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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 (SARDs) 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 the Massachusetts General Hospital with antineutrophil cytoplasmic antibody-associated vasculitis (AAV), IgG4-related disease (IgG4-RD), and systemic sclerosis (SSc) completed the Mishel Uncertainty in Illness Scale, 8-item Patient Health Questionnaire depression scale, 7-item General Anxiety Disorder scale, 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. One hundred thirty-two patients with AAV (n = 41, 31%), IgG4-RD (n = 61, 46%), or SSc (n = 30, 23%) participated. The mean age was 64 years, 52% were female, and 83% were White. Greater illness-related uncertainty was positively correlated with higher levels of depression ($r = 0.43$, $P < 0.001$), anxiety ($r = 0.33$, $P < 0.001$), 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 compared to IgG4-RD. The primary 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.

Key Indexing Terms: autoimmune diseases, mental health, uncertainty

After the 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 as a patient, including when and how to engage in medical visits and tests.[1,2,3,4] Illness-related uncertainty has been established as a chief concern across many of the most debilitating illnesses, such as cancer (eg, fear of cancer recurrence), cardiovascular disease (eg, fear of myocardial infarction recurrence), chronic pain (eg, fear of exacerbation), HIV (eg, fear of progression to AIDS), and multiple sclerosis (eg, 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 as a result of mind–body interactions between somatic symptoms (eg, pain, fatigue, sleep disturbance), psychological factors (eg, interpretation of somatic symptoms, optimism about future health), and behavioral responses (eg, excessive self-examination, urgent doctor visits, avoidance behaviors like substance use).[4,18,19,20,21] 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

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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 antineutrophil cytoplasmic antibody–associated vasculitis (AAV), systemic sclerosis (SSc), and IgG4-related disease (IgG4-RD), share common features (eg, multiorgan involvement), natural histories (eg, risk of flare, disease progression), complications (eg, organ failure, death), and immunosuppressive treatments. There has been limited prior literature on illness-related uncertainty in other SARDs, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).[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 affect these themes, each of these factors can, in theory, trigger and sustain illness-related SARDs-related uncertainty. Empirical examinations of these associations are lacking.[1,2,3,4]

The 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.

METHODS

Patient recruitment. In this cross-sectional study, we identified patients with AAV, IgG4-RD, and SSc at Massachusetts General Hospital (MGH). We focused on these 3 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 January 1, 2020, and November 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 postal 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 postal 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 2 weeks of their initial letter, patients were contacted up to 2 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 through 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 Supplementary Material, available with the online version of this article); (2) Mishel Uncertainty in Illness Scale (MUIS) of 22 items, anchored to SARDs, with higher scores reflecting higher SARDs-related uncertainty[26]; (3) Sickness Impact Profile (SIP) of 68 items, with higher scores reflecting higher negative effect of SARDs on one's behavior[27]; (4) 8-item Patient Health Questionnaire (PHQ-8)[28]; (5) 7-item General Anxiety Disorder (GAD-7)[29]; (6) Health Behavior Questionnaire (see Supplementary Material); and (7) Needs Survey (see Supplementary 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 (eg, virtual, in-person). Some questions on the MUIS were slightly modified to make them relevant to the SARD population (see Supplementary 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 (SD) or median (IQR), as appropriate. Correlations between MUIS with GAD-7, PHQ-8, and SIP were assessed using Pearson 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 2-sample *t* test and standardized Cohen *d* effect size with Hedges correction (ie, Hedges *g*). Formal mean comparisons were not tested for 3 items where < 10% of participants indicated unmet need (ie, managing social concerns, managing sexual/reproductive concerns, finding resources). The level of significance for all analyses was set as a 2-tailed $P < 0.05$, and statistical analyses were completed using SAS statistical software (version 9.4; SAS Institute).

