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## The Association of Illness-Related Uncertainty with Mental Health in Systemic Autoimmune Rheumatic Diseases

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## Abstract

**Objective:** Patients with systemic autoimmune rheumatic diseases (SARD) face illness-related uncertainty, but little is known about the psychological profiles and psychosocial and health needs associated with uncertainty among adults with SARDs.

**Methods:** Patients from Massachusetts General Hospital with ANCA-associated vasculitis (AAV), IgG4-related disease (IgG4-RD), and systemic sclerosis (SSc) completed the Mishel Uncertainty in Illness Scale, Patient Health Questionnaire depression scale, General Anxiety Disorder, Sickness Impact Profile, and a survey of psychosocial needs. The associations of uncertainty and self-reported needs with depression, anxiety, and sickness impact were assessed.

**Results:** 132 patients with AAV (41, 31%), IgG4-RD (61, 46%), or SSc (30, 23%) participated. The mean age was 65 years, 52% were female, and 83% were white. Greater illness-related uncertainty was positively correlated with higher levels of depression ( $r=0.43$ ,  $p<0.0001$ ), anxiety ( $r=0.33$ ,  $p<0.0001$ ), and sickness impact ( $r=0.28$ ,  $p<0.001$ ). We observed variations in these measures across SARDs, such that uncertainty was more strongly associated with depression and sickness impact in AAV or SSc as compared to IgG4-RD. The chief needs that patients endorsed were services for managing physical symptoms (53%), self-care (37%), and emotional concerns (24%), with greater needs strongly associated with greater illness-related uncertainty.

**Conclusion:** Among patients with SARDs, illness-related uncertainty is correlated with levels of depression, anxiety, and sickness impact, as well as psychosocial needs. Findings also implicate the need for targeted interventions to address uncertainty and needs among subgroups of patients with different illness profiles.

## Keywords

Uncertainty; mental health; autoimmune diseases

## Introduction

After diagnosis of a chronic illness, patients are confronted with uncertainty about recurrence or progression, how to manage their disease, how to interpret physiological changes in their bodies, and new roles, including when and how to engage in medical visits and tests (1–4). Illness-related uncertainty has been established as a chief concern across many of the most debilitating illnesses, such as cancer (e.g., fear of cancer recurrence), cardiovascular disease (e.g., fear of myocardial infarction recurrence), chronic pain (e.g., fear of exacerbation), HIV (e.g., fear of progression to AIDS), and multiple sclerosis (e.g., fear of worsening disease) (5–17). Patients with systemic autoimmune rheumatic

disease (SARD) may be particularly at risk for deleterious effects of uncertainty, given common complexities of care and the presence of somatic symptoms that may be transient, unpredictable, or lack a clear etiology or explanation. However, there is a paucity of research establishing the role of illness uncertainty in the mental and physical health of patients with SARDs.

Indeed, illness-related uncertainty can create an impairing cycle driven by the stress response. Theoretical models indicate that illness-related uncertainty arises and persists due to mind-body interactions between somatic symptoms (e.g., pain, fatigue, sleep disturbance), psychological factors (e.g., interpretation of somatic symptoms, optimism about future health), and behavioral responses (e.g., excessive self-examination, urgent doctor visits, avoidance behaviors like substance use) (4, 18–21). In the context of illness-related uncertainty, somatic symptoms, psychological factors, and behavioral responses can form a negative feedback loop, which, if untreated, can lead to clinically-significant mental and physical health impairment (7, 9, 12, 22, 23). In light of these risks, patients stand to benefit greatly from brief intervention targeting uncertainty and related psychological sequelae.

To guide the development of interventions that address illness-related uncertainty in patients living with SARDs, a more comprehensive understanding of uncertainty and its associations with psychologic health and well-being is needed. SARDs, including ANCA-associated vasculitis, systemic sclerosis, and IgG4-related disease, share common features (e.g., multi-organ involvement), natural histories (e.g., risk of flare, disease progression), complications (e.g., organ failure, death), and immunosuppressive treatments. There has been limited prior literature on illness-related uncertainty in other SARDs, such as rheumatoid arthritis and systemic lupus erythematosus (7, 24, 25). These studies have highlighted several themes of illness-related uncertainty, including symptoms and prognosis, medical management, self-management, and social functioning. While uncertainty can impact these themes, each of these factors can, in theory, trigger and sustain illness-related SARDs-related uncertainty. Empirical examinations of these associations are lacking (1–4).

Objectives of the present study were as follows: 1) Characterize levels of uncertainty in individuals with prototypic SARDs; 2) Explore the role of uncertainty in the mental health of individuals with rheumatic disease, explicating by illness subtype and disease activity, to identify patients who may benefit most from intervention; and 3) Query perceived unmet needs for psychosocial services among this group.

