Utilisation of primary healthcare services by Sjögren's syndrome patients in the Community of Madrid and associated factors: a population-based cross-sectional study

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Abstract

Objective

To describe the utilisation of primary health care (PHC) services and factors associated with its use by patients diagnosed with Sjögren's syndrome (SS).

Methods

Population-based cross-sectional cohort of SS patients in Madrid, Spain (SIERMA). Sociodemographic, diagnostic, clinical and PHC service utilisation variables were studied by bivariate analyses and regression models.

Results

A total of 4,778 SS patients were included, 65.2% classified as primary SS (pSS), while 34.8% associated with another autoimmune disease (associated SS). Mean age was 64.3 years, and 92.8% of the patients were women. A total of 87.5% used PHC services, with a mean of 19.8 consultations/year. The general practitioner was the most visited health professional, with a mean of 10.9 consultations/year, followed by the nurse, with a mean of 5.7. Characteristics associated with a greater use of PHC services in SS patients were associated SS, higher adjusted morbidity groups (AMG) risk level and older age. Additional factors included symptoms such as dry mouth, fatigue, dry vagina and joint and muscle pain; comorbidities such as atrial fibrillation, diabetes, hypertension, solid malignant neoplasms, coronary heart disease and chronic obstructive pulmonary disease; and treatments such as sterile saline solution, corticosteroids, opioids and biologic disease-modifying anti-rheumatic drugs.

Conclusion

Most SS patients used PHC services during the study period, and the mean number of consultations was remarkably high. Utilisation was mainly associated with AMG risk level, ageing, glandular and extra-glandular symptoms, substantial comorbidities and various treatments. An optimised design of PHC policies will facilitate early diagnosis, improved management and better quality of life for SS patients.

Key words

Sjögren's syndrome, epidemiology, use of services, primary health care

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Received on June 21, 2023; accepted in revised form on July 17, 2023.

Funding: this work received funding for English language editing from the Foundation for Biosanitary Research and Innovation in Primary Care in Madrid, Spain.
The authors received no direct compensation related to the development of this manuscript.

Competing interests: none declared.

Introduction

Sjögren's syndrome (SS) is a systemic chronic autoimmune disorder characterised by lymphocytic infiltration of the exocrine glands caused by the production of proinflammatory cytokines by epithelial cells, which leads to glandular dysfunction and consequent irreversible tissue damage and B-cell dysfunction (1). The principal targets are the lacrimal and salivary glands associated with clinical manifestations of dry eyes (xerophthalmia) and dry mouth (xerostomia), referred to as sicca syndrome (2). In most cases, the clinical presentation of SS is phenotypically polymorphic, with extra-glandular involvement affecting joints, muscles, skin, lung, heart, liver or kidney, along with the gastrointestinal, endocrine, central and peripheral nervous systems. Moreover, the impaired function of the immune system confers a high risk of lymphoproliferation (3).

SS is classified into primary SS (pSS), when it appears alone, and into associated SS, when it occurs in association with other autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, limited and progressive systemic sclerosis or vasculitis (4).

Several studies of SS performed in recent years have estimated a prevalence between 1/10,000 and 483/10,000 inhabitants (5–7). A systematic review demonstrated that women are the most consistently affected, showing a female:male ratio of almost 11:1 (5). SS is commonly diagnosed in the fifth decade of life, although most patients present the first clinical manifestations years before its diagnosis (8).

To date, the diagnosis of SS is undeniably a difficult task due to its heterogeneous clinical manifestations and the lack of universally standardised diagnostic criteria (9). Although the Sjögren's Foundation achieved a reduction in the average diagnosis delay from 6 to 2.8 years in 2018 (10), this delay still results in a worse quality of life for patients and a higher use of healthcare services, which imply elevated costs for the healthcare system owing to years of incorrect diagnostic tests and treatments (11). This delay is worsened because of insufficient awareness and knowledge of the syndrome among healthcare professionals, especially in primary health care (PHC) settings, thereby driving an absence of established clinical practice guidelines and pathways for the management of patients (12).

Addressing the above-mentioned challenges directly through PHC by understanding the implications of the condition for the health service and by ameliorating the allocation of resources will ultimately enrich the quality of life of patients, improve clinical outcomes and reduce overall costs. However, little is known about PHC service utilisation and related factors in patients with SS. The few published studies concur that SS patients make remarkable use of PHC services, registering a high number of consultations with different healthcare professionals for a wide variety of reasons and generating high healthcare costs (13-19). There is an urgent need to elucidate the details of PHC utilisation, with the purpose of optimising healthcare resources and services for SS patients.

