

Physician and Patient Perspectives on Relevant and Burdensome Symptoms of Non-Advanced Systemic Mastocytosis

Frank Siebenhaar¹, Cem Akin², Mariana C Castells³, Jean Paty⁴, Chad Gwaltney⁴, Michelle Lim-Watson⁵, Jenna Zhang⁵, Hina Jolin⁵, Casey Judge⁵, Jennifer Nicoloro SantaBarbara⁶

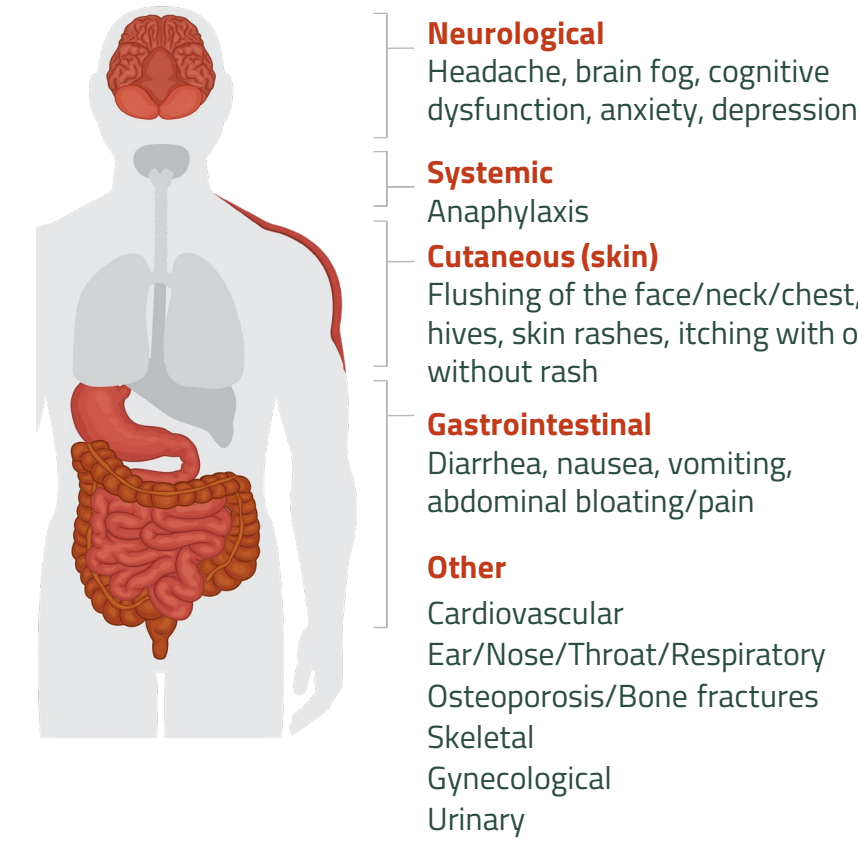
¹Institute of Allergy, Charité - Universitätsmedizin Berlin, Berlin, Germany ²University of Michigan, Ann Arbor, MI ³Mastocytosis Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA ⁴IQVIA, New York, NY ⁵Cogent Biosciences Inc., Waltham, MA

⁶Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

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INTRODUCTION

- Systemic mastocytosis (SM), which includes subtypes that range from non-advanced to advanced, is a rare, debilitating disease due to activation of and organ infiltration by mast cells¹
- Non-Advanced SM (NonAdvSM) includes three subvariants, indolent systemic mastocytosis (ISM), bone marrow mastocytosis (BMM - a former subtype of ISM) and smoldering systemic mastocytosis (SSM)²
- Patients with NonAdvSM experience a variety of debilitating, potentially serious and severe multi-organ symptoms, including some that are life-threatening like anaphylaxis^{3,4,5}
- Physicians report and patients experience multiple burdensome symptoms and impacts to health-related quality of life (HRQoL) impacts due to their NonAdvSM^{5,6}
- Patient-reported outcome measures (PROMs) utilized to assess treatment benefit in clinical trials must demonstrate "fit for purpose", and are often publicly unavailable or have measurement property limitations⁷
- The objective of this study was to identify the most relevant and bothersome symptoms as observed by healthcare providers (HCPs) and experienced by patients to support the development of a de novo disease-specific PROM



