Ocular Manifestations and Burden Related to Sjögren Syndrome: Results of a Patient Survey

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• PURPOSE: To compare the burden related to dry eye with systemic symptoms of Sjögren syndrome; to estimate the burden related to ocular treatments; and to compare the impact of dry eye and extraocular manifestations of Sjögren syndrome on various aspects of patient life.

• DESIGN: Cross-sectional study.

• METHODS: We conducted a postal survey of adult patients with a history of physician-diagnosed Sjögren syndrome.

• RESULTS: The survey was completed by 2,961 patients (mean age 65.1 years, standard deviation 11.7 years), most of whom were women (96%) and white (94%). Forty-one patients younger than 18 years of age were excluded. More than half (53%) experienced severe dry eye (ie, dry eye daily/almost daily with major impact on their life). Corresponding proportions for dry mouth and fatigue were 48% and 45%, respectively. Almost all patients (97%) had used nonprescription eye drops/artificial tears/ointments. Compared with patients who did not experience dry eye, those who experienced significant dry eye (ie, daily/almost daily dry eye) more often agreed that living with Sjögren syndrome made every day a challenge (adjusted odds ratio [OR] 3.81, 95% confidence interval [CI] 2.49 to 5.86) and added a significant emotional burden (adjusted OR 2.22, 95% CI 1.49 to 3.31). Adjusted ORs for the impact of dry eye were generally lower than those for fatigue, but were similar to dry mouth and considerably higher than use of systemic treatments for serious manifestations of the disease and diagnosis of lymphoma.

• CONCLUSIONS: Sjögren-related dry eye is more burdensome than systemic manifestations of the disease. While fatigue has the greatest impact on patient life, the impact of dry eye is comparable to that of other systemic manifestations. **(Am J Ophthalmol 2020;219:40–48.**

SJÖGREN SYNDROME (“SJÖGREN’S”) IS A COMMON autoimmune disease characterized by exocrine glandular involvement, which leads to ocular and oral dryness, and extraglandular involvement characterized by a variety of systemic manifestations. Sjögren’s is one of the most common autoimmune diseases in the general population, affecting an estimated 4 million Americans.[1]

Although the advent of targeted biological treatments and other factors have led to renewed interest in Sjögren’s among rheumatologists and immunologists, its ocular manifestations and burden remain underappreciated.[2] As an example, the most widely used Sjögren disease activity tool, the EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI), does not include the extraglandular ocular manifestations of Sjögren’s, such as corneal melt/perforation, uveitis, scleritis, retinal vasculitis, and optic neuritis.[3] In addition, the EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI) includes only 1 item that addresses the severity of dryness, but this refers to *overall* dryness and not specifically ocular dryness.[4] Most importantly, these tools do not include any *visual* symptoms related to dry eye, such as blurred vision and visual or ocular fatigue.

Sjögren’s is also underappreciated among ophthalmologists who manage patients with dry eye. In a 2018 survey, approximately half of the ophthalmologists reported referring fewer than 5% of patients for Sjögren’s evaluation, and approximately 20% reported *never* referring any patients.[5] This low referral rate, along with the complexity of diagnosis, likely contributes to long delays in diagnosis of the disease.

We previously reported on the need for a “paradigm shift,” in which physicians managing patients with Sjögren’s should become more familiar with the various ocular manifestations of this multisystem disease.[2] To facilitate this, we need active dissemination of evidence that describes the burden of ocular symptoms and treatments on patients with Sjögren’s, and the resulting impact on various aspects of their lives and overall quality of life.

• OBJECTIVES: We conducted a large cross-sectional survey of adult patients with Sjögren’s to (1) estimate and compare the burden related to dry eye with systemic symptoms; (2) estimate the burden related to ocular treatments;

AJO.com Supplemental Material available at AJO.com.
Accepted for publication May 29, 2020.

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0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2020.05.043

and (3) examine and compare the impact of dry eye with systemic manifestations of Sjögren's on various aspects of patient life.

METHODS

- **SURVEY DESIGN AND PATIENT SAMPLE:** This study was a cross-sectional survey of patients with Sjögren's. Harris Poll, a market research company, developed, reviewed, and refined the survey instrument, with input from the Sjögren's Foundation (formerly the Sjögren's Syndrome Foundation) and a group of 10 volunteers, including patients and healthcare providers. Printed copies of the final survey were mailed to potential respondents in the United States identified from the Sjögren's Foundation patient database. Surveys were mailed once between May 11, 2016, and July 11, 2016. No reminders were sent. Patient responses to the survey were anonymous and entirely voluntary. Respondents were informed that their completion and return of the survey implied their consent to participate. The Western Institutional Review Board approved the survey prospectively (WIRB 20160808 #14329711).