This research was developed within the Horizon2020 European Union funded project "HarmonicSS" (HARMONIzation and integrative analysis of regional, national and international cohorts on primary Sjögren's syndrome towards improved stratification, treatment and health policy making), a research and innovation programme designed to successfully harmonise and integrate the maximum amount of data from the largest European cohorts of pSS patients, with the mission of answering some major clinical unmet needs and public healthcare requirements (20).

The aim of the present study was to describe the utilisation of PHC services and the differences in utilisation by type of SS and sex as well as the associated factors in a population-based wide cohort of patients with SS in the Community of Madrid.

Methods

Study design

This was a population-based cross-sectional observational study.

Setting

The research was carried out in the Community of Madrid, Spain, which

had 6,401,162 citizens registered in the municipal census records in 2015.

Participants

The included patients were SS cases confirmed by a trained physician who evaluated all SS patients (initially as unspecified SS) in the Regional Registry for Rare Diseases of the Community of Madrid (SIERMA) (21) for eligibility by examining each clinical diagnosis in every individual's medical history and determining whether they met the classification or exclusion criteria according to the 2002 American-European Consensus Group (AECG) (22), the 2012 American College of Rheumatology (ACR) (23) or the 2016 ACR/European League Against Rheumatism (EULAR) (24). The SIERMA database, as well as case identification and case selection, are explained in detail in previous research by Barrio-Cortes *et al*. (7).

This study was approved by the Drug Research Ethics Committee of the 12 de Octubre University Hospital and received a favourable report from the Local Research Commission of the Primary Care Management of Madrid. All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was not required because the manuscript does not include any individual personal information since the data were obtained from a secondary database with anonymised and dissociated information as stipulated by legislation.

Data sources and variables

The analysed variables were sociodemographic (age, sex and country of birth), diagnostic (classification as pSS or associated SS and time from the date of SS diagnosis registered in the electronic clinical record until the date of data collection), and clinical (risk levels by adjusted morbidity groups [AMGs], symptoms related to SS reported to PHC [Supplementary Table S1], associated comorbidities [Suppl. S2] and drugs prescribed [Suppl. Table S3]). These variables were obtained from SIERMA and the PHC electronic health record in July 2015. Variables for the use of PHC services (number of annual consultations and type of healthcare professional [general practitioner, nurse, administrative, physiotherapist, dentist, dental hygienist, midwife, social worker, psychologist or others]) were collected from the PHC electronic health record throughout the span of a year, from June 30, 2015, to June 30, 2016.

The AMG stratification tool classifies the population into low risk, medium risk, high risk or without risk according to the patient's comorbidity and complexity diagnostics codes recorded in the electronic health record (25). This morbidity measurement tool has been included in the PHC electronic health record of the Community of Madrid to assist in the management of chronic patients (26) and has proven its validity compared to other similar tools, such as clinical risk groups (CRGs) or adjusted clinical groups (ACGs) (27).

Statistical methods

To characterise the sample, descriptive statistics were calculated for all the variables in the study. Categorical variables are defined as counts and percentages, whereas quantitative characteristics are presented as the means and medians and their corresponding standard deviation and interquartile range, respectively, as dispersion parameters. The distribution of quantitative data was determined through the Kolmogorov-Smirnov test. Bivariate analyses were executed by applying chi-square tests to analyse the relationship between SS classification and categorical data, while parametric or non-parametric tests were employed to evaluate the connection between SS classification and quantitative data. To analyse the factors associated with the use of PHC services, we considered the number of total contacts with the health system as the dependent variable and clinical and demographic variables as covariates of a regression model. Healthcare utilisation data, as the total contacts with the health system, are typically non-negative data that exhibit substantial positive skewness and a mass at zero for non-users, as in our study, for those patients who did not have any access to PHC services in the observation period. We therefore tested the following regression models: Poisson regression, negative binomial (NB) regression, and the hurdle model (logit and truncated at zero negative binomial) (28). We then used the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) to evaluate the performance of the abovementioned models and found that the hurdle model with a negative binomial distribution was adequate compared to the others. All statistical analyses were performed using the statistical software IBM SPSS Statistics v. 25 (IBM Corp., Armonk, New York, USA) and STATA Software v. 17 (Stata Corporation, College Station, TX).