Neurological
Headache, brain fog, cognitive dysfunction, anxiety, depression

Systemic
Anaphylaxis

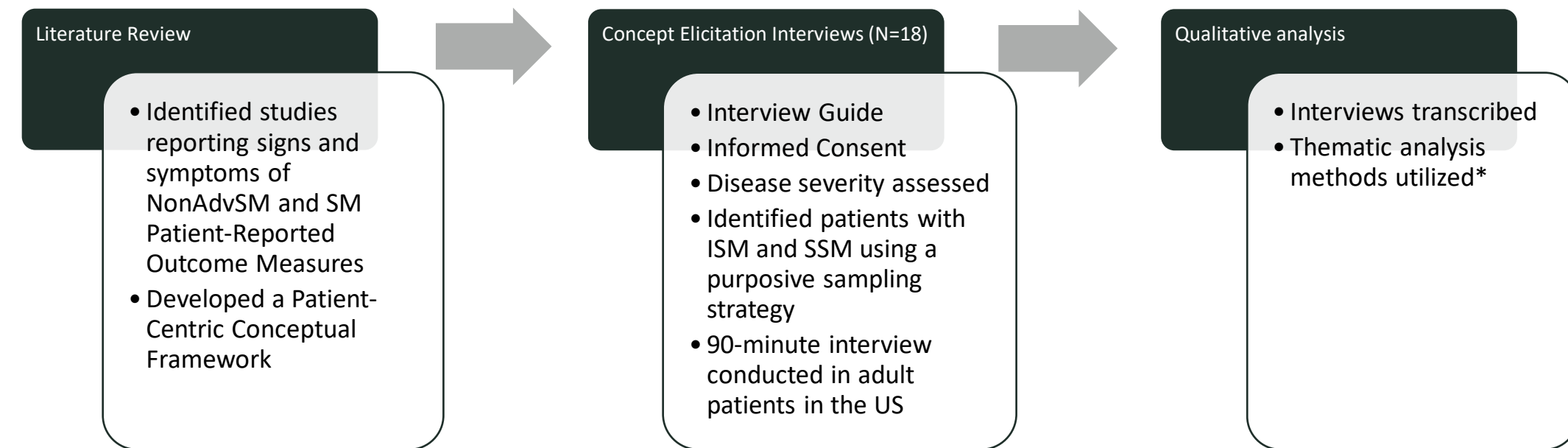
Cutaneous (skin)
Flushing of the face/neck/chest, hives, skin rashes, itching with or without rash

Gastrointestinal
Diarrhea, nausea, vomiting, abdominal bloating/pain

Other
Cardiovascular
Ear/Nose/Throat/Respiratory
Osteoporosis/Bone fractures
Skeletal
Gynecological
Urinary

METHODS

Fig. 1: Study Methodology Identifies HCP observed Symptoms and Health-Related Quality of Life (HRQoL) Impacts in Patients



*Utilized Atlas.ti9 qualitative analysis software using thematic analysis methods (Braun V, 2006)

- Participants were diagnosed with ISM or SSM prior to signing informed consent
- Four cohorts of participants with NonAdvSM (ISM/SSM) underwent semi-structured elicitation interviews (1:1) to determine the concepts of interest in this disease type between August and September 2021
- Identification of new concepts in each interview group contributed to conceptual saturation
- Healthcare providers (HCPs) must have practiced for >5 and <=30 years and treat >=2 unique NonAdvSM patients per month or >=24 per year

RESULTS

Table 1: Patient Demographics and Characteristics

18 NonAdvSM patients participated in qualitative interviews

Baseline Characteristics	Total (N=18)
Female, n (%)	18 (100)
NonAdvSM Subtype, n (%)	
ISM	15 (83)
SSM	3 (17)
Disease Severity, ISM, n (%)	
Mild	2 (11)
Moderate	11 (61)
Severe	2 (11)
Disease Severity, SSM, n (%)	
Mild	0 (0)
Moderate	1 (6)
Severe	2 (11)

