The Enduring Experience in Dry Eye Diagnosis: A Non-Interventional Study Comparing the Experiences of Patients Living With and Without Sjögren's Syndrome

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ORIGINAL RESEARCH

The Enduring Experience in Dry Eye Diagnosis: A Non-Interventional Study Comparing the Experiences of Patients Living With and Without Sjögren's Syndrome

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ABSTRACT

Introduction: Previous studies have examined the patient experience regarding the diagnosis and management of dry eye disease (DED). The current study explored the ways in which the DED diagnostic pathway differs for those living with and without Sjögren's syndrome (SS), to identify aspects that influence the patient experience and associated quality of life (QoL).

Methods: An observational/descriptive, non-interventional, retrospective, self-reported online survey was conducted among adults living in France, Spain and Italy who were diagnosed with DED (with/without SS), were using topical DED treatments (≥ 6 months), and were not contact lens users. Recruitment was via an online database for non-SS participants and through local patient advocacy groups for SS respondents.

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Results: The analysis included 827 respondents; 416 (50.3%) had SS and 82% were female. The mean age was 55 (SD 11; range 16–99) years. The mean age at diagnosis was 46 (SD 12; range 13–78) years and 50 (SD 10; range 21–73) years for SS and non-SS groups, respectively ($p < 0.0001$). The mean time to diagnosis was extended for SS participants [32 (SD 62) months] versus non-SS individuals [8.6 (SD 28) months ($p < 0.0001$)] and was associated with reduced QoL scores ($r = 0.113$; $p = 0.0169$). More SS participants (31%) consulted ≥ 4 healthcare professionals (HCPs) before DED diagnosis, versus non-SS individuals (6%) ($p < 0.0001$). Diagnosing clinician varied for SS respondents according to country, probably due to differences in healthcare systems/structures. More SS participants viewed their condition as a handicap than a discomfort, reporting greater QoL impact ($p < 0.0001$).

Conclusions: Patient experiences in DED diagnosis vary substantially when comparing SS and non-SS individuals. Time to diagnosis significantly impacts QoL for SS patients, who see more HCPs ahead of DED diagnosis. The number of HCPs consulted before diagnosis and perceptions of DED are important for both groups. Country-specific variations highlight opportunities to improve consistency and efficiency across DED diagnostic pathways. These data should be considered alongside existing evidence from high-quality sources (e.g. clinical records).

Keywords: Country differences; Dry eye disease; Quality of life; Patient experience; Non-Sjögren's syndrome; Sjögren's syndrome; Survey

Key Summary Points

Why carry out this study?

Dry eye disease (DED) is a multifactorial and debilitating condition affecting the ocular surface that is characterized by a vicious circle of tear film instability and hyperosmolarity, resulting in symptoms such as pain, ocular irritation and blurred vision.

Sjögren's syndrome (SS) is a chronic autoimmune disorder and a leading cause of moderate to severe DED.

The current study examined self-reported online patient survey data and aimed to explore the ways in which the diagnostic pathway for DED and associated patient experience may differ for those living with/without SS as well as the aspects that may influence quality of life (QoL).

What was learned from the study?

The length of time taken to obtain a diagnosis of DED was extended for people with SS and was associated with a significant reduction in global QoL score, compared with non-SS survey respondents ($p < 0.0001$).

People with SS also consulted a greater number of healthcare professionals before receiving an accurate DED diagnosis, and this was associated with a negative impact on QoL.

Patient perceptions of DED differed according to whether survey respondents had SS, and were also shown to influence QoL score.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.14192309.

INTRODUCTION

Dry eye disease (DED) is a multifactorial and debilitating condition affecting the ocular surface. Studies suggest that the prevalence of DED may range between 5 and 50%, and symptomatic disease tends to increase with age [1, 2].

The condition is associated with major changes to the structure and function of the tear film and the ocular surface, although further studies are required to fully understand the underlying biological changes that result in the development of DED [2]. Dry eye is characterized by a vicious circle of tear film instability and hyperosmolarity, which leads to increased ocular surface inflammation, damage and neurosensory abnormalities [1–4]. Stinging, burning or scratching sensations can be triggered by neurosensory abnormalities, which may be responsible for the discrepancy between signs and symptoms in DED [1, 2].

Pain, ocular irritation and blurred vision are key symptoms that can limit the ability to perform daily tasks and significantly impact on quality of life (QoL) [5]. DED symptoms may be exacerbated by topical and systemic medications, environmental factors (e.g. air conditioning, computer screen usage) and allergies [6–9]. The economic burden of DED is largely due to indirect societal costs associated with loss of productivity, presenteeism (attendance at work when unable to function effectively due to sickness) and absenteeism (frequent absence from work) [6, 8, 10]. Annual costs for absenteeism and presenteeism alone are estimated at $11,302 per patient with DED [6, 8, 10]. The impact on physical and psychological function (e.g. anxiety and depression) is also well evidenced [7, 9, 10].