Results

A total of 4,778 SS cases were confirmed in the SIERMA database, 65.2% of which were pSS and 34.8% of which were associated SS. Women constituted 92.8% of the population, and 86.7% were born in Spain. The mean age was 64.3 years (SD=15.4), 67.3 (SD=14.8) for men and 64.1 (SD=15.5) for women, while the average time since diagnosis was 5.8 years (SD=5.0). According to the AMG risk classification, 1,650 (34.5%) were at no risk, 1,309 (27.4%) were low-risk patients, 1,145 (24.0%) were medium-risk patients, and 674 (14.1%) were high-risk patients, with significant differences between sexes. Among the 3,116 pSS cases, 93.2% were female, and 87.6% were Spanish. The mean age was 64.1 (SD=15.6), 66.7 (SD=15.7) for males and 63.9 (SD=15.5) for females. The time from diagnosis was 5.6 years (SD=4.8); 33.3% of patients were without risk, 29.4% had low risk, 24.0% had medium risk and 13.4% had high risk, with significant differences between sexes. In contrast, among the 1,662 associated SS patients, 92% were female, and 85% were born in Spain. The average age was 64.7 (SD=15.2) years, with 68.4 (SD=13.3) years for men and 64.4 (SD=15.3) years for women. The time elapsed from diagnosis was 6.1 years (SD=5.4), and 36.9% were no risk patients, while 23.7% were low risk, 23.9% were medium risk, and 15.5% were high risk. Differences stratified by type of SS and sex are shown in Table I. The most common symptoms related to SS reported in PHC were fatigue (29.2%, 21.5% for males and 29.8% for

Table I. Characteristics of patients with Sjögren's syndrome (SS) according to type of SS and sex.

Characteristic n (%)	SS 4,778 (100)			Primary SS 3,116 (65.2)			Associated SS 1,662 (34.8)			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0[a])	Female 1,529 (92.0)	*p*	
Age*										
Mean (SD)	67.3 (14.8)	64.1 (15.5)	[d]	66.7 (15.7)	63.9 (15.5)	[c]	68.4 (13.3)	64.4 (15.3)	[c]	
Median (IQR)	69 (57-79)	65 (53-76)		69 (55-80)	65 (53-76)		69 (59.5-79)	65 (53-77)		
Country of birth										
Spain	312 (90.7)	3,830 (86.4)	[c]	189 (89.6)	2,540 (87.4)		123 (92.5)	1,290 (84.4)	[c]	[a]
Other	32 (9.3)	604 (13.6)		22 (10.4)	365 (12.6)		10 (7.5)	239 (15.6)		
Time from diagnosis*										
Mean (SD)	5.4 (4.2)	5.8 (5.1)		5.0 (4.1)	5.6 (4.8)	[c]	5.9 (4.2)	6.1 (5.5)		[a]
Median (IQR)	5 (2-8)	5 (2-9)		4 (2-8)	5 (2-8)		5 (2-9.5)	5 (2-9)		
Risk level by AMG										
No risk	146 (42.4)	1,504 (33.9)	[d]	90 (42.7)	947 (32.6)	[c]	56 (42.1)	557 (36.4)	[c]	[b]
Low	66 (19.2)	1,243 (28.0)		44 (20.9)	871 (30.0)		22 (16.5)	372 (24.3)		
Medium	71 (20.6)	1,074 (24.2)		44 (20.9)	704 (24.2)		27 (20.3)	370 (24.2)		
High	61 (17.7)	613 (13.8)		33 (15.6)	383 (13.2)		28 (21.1)	230 (15.0)		

AMG: adjusted morbidity group; IQR: interquartile range; SD: standard deviation.
* Age and time from diagnosis are measured in years.
[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

Table II. Main symptoms of patients with Sjögren's syndrome (SS) reported in PHC according to type of SS and sex.