Table 2: HCP Demographics and Characteristics

5 Board-Certified US Physicians

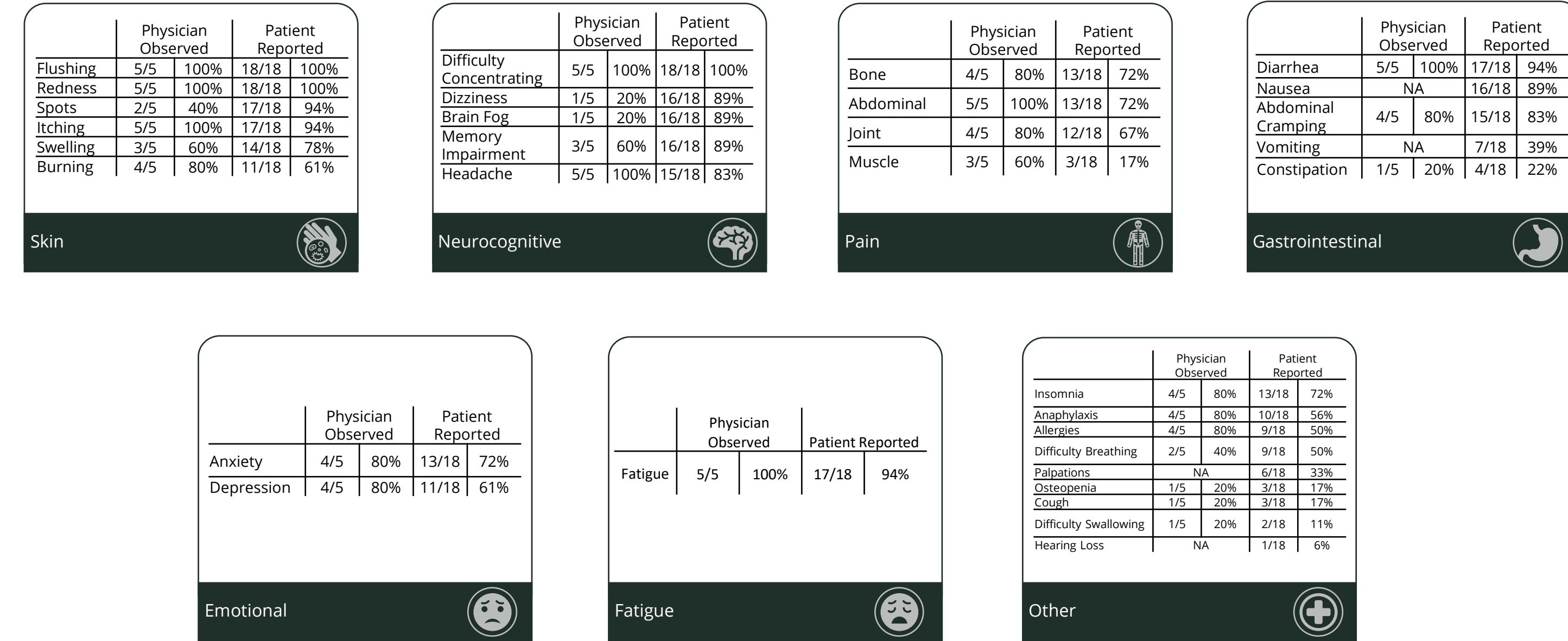
Years of clinical experience	Type of practice setting	# of NonAdvSM patients treated per year*	Specialty	Institution
12	Out-patient / office	~24-42**	Hematology / Oncology	Augusta University Medical Center
10	Academic practice within community	4	Hematology	Stanford Medical Center
30	Out-patient w/academic affiliation	~25	Hematology	University of Pennsylvania
18	Academic hospital	25	Hematology	Medical College of Georgia
20	In-patient / hospital	2	Oncology	University of Pennsylvania

*Numbers reflect those reported by clinicians during the interviews (and may not align with screening eligibility criteria)
** "For smoldering, I would say we specifically see around 3 patients or so every month... But in terms of the indolent, we would say we're seeing around 3 or 4 patients in that category as well... Most of the times these patients will be seen ideally between 4-6 months..." - C-01

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RESULTS

Fig. 2: HCP Observed and Patient Reported NonAdvSM Symptoms Identified Across Multiple Domains



- NonAdvSM patients reported a total of 32 relevant symptoms
- Reporting of domains and symptoms significantly overlapped between HCPs and patients, with both identifying 28 of the 32 identified symptoms

Fig. 3: Fatigue was reported by patients as their most bothersome symptom



Fig. 4: Impact to work (e.g., employment status), care management, mental well-being, and social interactions were most frequently reported by patients

