

Assessing Real-world Natural History of Indolent Systemic Mastocytosis: A Retrospective Matched Cohort Study from Mayo Clinic Electronic Health Records

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Evaluating the real-world disease burden and natural history of ISM compared to a propensity-matched control cohort

Background

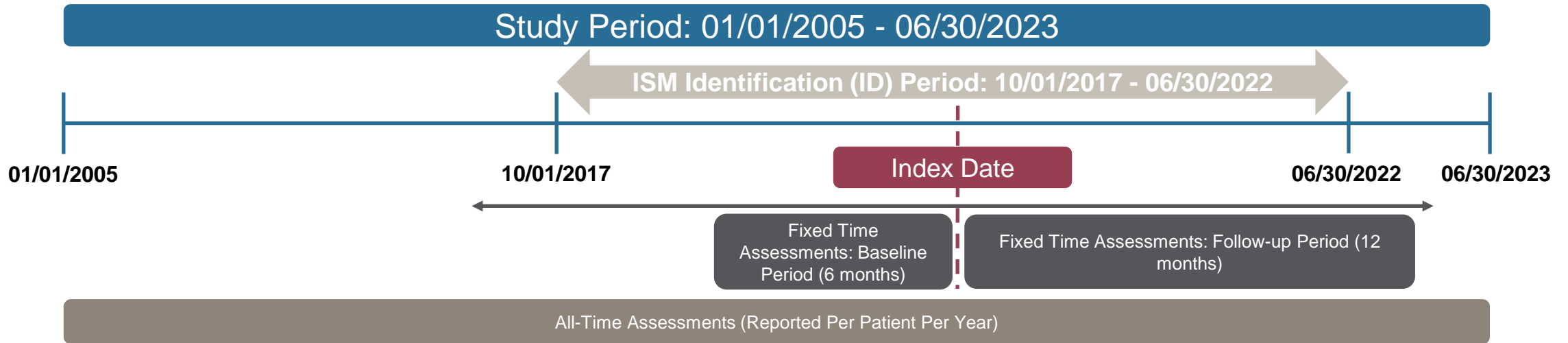
- Systemic mastocytosis (SM) is a clonal mast cell disease primarily driven by the KIT D816V mutation in ~95% of cases.¹
- ISM is the most common SM subtype, accounting for over 80% of all cases of SM.^{2,3}
- ISM patients often experience severe, unpredictable, and debilitating skin, gastrointestinal (GI), and systemic symptoms, including potentially life-threatening anaphylactic reactions.⁴⁻⁶
- Uncontrolled symptoms may worsen over time and can result in patients developing comorbid conditions.⁷⁻¹¹
- These symptoms lead to deterioration of patient quality of life, including impairment of daily activities, mood, and ability to work, and increased use of healthcare resources.⁴⁻⁶

References:

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Design: matched, retrospective, cohort study

Source	De-identified, retrospective data queried from the Mayo Clinic EMR database (all Mayo Clinic sites in the US): <ul style="list-style-type: none">Rochester, MinnesotaPhoenix/Scottsdale, ArizonaJacksonville, FloridaMayo Clinic locations in Minnesota, Iowa, and Wisconsin
Curation	Structured EMR data extraction and use of natural language processing (NLP) to review unstructured clinical notes
Assessment	Patient demographics, diagnostic workup (for ISM patients), symptoms, comorbidities, healthcare resource use, medication use
Approach	Employs a control cohort matched (10:1) on demographic and clinical characteristics



Index Date

- First observed ISM diagnosis (by ICD code or identification with NLP) serves as the Index date for the ISM cohort.
- The matched control cohort uses the first encounter that is at least 6 months after 2 prior encounters during the study period as the index date.