## **Patients and Methods**

### **Patient Recruitment**

In this cross-sectional study, we identified patients with ANCA-associated vasculitis (AAV), IgG4-related disease (IgG4-RD), and systemic sclerosis (SSc) at Massachusetts General Hospital (MGH). We focused on these three conditions because the MGH Rheumatology Unit has specialized care centers for these conditions and because they are among prototypic SARDs, but also have distinguishing features that may affect uncertainty and mental and physical health.

Patients with AAV seen in our Rheumatology Unit between 1/1/2020 and 11/1/2020 were identified from our electronic health record. Recruitment of IgG4-RD and SSc was done through ongoing prospective registries that include patients with these conditions managed in our Rheumatology Unit. We obtained permission from providers to contact patients.

Patients identified as eligible to participate by their provider were contacted through either electronic or US mail letter. Patients who used the MGH Patient Portal were invited to participate through an electronic letter they received through this Portal; the letter included a secure link to a Research Electronic Data Capture (REDCap) survey. Patients without access to the Patient Portal were sent a US mail letter inviting them to participate in the study; this letter also included the link to the same REDCap survey. Patients could respond to the initial contact by completing the survey, opting out of further contact, or requesting to complete the survey by phone or mail. If no response was received to the initial contact within two weeks of their initial letter, patients were contacted up to two additional times by phone. Patients who opted out of further contact were not contacted. In addition to electronic completion, patients also had the option of completing the survey over the phone with a research coordinator or on paper via a mailed survey.

### **Informed Consent**

Consent was implied by completion of the survey. This study was approved by the Mass General Brigham Institutional Review Board (Protocol # 2020P000049).

### **Survey Instrument**

Participants completed a series of surveys: (1) Demographics, comorbidities, and self-reported disease activity (see Supplemental Material); (2) Mishel Uncertainty in Illness Scale (MUIS; 22 items, anchored to SARDs, with higher scores reflecting higher SARDs-related uncertainty; (26); (3) Sickness Impact Profile (68 items, with higher scores reflecting higher negative impact of SARDs on one's behavior; (27); (4) Patient Health Questionnaire-8 (PHQ-8; (28); (5) General Anxiety Disorder-7 (GAD-7; (29); (6) Health Behavior Questionnaire (see Supplemental Material); and (7) Needs Survey (see Supplemental Material) asking about type of intervention needed, whether this need had been previously communicated to providers, and the preferred manner in which that intervention would be delivered (e.g., virtual, in-person). Some questions on the MUIS were slightly modified to make them relevant to the SARD population (see Supplemental Material). Patients had the option of skipping questions that they were uncomfortable completing and could complete the surveys anonymously. The surveys were only available in English.

### **Statistical Analysis**

Categorical variables are presented as number (percentage) and continuous variables are presented as mean  $\pm$  standard deviation or median  $\pm$  interquartile range, as appropriate. Correlations between MUIS with GAD-7, PHQ-8, and SIP were assessed using Pearson's correlation coefficient. The association of psychological measures, considered categorically based on severity group, with self-reported needs were assessed using the Cochran-Mantel-Hanszel test and reported as P-for-trend. Psychological variables (MUIS, GAD-7, PHQ-8,

and SIP) were also considered on a continuous scale and were compared using a two-sample t-test and standardized Cohen's D effect size with Hedges' correction (i.e., Hedges' G). Formal mean comparisons were not tested for three items where fewer than 10% of participants indicated unmet need (i.e., managing social concerns, managing sexual/reproductive concerns, finding resources). The level of significance for all analyses was set as a two-tailed  $p < 0.05$ , and statistical analyses were completed using SAS statistical software (version 9.4; SAS Institute, Inc.).

## Results

### Participants

Participant demographics are reported in full in Table 1 and Supplementary Table 1. Of 369 patients invited to complete study surveys, 132 patients completed the full survey, including 41 (31%) with AAV, 61 (46%) with IgG4-RD, and 30 (23%) with SSc. Of the patients who completed the survey, 122 (92%) did so online and 10 (8%) did so by paper; no respondents did so by phone. Compared with those who did not participate, those who participated were older (64 [12] vs 59 [16],  $p < 0.001$ ) and tended to be White (103 [83%] vs 180 [75%],  $p = 0.2$ ). A similar proportion of participants and non-participants were female (65 [52%] vs 122 [51%],  $p = 0.8$ ). The majority of those who participated reported being retired ( $n = 69$ , 52%). Participant demographics are reported in full in Table 1 and Supplementary Table S1.