The ultimate aim of DED treatment is to improve QoL and ocular comfort while reducing chronic complications. Treatment usually focuses on the use of topical medications. Artificial tears are the first line for all types of DED, high molecular weight hyaluronan eye drops may be helpful for severe dry eye, and lid hygiene (plus lipidic substitutes) should be recommended in cases of Meibomian gland dysfunction (MGD) [11, 12]. Topical steroids can help to relieve signs and symptoms of acute inflammatory flare-up and enable other topical therapies to work more effectively at the ocular surface, but long-term control of inflammation relies on immunomodulatory drugs, such as cyclosporin A and lifitegrast [11–16].

DED is often associated with systemic conditions such as diabetes mellitus and autoimmune diseases [17–19]. Sjögren's syndrome (SS) is among the chronic autoimmune disorders most typically associated with DED [18, 20]. SS is characterized by lymphocytic inflammation of the exocrine glands and epithelia, resulting in salivary and lacrimal gland dysfunction [8, 21]. SS is one of the leading causes of moderate to severe aqueous deficient DED, and accompanying MGD (evaporative dry eye) leads to mixed DED in most cases (evaporative and aqueous deficient) [22, 23]. Although moderate to severe DED is a fundamental aspect of SS, specific criteria have not been developed to support DED diagnosis in people with SS [17].

SS may occur in isolation (primary SS) or alongside other autoimmune conditions (secondary SS), such as rheumatoid arthritis or lupus. Symptoms vary but must include DED and oral dryness [8, 20, 24]. Ocular surface staining score and tear production tests (Schirmer's test with/without anesthesia) play a crucial role in diagnosis [8, 24, 25]. Other symptoms include musculoskeletal pain, fatigue and a number of neurological disorders [8, 20, 24]. SS is predominantly found in females, but estimates concerning the global prevalence of SS have varied widely depending on epidemiological study design and the definition of disease applied [24, 26–28]. However, the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have published a joint definition for classification and diagnostic criteria of SS, with specific criteria concerning ocular symptoms [29, 30]. Population-based European data suggest that primary SS may occur at a rate of approximately 48.9 cases per 100,000, which equates to approximately 30,000 cases in countries such as the UK and France [27]. As is the case with many chronic progressive conditions, symptoms may be associated with physically disabling levels of psychological stress and significantly reduced QoL [7].

This study aimed to examine the patient experience concerning the diagnosis and management of DED for those living with or without SS (non-SS). The study was designed to add further insights to those gained through a previously published survey (conducted in 2013)

examining the experiences of DED patients and aspects of seasonality relating to dry eye symptoms across five European countries: France, Spain, Italy, Germany and the United Kingdom (UK) [31, 32]. The previous survey mainly included subjects who did not suffer from SS, leaving some unanswered questions regarding the potential impact of SS on the care pathway and providing an opportunity to leverage these data to explore patient perceptions in the presence or absence of this long-term and often challenging autoimmune condition.

METHODS

An observational/descriptive, non-interventional, retrospective study was conducted to examine the patient experience accompanying the diagnosis and management pathway of DED in individuals with or without SS, including their perception of disease and the overall associated impact on global QoL scores.

Self-reported data were collected via a specifically designed, 35-question online survey (questionnaire provided in Appendix 1) [32]. All survey respondents completed the same questionnaire (translated into the local language) and were based in France, Spain and Italy. The country of residence was recorded during survey completion. The survey was developed by a specialist healthcare market research provider (Listening Pharma, France) in consultation with a group of DED patients and a small panel of expert clinician advisers from across Europe. The questions were validated for usability and timing on a subset of respondents before being made available online. The study followed the tenets of the Declaration of Helsinki. The survey was approved by the ethical committee of the Société Française d'Ophtalmologie. Participants completed the questionnaire on a voluntary basis and were able to withdraw from the study at any stage during the process.

Before completing the main study survey, participants were required to answer nine screening questions to ensure eligibility. Inclusion criteria comprised a formal DED diagnosis, with or without SS, obtained from a registered healthcare professional (HCP) and regular use of a topical DED treatment for 6 months or more. Participants were excluded if they wore contact lenses.

Data for non-SS participants living in France, Spain and Italy were extracted from the initial online survey conducted in 2013 [32]. These individuals had been recruited via an online database (Lightspeed GMI, Kantar Group, France). Participants with DED who had received a formal clinical diagnosis of SS from an HCP were recruited through their local patient advocacy groups and completed the survey in 2014: Association Française du Gougerot Sjögren et des Syndromes Secs (AFGS), Associazione Nazionale Italiana Malati Sindrome di Sjögren (A.N.I.Ma.S.S.) and Asociación Española de Síndrome de Sjögren (AESS). These patient organizations also provided ethical approval for the survey.

Survey data obtained for non-SS participants who completed the 2013 survey included only individuals aged 40 years and above. SS survey respondents (completing the same questionnaire in 2014) had been allowed to participate in the survey if they were aged 16 years and above. However, the age difference between the study groups (SS and non-SS) was not expected to be a problem, as SS had been previously shown to mainly affect individuals aged between 40 and 60 years of age, with the disease most frequently occurring in people around 50 years of age [33].