Respondents were considered eligible to be included in this study if they were at least 18 years of age and reported having been diagnosed with Sjögren's by a medical professional.

- **SURVEY DESCRIPTION:** The overall purpose of the Sjögren's Foundation survey was to better understand the experiences of patients with Sjögren's, including symptoms, diagnoses, and disease impact on various aspects of their life. The survey included 7 sections: (A) patient profile (including years of diagnosis and Sjögren's-related conditions and manifestations), (B) frequency and impact of various symptoms, (C) emotional and physical well-being, (D) effect of Sjögren's on quality of life, (E) treatment history, (F) financial and work impact, and (G) demographic information. The current study summarizes aspects of the survey that are relevant to our objectives related to dry eye and ocular manifestations of Sjögren's summarized above.

- **STATISTICAL ANALYSIS:** To estimate the burden related to ocular symptoms (objective 1), we calculated the percentage of respondents who experienced each symptom (1) monthly/almost monthly, (2) daily/almost daily (classified as "significant" dry eye), and (3) daily/almost daily with a major impact on the patient's life (classified as "severe" dry eye). We also stratified these percentages by time since Sjögren's diagnosis, age, sex, race/ethnicity, employment status, receipt of Social Security Disability, and presence of corneal scarring (Supplemental Table 1; Supplemental Material available at AJO.com). We compared percentages by conducting χ^2 tests and computing P values. The burden related to experiencing severe dry eye was then compared with the burden related to experiencing severe levels of other Sjögren's symptoms, such as dry mouth, fatigue, trouble sleeping, dry or itchy skin, and morning stiffness (Table 2). To estimate burden related to ocular treatments (objective 2), we calculated the proportion of respondents using various ocular

TABLE 1. Baseline Characteristics of All Survey Participants (Patients With Sjögren Syndrome)

Characteristic	Result (N = 2,961 Respondents)
Time since diagnosis of Sjögren syndrome, n (%)	
<5 years	758 (26)
5-9 years	622 (21)
10-14 years	478 (16)
15-19 years	362 (12)
≥20 years	611 (21)
Missing or declined to answer	130 (4)
Age, years	
Mean	65.1
Standard deviation	11.7
Minimum	19
Maximum	95
Sex, n (%)	
Women	2,831 (96)
Men	130 (4)
Race/ethnicity,[a] n (%)	
White	2,790 (94)
Black/African American	71 (2)
Asian	43 (1)
American Indian or Alaskan Native	23 (1)
Hispanic or Latino	68 (2)
Hawaiian or other Pacific Islander	2 (0)
Other	18 (1)
Employment status, n (%)	
Employed full time	569 (19)
Employed part time	178 (6)
Self-employed	128 (4)
Not employed, but looking for work	28 (1)
Not employed and not looking for work	48 (2)
Not employed, unable to work owing to disability or illness	331 (11)
Retired	1,398 (47)
Student	11 (0)
Stay-at-home spouse or partner	111 (4)
Declined to answer	159 (5)
Currently receiving Social Security disability owing to Sjögren syndrome, n (%)	
Yes	239 (8)
No	2,683 (91)
Declined to answer	39 (1)

[a] Respondents could select more than 1 response.

TABLE 2. Comparison of Burden of Daily/Almost Daily and Major Impact on Patient's Life ("Severe") of Dry Eye With the 5 Most Frequent Nonocular Symptoms Experienced in the Past 12 Months by Patients With Sjögren Syndrome