RESULTS

Participants. Participant demographics are reported in full in Table 1 and Supplementary Table 1 (available with the online version of this article). Of 369 patients invited to complete study surveys, 132 patients completed the full survey, including 41 (31.1%) with AAV, 61 (46.2%) with IgG4-RD, and 30 (22.7%) with SSc. Of the patients who completed the survey, 122 (92.4%) did so online and 10 (7.6%) did so by paper; no respondents did so by phone. Compared with those who did not participate, those who participated were older (64.2 yrs [11.7] vs 59 yrs [16.0], $P < 0.001$) and tended to be White (110 [83.3%] vs 180 [75.0%], $P = 0.20$). A similar proportion of participants and nonparticipants were female (65 [52%] vs 122 [51%], $P = 0.80$). The majority of those who participated reported being retired (n = 69, 52%). Participant demographics are reported in full in Table 1 and Supplementary Table 1.

Age and race distribution were similar across disease groups, but the proportion of female patients significantly differed by group, such that 56.1% of patients with AAV, 27.9% of patients with IgG4-RD, and 96.7% of patients with SSc 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

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Table 1. Demographics of survey respondents.

	Total	AAV	IgG4-RD	SSc
N	132	41	61	30
Age, yrs, mean (SD)	64.2 (11.7)	60.1 (13.8)	66.5 (10.0)	65.8 (10.2)
Race/ethnicity				
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)
Sex, n (%)				
Female	69 (52.3)	23 (56.1)	17 (27.9)	29 (96.7)
Relationship status				
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)
Children				
Yes	102 (77.3)	33 (80.5)	49 (80.3)	20 (66.7)
Caretaker				
Yes	22 (16.7)	6 (14.6)	12 (19.7)	4 (13.3)
Level of education				
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)
Employment status				
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)
Annual household income				
< $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)
$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	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)
Health insurance				
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)
Comorbidities				
Cardiovascular disease (ie, 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 (eg, asthma, COPD, sleep apnea)	43 (32.6)	20 (48.8)	16 (26.2)	7 (23.3)

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Table 1. Continued.

	Total	AAV	IgG4-RD	SSc
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)
Self-reported disease activity				
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)

Values are n (%) unless otherwise indicated. AAV: antineutrophil cytoplasmic antibody-associated vasculitis; COPD: chronic obstructive pulmonary disease; IgG4-RD: IgG4-related disease; SSc: systemic sclerosis.

to employer-sponsored (n = 54, 40.9%), individual (n = 8, 6.1%), or Medicare (n = 64, 48.5%) health 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 than those with IgG4-RD (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

Table 2. Uncertainty and mental health (overall and stratified by disease).

	Overall	AAV	IgG4-RD	SSc	*P*
N	132	41	61	30	
MUIS					
Median, IQR	55.0 (48.0–62.0)	56.0 (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)	
PHQ-8					
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 (3.3)	
Moderately Severe (15–19)	5 (3.8)	2 (4.9)	2 (3.3)	1 (3.3)	
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 (3.3)	
GAD-7					
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)	
SIP					
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)	

Values are n (%) unless otherwise indicated. * P value compares the proportion of patients with at least mild depression or anxiety across the 3 disease groups. AAV: antineutrophil cytoplasmic antibody-associated vasculitis; GAD-7: 7-item General Anxiety Disorder; IgG4-RD: IgG4-related disease; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: 8-item Patient Health Questionnaire depression scale; Q: quartile; SIP: Sickness Impact Profile; SSc: systemic sclerosis.

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depression (PHQ-8 ≥ 5). Similar rates of depression symptoms were observed across subgroups, but there was again a trend toward patients with AAV and SSc reporting depression symptoms more often than patients with IgG4-RD (n = 20, 48.7% and n = 11, 37%, respectively, vs n = 17, 27.9%, $P = 0.10$). Anxiety was also common in this cohort, with 42 (41.8%) reporting at least mildly severe symptoms (GAD-7 ≥ 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 effect was generally higher among patients with SSc who were unaware of their status (see Supplementary Tables 2A–C, available with the online version of this article).