Aspects of the Patient Experience Examined and QoL Measures

Data regarding different aspects of the patient experience leading up to the diagnosis of DED were collected via the survey questionnaire. Factors that were examined included time to DED diagnosis, age at DED diagnosis, pharmacological treatments, the number of HCPs consulted before a definitive DED diagnosis was established, and the HCP responsible for providing a DED diagnosis.

Where the type of HCP involved in the diagnostic pathway was reported, options comprised allergy specialist/immunologist, internist, dermatologist, family doctor/general

physician (GP), gynecologist, ophthalmologist, optometrist/optician, rheumatologist and other (participant specified using free text).

Participants indicated whether they perceived their condition as a discomfort, disease, handicap or none of these options. For the purposes of this study, the term "handicap" was described as (and considered to be) the most severe in terms of limiting daily activities, followed by disease and then discomfort.

Respondents reported the global impact of DED on their QoL using a numerical scale ranging from 0 to 10, in which impact on QoL was categorized as low (0 − 3), medium (4 − 6) or high (7 − 10).

Statistical Analysis

Statistical analysis comprised *t* tests for continuous variables (e.g. age, time to diagnosis) and contingency tables. Patient responses were divided into non-overlapping QoL impact categories (low, medium, high). Analysis of variance (ANOVA) with post hoc Tukey and χ^2 test revealed distribution, compared with overall average.

Table 1 Participant demographics

	Non-Sjögren's	Sjögren's	Total
Survey participants/ respondents	411	416	827
Survey participants, by country			
France, *n* (%)	135 (33)	136 (33)	271 (33)
Spain, *n* (%)	147 (36)	94 (23)	241 (29)
Italy, *n* (%)	129 (31)	186 (45)	315 (38)
Mean age (SD, range), years	54 (9, 40–99)	56 (12, 16–88)	55 (11, 16–99)
France	57 (10, 40–78)	61 (10, 34–84)	59 (10, 34–84)
Spain	52 (8, 40–75)	50 (13, 16–88)	51 (10, 16–88)
Italy	52 (9, 40–99)	55 (11, 26–83)	54 (11, 26–99)
Gender			
Male, *n* (%)	124 (30)	21 (5)	145 (18)
Female, *n* (%)	287 (70)	395 (95)	682 (82)

RESULTS

Study Population Demographics

The study population comprised 827 survey respondents with a diagnosis of DED. The analysis included 411 non-SS and 416 SS respondents (Table 1). Among the non-SS participants, 135 were based in France, 147 in Spain and 129 in Italy. Of those with SS, 186 lived in Italy, 136 in France and 94 Spain at the time of the survey (Table 1). Overall, 82% of the study population were female: 95% of SS respondents and 70% of non-SS participants (Table 1). The mean age was 55 (SD 11; range 16–99) years. Mean age was comparable across study groups: 56 (SD 12; range 16–88) years in the SS group versus 54 (SD 9, range 40–99) years in the non-SS group ($p > 0.05$). (Table 1). On average, participants in France were older than those in Spain and Italy across both non-SS and SS groups (Table 1).

The main symptoms of DED highlighted by survey participants were ocular dryness and foreign body sensation. More non-SS respondents remarked on having itchy eyes, feeling burdened and experiencing scratching sensations, while SS participants reported experiencing burning sensations, lack of tears, blurred vision and swollen eyes at greater frequencies. Other symptoms highlighted by both groups included sticky and painful eyes.

Around half of all participants (51%) were in full-time or part-time employment, 33% were retired and 15% were unemployed. Forty-five percent of those with SS and 58% of non-SS participants were full-time or part-time employed. Level of unemployment was comparable across SS and non-SS groups. More individuals with SS were retired compared with non-SS participants, 39% versus 26%,

respectively. Overall, 15.9% of SS respondents and 13.1% of non-SS individuals were retired and below the age of 65 years (the average age for retirement in Europe) at the time of completing the survey.

Age-Related Measures and QoL

There was no overall correlation between age at the time of survey completion and impact on QoL in either group. On average, people with SS were diagnosed with DED at a younger age than non-SS participants (Fig. 1). Mean (SD) age at diagnosis was 46 (SD 12; range 13–78) years in the SS group and 50 (SD 10; 21–73) years in the non-SS group ($p < 0.0001$). Age at diagnosis was weakly (but significantly) correlated with impact on global QoL in the SS group ($r = -0.112$; $p = 0.017$), but no correlation was observed in the non-SS group ($p = 0.24$).

Time Living with DED Symptoms and Timing of Diagnosis

The mean length of time living with symptoms of DED ahead of diagnosis was 11.6 (SD 8.7) years among SS participants and 5.1 (SD 5.8) years in the non-SS group ($p < 0.0001$) (Fig. 2a). The reported length of time living with DED symptoms correlated significantly with the impact on global QoL in the non-SS group ($r = 0.128$; $p = 0.0095$), while only a tendency was observed in the SS group ($r = 0.0625$; $p = 0.204$) (Fig. 2b).