		Dry Eye	Dry Mouth	Fatigue	Trouble Sleeping	Dry or Itchy Skin	Morning Stiffness
		Severe	Severe	Severe	Severe	Severe	Severe
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
All respondents	2,961	1,556 (53)	1,422 (48)	1,326 (45)	573 (19)	506 (17)	452 (15)
Time since diagnosis of Sjögren syndrome (years)							
<5	758	348 (46)	296 (39)	360 (48)	174 (23)	127 (17)	106 (14)
5-9	622	318 (51)	280 (45)	296 (48)	143 (23)	113 (18)	107 (17)
10-14	478	255 (53)	239 (50)	203 (43)	83 (17)	82 (17)	73 (15)
15-19	362	199 (55)	194 (54)	154 (42)	57 (16)	66 (18)	62 (17)
≥20	611	371 (61)	341 (56)	263 (43)	93 (15)	97 (16)	87 (14)
Declined to answer	130	65 (50)	72 (55)	50 (39)	23 (18)	21 (16)	17 (13)
Age (years)							
<20	1	0 (0)	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)
20-39	78	35 (45)	22 (28)	43 (55)	16 (21)	13 (17)	12 (15)
40-59	783	373 (48)	330 (42)	364 (45)	184 (24)	122 (16)	146 (19)
60-79	1,800	986 (55)	910 (51)	803 (45)	335 (19)	317 (18)	250 (14)
≥80	299	162 (54)	160 (54)	115 (38)	37 (12)	54 (18)	44 (15)
Sex							
Female	2,832	1,516 (54)	1,387 (49)	1,282 (45)	553 (20)	492 (17)	433 (15)
Male	129	40 (32)	35 (28)	44 (34)	20 (15)	14 (11)	19 (15)
Race/ethnicity							
White	2,790	1,472 (53)	1,335 (48)	1,254 (45)	531 (19)	470 (17)	426 (15)
Black/African American	71	30 (42)	33 (47)	31 (44)	23 (32)	14 (20)	8 (11)
Asian	43	23 (54)	21 (49)	12 (28)	7 (16)	6 (14)	7 (16)
American Indian or Alaskan Native	23	12 (52)	10 (44)	15 (65)	4 (17)	8 (35)	6 (26)
Hispanic or Latino	68	40 (59)	42 (62)	32 (47)	17 (25)	17 (25)	14 (21)
Hawaiian or other Pacific Islander	2	2 (100)	2 (100)	2 (100)	1 (50)	1 (50)	0 (0)
Other	18	8 (44)	10 (56)	9 (50)	3 (17)	2 (11)	3 (17)
Employment status							
Employed, self-employed, or student	886	419 (47)	367 (41)	357 (40)	157 (18)	108 (12)	108 (12)
Not employed and not a student	1,916	1,051 (55)	973 (51)	891 (47)	382 (20)	361 (19)	315 (16)
Declined to answer	159	86 (54)	82 (52)	78 (49)	34 (21)	37 (23)	29 (18)
Currently receiving SSD owing to Sjögren syndrome							
Yes	239	147 (62)	136 (57)	176 (74)	82 (34)	63 (26)	81 (33)
No	2,683	1,394 (52)	1,269 (47)	1126 (42)	484 (18)	434 (16)	358 (13)
Declined to answer	39	15 (39)	12 (31)	24 (62)	7 (18)	9 (23)	13 (33)

SSD = Social Security disability.

All percentages are row percentages.

"Severe" was defined as daily/almost daily AND major impact on patient's life.

treatments, stratified by frequency of dry eye (Table 3). To estimate the impact of dry eye on various aspects of patient life (objective 3), we calculated adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for the associations between significant dry eye and various survey questions related to emotional and physical well-being (Table 4), quality of life (Table 5), work impact (Supplemental Table 2; Supplemental Material available at AJO.com), depression (Supplemental Table 3; Supplemental Material available at AJO.com), and use of systemic immunosuppressive therapy (Supplemental Table 4; Supplemental Material available at AJO.com). For the sake of comparison, Tables 4 and 5 and Supplemental Tables 2-4 also provide corresponding adjusted ORs for significant dry mouth, significant fatigue, current use of disease-modifying antirheumatic drugs (DMARDs) for systemic manifestations of Sjögren's, and diagnosis of lymphoma. Adjusted ORs were calculated using multivariable logistic regression analyses that were adjusted for age, sex, race, and employment status.

TABLE 3. Burden Related to Ocular Treatments in the Past 12 Months by Patients With Sjögren Syndrome

		Dry Eye		
Ocular Treatment	All Participants N = 2,961	Monthly/Almost Monthly or More Frequently (N = 2,835) n (%)	Significant (ie, Daily/Almost Daily) (N = 2,502) n (%)	Severe (ie, Daily/Almost Daily and Major Impact on Patient's Life) (N = 1,556) n (%)
Nonprescription eye drops, artificial tears, or ointments				
Never used	77 (3)	58 (2)	44 (2)	27 (2)
Ever used	2,884 (97)	2,777 (98)	2,458 (98)	1,529 (98)
Currently use	2,684 (91)	2,615 (92)	2,351 (94)	1,478 (95)
Autologous serum drops				
Never used	2,351 (79)	2,247 (79)	1,970 (79)	1,177 (76)
Ever used	610 (21)	588 (21)	532 (21)	379 (24)
Currently use	170 (6)	168 (6)	164 (7)	139 (9)
Tear duct surgery/plugs				
Never used	1,346 (45)	1,263 (45)	1,049 (42)	521 (34)
Ever used	1,615 (55)	1,572 (55)	1,453 (58)	1,035 (66)
Currently use	861 (29)	846 (30)	804 (32)	599 (39)
Antibiotic eye ointments				
Never used	1,351 (46)	1,265 (45)	1,078 (43)	568 (36)
Ever used	1,610 (54)	1,570 (55)	1,424 (57)	988 (64)
Currently use	298 (10)	295 (10)	277 (11)	230 (15)
Adjunctive dry eye therapies				
Never used	1,480 (50)	1,391 (49)	1,166 (47)	609 (39)
Ever used	1,481 (50)	1,444 (51)	1,336 (53)	947 (61)
Currently use	746 (25)	735 (26)	698 (28)	537 (35)