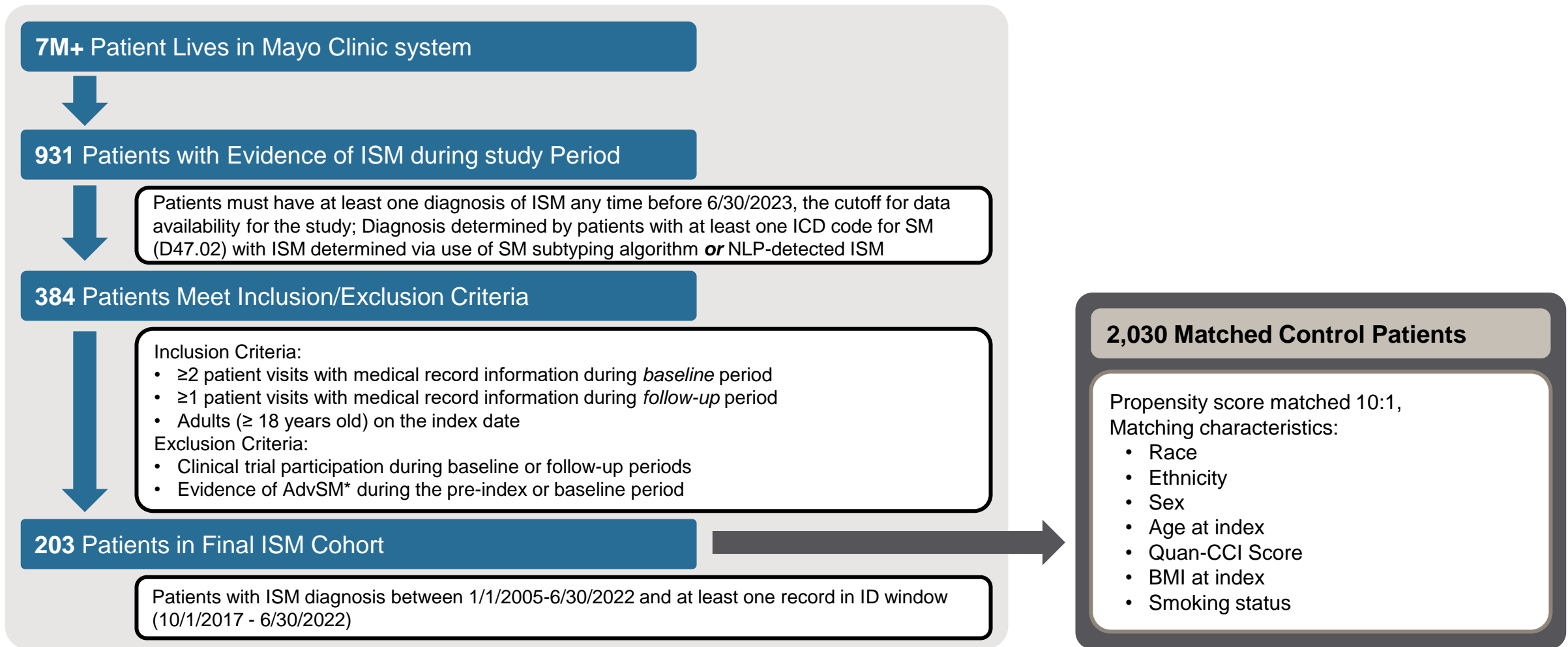
Innovative application of AI methods allows for the collection of more varied data elements than traditional analysis

SUBJECTIVE HISTORY OF PRESENT ILLNESS: [redacted] returns for followup of **indolent systemic mastocytosis**. Recall that she has about 5% involvement of the **bone marrow**. She was doing quite **well**, **exercising** regularly and carrying on with her normal activities, until an episode of **COVID** in **February**. Following about a **2-week** course of **COVID**, she developed a **generalized reaction** with rash, **palpitations**, **angioedema**, **diffuse musculoskeletal pains**, and **itching**. She developed **confluent areas of hives** on the **skin** which did not respond to **Benadryl**. She may have lost **consciousness** in addition. She did not use her **EpiPen**, however. She was seen in an emergency room setting and treated with **intravenous steroids** and was given a **2-week** course of **tapering prednisone** which ended in **March**. Since that time, she has nearly fully recovered from this **spell**. She feels that she **flushes** easier at this time. Her **skin** has cleared, however. She has had no **digestive issues**, **lymphadenopathy**, or **fevers**. She did have a **bone density** done **today**. She has had no **skeletal** complaints or **fractures**.

Clinical Encounter Note Examples	Data Label
<i>Patient returns for followup of indolent systemic mastocytosis</i>	Has disease
<i>Diagnosis of systemic mastocytosis pending tryptase levels and KIT mutation testing</i>	Maybe/unknown
<i>The KIT D816V mutation is associated with SM</i>	Other
<i>Based on the workup and normal serum tryptase and LTE4 levels I do not believe this patient has ISM</i>	Does not have disease

To Supplement Structured Data Review, Natural Language Processing (NLP) was Used for Additional Data and Context

203 eligible patients with ISM were identified and propensity score matched with 2,030 similar patients without ISM



