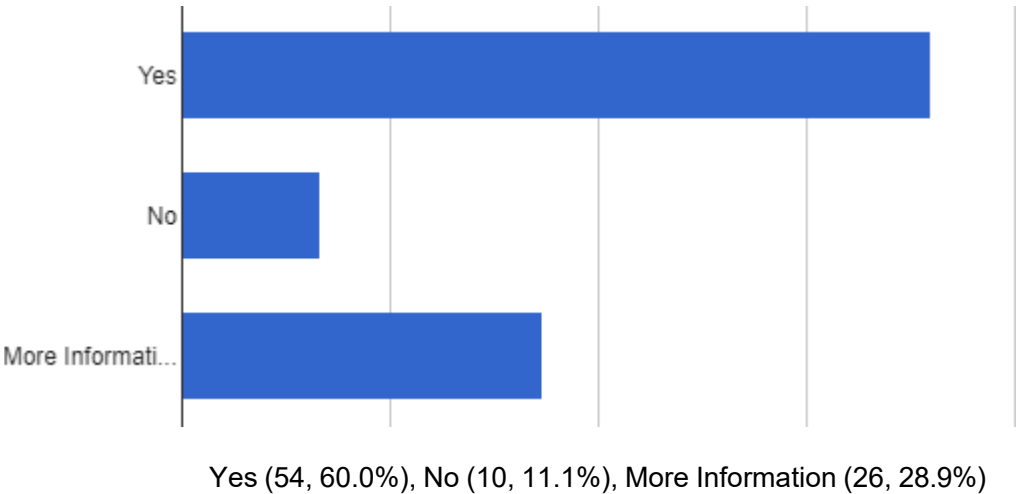
## Antioxidant Observational Community Study



## Bio Repository Specimen Donation



## Informational and Observational Studies and Papers



# CONCLUSION

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While the patient registry increased enrollment numbers in 2022, survey and poll responses were slightly under the 2021 level. Since registry members are never required to respond to a question, the response rate may vary in some areas.

The Research Participation Survey revealed that an adequate number of interested participants would be available for enrollment in all areas of research interest. The data compiled from the Patient Assessment of Care for Chronic Conditions (PACIC) survey disclosed a stark assessment of chronic care management throughout the superficial siderosis patient community. One respondent out of 91 scored their clinical care at a perfect 100. The following two highest scored their clinical care at 86 (mean 4.3) and 87 (mean 4.4), respectively. From there, it drops off a cliff.

Our primary focus for 2023 remains increasing enrollment worldwide by identifying SS patients through clinical care referrals, social media outreach, and Superficial Siderosis Research Alliance patient community advocacy. Evaluation of patterns in real-world clinical practice and self-reported patient experiences contribute to advancing the understanding of superficial siderosis, management practices, quality-of-life, and improving long-term health outcomes.

# Data Source

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The [Superficial Siderosis Patient Registry](#) provided the data used to complete this report from 106 volunteer respondents who completed three surveys and one assessment questionnaire intended for advocacy, research project design, and funding applications.

# Acknowledgments

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[Superficial Siderosis Research Alliance](#)

[Superficial Siderosis Patient Registry](#)

***Our thanks and appreciation to the superficial siderosis patient community  
for their continued contribution***

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