Mean time to diagnosis was 8.6 (SD 28) months among non-SS respondents versus 32 (SD 62) months among SS participants ($p < 0.0001$; Fig. 3). Time to DED diagnosis correlated significantly with impact on global QoL for the SS group ($r = 0.113$, $p = 0.0169$), but not for the non-SS group ($r = 0.071$, $p = 0.15$).

Number and Type of HCPs Consulted

Overall, 64% of SS participants were referred for formal diagnosis and treatment by an HCP, while 61% of non-SS respondents sought diagnosis independently ($p < 0.0001$). The majority of non-SS participants (64%) saw only one HCP before receiving their DED diagnosis, while 67% of SS respondents consulted more than one HCP ahead of diagnosis (Fig. 4a). SS respondents consulted four or more HCPs before diagnosis in

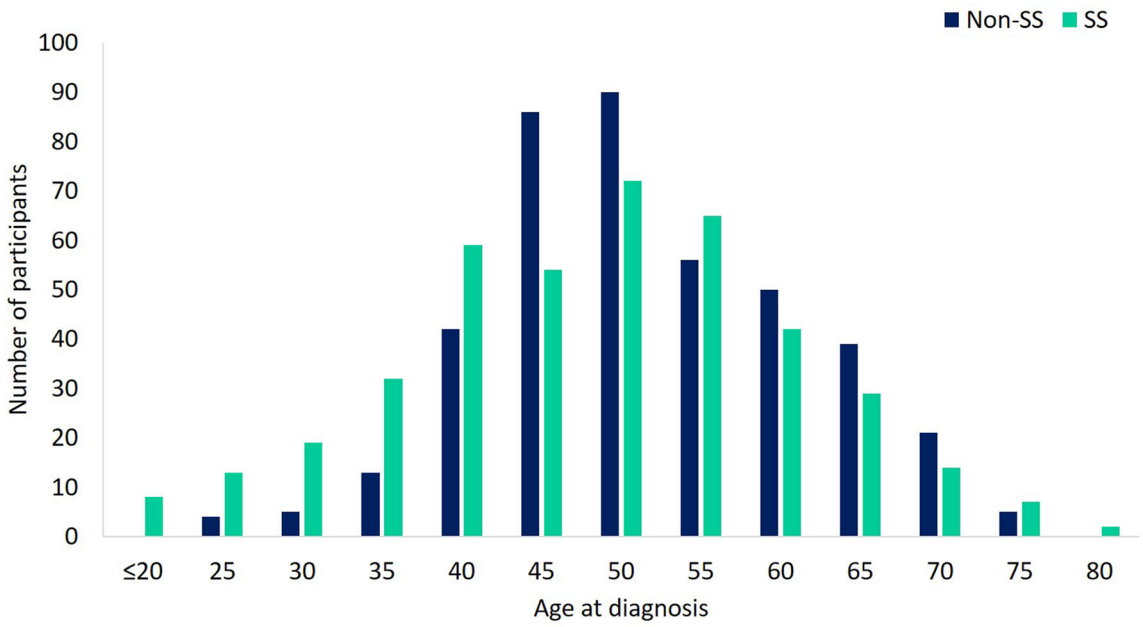

Fig. 1 Age of survey participants at diagnosis

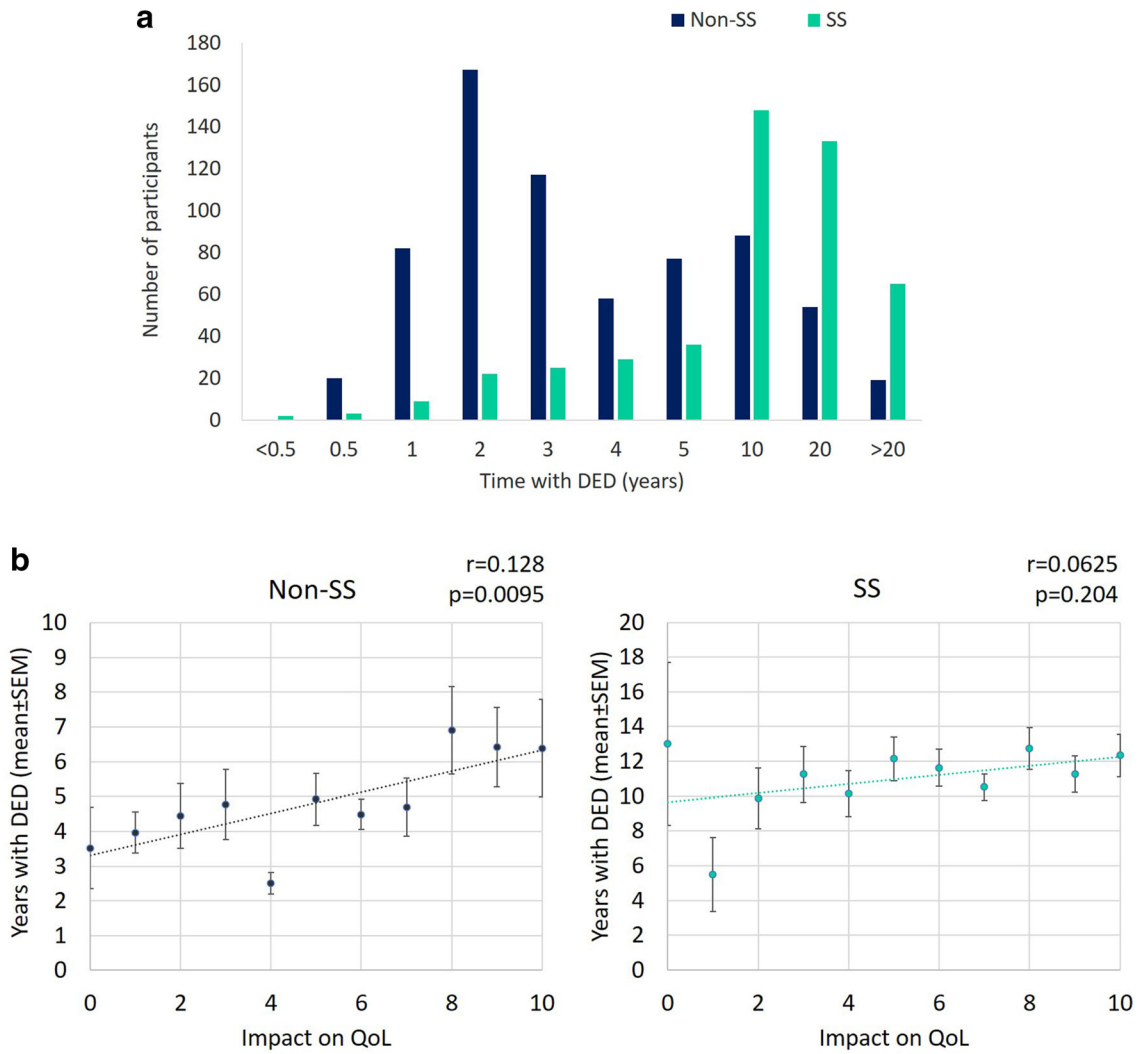

Fig. 2 **a** Length of time that participants had lived with DED. **b** Impact of time with DED on global QoL. Self-reported impact on QoL was categorized as low (0–3), medium (4–6) or high (7–10)

31% of cases, compared with just 6% of the non-SS population ($p < 0.0001$).

Respondents who saw three or four HCPs before receiving a DED diagnosis were significantly more likely to report a higher impact on QoL than those who only needed to see one HCP for diagnosis ($p < 0.0001$ for both groups) (Fig. 4b).