Age and race distribution were similar across disease groups, but the proportion of female patients significantly differed by group, such that 56.1% of AAV patients, 27.9% of IgG4-RD patients, and 96.7% of SSc patients were female ( $p < 0.001$ ). Most patients were relatively well-resourced, with 43.2% ( $n = 57$ ) indicating possession of an advanced educational degree beyond college, 54.6% ( $n = 72$ ) reporting annual household income of at least \$80,000 as well as access to employer-sponsored ( $n = 54$ , 40.9%), individual ( $n = 8$ , 6.1%), or Medicare ( $n = 64$ , 48.5%) insurance. Of note, patients in this sample endorsed diverse medical comorbidities; nearly half experienced cardiovascular disease ( $n = 59$ , 44.7%), with lung disease ( $n = 43$ , 32.6%), overweight/obesity ( $n = 26$ , 19.7%), kidney disease ( $n = 17$ , 12.9%), and diabetes ( $n = 15$ , 11.4%) also commonly reported.

### Uncertainty and Mental Health in SARDs

As outlined in Table 2, reports of uncertainty were similar across illness groups but there was a trend toward those with AAV or SSc more often having higher MUIS scores (median = 55 [IQR 48, 62] and 59 [IQR 55, 66] vs 53 [IQR 48, 58],  $p = 0.002$ ). Self-reported depression was common in this cohort with 48 (36%) patients overall reporting at least mild depression (PHQ-8  $\geq 5$ ); similar rates of depression symptoms were observed across subgroups but there was again a trend towards AAV and SSc patients reporting depression symptoms more often than IgG4-RD patients ( $n = 20$ , 48.7% and  $n = 11$ , 37%, respectively, vs  $n = 17$ , 27.9%,  $p = 0.1$ ). Anxiety was also common in this cohort with 42 (41.8%) reporting at least mildly severe symptoms (GAD-7  $\geq 5$ ). Again, differences between illness group were observed such that a larger proportion of patients with AAV and SSc compared with IgG4-RD reported at least mild anxiety ( $n = 21$ , 51.2% and  $n = 8$ , 26.7%, respectively, vs  $n = 13$ , 21.3%,  $p = 0.005$ ).

Uncertainty, depression, anxiety, and illness impact varied according to self-reported disease activity. For patients with AAV and IgG4-RD, uncertainty, depression, anxiety, and illness impact were generally lower for individuals whose illness was in self-reported remission, compared to those with illness not in remission or those unaware of their disease status. Patients with SSc experienced similar uncertainty regardless of disease activity, although illness impact was generally higher among SSc patients who were unaware of their status (see Supplemental Tables S2a–S2c).

We also found that uncertainty varied according to gender (see Supplemental Tables S3a–S3e). Female patients had higher uncertainty than male patients (median 58 [IQR 52, 63] vs 52.0 [IQR 46, 58],  $p=0.002$ ). When stratifying our analysis according to gender, our findings remained consistent though the statistical significance of some differences across disease groups were attenuated, likely related in part to the reduced sample size in some analyses.

### The Association of Uncertainty with Mental Health

As outlined in Table 3, we observed moderately strong associations between patient-reported illness uncertainty and depression ( $r=0.43$ ,  $p<0.001$ ), anxiety ( $r=0.33$ ,  $p<0.001$ ), and sickness impact ( $r=0.28$ ,  $p=0.001$ ). However, associations between patient-reported illness uncertainty and mental health varied across illness groups. Whereas moderately large associations of uncertainty with depression (AAV:  $r=0.56$ ,  $p<0.001$ ; SSc:  $r=0.60$ ,  $p<0.001$ ) and sickness impact (AAV:  $r=0.57$ ,  $p<0.001$ ; SSc:  $r=0.59$ ,  $P<0.001$ ) were observed in AAV and SSc patients, little association of uncertainty with depression ( $r=0.17$ ,  $p=0.20$ ) and sickness impact ( $r=0.01$ ,  $p=0.93$ ) was observed in IgG4-RD patients. Associations between uncertainty and anxiety also varied by group, with a moderately large association reported by patients with AAV ( $r=0.45$ ,  $p=0.003$ ) and smaller effect sizes for those with IgG4-RD ( $r=0.22$ ,  $p=0.09$ ) and SSc ( $r=0.25$ ,  $p=0.20$ ).

### Self-Reported Needs by Patients with SARDs

Finally, patients indicated considerable interest in additional support to promote psychosocial health and well-being (Table 4), particularly with reference to management of physical symptoms ( $n = 70$ , 53.0%), learning strategies to increase self-care ( $n = 49$ , 37.1%), and coping with emotional concerns ( $n = 32$ , 24.2%). There was also interest among some patients in obtaining support to manage social concerns ( $n=10$ , 7.6%), managing sexual and reproductive concerns ( $n=4$ , 3%), and finding resources to help with daily concerns ( $n=11$ , 8%). Trends in interest in additional support were similar across illness subgroups (Supplementary Table S4).