ISM patient demographics, diagnosis, and high symptom burden

Demographics



Total participants: **203**
Mean age: **51.4 years**
Female: **66.5%**

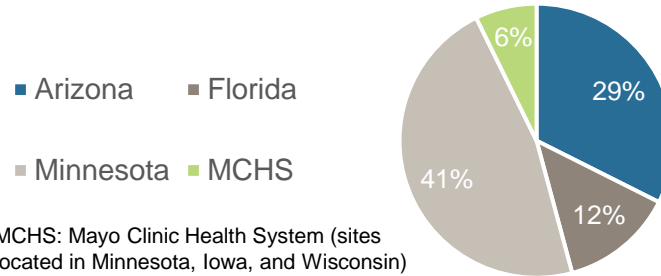
Average Length of follow-up: **4.4 years**

Race and Ethnicity

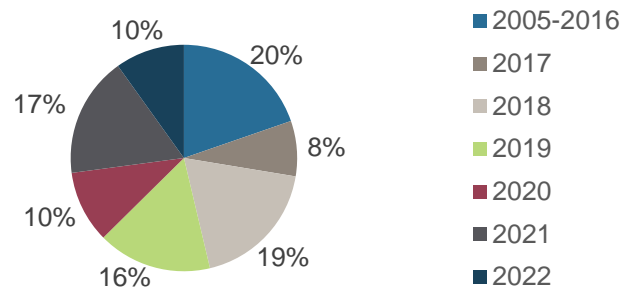
White: **93%**
Black or African American, Asian, Other/Unknown: **7%**
Hispanic or Latino: **5%**

Diagnosis

Clinic Site of ISM Diagnosis



Year of Index Diagnosis



Symptoms

Average number of distinct symptoms reported:

10.6 Baseline **13.3** Follow-up

Prevalence of most reported symptoms during 6-month baseline:

Allergic Reaction: **58%**
Lymphadenopathy: **57%**
Diarrhea: **54%**
Dyspnea: **53%**
Nausea: **53%**
Fatigue: **52%**
Dermatologic*: **66%**



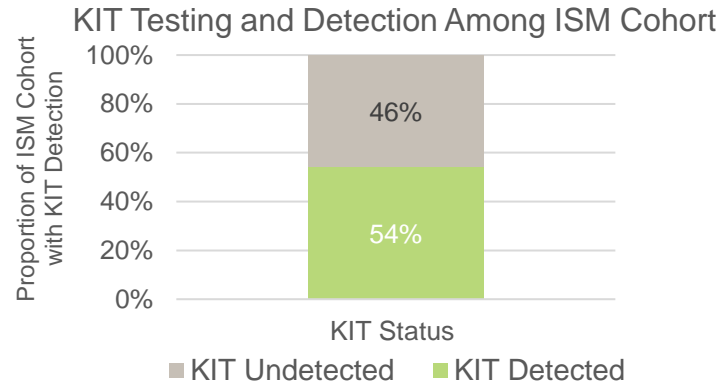
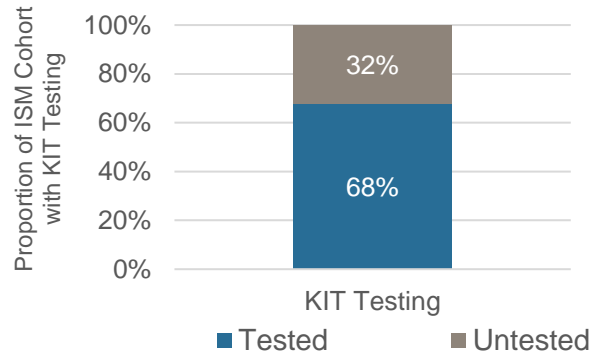
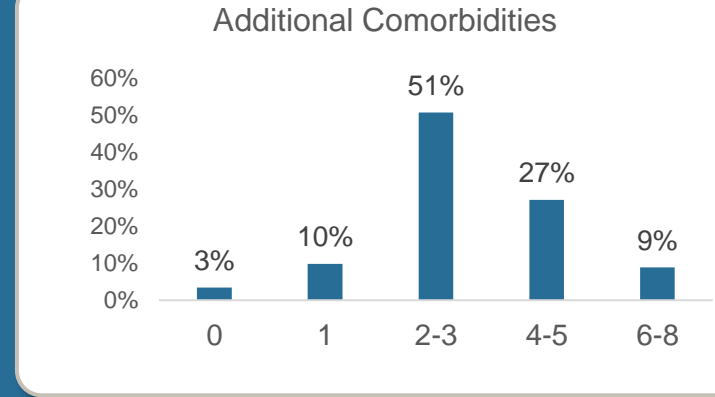
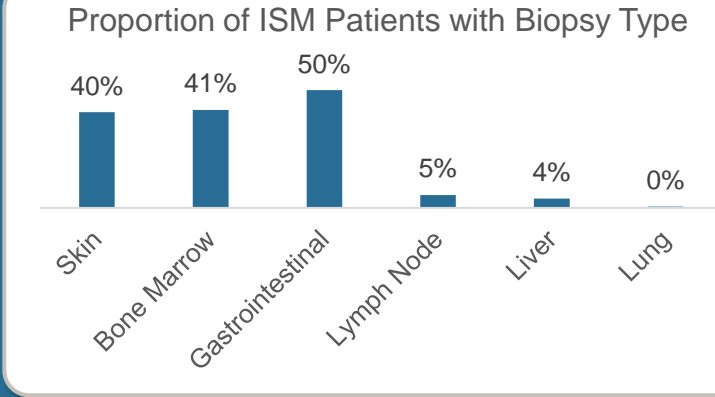
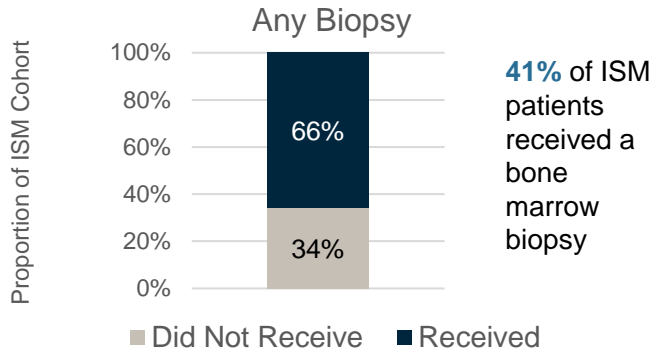
At time of diagnosis, ISM patients present with numerous, burdensome, and heterogenous symptoms that increase following diagnosis.