We also found that uncertainty varied according to sex (see Supplementary Tables 3A–E, available with the online version of this article). 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 sex, 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 patients with AAV and SSc, little association of uncertainty with depression ($r = 0.17$, $P = 0.20$) and sickness impact ($r = 0.01$, $P = 0.93$) was observed in patients with IgG4-RD. 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 ($r = 0.25$, $P = 0.18$).

Table 3. The association of uncertainty with mental health.

	Correlation Coefficient	*P*
Overall		
MUIS and PHQ-8	0.43	< 0.0001
MUIS and GAD-7	0.33	< 0.0001
MUIS and SIP	0.28	0.001
AAV		
MUIS and PHQ-8	0.56	0.0001
MUIS and GAD-7	0.45	0.003
MUIS and SIP	0.57	0.0001
IgG4-RD		
MUIS and PHQ-8	0.17	0.20
MUIS and GAD-7	0.22	0.09
MUIS and SIP	0.01	0.93
SSc		
MUIS and PHQ-8	0.60	0.0007
MUIS and GAD-7	0.25	0.18
MUIS and SIP	0.59	0.0005

AAV: antineutrophil cytoplasmic antibody-associated vasculitis; GAD-7: 7-item General Anxiety Disorder; IgG4-RD: IgG4-related disease; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: 8-item Patient Health Questionnaire depression scale; SIP: Sickness Impact Profile; SSc: systemic sclerosis.

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%), manage sexual and reproductive concerns (n = 4, 3%), and find resources to help with daily concerns (n = 11, 8%). Trends in interest in additional support were similar across illness subgroups (Supplementary Table 4, available with the online version of this article).

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 ($t(126.29) = -2.93$, $P = 0.004$, $g = -0.50$; $t(103.49) = -2.76$, $P = 0.007$, $g = -0.47$, 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 ($t(130) = -2.37$, $P = 0.02$, $g = -0.43$; $t(74.52) = -2.10$, $P = 0.04$, $g = -0.42$; $t(76.54) = -2.16$, $P = 0.03$, $g = -0.42$, respectively). Perceived need for support with emotional concerns had moderate-to-large associations with all psychological domains assessed, including uncertainty ($t(130) = -2.96$, $P = 0.004$, $g = -0.60$), sickness impact ($t(130) = -1.99$, $P = 0.049$, $g = -0.40$), depression ($t(128) = -2.17$, $P = 0.03$, $g = -0.45$), and anxiety ($t(41.21) = -3.35$, $P = 0.002$, $g = -0.81$).

Importantly, the need for these resources were often not communicated from the patient to the provider (Supplementary Table 5, available with the online version of this article). 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.

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Table 4. Needs identified by patients according to uncertainty and mental health (N = 132).

	Total	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	
		n (%)	*P* for Trend	n (%)	*P* for Trend	n (%)	*P* for Trend	n (%)	*P* for Trend	n (%)	*P* for Trend	n (%)	*P* for Trend
PHQ-8	132 (100.0)	68 (51.5)	**0.03**	48 (36.4)	**0.03**	31 (23.5)	0.07	10 (7.6)	**0.008**	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 (20.0)		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)	
GAD-7	132 (100.0)	70 (53.0)	0.52	49 (37.1)	**0.03**	32 (24.2)	**< 0.0001**	10 (7.6)	**0.01**	11 (8.3)	0.08	4 (3.0)	**0.008**
Minimal	90 (68.2)	48 (53.3)		30 (33.3)		12 (13.3)		4 (4.4)		6 (6.7)		1 (1.1)	
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)	
MUIS	132 (100.0)	70 (53.0)	**0.003**	49 (37.1)	**0.04**	32 (24.2)	**0.04**	10 (7.6)	**0.03**	11 (8.3)	0.77	4 (3.0)	0.86
Q1	21 (15.9)	7 (33.3)		6 (28.8)		1 (4.8)		1 (4.8)		1 (4.8)		0 (0.0)	
Q2	97 (73.5)	51 (52.6)		33 (34.0)		26 (26.8)		5 (5.2)		10 (10.3)		4 (4.1)	
Q3	13 (9.8)	11 (84.6)		10 (76.9)		5 (38.5)		4 (30.8)		0 (0.0)		0 (0.0)	
Q4	1 (0.8)	1 (100.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
SIP	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)	**0.001**
Q1	92 (69.7)	47 (51.1)		32 (34.8)		19 (20.7)		6 (6.5)		4 (4.3)		0 (0.0)	
Q2	34 (25.8)	18 (52.9)		13 (38.2)		11 (32.4)		4 (11.8)		7 (20.6)		3 (8.8)	
Q3	6 (4.5)	5 (83.3)		4 (66.7)		2 (33.3)		0 (0.0)		0 (0.0)		1 (16.7)	
Q4	0 (0.0)	0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	