All percentages are column percentages.

RESULTS

• PATIENT SAMPLE: In total, 9,252 paper surveys were mailed, of which 3,072 completed surveys (33%) were returned. We excluded 111 respondents who did not meet our eligibility criteria: 68 were not diagnosed with Sjögren's by a medical professional, 41 were younger than 18 years of age, and 2 did not respond to the survey questions pertaining to our eligibility criteria. This study includes responses from 2,961 patients with Sjögren's.

Almost half of the 2,961 patients (47%) had been diagnosed with Sjögren's within the preceding 10 years (Table 1). The mean age of patients was 65.1 years (standard deviation [SD] 11.7 years). The majority of respondents were women (96%) and white (94%). Almost half of the patients (47%) were retired and 11% were unable to work owing to disability or illness. Fewer than 1 in 5 patients (19%) were employed full time. Eight percent of patients were receiving Social Security disability benefits owing to Sjögren's-related manifestations.

• BURDEN RELATED TO OCULAR SYMPTOMS—DRY EYE: Almost all patients (96%) experienced dry eye monthly/almost monthly or more frequently, and the majority (85%) experienced significant dry eye. More than half (53%) experienced severe dry eye (Supplemental Table 1). The proportion of patients with severe dry eye seemed to increase with greater time since diagnosis of Sjögren's (46% when <5 years to 61% when ≥20 years) and advancing age (45% when 20-39 years to 54% when ≥80 years), suggesting progression of the disease process.

A higher proportion of women than men experienced significant dry eye (85% vs 75%; $P = .001$) and severe dry eye (54% vs 32%; $P < .001$). A similar pattern was observed for employment status: a higher proportion of unemployed patients than employed patients experienced significant dry eye (86% vs 81%; $P = .001$) and severe dry eye (55% vs 47%; $P < .001$). These differences also held when comparing patients who were not currently receiving Social Security disability owing to Sjögren's with those who were. Similar patterns were also observed when examining corneal scarring: a higher proportion of patients with corneal scarring than those without corneal scarring had experienced significant dry eye (96% vs 84%; $P < .001$) and severe dry eye (79% vs 50%; $P < .001$).

• BURDEN RELATED TO OCULAR SYMPTOMS—PHOTOSENSITIVITY: Almost 7 in 10 patients (69%) experienced

TABLE 4. Association Between Various Aspects of Sjögren Syndrome (Exposures) and Emotional and Physical Well-Being (Outcome)

Questions How much do you agree or disagree with each of the following statements about living with Sjögren's?	Dry Eye	Dry Mouth	Fatigue	Disease-Modifying Antirheumatic Drugs (DMARDs)[a]	Diagnosis of Lymphoma
	Significant (ie, Daily/ Almost Daily)	Significant (ie, Daily/ Almost Daily)	Significant (ie, Daily/ Almost Daily)	Current	Ever
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Statements that are construed as "negative" statements					
Living with Sjögren's makes every day a challenge.	3.81 (2.49, 5.86)[b]	2.84 (1.85, 4.34)[b]	11.73 (8.34, 16.48)[b]	1.79 (1.39, 2.31)[b]	1.07 (0.55, 2.11)
I struggle to cope with my Sjögren's.	2.60 (1.77, 3.83)[b]	2.16 (1.50, 3.12)[b]	6.44 (4.88, 8.51)[b]	1.33 (1.10, 1.60)[c]	1.15 (0.70, 1.88)
Living with Sjögren's adds a significant financial burden to my life.	2.11 (1.43, 3.12)[b]	2.60 (1.80, 3.76)[b]	3.11 (2.38, 4.07)[b]	1.47 (1.22, 1.76)[b]	0.89 (0.56, 1.41)
Living with Sjögren's adds a significant emotional burden to my life.	2.22 (1.49, 3.31)[b]	2.14 (1.47, 3.11)[b]	6.00 (4.53, 7.93)[b]	1.33 (1.09, 1.63)[c]	0.94 (0.57, 1.54)
My Sjögren's gets in the way of the things I need to do each day.	2.10 (1.41, 3.11)[b]	2.10 (1.45, 3.05)[b]	9.30 (6.99, 12.38)[b]	1.50 (1.24, 1.82)[b]	0.73 (0.46, 1.15)
I wish there were additional treatments available for my Sjögren's.	3.88 (1.85, 8.13)[b]	2.18 (0.92, 5.17)	3.60 (1.91, 6.78)[b]	2.25 (1.32, 3.82)[c]	1.15 (0.28, 4.77)
Statements that are construed as "positive" statements					
I am able to live a fulfilling life despite having Sjögren's.	1.02 (0.64, 1.64)	0.92 (0.59, 1.43)	0.23 (0.15, 0.36)[b]	0.74 (0.60, 0.93)[c]	0.96 (0.57, 1.61)
Living with Sjögren's isn't that bad.	0.55 (0.37, 0.81)[c]	0.55 (0.38, 0.80)[c]	0.22 (0.17, 0.29)[b]	0.61 (0.51, 0.73)[b]	1.08 (0.68, 1.72)