Symptoms n (%)	SS 4,778 (100)			Primary SS 3,116 (65.2)			Associated SS 1,662 (34.8)			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0)	Female 1,529 (92.0)	*p*	
Fatigue	74 (21.5)	1,320 (29.8)	[c]	48 (22.7)	946 (32.6)	[c]	26 (19.5)	374 (24.5)		[b]
Dry eye	80 (23.3)	1,082 (24.4)		53 (25.1)	731 (25.2)		27 (20.3)	351 (23.0)		
Muscle pain, myalgia or fibromyalgia	46 (13.4)	1,016 (22.9)	[d]	25 (11.8)	727 (25.0)	[d]	21 (15.8)	289 (18.9)		[b]
Dry mouth	57 (16.6)	930 (21.0)		40 (19.0)	639 (22.0)		17 (12.8)	291 (19.0)		[a]
Cough	63 (18.3)	883 (19.9)		40 (19.0)	570 (19.6)		23 (17.3)	313 (20.5)		
Dry vagina	-	602 (13.6)	[d]	-	430 (14.8)	[d]	-	172 (11.2)	[d]	[b]
Joint pain, swelling or stiffness	29 (8.4)	565 (12.7)	[c]	21 (10.0)	411 (14.1)		8 (6.0)	154 (10.1)		[b]
Dysphagia	37 (10.8)	555 (12.5)		23 (10.9)	395 (13.6)		14 (10.5)	160 (10.5)		[a]
Lymphadenopathy	25 (7.3)	466 (10.5)		17 (8.1)	327 (11.3)		8 (6.0)	139 (9.1)		[a]
Purpura	37 (10.8)	351 (7.9)		28 (13.3)	238 (8.2)	[c]	9 (6.8)	70 (4.6)		
Gastroesophageal reflux	23 (6.7)	359 (8.1)		15 (7.1)	248 (8.5)		8 (6.0)	111 (7.3)		
Raynaud	30 (8.7)	237 (5.3)	[c]	15 (7.1)	128 (4.4)		15 (11.3)	109 (7.1)		[b]
Neuritis	31 (9.0)	235 (5.3)	[c]	19 (9.0)	165 (5.7)		12 (9.0)	113 (7.4)	[c]	
Swollen glands	15 (4.4)	112 (2.5)		12 (5.7)	80 (2.8)	[c]	3 (2.3)	32 (2.1)		
Dry skin	3 (0.9)	53 (1.2)		2 (0.9)	37 (1.3)		1 (0.8)	16 (1.0)		
Pericarditis	4 (1.2)	28 (0.6)		2 (0.9)	13 (0.4)		2 (1.5)	15 (1.0)		[a]

[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

females); dry eye (24.3%); muscle pain, myalgia or fibromyalgia (22.2%, 13.4% in men and 22.9 in women); dry mouth (20.7%); cough (19.8%); dry vagina (13.6% of women); joint pain, swelling and stiffness (12.4%, 8.4% for males and 12.7% for females); and dysphagia (12.4%). Among the pSS patients, the main recurrent symptoms were fatigue (31.9%, 22.7% of men and 32.6% of women); dry eye (25.2%); muscle pain, myalgia and fibromyalgia (24.1%, 11.8% of males and 25.0% of females); and dry mouth (21.8%). Among the associated SS patients, the most prevalent manifestations were fatigue (24.1%); dry eye (22.7%); cough (20.2%); and muscle pain, myalgia and fibromyalgia (18.7%). The main symptoms of patients with SS and their differences by type of SS and sex are described in Table II.

The most common comorbidity suffered by SS patients was hypertension, affecting 40.2% of the participants in

Table III. Main comorbidities of patients with Sjögren's syndrome (SS) according to subtype of SS and sex.