ISM: Indolent Systemic Mastocytosis

*Dermatologic symptoms include angioedema, flushing, cutaneous mastocytosis, pruritic, urticaria.

Real-world diagnosis of patients with ISM

SM Workup



Most testing occurred prior to the widespread availability of high-sensitivity KIT testing

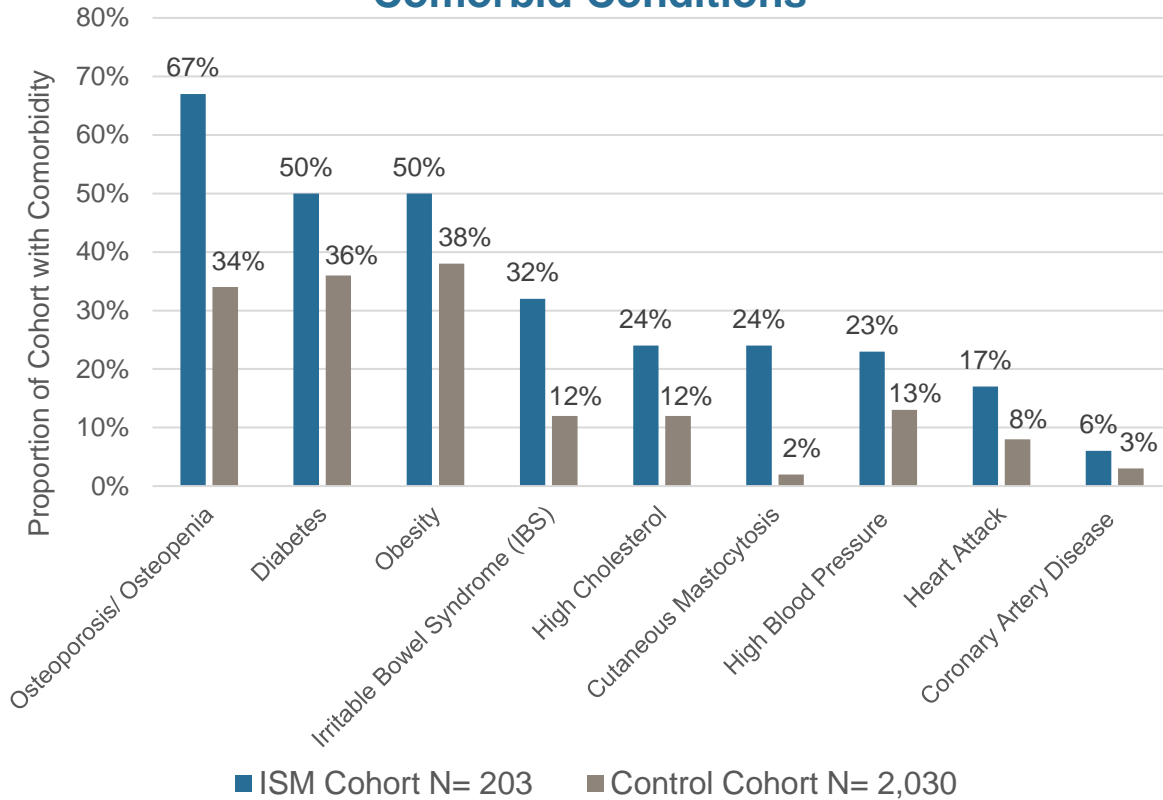


Disease awareness, education, and high sensitivity testing for KIT D816V can assist in the proper workup of ISM and is a critical tool enabling accurate diagnosis.

Note: Even with mixed methodology using structured EMR data and NLP, specific information related to testing and diagnostic workup that occurred outside of the Mayo system may not end up in clinical notes.