Non-SS participants were diagnosed almost entirely by ophthalmologists (89%), while the SS group were diagnosed by a range of different HCP types: ophthalmologists (38%), rheumatologists (36%), other (26%). Overall, the type of HCP responsible for diagnosing DED did not affect QoL score ($p > 0.05$). However, participants across both groups who consulted an ophthalmologist initially and were not diagnosed, and then went on to be diagnosed by a different HCP (e.g. second ophthalmologist, rheumatologist), reported higher than average impact on global QoL (mean score of 6.57; $p = 0.0056$).

Country Sub-Analysis

Figure 5a shows the proportion of respondents in each country who saw more than one HCP

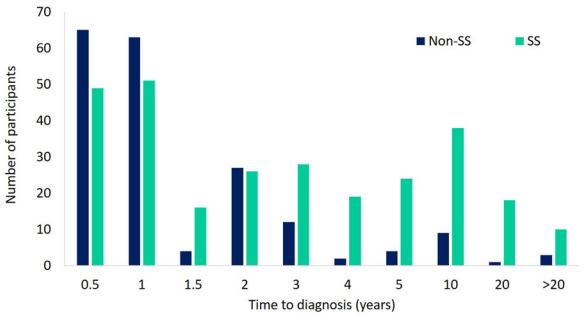

Fig. 3 Length of time to DED diagnosis from symptom onset. Difference between responses to questions: "How long have you had this eye condition" and "When was your dry eyes diagnosis confirmed?"

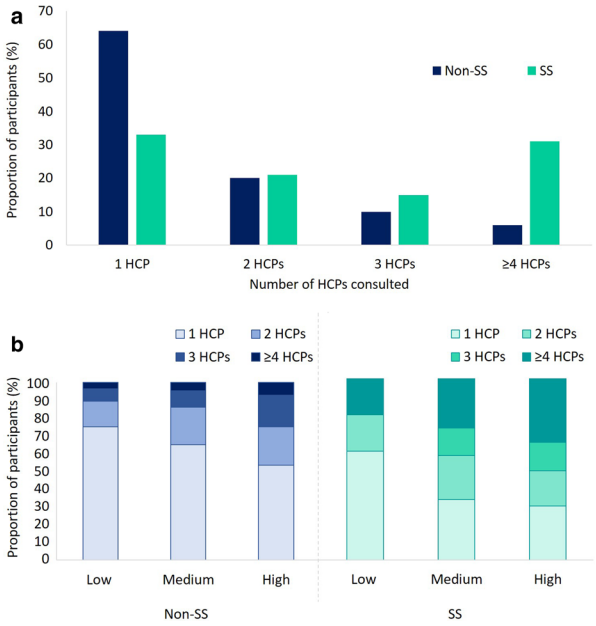

Fig. 4 **a** Number of HCPs consulted ahead of diagnosis and survey responses to the question: "How many different health care professionals did you see regarding your eyes condition before the diagnosis of your dry eyes?" **b** Impact of number of HCPs seen before diagnosis on global QoL score

before receiving their DED diagnosis. Significant variation was observed between countries in both the non-SS and SS groups (non-SS: $p = 0.001$; SS: $p = 0.0086$). However, SS respondents were typically more likely to have consulted more than one HCP ahead of diagnosis in each country.