Comorbidity n (%)	SS 4,778 (100)			Primary SS 3,116 (65.2)			Associated SS 1,662 (34.8)			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0)	Female 1,529 (92.0)	*p*	
Hypertension	151 (43.9)	1,769 (39.9)		85 (40.3)	1,127 (38.8)		66 (49.6)	642 (42.0)		[a]
Lipid disorder	115 (33.4)	1,448 (32.7)		66 (31.3)	966 (33.3)		49 (36.8)	482 (31.5)		
Osteoarthritis	86 (25.0)	1,239 (27.9)		45 (21.3)	829 (28.5)	[c]	41 (30.8)	410 (26.8)		
Osteoporosis	19 (5.5)	1,123 (25.3)	[d]	9 (4.3)	743 (25.6)	[d]	10 (7.5)	380 (24.9)	[d]	
Depression	40 (11.6)	966 (21.8)	[d]	27 (12.8)	669 (23.0)	[d]	13 (9.8)	297 (19.4)	[c]	[a]
Rheumatoid arthritis	98 (28.5)	872 (19.7)	[d]	-	-	-	98 (73.3)	872 (57.0)	[d]	[b]
Hypothyroidism	23 (6.7)	947 (21.4)	[d]	13 (6.2)	651 (22.4)	[d]	10 (7.5)	296 (19.4)	[c]	[a]
Obesity	32 (9.3)	576 (13.0)		19 (9.0)	406 (14.0)		13 (9.8)	170 (11.1)		[a]
Solid malignant neoplasm	56 (16.3)	431 (9.7)	[d]	31 (14.7)	294 (10.1)	[c]	25 (18.8)	137 (9.0)	[d]	
Type II diabetes	60 (17.4)	388 (8.8)	[d]	36 (17.1)	263 (9.1)	[d]	24 (18.0)	125 (8.2)	[d]	
Systemic lupus erythematosus	19 (5.5)	389 (8.8)	[c]	-	-	-	19 (14.3)	389 (25.4)	[c]	[b]
COPD	17 (4.9)	343 (7.7)		11 (5.2)	244 (8.4)		6 (4.5)	99 (6.5)		[a]
Atrial fibrillation/flutter	31 (9.0)	256 (5.8)	[c]	18 (8.5)	150 (5.2)		13 (9.8)	106 (6.9)		[a]
Coronary heart disease	41 (11.9)	184 (4.1)	[d]	26 (12.3)	119 (4.1)	[d]	15 (11.3)	65 (4.3)		[d]
Heart failure	14 (4.1)	204 (4.6)		5 (2.4)	107 (3.7)		9 (6.8)	97 (6.3)		[b]
Systemic sclerosis	8 (2.3)	172 (3.9)		-	-		8 (6.0)	172 (11.2)		[b]
Mixed connective tissue disease	6 (1.7)	61 (1.4)		-	-		6 (4.5)	61 (4.0)		[b]
Idiopathic inflammatory myopathies	2 (0.6)	36 (0.8)		-	-		6 (4.5)	36 (2.4)		[b]
Lymphomas	3 (0.9)	26 (0.6)		2 (0.9)	18 (0.6)		1 (0.8)	8 (0.5)		
Coeliac disease	1 (0.3)	25 (0.6)		1 (0.5)	21 (0.7)		0	4 (0.3)		
Leukaemia	2 (0.6)	16 (0.4)		1 (0.5)	11 (0.4)		1 (0.8)	5 (0.3)		
Vasculitis	2 (0.6)	13 (0.3)		-	-		2 (1.5)	13 (0.9)		[b]

COPD: chronic obstructive pulmonary disease.
[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

the study and showing a lower prevalence in pSS (38.9%) than in associated SS (42.6%). The second most frequent comorbidity was lipid disorder (32.7%), followed by osteoarthritis (27.7%) and osteoporosis (23.9%), which had a significantly higher prevalence in women. This was followed by depression (21.1%) and hypothyroidism (20.3%), both of which had higher rates in pSS patients and in females. More than half of associated SS subjects (58.4%) suffered from rheumatoid arthritis, which was present in 73.3% of associated SS men and in 57.0% of associated SS women. The most common autoimmune diseases in associated SS individuals were systemic lupus erythematosus (24.5%, present in 14.3% of males and 25.4% of females) and systemic sclerosis (10.8%). Differences by type of SS and sex are shown in Table III.

Regarding the main SS-related treatments prescribed, anti-inflammatory drugs were the most commonly used drugs in 31.9% of patients; they were used in 28.9% of pSS patients and 37.4% of associated SS patients and in 25.6% of men and 32.4% of women. The next most common treatment was topical ophthalmic therapies in 31.2% (32.4% of pSS patients and 29.0% of associated SS patients), followed by corticosteroids in 28% (15.6% of pSS patients and 51.3% of associated SS patients) and conventional immunosuppressive drugs and non-biologic disease-modifying anti-rheumatic drugs (DMARDs) in 26.0% (19.2% of pSS patients and 38.6% of associated SS patients). The differences among the main drugs prescribed by type of SS and sex are shown in Table IV.

Regarding the use of services, 4,182 (87.5%) patients experienced at least one interaction with the PHC system during a one-year period, including 88.7% of pSS patients and 85.4% of associated SS patients and 83.1% of men and 87.9% of women. A total of 86.8% consulted the general practitioner (GP) (87.8% of pSS patients and 85.0% of associated SS patients, 82.8% of men and 87.1% of women), whereas 74.0% visited the nurse and 26.5% visited the administrative department. The overall total of appointments calculated for this time interval was 94,470. More than half of the contacts were with the GP, 29.0% with nurses, 8.4% with administrative personnel and 3.1% with physiotherapists. Differences by type of SS and sex are shown in Table V.