Values in bold are statistically significant. GAD-7: 7-item General Anxiety Disorder; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: 8-item Patient Health Questionnaire depression scale; Q: quartile; SIP: Sickness Impact Profile.

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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	**−0.47 (−0.82 to −0.12)**
GAD-7	0.33	−0.98	130	−0.17 (−0.51 to 0.17)
MUIS	0.004	−2.93	126.29	**−0.50 (−0.85 to −0.15)**
SIP	0.08	−1.74	130	−0.30 (−0.65 to 0.04)
Coping with emotional concerns				
PHQ-8	0.03	−2.17	128	**−0.45 (−0.85 to −0.04)**
GAD-7	0.002	−3.35	41.21	**−0.81 (−1.22 to −0.40)**
MUIS	0.004	−2.96	130	**−0.60 (−1.01 to −0.20)**
SIP	0.049	−1.99	130	**−0.40 (−0.80 to 0.00)**
Learning strategies to increase self-care				
PHQ-8	0.04	−2.10	74.52	**−0.42 (−0.78 to −0.06)**
GAD-7	0.03	−2.16	76.54	**−0.42 (−0.78 to −0.07)**
MUIS	0.02	−2.37	130	**−0.43 (−0.78 to −0.07)**
SIP	0.28	−1.09	130	−0.20 (−0.55 to 0.16)

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% CI. Hedges *g* effect size is interpreted as 0.20 = small, 0.50 = medium, and 0.80 = large. Values in bold are statistically significant. DF: degrees of freedom; GAD-7: General Anxiety Disorder; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; SIP: Sickness Impact Profile.

DISCUSSION

We found that illness-related uncertainty is common in patients with AAV, IgG4-RD, and SSc, and that patients with greater uncertainty tended to have worse mental health outcomes, including greater depression, anxiety, and the perceived effect 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 patients with SARDs 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 antirheumatic 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 RA.[31,32] A previous randomized trial in patients with SSc found that compared to a wait-listed control, a 12-session, videoconference-based group intervention providing education about coping strategies (ie, fostering social connection, relaxation training, managing worry, and physical activity) improved depression and anxiety symptoms within 6 weeks of randomization.[33] Importantly, we observed strong interest among patients with SARDs 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, to our knowledge, ours is the first to explore this in AAV, IgG4-RD, and SSc. A previous qualitative study in patients with SSc found that the need for navigating uncertainty (eg, diagnostic ambiguity, unpredictable illness course) was an important concern raised by patients.[24] Additionally, a different uncertainty instrument has been previously developed for RA and SLE.[25] As part of the development and validation of that instrument, associations were observed between uncertainty, 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.

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

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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 effects of illness.[41,42,43,44]

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 (eg, sex distribution) or the underlying disease (eg, 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 reduced 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 3 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.