Ophthalmologists diagnosed the majority of non-SS DED cases in each location, while the predominant diagnosing professional varied in each country for those with SS (Fig. 5b). In France, 52% of SS DED cases were diagnosed by ophthalmologists and just 12% were diagnosed by a rheumatologist, while 53% were diagnosed by rheumatologists and 27% by ophthalmologists in Italy. In Spain, ophthalmologists and rheumatologists were responsible for comparable proportions of DED diagnoses among those with SS (38% and 39%, respectively).

Pharmacological Treatments

In accordance with inclusion criteria, all survey participants were prescribed topical medication (e.g. artificial tears, other non-specified eye drops) for the treatment of DED. However, the survey did not collect data concerning specific categories of eye drops prescribed (e.g. topical anti-inflammatory treatments). The types of treatment used did not appear to impact QoL scores.

Perceptions of DED

SS participants were significantly more likely to consider DED a disease or handicap, while more non-SS individuals tended to perceive DED as a discomfort ($p < 0.0001$). SS respondents who viewed DED as a handicap were more likely to report high impact on global QoL ($p < 0.0001$). Those non-SS individuals who perceived DED to be a disease reported higher impact on global QoL ($p < 0.0001$).

Country sub-analysis showed that a greater proportion of respondents in Spain viewed their condition as a disease, compared with those in France and Italy ($p < 0.0001$). However, respondents in France had a higher tendency to consider DED to be a handicap ($p < 0.0001$), compared with Italy or Spain.

Comorbidities

SS participants reported more comorbidities compared with non-SS participants ($p < 0.0001$). However, the presence of