Significantly higher rates of comorbid conditions in ISM patients compared to matched controls

Proportion of Cohort with Specified Comorbid Conditions



Comorbid Condition	χ ² test p-value	Comorbid Condition	χ ² test p-value
Osteoporosis/ Osteopenia	<0.0001	Cutaneous Mastocytosis	<0.0001
Diabetes	0.0001	High Blood Pressure	0.0001
Obesity	0.0008	Heart Attack	<0.0001
Irritable Bowel Syndrome (IBS)	<0.0001	Coronary Artery Disease	0.0220
High Cholesterol	<0.0001		

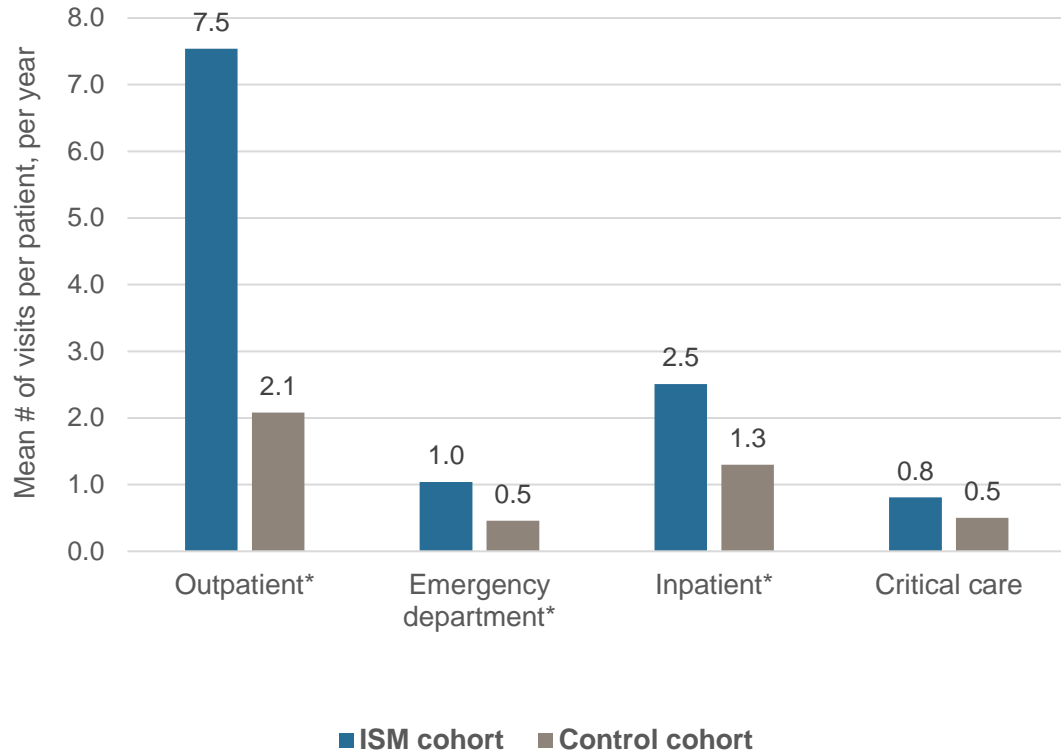
Proportion of Cohort with Specified Allergies