Mean comparisons for interest in management of physical symptoms, learning self-care strategies, and coping with emotional concerns revealed significant group differences in illness-related uncertainty, depression, and anxiety (Table 5). For instance, uncertainty and depression had moderately strong associations with perceived need for support for physical symptoms ( $t(126.29) = -2.93$ ,  $p = .004$ ,  $D = -0.50$ ;  $t(103.49) = -2.76$ ,  $p = .007$ ,  $D = -0.47$ , respectively). Similarly, higher levels of uncertainty, depression, and anxiety were moderately strongly associated with being more likely to be interested in learning strategies to increase self-care ( $t(130) = -2.37$ ,  $p = .02$ ,  $D = -0.43$ ;  $t(74.52) = -2.10$ ,  $p = .04$ ,  $D =$

= -0.42;  $t(76.54) = -2.16$ ,  $p = .03$ ,  $D = 0.42$ , respectively). Perceived need for support with emotional concerns had moderate-to-large associations with all psychological domains assessed, including uncertainty ( $t(130) = -2.96$ ,  $p = .004$ ,  $D = -0.60$ ), sickness impact ( $t(130) = -1.99$ ,  $p = .049$ ,  $D = -0.40$ ), depression ( $t(128) = -2.17$ ,  $p = .03$ ,  $D = -0.45$ ), and anxiety ( $t(41.21) = -3.35$ ,  $p = .002$ ,  $D = -0.81$ ).

Importantly, the need for these resources were often not communicated from the patient to the provider (Supplemental Table S5). For instance, whereas a majority of interested patients voiced their need for support managing physical symptoms to their providers ( $n = 50$ , 71.4%), a minority articulated desire for support around self-care ( $n = 17$ , 34.7%) or emotional concerns ( $n = 10$ , 31.3%). With regard to future interventions, patients endorsed interest in receiving additional information about these areas of interest and receiving this information virtually.

## Discussion

We found that illness-related uncertainty is common in patients with ANCA-associated vasculitis, IgG4-related disease, and systemic sclerosis, and that patients with greater uncertainty tended to have worse mental health outcomes, including greater depression, anxiety, and the perceived impact of being sick on their daily functioning. While most patients expressed a desire for access to psychosocial services -- including learning strategies for managing their physical health, promoting self-care, and coping with emotional distress -- patients with greater uncertainty were more likely to have these unmet needs. Overall, findings support theoretical conceptualizations of uncertainty in illness and highlight several clinical and research opportunities to improve patient outcomes.

Interventions that address illness-related uncertainty among SARDs patients are important for improving mental health outcomes, an important unmet need in this patient population. Indeed, mental health outcomes have not been found to meaningfully improve as much as clinical measures of disease activity in trials evaluating the efficacy of disease-modifying anti-rheumatic drugs (30). Few studies have evaluated the role of interventions for improving mental health and well-being in patients with SARDs and most have focused on cognitive behavioral therapy in rheumatoid arthritis (31, 32). A recent randomized trial in patients with SSc found that compared to a waitlist control, a 12-session, videoconference-based group intervention providing education about coping strategies (i.e., fostering social connection, relaxation training, managing worry, and physical activity) improved depression and anxiety symptoms by a six-week follow-up (33). Importantly, we observed strong interest among SARDs patients in interventions to address mental health needs, especially those with greater illness-related uncertainty, depression, and anxiety. Distinct patterns of associations of illness-related uncertainty with mental health emerged according to disease subtype, suggesting that interventions may need to be adapted to the needs of patients with different conditions.

Prior studies of mental health in SARDs have focused on measuring the reduced quality of life in patients with these conditions as well as the burden of depression and anxiety (34–40). Few studies have evaluated rheumatological uncertainty and ours is the first to

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explore this in AAV, IgG4-RD, and SSc. A previous qualitative study in SSc patients found that the need for navigating uncertainty (e.g., diagnostic ambiguity, unpredictable illness course) was an important concern raised by patients (24). Additionally, a different uncertainty instrument has been previously developed for rheumatoid arthritis and systemic lupus erythematosus (25). As part of the development and validation of that instrument, associations were observed between uncertainty and anxiety and depression. We expand upon these findings using a previously validated measure of illness-related uncertainty in patients with different SARDs and assessing the association of this measure of uncertainty with mental health outcomes and psychosocial needs. We chose to use an instrument to measure uncertainty (MUIS) that has been more widely used across diverse illnesses to measure illness-related uncertainty.

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The significant associations between uncertainty and distressing emotions found in this study are consistent with Uncertainty in Illness Theory (4), which posits that uncertainty about health-related events and symptoms can trigger a stress response that includes anxiety, depression, and perceived illness burden. Although we were unable to test the directionality of these associations, our findings are consistent with evidence-based treatment models for managing uncertainty and fear in chronic illness that offer coping skills for tolerating uncertainty and stress in order to reduce anxiety, depression, and negative impacts of illness (41–44).