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 patients with SARDs 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 1 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; 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]

DATA AVAILABILITY

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

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Becker G, Janson-Bjerklie S, Benner P, Slobin K, Ferketich S. The dilemma of seeking urgent care: asthma episodes and emergency service use. Soc Sci Med 1993;37:305-13.
2. Cohen MH. Diagnostic closure and the spread of uncertainty. Issues Compr Pediatr Nurs 1993;16:135-46.
3. Hilton BA. The phenomenon of uncertainty in women with breast cancer. Issues Ment Health Nurs 1988;9:217-38.
4. Mishel MH. Reconceptualization of the uncertainty in illness theory. Image J Nurs Sch 1990;22:256-62.
5. Brashers DE, Neidig JL, Reynolds NR, Haas SM. Uncertainty in illness across the HIV/AIDS trajectory. J Assoc Nurses AIDS Care 1998;9:66-77.
6. Carroll DL, Hamilton GA, McGovern BA. Changes in health status and quality of life and the impact of uncertainty in patients who survive life-threatening arrhythmias. Heart Lung 1999;28:251-60.
7. Cleanthous S, Newman SP, Shipley M, Isenberg DA, Cano SJ. What constitutes uncertainty in systemic lupus erythematosus and rheumatoid arthritis? Psychol Health 2013;28:171-88.