Multivariable analysis that adjusts for age, sex, race, and employment status.

Outcome variables (rows) – each statement. Defined as: 1 = "Somewhat agree" or "Strongly agree"; 0 = "Somewhat disagree" or "Strongly disagree."

[a] Hydroxychloroquine, methotrexate, azathioprine, mycophenolate, leflunomide, sulfasalazine, etc.

[b] Statistically significant at the 95% confidence level; $P < .001$.

[c] Statistically significant at the 95% confidence level; $P < .05$.

TABLE 5. Association Between Various Aspects of Sjögren Syndrome (Exposures) and Quality of Life (Outcome)

Questions To what extent, if at all, have each of the following aspects of your life been negatively affected by your Sjögren's?	Dry Eye	Dry Mouth	Fatigue	Disease-Modifying Antirheumatic Drugs (DMARDs)[a]	Diagnosis of Lymphoma
	Significant (ie, Daily/ Almost Daily)	Significant (ie, Daily/ Almost Daily)	Significant (ie, Daily/ Almost Daily)	Current	Ever
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Performing activities of daily life (eg, dressing, cooking, cleaning)	3.13 (1.79, 5.47)[b]	2.79 (1.70, 4.57)[b]	9.29 (5.98, 14.45)[b]	1.48 (1.26, 1.74)[b]	1.06 (0.66, 1.69)
Relationships with friends and family	1.67 (0.98, 2.86)	2.58 (1.48, 4.50)[c]	9.25 (5.33, 16.06)[b]	1.38 (1.15, 1.65)[c]	0.60 (0.33, 1.11)
Relationships with spouse/partner	2.24 (1.17, 4.27)[c]	1.68 (0.98, 2.90)	6.37 (3.77, 10.75)[b]	1.13 (0.93, 1.38)	0.78 (0.43, 1.42)
Overall mood	2.42 (1.44, 4.08)[c]	1.92 (1.23, 2.99)[c]	8.09 (5.24, 12.52)[b]	1.15 (0.98, 1.36)	0.71 (0.42, 1.19)
Caring for your children	2.07 (0.80, 5.33)	3.19 (1.12, 9.14)[c]	12.37 (4.47, 34.21)[b]	1.68 (1.22, 2.32)[c]	0.48 (0.14, 1.66)
Job/career or ability to work	3.84 (1.70, 8.70)[c]	2.48 (1.50, 4.10)[b]	8.72 (5.72, 13.28)[b]	1.44 (1.18, 1.75)[b]	1.15 (0.62, 2.13)
School attendance/performance	1.74 (0.65, 4.62)	6.04 (0.80, 45.87)	6.26 (2.42, 16.16)[b]	1.85 (1.20, 2.86)[c]	0.24 (0.03, 1.93)
Participating in hobbies, social activities, and extracurricular activities (eg, play sports, play instruments, join clubs)	2.53 (1.63, 3.95)[b]	1.66 (1.12, 2.45)[c]	9.65 (6.84, 13.62)[b]	1.54 (1.32, 1.81)[b]	0.77 (0.49, 1.22)
Sex life	3.35 (1.85, 6.07)[b]	3.93 (2.21, 6.99)[b]	5.77 (3.93, 8.48)[b]	1.32 (1.10, 1.58)[c]	0.79 (0.47, 1.34)
Ability to be independent	2.62 (1.35, 5.11)[c]	2.53 (1.40, 4.58)[c]	7.24 (4.30, 12.19)[b]	1.43 (1.18, 1.73)[b]	0.93 (0.53, 1.61)
Ability to drive	1.62 (0.77, 3.41)	1.81 (0.90, 3.65)	3.12 (1.84, 5.30)[b]	1.32 (1.04, 1.67)[c]	0.90 (0.44, 1.85)
Traveling or taking a vacation	3.07 (1.76, 5.37)[b]	1.55 (1.02, 2.38)[c]	5.72 (3.92, 8.33)[b]	1.38 (1.17, 1.63)[b]	0.70 (0.43, 1.17)
Remembering details at home or work	2.52 (1.48, 4.30)[c]	2.58 (1.59, 4.21)[b]	11.82 (7.03, 19.87)[b]	1.58 (1.34, 1.87)[b]	0.67 (0.40, 1.15)
Concentrating on a task	2.28 (1.35, 3.85)[c]	2.94 (1.77, 4.88)[b]	8.67 (5.46, 13.75)[b]	1.58 (1.33, 1.87)[b]	0.68 (0.40, 1.16)
Concentrating on more than 1 task at a time	2.29 (1.42, 3.68)[c]	2.48 (1.59, 3.86)[b]	9.20 (6.08, 13.92)[b]	1.66 (1.41, 1.95)[b]	0.70 (0.43, 1.15)
Finding the correct word during conversations	1.69 (1.11, 2.57)[c]	2.22 (1.48, 3.33)[b]	6.13 (4.35, 8.64)[b]	1.51 (1.30, 1.77)[b]	0.62 (0.39, 1.00)
Making adjustments to diet	1.75 (1.11, 2.76)[c]	2.82 (1.76, 4.53)[b]	4.86 (3.37, 6.99)[b]	1.18 (1.00, 1.39)[c]	1.33 (0.84, 2.11)