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The varying strength of associations between illness-related uncertainty and mental health outcomes was unexpected and warrants greater consideration in qualitative research. These observations may be related to differences in the patient populations (e.g., sex distribution) or the underlying disease (e.g., spectrum or severity of organ involvement). For instance, associations of illness-related uncertainty with depression, anxiety, and sickness impact in AAV were consistently stronger than those observed in IgG4-RD. In contrast to IgG4-RD, AAV is often more acute in its presentation and is commonly associated with organ- and life-threatening manifestations, including glomerulonephritis and diffuse alveolar hemorrhage. IgG4-RD often has a more indolent presentation and typically presents with fibro-inflammatory lesions in the salivary glands, lacrimal glands, hepatobiliary tract, and other areas where it may compromise organ function, cause symptoms and distress, and contribute to reduce quality of life, but does not typically lead to major organ failure or death, as seen in AAV or SSc. Disease duration was not collected as a covariate in our study so additional studies are needed to understand how uncertainty and patient needs temporally evolve over the course of illness and whether this drives some of the observed difference across disease groups. Regardless, patients with all three diseases expressed interest in additional resources to support their needs with managing physical symptoms, emotional concerns, and increasing self-care, suggesting that interventions to address illness-related uncertainty, mental health outcomes, and the needs of patients may need to be tailored to specific diseases.

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Strengths of our study include the inclusion of patients with different SARDs in which illness-related uncertainty has not been previously well-studied. We included patients across the spectrum of disease activity. Additionally, we used a previously validated instrument to measure illness-related uncertainty as well as those used to assess mental health outcomes.



Despite these strengths, our study has certain limitations. First, this study was conducted in a single center, surveys were only available in English, and the study population included a largely White, well-educated population of higher socioeconomic status, which may limit generalizability. Despite this, we observed strong associations of illness-related uncertainty with mental health outcomes and patient needs for relevant resources. Additional studies are needed to confirm these associations and the psychosocial needs of SARDs patients from diverse racial, ethnic, and socioeconomic backgrounds. Second, we conducted a cross-sectional study which limits our ability to establish causal associations and only afforded one opportunity to capture patients' responses, reflected in our modest response rate. However, our theoretical framework of illness-related uncertainty with mental health outcomes provides context for interpreting the significance of the observed associations. Third, this study was conducted during the COVID-19 pandemic which may have impacted some responses. Nevertheless, the ongoing pandemic is known to have strongly affected the health and well-being of patients with SARDs (45) and our findings regarding the association of illness-related uncertainty with mental health outcomes remain relevant. Fourth, patient participation was voluntary and those who self-selected for participation may be those more likely to have illness-related uncertainty, depression, anxiety, or high psychosocial needs. Reassuringly, we saw substantial variation in uncertainty, depression, anxiety, and psychosocial needs across participants. Fifth, some patients contacted chose not to participate and the reasons for declining participation are unknown. Future studies are needed to determine how best to engage with these populations to conduct this type of research. Because our sample size was small in subgroups, we were limited in the comparisons we were able to make across these groups. Larger studies are planned to confirm our observations.

Findings from this study could be useful for clinicians and healthcare professionals caring for patients with SARDs. These patients are likely to have concerns about the ambiguity, complexity, or unpredictability of their symptoms or may feel that they lack information about available treatments. Clinicians can inquire about these uncertainties, and our findings suggest that patients may be particularly interested in referrals for psychosocial services that address psychological and physical health demands. In addition to available services in clinical settings, remotely delivered interventions for coping with rheumatological uncertainty are especially needed. Our findings suggest that rheumatology patients would like to access these skills virtually, which is consistent with preferences from other chronic illness populations who face logistical and physical barriers to accessing care in-person (46).

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Conflicts of Interest:**

ZSW reports research support from Bristol-Myers Squibb and Principia and consulting fees from Viela Bio and Medpace. No other disclosures relevant to this article were reported.

**Data availability:**

The data underlying this article will be shared on reasonable request to the corresponding author.

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**Key messages**

- Illness-related uncertainty may be an important target for interventions to improve quality of life.
- We observed generally strong associations of illness-related uncertainty with depression, anxiety, and symptom impact.
- Patients expressed a strong desire for interventions that address illness-related uncertainty.