Downloaded on November 11, 2026 from www.jrheum.org

8. Eastwood JA, Doering L, Roper J, Hays RD. Uncertainty and health-related quality of life 1 year after coronary angiography. Am J Crit Care 2008;17:232-42.
9. Jamison M, Neuberger GB, Miller PA. Correlates of falls and fear of falling among adults with rheumatoid arthritis. Arthritis Rheum 2003;49:673-80.
10. Jurgens CY. Somatic awareness, uncertainty, and delay in care-seeking in acute heart failure. Res Nurs Health 2006;29:74-86.
11. Mattsson M, Möller B, Stamm T, Gard G, Boström C. Uncertainty and opportunities in patients with established systemic lupus erythematosus: a qualitative study. Musculoskeletal Care 2012; 10:1-12.
12. Fessel KD, Nevitt MC. Correlates of fear of falling and activity limitation among persons with rheumatoid arthritis. Arthritis Care Res 1997;10:222-8.
13. McKinley ED. Under Toad days: surviving the uncertainty of cancer recurrence. Ann Intern Med 2000;133:479-80.
14. Regan-Kubinski MJ, Sharts-Hopko N. Illness cognition of HIV-infected mothers. Issues Ment Health Nurs 1995;16:327-44.
15. Searle C, Jeffrey J. Uncertainty and quality of life of adults hospitalized with life-threatening ventricular arrhythmias. Can J Cardiovasc Nurs 1994;5:15-22.
16. Solomon P, O'Brien K, Wilkins S, Gervais N. Aging with HIV and disability: the role of uncertainty. AIDS Care 2014;26:240-5.
17. Weitz R. Uncertainty and the lives of persons with AIDS. J Health Soc Behav 1989;30:270-81.
18. Carleton RN. Into the unknown: a review and synthesis of contemporary models involving uncertainty. J Anxiety Disord 2016;39: 30-43.
19. Curran L, Sharpe L, Butow P. Anxiety in the context of cancer: a systematic review and development of an integrated model. Clin Psychol Rev 2017;56:40-54.
20. de Boer AG, Wijker W, de Haes HC. Predictors of health care utilization in the chronically ill: a review of the literature. Health Policy 1997;42:101-15.
21. Hall DL, Jimenez RB, Perez GK, et al. Fear of cancer recurrence: a model examination of physical symptoms, emotional distress, and health behavior change. J Oncol Pract 2019;15:e787-97.
22. Byrne SK. Healthcare avoidance: a critical review. Holist Nurs Pract 2008;22:280-92.
23. Heiberg T, Finset A, Uhlig T, Kvien TK. Seven year changes in health status and priorities for improvement of health in patients with rheumatoid arthritis. Ann Rheum Dis 2005;64:191-5.
24. Nakayama A, Tunnicliffe DJ, Thakkar V, et al. Patients' perspectives and experiences living with systemic sclerosis: a systematic review and thematic synthesis of qualitative studies. J Rheumatol 2016;43:1363-75.
25. Cleanthous S, Isenberg DA, Newman SP, Cano SJ. Patient Uncertainty Questionnaire–Rheumatology (PUQ-R): development and validation of a new patient-reported outcome instrument for systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) in a mixed methods study. Health Qual Life Outcomes 2016;14:33.
26. Mishel MH. The measurement of uncertainty in illness. Nurs Res 1981;30:258-63.
27. Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. Med Care 1981;19:787-805.
28. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Dis 2009;114:163-73.
29. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092-7.
30. Matcham F, Galloway J, Hotopf M, et al. The impact of targeted rheumatoid arthritis pharmacologic treatment on mental health: a systematic review and network meta-analysis. Arthritis Rheumatol 2018;70:1377-91.
31. Cramp F. The role of non-pharmacological interventions in the management of rheumatoid-arthritis-related fatigue. Rheumatology 2019;58 Suppl 5:v22-8.
32. Shen B, Li Y, Du X, et al. Effects of cognitive behavioral therapy for patients with rheumatoid arthritis: a systematic review and meta-analysis. Psychol Health Med 2020;25:1179–91.
33. Thombs BD, Kwakkenbos L, Levis B, et al. Effects of a multi-faceted education and support programme on anxiety symptoms among people with systemic sclerosis and anxiety during COVID-19 (SPIN-CHAT): a two-arm parallel, partially nested, randomised, controlled trial. Lancet Rheumatol 2021;3:e427–37.
34. Aitken M, Basu N. Improving quality of life in vasculitis patients. Rheumatology 2020;59 Suppl 3:iii132-5.
35. Basu N, McClean A, Harper L, et al. The characterisation and determinants of quality of life in ANCA associated vasculitis. Ann Rheum Dis 2014;73:207-11.
36. Hudson M, Thombs BD, Steele R, et al. Health-related quality of life in systemic sclerosis: a systematic review. Arthritis Rheum 2009;61:1112-20.
37. Moustafa AT, Moazzami M, Engel L, et al. Prevalence and metric of depression and anxiety in systemic lupus erythematosus: a systematic review and meta-analysis. Semin Arthritis Rheum 2020;50:84-94.
38. Pittam B, Gupta S, Ahmed AE, Hughes DM, Zhao SS. The prevalence and impact of depression in primary systemic vasculitis: a systematic review and meta-analysis. Rheumatol Int 2020; 40:1215-21.
39. Sturgeon JA, Finan PH, Zautra AJ. Affective disturbance in rheumatoid arthritis: psychological and disease-related pathways. Nat Rev Rheumatol 2016;12:532-42.
40. Thombs BD, Taillefer SS, Hudson M, Baron M. Depression in patients with systemic sclerosis: a systematic review of the evidence. Arthritis Rheum 2007;57:1089-97.
41. Hall DL, Park ER, Cheung T, Davis RB, Yeh GY. A pilot mind-body resiliency intervention targeting fear of recurrence among cancer survivors. J Psychosom Res 2020;137:110215.
42. Luberto CM, Hall DL, Chad-Friedman E, Park ER. Theoretical rationale and case illustration of mindfulness-based cognitive therapy for fear of cancer recurrence. J Clin Psychol Med Settings 2019;26:449-60.
43. Park ER, Luberto CM, Chad-Friedman E, et al. A comprehensive resiliency framework: theoretical model, treatment, and evaluation. Glob Adv Health Med 2021;10:21649561211000306.
44. Salkovskis PM, Warwick HM. Meaning, misinterpretations, and medicine: a cognitive-behavioral approach to understanding health anxiety and hypochondriasis. In: Hypochondriasis: modern perspectives on an ancient malady. Oxford University Press; 2001:202-22.
45. Adnine A, Nadiri K, Soussan I, et al. Mental health problems experienced by patients with rheumatic diseases during COVID-19 pandemic. Curr Rheumatol Rev 2021;17:303-11.
46. Park ER, Chiles C, Cinciripini PM, et al. Impact of the COVID-19 pandemic on telehealth research in cancer prevention and care: a call to sustain telehealth advances. Cancer 2021;127:334-8.

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