Multivariable analysis that adjusts for age, sex, race, and employment status.

Outcome variables (rows) – each statement. Defined as: 1 = "A lot of negative impact" or "A great deal of negative impact"; 0 = "Some negative impact" or "no negative impact." Respondents who rated the statement as "Not applicable" were excluded from this analysis.

[a] Hydroxychloroquine, methotrexate, azathioprine, mycophenolate, leflunomide, sulfasalazine, etc.

[b] Statistically significant at the 95% confidence level; $P < .001$.

[c] Statistically significant at the 95% confidence level; $P < .05$.

photosensitivity monthly/almost monthly or more frequently, almost half (49%) experienced significant photosensitivity, and almost a quarter (23%) experienced severe photosensitivity (Supplemental Table 1). Similar to dry eye, an increase in photosensitivity was observed with greater time since diagnosis of Sjögren's and advancing age. Differences by sex, employment status, Social Security Disability status, and corneal scarring were also similarly observed.

- **COMPARISON OF BURDEN RELATED TO DRY EYE VS COMMON NONOCULAR SJÖGREN'S SYMPTOMS:** Table 2 compares the proportion of patients with severe dry eye with the proportions of patients with severe levels of 5 common nonocular Sjögren's-related symptoms: dry mouth, fatigue, trouble sleeping, dry or itchy skin, and morning stiffness. Dry eye was the symptom that impacted the daily life of the largest proportion of patients with Sjögren's (53%), followed by dry mouth (48%), fatigue (45%), trouble sleeping (19%), dry or itchy skin (17%), and morning stiffness (15%). Similar patterns by age, time since diagnosis of Sjögren's, sex, employment status, and Social Security Disability status were observed for the nonocular symptoms as were observed for dry eye and photosensitivity.

- **BURDEN RELATED TO OCULAR TREATMENTS:** Patients with Sjögren's experienced a considerable burden related to ocular treatments (Table 3). Almost all surveyed patients (97%) had used nonprescription eye drops, artificial tears, or ointments, and 91% were currently using them. Approximately half of the patients had used tear duct surgery/plugs, prescription antibiotic eye ointments, and other adjunctive dry eye therapies.

The proportion of patients who had ever used and were currently using each treatment generally increased with increasing frequency and impact of dry eye (Table 3).