**Table 1:**

## Demographics of Survey Respondents

	<b>Total</b>	<b>AAV</b>	<b>IgG4-RD</b>	<b>SSc</b>
<b>N</b>	132	41	61	30
<b>Age (Mean, SD)</b>	64.7, 11.3	64.7, 10.3	64.5, 12.0	64.9, 11.8
<b>Race/Ethnicity n (%)</b>				
American Indian or Alaskan Native	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Asian	13 (9.8)	2 (4.9)	9 (14.8)	2 (6.7)
Black or African American	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Hispanic or Latino	6 (4.5)	1 (2.4)	3 (4.9)	2 (6.7)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White	110 (83.3)	38 (92.7)	46 (75.4)	26 (86.7)
Other	4 (3.0)	1 (2.4)	3 (4.9)	0 (0.0)
<b>Sex n (%)</b>				
Female	69 (52.3)	23 (56.1)	17 (27.9)	29 (96.7)
<b>Relationship status n (%)</b>				
Single, never married	12 (9.1)	7 (17.1)	2 (3.3)	3 (10.0)
Married/Living with partner	101 (76.5)	28 (68.3)	54 (88.5)	19 (63.3)
Widowed/Divorced	16 (12.1)	5 (12.2)	4 (6.6)	7 (23.3)
Other	2 (1.5)	1 (2.4)	0 (0.0)	1 (3.3)
<b>Children n (%)</b>				
Yes	102 (77.3)	33 (80.5)	49 (80.3)	20 (66.7)
<b>Caretaker n (%)</b>				
Yes	22 (16.7)	6 (14.6)	12 (19.7)	4 (13.3)
<b>Level of Education n (%)</b>				
High school or some college	27 (20.5)	7 (17.1)	9 (14.8)	11 (36.7)
College degree	47 (35.6)	18 (43.9)	21 (34.4)	8 (26.7)
Advanced degree	57 (43.2)	16 (39)	30 (49.2)	11 (36.7)
<b>Employment status n (%)</b>				
Full-time	37 (28)	12 (29.3)	19 (31.1)	6 (20.0)
Part-time	10 (7.6)	6 (14.6)	2 (3.3)	2 (6.7)
Unemployed and looking for work	5 (3.8)	1 (2.4)	3 (4.9)	1 (3.3)
Unable to work due to caring for family or home	2 (1.5)	2 (4.9)	0 (0.0)	0 (0.0)
Unable to work due to disability or illness	6 (4.5)	2 (4.9)	1 (1.6)	3 (10.0)
Retired	69 (52.3)	16 (39.0)	36 (59.0)	17 (56.7)
Student	1 (0.8)	1 (2.4)	0 (0.0)	0 (0.0)
Other	2 (1.5)	1 (2.4)	0 (0.0)	1 (3.3)
<b>Annual household income n (%)</b>				
Less than 20,000	4 (3.0)	1 (2.4)	3 (4.9)	0 (0.0)
20,000–39,999	16 (12.1)	4 (9.8)	6 (9.8)	6 (20.0)

	Total	AAV	IgG4-RD	SSc
40,000–59,999	11 (8.3)	6 (14.6)	2 (3.3)	3 (10.0)
60,000–79,999	14 (10.6)	4 (9.8)	5 (8.2)	5 (16.7)
80,000–99,999	8 (6.1)	3 (7.3)	3 (4.9)	2 (6.7)
100,000 and over	64 (48.5)	20 (48.8)	35 (57.4)	9 (30.0)
Don't know	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Prefer not to answer	14 (10.6)	0 (0.0)	6 (9.8)	0 (0.0)
<b>Health Insurance n (%)</b>				
Employer-sponsored	54 (40.9)	20 (48.8)	21 (34.4)	13 (43.3)
Individual insurance	8 (6.1)	4 (9.8)	4 (6.6)	0 (0.0)
Medicare	64 (48.5)	15 (36.6)	32 (52.5)	17 (56.7)
Medicaid	2 (1.5)	1 (2.4)	1 (1.6)	0 (0.0)
Military health care	2 (1.5)	0 (0.0)	2 (3.3)	0 (0.0)
Don't know	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	2 (1.5)	1 (2.4)	1 (1.6)	0 (0.0)
No health insurance	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Comorbidities n (%)</b>				
Cardiovascular disease (i.e. heart disease, stroke, high blood pressure, high cholesterol)	59 (44.7)	16 (39.0)	27 (44.3)	16 (53.3)
Diabetes	15 (11.4)	3 (7.3)	11 (18.0)	1 (3.3)
Kidney disease	17 (12.9)	4 (9.8)	11 (18.0)	2 (6.7)
Liver disease	3 (2.3)	0 (0.0)	3 (4.9)	0 (0.0)
Lung disease (e.g., asthma, COPD, sleep apnea)	43 (32.6)	20 (48.8)	16 (26.2)	7 (23.3)
Overweight/obesity	26 (19.7)	9 (22.0)	12 (19.7)	5 (16.7)
Underweight	2 (1.5)	0 (0.0)	0 (0.0)	2 (6.7)
Other	31 (23.5)	11 (26.8)	13 (21.3)	7 (23.3)
<b>Self-Reported Disease activity n (%)</b>				
In remission	56 (42.4)	21 (51.2)	32 (52.5)	3 (10.0)
Not in remission	42 (31.8)	13 (31.7)	13 (21.3)	16 (53.3)
I do not know	34 (25.8)	7 (17.1)	16 (26.2)	11 (36.7)

AAV: ANCA-Associated Vasculitis; IgG4-RD: IgG4-Related Disease; SSc: Systemic Sclerosis