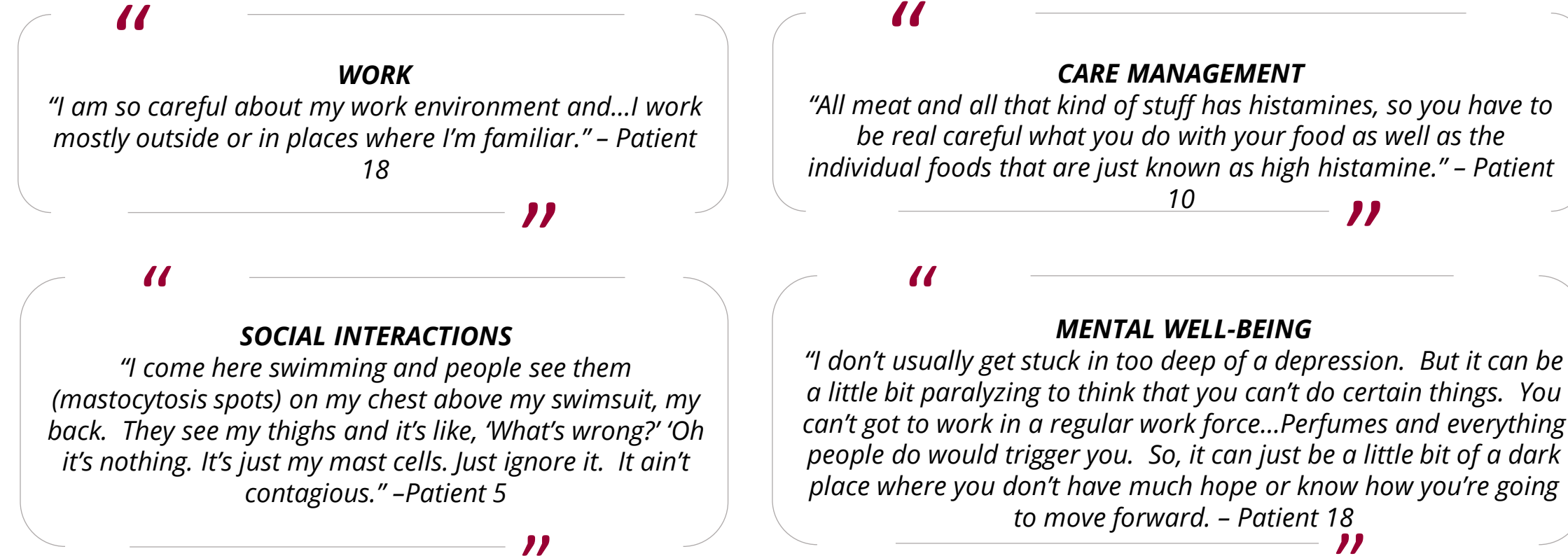


Table 3: Patient identified most bothersome symptom

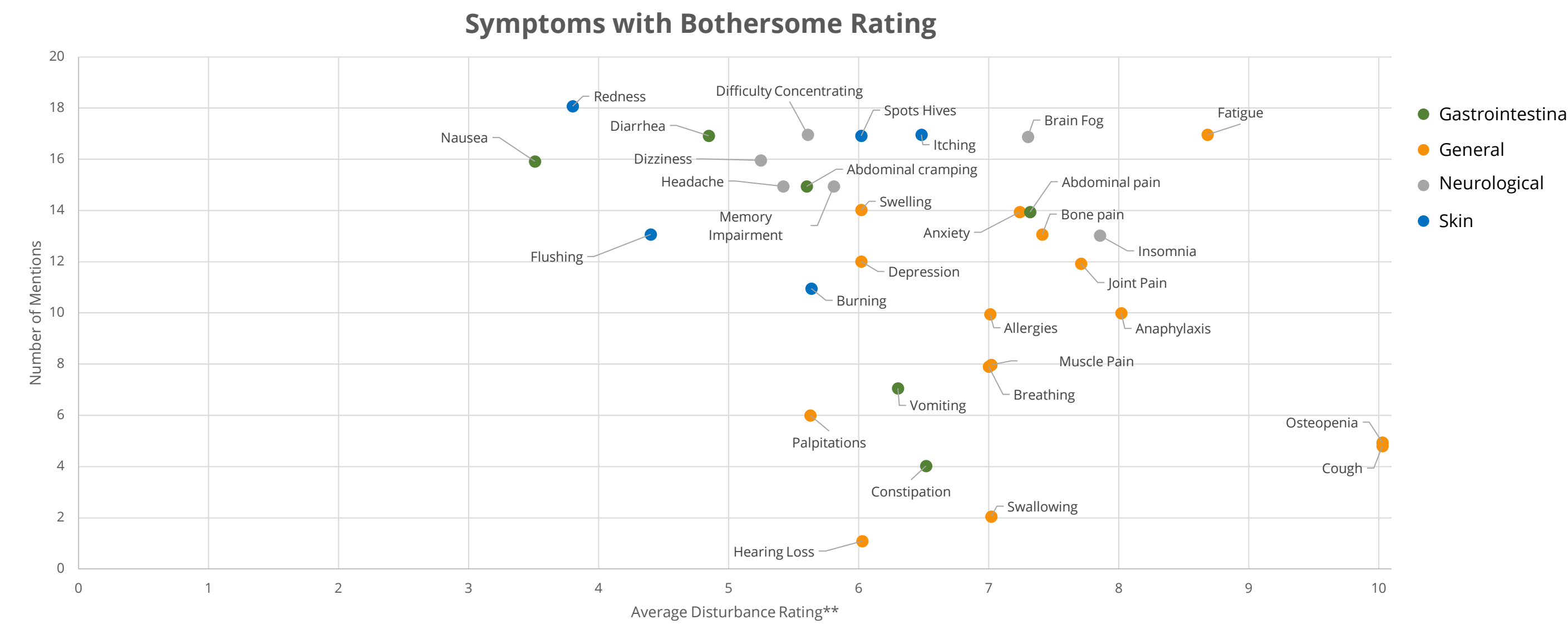
Symptom	Total Experienced	%	Average Bothersome Score*
Redness	18	100%	3.8
Flushing	18	100%	4.3
Difficulty concentrating	18	100%	5.0
Itching	17	94%	6.0
Spots	17	94%	3.2
Fatigue	17	94%	8.4
Diarrhea	17	94%	6.3
Nausea	16	89%	3.5
Dizziness	16	89%	4.3
Memory impairment	16	89%	5.6
Brain fog	16	89%	6.2
Headache pain	15	83%	7.5
Abdominal cramping	15	83%	6.2
Swelling	14	78%	6.0
Bone pain	13	72%	7.1
Insomnia	13	72%	7.0
Anxiety	13	72%	7.0
Abdominal pain	13	72%	4.4
Joint pain	12	67%	7.5
Burning	11	61%	4.2

*Bothersome score calculated from ratings provided in wave 2 and 3 patient interviews

- Redness, flushing, and difficulty concentrating were reported by all patients
- 14 (78%) participants experienced Mast Cell Reactions, and reported an average bothersome score of 7.5

- Saliency analysis was performed on symptoms and their most bothersome rating
- A concept was deemed salient if at least 50% of patients (i.e., at least 9/18 patients) mentioned the concept regardless of spontaneity
- Based on interviews of 18 patients, 16 signs and symptoms were considered salient: 'itching', 'flushing', 'skin redness', 'spots', 'nausea', 'diarrhea', 'abdominal pain', 'abdominal cramping', 'bone pain', 'joint pain', 'headache', 'concentration', 'memory impairment', 'brain fog', 'dizziness', and 'fatigue'

Fig. 5 Saliency of Patient-Reported Signs and Symptoms Based on Prevalence and Average Bothersome Rating



**Bothersome rating was based on patient responses for how bothersome their symptom was on a 0-10 scale

SUMMARY

- HCPs observe and NonAdvSM patients report substantial and debilitating symptom burden that impacts their overall HRQoL.
- Interestingly, the most bothersome symptoms (e.g., fatigue, mast cell reaction and joint pain) are not always the most frequently experienced by NonAdvSM patients.
- HCP and patient perspectives on disease severity and manifestations may differ. PROMs that accurately reflect the patient experience are necessary to optimize treatment outcomes in patients with NonAdvSM.
- Qualitative interviews provide relevant and important clinician and patient insights on NonAdvSM disease burden and HRQoL impacts. Results from these interviews coupled with a literature review, and development of a patient-centric conceptual framework can support the creation of a de novo disease-specific PROM for patients with NonAdvSM.
- This study was limited by small sample size (HCPs and participants) and all female population in the United States. As a result, there may be limitations to the conclusions drawn about symptom severity and HRQoL impact in NonAdvSM patients. Additional studies are needed to explore NonAdvSM disease manifestations across geographies, race, ethnicity, and gender.