The mean number of consultations/year with PHC services was 19.8 (SD=20.0), which increased to 22.6 when removing subjects without any PHC contact from the analysis. pSS subjects registered a mean of 18.6 (SD=17.8) consultations, and associated SS patients registered a mean of 22.0 (SD=23.4) consultations. The most common provider requested by the patients was the GP, with a mean of 10.9 (SD=9.9) interactions per year, 10.6 (SD=9.5) for pSS patients

Table IV. Pharmacological prescriptions for patients with Sjögren's syndrome (SS) according to type of SS and sex.

Pharmacological prescriptions n (%)	SS 4,778 (100)			Primary SS 3,116 (65.2)			Associated SS 1,662 (34.8)			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0)	Female 1,529 (92.0)	*p*	
Non-steroidal anti-inflammatory and anti-rheumatic products	88 (25.6)	1,435 (32.4)	[c]	40 (19.0)	862 (29.7)	[c]	48 (36.1)	573 (37.5)		[b]
Xerophthalmia treatment	97 (28.2)	1,394 (31.4)		68 (32.2)	941 (32.4)		29 (21.8)	453 (29.6)		[a]
Corticosteroids	108 (31.4)	1,229 (27.7)		31 (14.7)	454 (15.6)		77 (57.9)	775 (50.7)		[b]
Conventional immunosuppressive drugs and non-biologic DMARDs	75 (21.8)	1,166 (26.3)		28 (13.3)	571 (19.7)	[c]	47 (35.3)	595 (38.9)		[b]
Opioids	29 (8.4)	624 (14.1)	[c]	12 (5.7)	379 (13.0)	[c]	17 (12.8)	245 (16.0)		[a]
Biologic DMARDs	26 (7.6)	417 (9.4)		4 (1.9)	130 (4.5)		22 (16.5)	287 (18.8)		[b]
Xerostomia treatment	24 (7.0)	405 (9.1)		17 (8.1)	307 (10.6)		7 (5.3)	98 (6.4)		[b]
Sterile saline solutions	5 (1.5)	41 (0.9)		1 (0.5)	27 (0.9)		4 (3.0)	14 (0.9)		

DMARDs: disease-modifying anti-rheumatic drugs.
[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

and 11.4 (SD=10.6) for associated SS patients, followed by the nurse with a mean of 5.7 (SD=9.0) interactions (5.2 (SD=7.1) for pSS patients and 6.7 (SD=11.6) for associated SS patients) and the administrative personnel with an average of 1.7 (SD=5.3) interactions (1.2 (SD=4.2) for pSS patients and 2.5 (SD=6.8) for associated SS patients). The physiotherapist had a mean of 0.6 (SD=3.0) interactions, and the dentist had a mean of 0.1 (SD=0.7) interactions. Differences by type of SS and sex are shown in Table VI.

The predisposing factors significantly associated with the use of PHC services were associated SS (Exponentiation of B [ExpB]=1.15; 95% CI=1.08–1.22), a high AMG risk level (ExpB=1.09; 95% CI=1.06–1.12) and age (ExpB=1.01; 95% CI=1.01–1.01). The symptoms significantly associated with the use of PHC services were dry mouth (ExpB=1.16; 95% CI=1.09–1.22), fatigue (ExpB=1.14; 95% CI=1.09–1.20), dry vagina (ExpB=1.14; 95% CI=1.07–1.22), joint pain (ExpB=1.13; 95% CI=1.05-1.22), purpura (ExpB=1.10; 95% CI=1.01–1.19), muscle pain (ExpB=1.10; 95% CI=1.04–1.16) and lymphadenopathy (ExpB=1.09; 95% CI=1.01–1.17). The comorbidities significantly associated with a higher number of contacts with PHC were atrial fibrillation (ExpB=1.59; 95% CI=1.47–1.73), type II diabetes (ExpB=1.22; 95% CI=1.14–1.31), hypertension (ExpB=1.19; 95% CI=1.13–1.26), solid malignant neoplasm (ExpB=1.19; 95% CI=1.09–1.30), coronary heart disease (ExpB=1.16; 95% CI=1.04–1.30), chronic obstructive pulmonary disease (COPD) (ExpB=1.11; 95% CI=1.02–1.20), obesity (ExpB=1.10; 95% CI=1.03-1.17), depression (ExpB=1.09; 95% CI=1.03–1.15) and osteoarthritis (ExpB=1.06; 95% CI=1.00–1.12). The medications significantly linked with a greater use of PHC services were sterile saline solutions (ExpB=1.33; 95% CI=1.01–1.74), corticosteroids (ExpB=1.26; 95% CI=1.19–1.34), opioids (ExpB=1.19; 95% CI=1.12–1.27) and biologic DMARDs (ExpB=1.11; 95% CI=1.01-1.21). However, the only factor significantly associated with a lower utilisation of PHC services was vasculitis (ExpB=0.47; 95% CI=0.35–0.63) (Table VII).