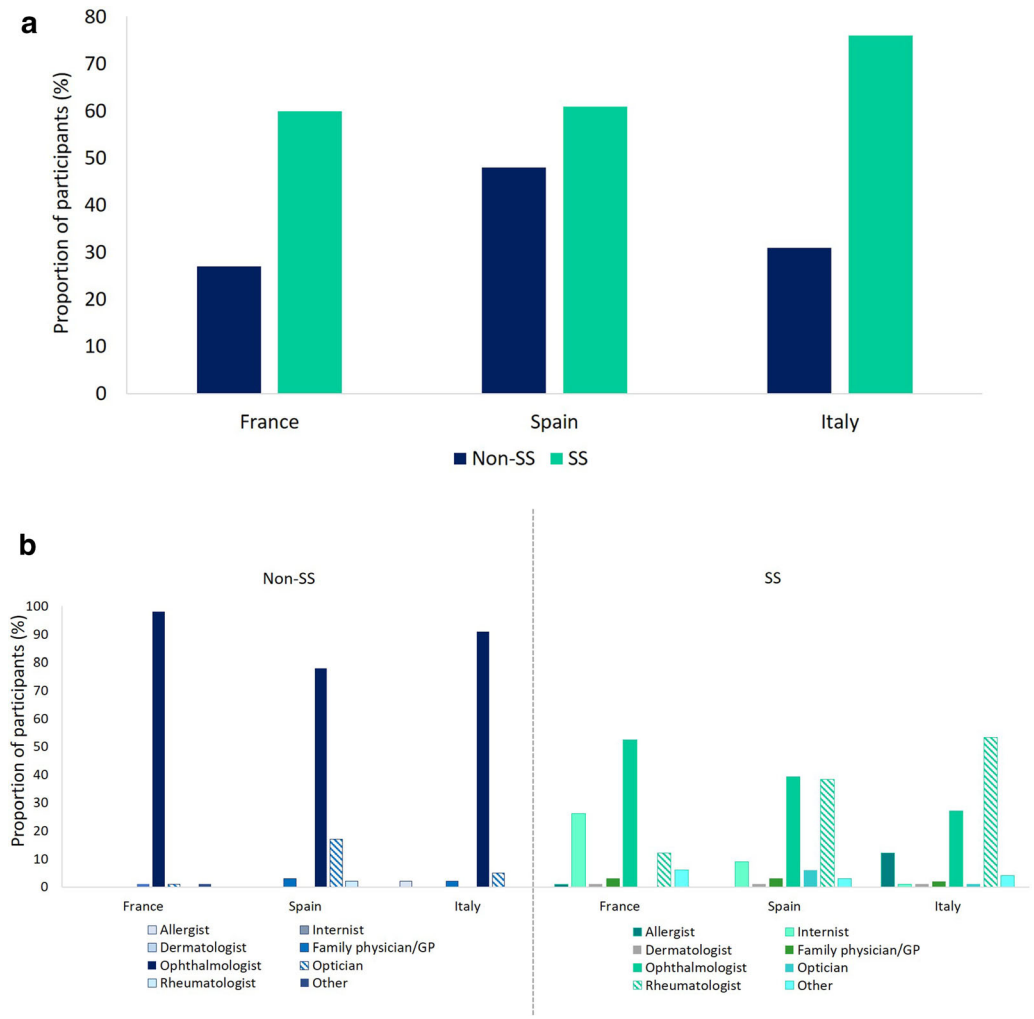

Fig. 5 **a** Number of survey participants who consulted more than one HCP before diagnosis, by country. **b** Diagnosing HCPs, by country

comorbid conditions was associated with a significant impact on QoL for non-SS respondents only ($p = 0.00076$; SS group: $p = 0.085$). The main comorbidities highlighted by respondents were eye disorders (non-SS:19%; SS: 40%), hypertension (non-SS: 18%; SS: 13%), depression (non-SS: 13%; SS: 11%), chronic pain (non-SS: 13%; SS 19%) and rheumatoid polyarthritis (non-SS: 6%; SS: 15%).

DISCUSSION

The study data highlight a number of important factors within the DED diagnostic pathway that may influence the patient experience and associated QoL for people living with/without Sjögren's.

A critical factor predicting impact on QoL was the time taken to obtain an accurate diagnosis. SS respondents reported longer mean time to diagnosis compared with non-SS survey participants. These results are surprising, as DED is a fundamental aspect and defining feature of SS [17, 29, 30]. However, SS and DED are both multifactorial conditions, and diagnosis may be complex. As described by Aragona and Rolando (2013), identification of dry eye requires an understanding of the multiple interrelated factors that define a healthy ocular surface (e.g.

corneal epithelium integrity, tear film osmolarity and stability) as well as the potential for variation according to patient gender, age and ethnicity [24–26, 34]. The clinical situation may also have been further complicated by the number of comorbidities reported by those with Sjögren's, and diagnosis often relies on the sensitivity and specificity of tests available to the clinician [35, 36]. SS patients consult a rheumatologist for management of their autoimmune condition, and DED would be diagnosed and treated secondary to this. Rheumatologists may prescribe lubricating eye drops to reduce the initial severity of dry eye symptoms, which might consequently delay referral to ophthalmology services. Timely referral is important in facilitating appropriate assessment and treatment, and avoidance of epithelial damage and loss of visual function. Delays in diagnosing DED may be as damaging to QoL as the evolution of the disease itself. Obtaining a definitive diagnosis can help patients to manage not only the symptoms of dry eye, but also the emotional and psychological aspects of living with DED [7, 24]. In addition, education at the point of diagnosis is a very important factor in helping patients to effectively understand and self-manage chronic conditions [37].

The need to consult more than one type of HCP before receiving a diagnosis of DED was associated with a significant impact on QoL in both groups. Overall, people with SS tended to see more than one type of HCP before receiving a diagnosis of DED, with approximately one-third consulting four or more clinicians ahead of diagnosis. SS respondents consulted more HCPs in each of the countries examined, although a significantly higher proportion of people with SS in Italy consulted multiple HCPs compared with Spain and France ($p = 0.0086$). The country-specific differences could simply be due to local referral practices and would warrant further investigation to identify key areas for service improvement. Better centralized services should be provided across Europe for patients suspected of having SS.

Participants reported higher than average QoL impact scores in cases where an ophthalmologist had failed to accurately identify DED and a diagnosis was subsequently provided by a different HCP or a second ophthalmologist. The type of HCP responsible for diagnosing DED varied significantly according to country and the presence of SS. Ophthalmologists provided the majority of diagnoses for non-SS individuals (89%), while SS participants were diagnosed by a range of different HCP types (ophthalmologists, rheumatologists, other). SS participants in France were more likely to be diagnosed by an ophthalmologist, while Italian SS individuals tended to be diagnosed by rheumatologists. In Spain, SS participants were equally likely to receive a diagnosis from either an ophthalmologist or a rheumatologist. As highlighted above, it is likely that people with SS begin their DED patient journey with the rheumatologist responsible for managing the autoimmune systemic aspects of Sjögren's, and this could explain why patients in Italy are mainly diagnosed in rheumatology services. In contrast with other countries across Europe, ophthalmologists are the first-line eye care providers in France, as optometrists are not widely recognized and are mainly responsible for dispensing of spectacles only. Patients in France are able to self-refer to ophthalmology services, which could be the reason ophthalmologists diagnosed more SS respondents here. Studies have shown that physicians across multiple specialties may provide different care for patients with similar medical conditions, and geographical location plays a significant role in the variation of clinical practice [38].

Although the survey did not specifically explore which topical eye medications had been prescribed, the type of diagnosing and/or treating HCP would likely have influenced treatment choice or preference. Country-specific variation and restrictions would also be expected to affect prescribing practices in DED management [38]. This highlights a potential area for exploration in future surveys/studies.