- **IMPACT OF DRY EYE AND EXTRAOCULAR MANIFESTATIONS OF SJÖGREN'S ON EMOTIONAL AND PHYSICAL WELL-BEING:** Dry eye had a considerable impact on emotional and physical well-being in patients with Sjögren's, and this impact was at least as strong as the impact of dry mouth (Table 4). For example, compared with patients who did not experience dry eye, those who experienced significant dry eye were almost 4 times as likely to agree that living with Sjögren's makes every day a challenge (adjusted OR 3.81, 95% CI 2.49 to 5.86) and to wish that there were additional treatments for their Sjögren's (adjusted OR 3.88, 95% CI 1.85 to 8.13). Patients with significant dry eye were also more than twice as likely to agree that they struggle to cope with their Sjögren's (adjusted OR 2.60, 95% CI 1.77 to 3.83), that living with Sjögren's adds a significant financial burden (adjusted OR 2.11, 95% CI 1.43 to 3.12), that living with Sjögren's adds a significant emotional burden (adjusted OR 2.22, 95% CI 1.49 to 3.31), and that Sjögren's gets in the way of things they need to do each day (adjusted OR 2.10, 95% CI 1.41 to 3.11).

Most of the above adjusted ORs for the impact of significant dry eye were similar in magnitude to the corresponding adjusted ORs for significant dry mouth, but higher than the adjusted ORs for current use of DMARDs and diagnosis of lymphoma. Notably, none of the adjusted ORs for the impact of diagnosis of lymphoma were statistically significant. As expected, the adjusted ORs for significant fatigue were generally the highest in magnitude. For example, patients with significant fatigue were much more likely to agree that living with Sjögren's makes every day a challenge (adjusted OR 11.73, 95% CI 8.34 to 16.48) and that Sjögren's gets in the way of things they need to do each day (adjusted OR 9.30, 95% CI 6.99 to 12.38).

- **IMPACT OF DRY EYE AND EXTRAOCULAR MANIFESTATIONS OF SJÖGREN'S ON QUALITY OF LIFE, WORK IMPACT, DEPRESSION, AND USE OF SYSTEMIC IMMUNOSUPPRESSIVE THERAPY:** The patterns of the impacts of dry eye and extraocular manifestations of Sjögren's on quality of life, work impact, depression, and use of systemic immunosuppressive therapy (Table 5 and Supplemental Tables 2-4) were similar to the impacts of dry eye and extraocular manifestations on emotional and physical well-being described in the previous section. The adjusted ORs for significant dry eye were similar in magnitude to corresponding adjusted ORs for significant dry mouth, but higher than current use of DMARDs and ever diagnosis of lymphoma. The adjusted ORs for significant fatigue were generally the highest in magnitude.

Here, we summarize the highest adjusted ORs for the impact of significant dry eye on quality of life, work impact, depression, and use of systemic immunosuppressive therapy. Patients with significant dry eye were more than 3 times as likely as patients without dry eye to agree that the following aspects related to their quality of life were negatively affected by their Sjögren's: job/career or ability to work (adjusted OR 3.84, 95% CI 1.70 to 8.70), sex life (adjusted OR 3.35, 95% CI 1.85 to 6.07), activities of daily life (adjusted OR 3.13, 95% CI 1.79 to 5.47), and traveling or taking a vacation (adjusted OR 3.07, 95% CI 1.76 to 5.37) (Table 5).

Patients with significant dry eye were approximately 3 times as likely as patients without dry eye to agree that they had to do the following work-related activities because of their Sjögren's: apply for Social Security Disability (adjusted OR 3.10, 95% CI 1.20 to 8.05), stop or cut back on housework (adjusted OR 2.86, 95% CI 1.88 to 4.36), and modify their living space to accommodate limited mobility (adjusted OR 2.68, 95% CI 1.40 to 5.14) (Supplemental Table 2).

Patients with significant dry eye were more than twice as likely as patients without dry eye to experience at least monthly symptoms of depression (adjusted OR 2.14, 95% CI 1.32 to 3.47) (Supplemental Table 3). Patients with significant dry eye were almost twice as likely as patients without dry eye to be currently using systemic immunosuppressive therapy (adjusted OR 1.94, 95% CI 1.28 to 2.95) (Supplemental Table 4).

DISCUSSION

IN THIS LARGE SURVEY OF 2,961 PATIENTS WITH SJÖGREN'S, we found that ocular manifestations are common and have a significant impact on patient quality of life. Most patients in this study experienced significant dry eye (ie, daily or almost daily), with more than half also experiencing severe dry eye (ie, daily/almost daily dry eye with a major impact on their life). Patients with more chronic disease and older age were more likely to experience severe dry eye, suggesting that dry eye might worsen with time. Women, unemployed patients, and patients with corneal scarring were significantly more likely to experience severe dry eye. Photosensitivity also was a common ocular symptom in our study, with almost 50% of patients experiencing significant photosensitivity and almost 25% experiencing severe photosensitivity. We have also conducted a separate analysis (to be published in a separate paper) that explores further the oral signs and symptoms of Sjögren's and their impact on patient life.