Discussion

Main findings

There is limited information available describing the utilisation of PHC resources by SS patients. This study is the first to characterise the use of services at the PHC level and the factors associated with its use in such a large cohort of SS patients, stratifying the results by type of SS and gender. SS mostly affected females over 60 years of age, and pSS was almost twice as common as associated SS. The use of PHC services by SS patients was very high, and the GP was the most contacted health professional, with twice the average number of consultations compared to the nurse. The main factors associated with PHC service use were a higher AMG risk level, ageing, glandular and extra-glandular symptoms, substantial comorbidities and various treatments.

Comparison with other studies

- Sociodemographic characteristics

The prevalence of SS in the Community of Madrid in participants over 18 years of age was 8.4 per 10,000 inhabitants (7), within the range from 1/10,000 to 483/10,000 inhabitants estimated by two systematic reviews and meta-analyses of SS performed in recent years (5,6). We identified a female:male ratio of approximately 13:1, greater than the 11:1 ratio reported in the 2015 systematic review (5). These differences with previously published studies could be attributed to the heterogeneity of the populations compared and the lack of consensus on the classification criteria in the past (29). The mean age of the SS patients in our study was 64.3, and

Table V. Utilisation of primary health care (PHC) services by Sjögren's syndrome (SS) patients in a year according to type of SS and sex.

PHC service n (%)	SS 4,778 (100)			Primary SS 3,116 (65.2)			Associated SS 1,662 (34.8)			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0)	Female 1,529 (92.0)	*p*	
Total PHC patients' consultation										
≥1 PHC visits	286 (83.1)	3,896 (87.9)	[c]	177 (83.9)	2,586 (89.0)	[c]	109 (82.0)	1,310 (85.7)		[a]
Total number of events	6,913 (100)	87,557 (100)		3,656 (100)	54,314 (100)		3,257 (100)	33,243 (100)		
Provider involved										
General practitioner										
≥1 PHC visits	285 (82.8)	3,863 (87.1)	[c]	176 (83.4)	2,560 (88.1)		109 (82.0)	1,303 (85.2)		[a]
Total number of events	3,664 (53.0)	48,311 (55.2)		2,032 (55.6)	31,055 (57.2)		1,632 (50.1)	17,256 (51.9)		
Nurse										
≥1 PHC visits	245 (71.2)	3,292 (74.2)		149 (70.6)	2,182 (75.1)		96 (72.2)	1,110 (72.6)		
Total number of events	2,064 (29.9)	25,358 (29.0)		1,069 (29.2)	15,199 (28.0)		995 (30.5)	10,159 (30.6)		
Administrative personnel										
≥1 PHC visits	97 (28.2)	1,167 (26.3)		49 (23.2)	715 (24.6)		48 (36.1)	452 (29.6)		[b]
Total number of events	774 (11.2)	7,125 (8.1)		334 (9.1)	3,472 (6.4)		440 (13.5)	3,653 (10.0)		
Physiotherapist										
≥1 PHC visits	12 (3.5)	278 (6.3)	[c]	7 (3.3)	209 (7.2)	[c]	5 (3.8)	69 (4.5)		[b]
Total number of events	131 (1.9)	2,767 (3.2)		89 (2.4)	2,254 (4.1)		42 (1.3)	513 (1.5)		
Dentist										
≥1 PHC visits	22 (6.4)	252 (5.7)		15 (7.1)	159 (5.5)		7 (5.3)	93 (6.1)		
Total number of events	57 (0.8)	569 (0.6)		40 (1.1)	337 (0.6)		17 (0.5)	232 (0.7)		
Midwife										
≥1 PHC visits	-	266 (6.0)	[c]	-	164 (5.6)	[d]	-	102 (6.7)	[c]	
Total number of events	-	461 (0.5)		-	270 (0.5)		-	191 (0.6)		
Social worker										
≥1 PHC visits	10 (2.9)	183 (4.1)		3 (1.4)	108 (3.7)		7 (5.3)	75 (4.9)		[a]
Total number of events	22 (0.3)	348 (0.4)		3 (0.1)	182 (0.3)		19 (0.6)	166 (0.5)		
Dental hygienist										
≥1 PHC visits	7 (2.0)	70 (1.6)		4 (1.9)	39 (1.3)		3 (2.3)	31 (2.0)		
Total number of events	11 (0.2)	136 (0.2)		8 (0.2)	68 (0.1)		3 (0.1)	68 (0.2)		
Psychologist										
≥1 PHC visits	0	5 (0.1)		0	4 (0.1)		0	1 (0.1)		
Total number of events	0	5 (0.0)		0	4 (0.0)		0	1 (0.0)		
Others										
≥1 PHC visits	45 (13.1)	607 (13.7)		22 (10.4)	420 (14.5)		23 (17.3)	187 (12.2)		
Total number of events	190 (2.7)	2,477 (2.8)		81 (2.2)	1,473 (2.7)		109 (3.3)	1,004 (3.0)		