**Table 2:**

## Uncertainty and Mental Health (Overall and Stratified by Disease)

	Overall	AAV	IgG4-RD	SSc	P-Value
<b>N</b>	132	41	61	30	
<b>MUIS n (%)</b>					
Median, IQR	55.0 [48.0, 62.0]	55.0 [48.0, 62.0]	53.0 [48.0, 58.0]	59.0 [55.0, 66.0]	0.002
Q1 (22–44)	21 (15.9)	8 (19.5)	12 (19.7)	1 (3.3)	
Q2 (44–66)	97 (73.5)	25 (61.0)	48 (78.7)	24 (80.0)	
Q3 (66–88)	13 (9.8)	7 (17.1)	1 (1.6)	5 (16.7)	
Q4 (88–110)	1 (0.8)	1 (2.4)	0 (0.0)	0 (0.0)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
<b>PHQ-8 n (%)</b>					
Median, IQR	3.0 [1.0, 6.0]	4.0 [2.0, 9.0]	2.5 [0.5, 5.0]	3.0 [1.0, 7.0]	0.03
Minimal (0–4)	84 (63.6)	21 (51.2)	44 (72.1)	19 (63.3)	0.10*
Mild (5–9)	31 (23.5)	10 (24.4)	13 (21.3)	8 (26.7)	
Moderate (10–14)	5 (3.8)	4 (9.8)	0 (0.0)	1 (3.4)	
Moderately Severe (15–19)	5 (3.8)	2 (4.9)	2 (3.3)	1 (3.4)	
Severe (20–24)	5 (3.8)	4 (9.8)	1 (1.6)	0 (0.0)	
Missing	2 (1.5)	0 (0.0)	1 (1.6)	1 (3.4)	
<b>GAD-7 n (%)</b>					
Median, IQR	2.0 [0.0, 5.5]	5.0 [2.0, 8.0]	1.0 [0.0, 4.0]	2.0 [0.0, 5.0]	0.002
Minimal (0–4)	90 (68.2)	20 (48.8)	48 (78.7)	22 (73.3)	0.005*
Mild (5–9)	34 (25.8)	16 (39.0)	11 (18.0)	7 (23.3)	
Moderate (10–14)	6 (4.5)	4 (9.8)	1 (1.6)	1 (3.3)	
Severe (15–21)	2 (1.5)	1 (2.4)	1 (1.6)	0 (0.0)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
<b>SIP n (%)</b>					
Median, IQR	1.0 [0.0, 6.0]	2.0 [0.0, 6.0]	1.0 [0.0, 7.0]	1.0 [0.0, 5.0]	0.60
Q1 (0–5)	92 (69.7)	27 (65.9)	41 (67.2)	24 (80.0)	
Q2 (6–11)	34 (25.8)	12 (29.3)	16 (26.2)	6 (20.0)	
Q3 (12–16)	6 (4.5)	2 (4.9)	4 (6.6)	0 (0.0)	
Q4 (17–22)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

AAV: ANCA-Associated Vasculitis; IgG4-RD: IgG4-Related Disease; SSc: Systemic Sclerosis; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder; SIP: Sickness Impact Profile

\* P-value compares the proportion of patients with at least mild depression or anxiety across the three disease groups.



**Table 3:**

## The Association of Uncertainty with Mental Health

	Correlation coefficient	p-value
<b>Overall</b>		
MUIS and PHQ-8	0.43	<0.0001
MUIS and GAD-7	0.33	<0.0001
MUIS and SIP	0.28	0.0012
<b>AAV</b>		
MUIS and PHQ-8	0.56	0.0001
MUIS and GAD-7	0.45	0.003
MUIS and SIP	0.57	0.0001
<b>IgG4-RD</b>		
MUIS and PHQ-8	0.17	0.20
MUIS and GAD-7	0.22	0.09
MUIS and SIP	0.01	0.93
<b>SSc</b>		
MUIS and PHQ-8	0.60	0.0007
MUIS and GAD-7	0.25	0.18
MUIS and SIP	0.59	0.0005

AAV: ANCA-Associated Vasculitis; IgG4-RD: IgG4-Related Disease; SSc: Systemic Sclerosis; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder; SIP: Sickness Impact Profile

**Table 4:**

Needs Identified by Patients According to Uncertainty and Mental Health (N=132)