Our findings regarding the ocular manifestations of Sjögren's are consistent with prior studies demonstrating that dry eye significantly impacts patient quality of life.[6–8] We found that dry eye reduced the quality of life in a greater proportion of patients than did other common Sjögren's symptoms, such as dry mouth, trouble sleeping, dry or itchy skin, and morning stiffness. We also found that dry eye had a considerable impact on the emotional, physical, and financial well-being of patients with Sjögren's. For example, compared with patients without dry eye, patients with significant dry eye were almost 4 times as likely to agree that living with Sjögren's made every day a challenge and more than twice as likely to agree that they struggle to cope with their Sjögren's. In addition, those with significant dry eye were more than twice as likely to agree that living with Sjögren's adds a significant financial burden, or that Sjögren's gets in the way of things that they need to do each day. This study points to a significant toll that the ocular manifestations of Sjögren's can have on patients emotionally, physically, and financially. Clinicians managing patients with Sjögren's should proactively assess patients with dry eye as well as have a low threshold for referring patients to an eye care specialist for further management.

We also found that large proportions of patients with Sjögren's have used a variety of ocular treatments, such as nonprescription eye drops, artificial tears, or ointments (almost all patients); tear duct surgery/plugs, antibiotic eye drops, or adjunctive dry eye therapies (each approximately 50% of patients); and autologous serum drops (more than 20% of patients). These are all expensive treatments, both for patients and for the healthcare system. In addition, these treatments contribute greatly to the burden of Sjögren disease management. Despite the variety of treatments used, patients with significant dry eye in this survey were almost 4 times as likely to wish there were additional treatments available for their Sjögren's. Effective modalities to treat dry eye and minimize loss of visual function remain an unmet need.

Our study has some limitations. First, although we had only a 33% response rate, it is either higher than or similar to other studies in the fields of ophthalmology and Sjögren's.[5,7,9,10] Second, the survey relied on patient self-report of physician diagnoses and of treatments received. It is possible that patients may have mischaracterized their diagnosis and/or underreported their prescribed treatments. Third, the survey was conducted in 2016. It is possible that responses would differ if the survey were conducted more recently, but we do not believe that this would have greatly impacted our findings. In future work, we plan to repeat the survey, with longitudinal follow-up, and compare those results with the current findings. Fourth, the current survey did not collect information related to the frequency of, or costs associated with, the use of the various treatments. In future work, we will examine these factors to better characterize the burden related to treatments for ocular manifestations of Sjögren's.

In conclusion, the ocular manifestations of Sjögren's, especially dry eye, are considerable and more burdensome than other key symptoms of the disease. Dry eye can worsen visual function, impact quality of life, and cause significant emotional and financial burden on patients with Sjögren's. Ocular symptoms and signs should be included as an integral component of any tool designed to evaluate Sjögren's. New therapies that specifically target Sjögren's-related dry eye are needed to alleviate this burden and improve patient quality of life.

FUNDING/SUPPORT: THE SJÖGREN'S FOUNDATION FUNDED THE SURVEY DEVELOPMENT AND DEPLOYMENT AND PAID FOR MR Makara's time spent working on this paper, but did not pay the other authors for the conduct of the analysis or writing the paper. Dr Bunya declares financial support from the National Eye Institute (grant number R01 EY026972). Dr McCoy declares funding from the Clinical and Translational Science Award (CTSA) program, through the National Institutes of Health National Center for Advancing Translational Sciences (NCATS) (grant number 1KL2TR002374). Drs Saldanha, Baer, and Akpek did not receive funding for this work. Financial Disclosures: Dr Bunya declares grant support from Bausch & Lomb (for a separate study) and consultant fees from Verily and Celularity, all outside the submitted work. Mr Makara declares employment by the Sjögren's Foundation. Dr Baer declares consultant fees from Bristol-Myers Squibb, AbbVie, Sanofi-Aventis, and Mitsubishi Tanabe Pharma America, all outside the submitted work. Dr Akpek declares grant support from Allergan, W.L. Gore & Associates, the Department of Defense, the National Institutes of Health, and EpiTech, and consultant fees from Regeneron and Novaliq, all outside the submitted work. Drs Saldanha and McCoy declare no other relevant financial disclosures. All authors attest that they meet the current ICMJE criteria for authorship.

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