Allergy Type	ISM Cohort N= 203 (%)	Control Cohort N= 2,030 (%)	χ ² test p-value
Food	24%	7%	<0.0001
Environmental	9%	5%	0.0159
Drug Allergies	8%	4%	0.0078
Stinging Insect	7%	1%	<0.0001
Latex	7%	3%	0.0026
Radiocontrast	5%	1%	<0.0001
Dander/pet	3%	1%	0.0120
Venom	<1%	<1%	0.3922

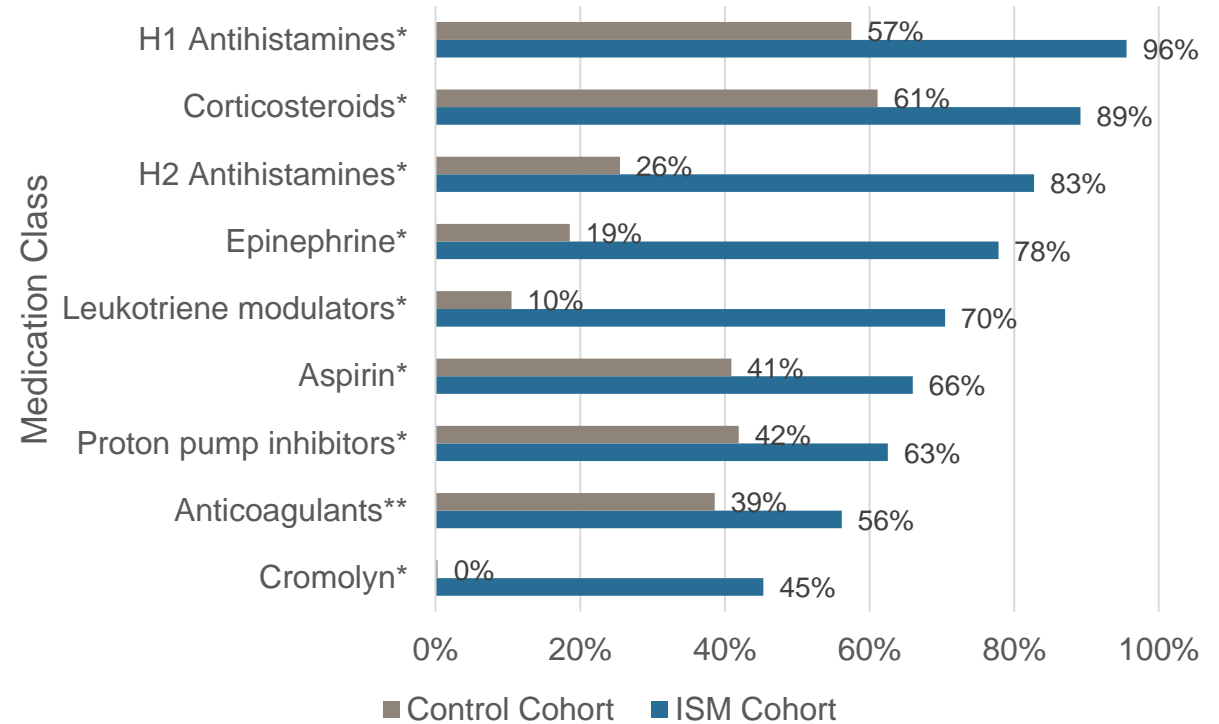
Patients with ISM are more likely to have allergies, including food (24% vs 7%) and stinging insect [hymenoptera] (7% vs 1%)

Significantly higher rates of healthcare and medication utilization in ISM patients compared to matched controls

Healthcare Resource Use



Proportion of Cohort with All-time Medication Use



Patients with ISM take **more classes of medications** compared to control patients (14.68 vs 5.79)

Note that emergency department visits are likely under reported in this data, as patients may seek emergency care outside of the Mayo Clinic system.

Statistical significance – χ^2 test: *p-value <0.001; **p-value = 0.001

Conclusions

- This study employed innovative methods combining structured data and unstructured data captured using NLP, providing deeper insight into patient symptoms and burden than traditional data alone.
- Patients with ISM present with multiple, diverse, and burdensome symptoms that increase in prevalence over time.
- This heterogeneous presentation complicates timely diagnosis that may be improved with disease education and high sensitivity testing.
- Patients with ISM were more likely to have serious comorbidities, including being twice as likely to have osteoporosis/osteopenia and key cardiovascular diseases.
- Patients with ISM had significantly higher rates of medication use and healthcare services, including inpatient stays, outpatient visits, emergency department visits, compared to the matched cohort.