		Managing physical symptoms		Learning strategies to increase self-care		Coping with emotional concerns		Managing social concerns or lack of support		Finding resources to help with daily concerns		Managing sexual and reproductive concerns	
	Total	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend
<b>PHQ8</b>	132 (100.0)	68 (51.5)	<b>0.03</b>	48 (36.4)	<b>0.03</b>	31 (23.5)	0.07	10 (7.6)	<b>0.008</b>	9 (6.8)	0.4	4 (3.0)	0.07
Minimal	84 (63.6)	42 (50.0)		25 (29.8)		15 (17.9)		2 (2.4)		4 (4.8)		1 (1.2)	
Mild	31 (23.5)	14 (45.2)		16 (51.6)		11 (35.5)		5 (16.1)		4 (12.9)		2 (6.5)	
Moderate	5 (3.8)	3 (60.0)		1 (20.0)		1 (2.0)		1 (20.0)		0 (0.0)		0 (0.0)	
Moderately Severe	5 (3.8)	4 (80.0)		2 (40.0)		2 (40.0)		1 (20.0)		0 (0.0)		0 (0.0)	
Severe	5 (3.8)	5 (100.0)		4 (80.0)		2 (40.0)		1 (20.0)		1 (20.0)		1 (20.0)	
<b>GAD7</b>	132 (100.0)	70 (53.0)	0.52	49 (37.1)	<b>0.03</b>	32 (24.2)	<b>&lt;0.0001</b>	10 (7.6)	<b>0.01</b>	11 (8.3)	0.08	4 (3.0)	<b>0.008</b>
Minimal	90 (68.2)	48 (53.3)		30 (33.3)		12 (13.3)		4 (4.4)		6 (6.7)		1 (11)	
Mild	34 (25.8)	16 (47.1)		13 (38.2)		15 (44.1)		4 (11.8)		3 (8.8)		2 (5.9)	
Moderate	6 (4.5)	4 (66.7)		4 (66.7)		3 (50.0)		1 (16.7)		1 (16.7)		0 (0.0)	
Severe	2 (1.5)	2 (100.0)		2 (100.0)		2 (100.0)		1 (50.0)		1 (50.0)		1 (50.0)	
<b>MUIS</b>	132 (100.0)	70 (53.0)	<b>0.003</b>	49 (37.1)	<b>0.04</b>	32 (24.2)	<b>0.04</b>	10 (7.6)	<b>0.03</b>	11 (8.3)	0.77	4 (3.0)	0.86
Quartile 1	21 (15.9)	7 (33.3)		6 (28.8)		1 (4.8)		1 (4.8)		1 (4.8)		0 (0.0)	
Quartile 2	97 (73.5)	51 (52.6)		33 (34.0)		26 (26.8)		5 (5.2)		10 (10.3)		4 (4.1)	
Quartile 3	13 (9.8)	11 (84.6)		10 (76.9)		5 (38.5)		4 (30.8)		0 (0.0)		0 (0.0)	
Quartile 4	1 (0.8)	1 (100.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
<b>SIP</b>	132 (100.0)	70 (53.0)	0.27	49 (37.1)	0.21	32 (24.2)	0.17	10 (7.6)	0.77	11 (8.3)	0.08	4 (3.0)	<b>0.001</b>
Quartile 1	92 (69.7)	47 (51.1)		32 (34.8)		19 (20.7)		6 (6.5)		4 (4.3)		0 (0.0)	
Quartile 2	34 (25.8)	18 (52.9)		13 (38.2)		11 (32.4)		4 (11.8)		7 (20.6)		3 (8.8)	
Quartile 3	6 (4.5)	5 (83.3)		4 (66.7)		2 (33.3)		0 (0.0)		0 (0.0)		1 (16.7)	
Quartile 4	0 (0.0)	0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	

MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder (GAD-7); SIP: Sickness Impact Profile

**Table 5.**

Comparison of PHQ-8/GAD-7/MUIS/SIP score means between did vs. did not endorse needs (reference)

	Overall			
	P	T	DF	Hedges' G
Managing physical symptoms				
PHQ-8	0.01	2.76	103.49	<b>0.47 (0.12, 0.82)</b>
GAD-7	0.33	0.98	130	0.17 (-0.17, 0.51)
MUIS	0.004	2.93	126.29	<b>0.50 (0.15, 0.85)</b>
SIP	0.08	1.74	130	0.30 (-0.04, 0.65)
Coping with emotional concerns				
PHQ-8	0.03	2.17	128	<b>0.45 (0.04, 0.85)</b>
GAD-7	0.002	3.35	41.205	<b>0.81 (0.40, 1.22)</b>
MUIS	0.004	2.96	130	<b>0.60 (0.20, 1.01)</b>
SIP	0.049	1.99	130	<b>0.40 (0.00, 0.80)</b>
Learning strategies to increase self-care				
PHQ-8	0.04	2.10	74.519	<b>0.42 (0.06, 0.78)</b>
GAD-7	0.03	2.16	76.543	<b>0.42 (0.07, 0.78)</b>
MUIS	0.02	2.37	130	<b>0.43 (0.07, 0.78)</b>
SIP	0.28	1.09	130	0.20 (-0.16, 0.55)

MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder (GAD-7); SIP: Sickness Impact Profile

*Notes.* Individuals who endorsed needs consistently had higher symptom scores in group comparisons. Degrees of freedom were corrected for t-tests as appropriate when the assumption of equal variance between groups was violated. Values in parentheses for Hedges' G indicate 95% confidence interval. Hedges' G effect size is interpreted as 0.20 = small, 0.50 = medium, 0.80 = large.