DED represents a significant economic burden for healthcare systems; annual costs for services in Europe are estimated to be in the region of $664 per patient (average across France, Germany, Italy, Spain and the UK), excluding expenditure on pharmacological treatments [5, 6, 39]. As many patients self-

manage dry eye symptoms using over-the-counter medicines, the cost of pharmacological treatments for DED is difficult to assess [39]. The cumulative cost of care for each DED case in which multiple HCP opinions are required will also be increased considerably compared with cases where only one consultation or HCP is required to obtain an accurate diagnosis. More integrated, multidisciplinary and collaborative approaches to care provision are believed to provide benefits and efficiencies regarding diagnosis and management of chronic conditions such as DED [40–42].

Perceptions regarding DED clearly impacted QoL across both study groups. Those who perceived DED to be a clinical disease or handicap reported a greater impact on global QoL in the non-SS and SS groups, respectively, compared with individuals who described DED as merely a discomfort. These data are aligned with previous results showing that negative perceptions of disease are associated with poorer QoL measures [32]. Participants with SS were more likely to regard DED as a disease or handicap than non-SS individuals. Ongoing perceptions of disease or handicap associated with a chronic condition, such as SS, may influence global QoL measures over time, and HCPs working in this area should be aware of the cumulative impact that such perceptions can have on each patient's life. The multilingual nature of the survey provides some interesting insights concerning the ways in which people may describe or perceive DED according to their country of residence. For example, the terms "handicap" and "disease" (used in the survey questionnaire) might have different connotations regarding severity of impact in France compared with Italy and Spain. Similarly, country-specific healthcare, insurance and DED management systems may also have influenced disease perception and terminology [32]. This might have implications for the reimbursement of healthcare costs. For example, a person in France who is registered as having a handicap or diagnosed with a severe chronic disease, such as SS, will have future healthcare costs paid for them by the authorities. Severity of disease and subsequent perceptions of dry eye may also be influenced by country-specific environmental factors, such as levels of humidity and use of air conditioning. For example, hot and dry climates or environments where use of air conditioning is widespread will be associated with higher rates of DED exacerbations, and patients may therefore perceive their symptoms to be a disability or handicap rather than a source of discomfort [31].

Strengths and Limitations of the Study

The self-reported evidence obtained via the online survey design provided access to psychological and QoL measures that would be challenging to obtain under conventional clinical trial conditions. Participants were able to provide honest, anonymous and independent information concerning their experience, with the knowledge that their diagnosing HCP would not have access to this information. However, this approach relies on the accuracy of the self-reported information submitted, without the means to validate the data via clinical records, which may have provided a more reliable data source.

The analysis was based upon the outcomes of two separate surveys, which were conducted just one year apart. Some inconsistencies existed concerning the matching of participants across age groups (the SS group included younger participants). However, this is reflective of real life in that DED with SS tends to develop at an earlier age, and non-SS is commonly associated with advancing age and often related to menopause in females. Mean age at survey completion was comparable across the study groups, and no overall correlation was observed concerning age and global QoL scores. Gender differences across the groups may have influenced perceptions of disease and QoL (a higher proportion of the SS group were female). Future studies should ensure consistency of demographics and could, for example, be conducted with patients attending ophthalmology clinics where access to clinical records would allow information to be checked. The survey was designed specifically to explore the patient experience in DED diagnosis in the real-world setting. It provided an opportunity for

respondents to share their perspectives with the aim of increasing understanding of a broader spectrum of factors that affect their QoL, which may not be captured using traditional validated tools. Similar studies or surveys in the future may benefit from a blended approach, which includes the use of high-quality validated tools or questionnaires (e.g. DEQ-5) and/or clinical records alongside self-reported information, with analyses conducted to compare and contrast the data collected via both methods.

CONCLUSIONS

Self-reported online survey data from dry eye patients provide valuable additional insights when considered alongside existing evidence from high-quality sources such as validated QoL questionnaires and clinical records. The survey data suggest that patients living with DED and SS have substantially different experiences from those without Sjögren's. Delays in diagnosis and the number of HCPs consulted before dry eye is effectively diagnosed are key factors impacting the patient experience and reported QoL, as are perceptions of disease. Improved education and emphasis on accurate diagnosis of DED, particularly for those with SS, would be of benefit for clinicians practicing in Europe and for their patients. Simplified referral pathways that prioritize the requirement for specialist ophthalmologist examination should reduce the time taken to identify DED and the number of HCPs consulted, improving the efficiency and accuracy of diagnosis as well as associated QoL outcomes.

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Sindrome di Sjögren (A.N.I.Ma.S.S.), and Asociación Española de Síndrome de Sjögren (AESS). The study complied with the Tenets of the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All respondents gave consent to survey participation, acknowledging provided information would remain anonymous and confidential, and they could discontinue it at any time. Survey participants were required to give informed consent before completing the online survey and were able to withdraw from the study at any stage. Upon providing informed consent, survey participants also gave permission for data to be published.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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