PHC: primary health care.
[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

the average time since diagnosis was approximately 5.8 years, consistent with the fact that SS is regularly diagnosed within the fifth decade of life (8). Women were diagnosed at a younger age than men, in accordance with the results from other studies (30, 31).

- Clinical characteristics

According to the AMG morbidity classification, almost 40% of our population was at a medium- or high-risk level, contrasting with the mild severity and favourable prognosis that usually characterise this syndrome (4). In the Community of Madrid, the percentage of individuals at medium and high risk has been reported to be approximately 20% (32). The higher risk level observed could be attributable to the presence of diverse serious and concerning comorbidities, in addition to advanced age, which implies a worsened and deteriorated health status (33). The AMG classifier is an excellent indicator that allows the identification of the different healthcare needs required by patients, considering their morbidity, risk of admission, PHC visits and prescriptions (25).

The main symptoms in our population were consistent with the typical triad of sicca symptoms, fatigue and pain (1). Curiously, although xerophthalmia and xerostomia are considered the hallmark symptomatology features of SS and are usually present in most cases (34), in our population, only 24.3% reported dry eye and 20.7% reported dry mouth. Additionally, the prevalence of fatigue in our population was lower than normally described (35). Cough was also a common ailment, in some cases attributed to the desiccation of the tracheobronchial mucosa known as xerotrachea originated by SS but not related to SS in other cases because cough is the most common symptom for which adults see the PHC physician (36). The

Table VI. Utilisation of primary health care (PHC) services by Sjögren's syndrome (SS) patients in a year according to type of SS and sex.

PHC service	SS n=4,778			Primary SS n=3,116			Associated SS n=1,662			*p*
	Male 344 (7.2)	Female 4,434 (92.8)	*p*	Male 211 (6.8)	Female 2,905 (93.2)	*p*	Male 133 (8.0)	Female 1,529 (92.0)	*p*	
PHC consultation										
Total										
Mean (SD)	20.1 (20.1)	19.8 (20.0)		17.3 (17.1)	18.7 (17.9)		24.5 (23.4)	21.7 (23.4)		[b]
Median (IQR)	14 (4-32.5)	15 (6-27)		13 (4-25)	14 (6-26)		19 (4.5-39.5)	16 (5-30)		
Provider involved										
General practitioner										
Mean (SD)	10.7 (10.1)	10.9 (9.9)		9.6 (9.0)	10.7 (9.5)		12.3 (11.5)	11.3 (10.5)		[a]
Median (IQR)	9 (2-16)	9 (4-15)		8 (2-15)	9 (4-15)		11 (3-18)	9 (4-16)		
PHC nurse										
Mean (SD)	6.0 (8.4)	5.7 (9.0)		5.1 (6.7)	5.2 (7.2)		7.5 (10.3)	6.6 (11.7)		[b]
Median (IQR)	3 (0-8)	3 (0-7)		3 (0-7)	3 (1-7)		3 (0-10)	3 (0-8)		
Administrative personnel										
Mean (SD)	2.3 (5.5)	1.6 (5.3)	[c]	1.6 (4.7)	1.2 (4.1)		3.3 (6.5)	2.4 (6.9)		[b]
Median (IQR)	0 (0-1)	0 (0-1)		0 (0-0)	0 (0-0)		0 (0-2.5)	0 (0-1)		
Physiotherapist										
Mean (SD)	0.4 (2.4)	0.6 (3.0)		0.4 (2.6)	0.8 (3.4)		0.3 (1.9)	0.3 (2.0)	[d]	
Median (IQR)	0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		
Dentist										
Mean (SD)	0.2 (0.8)	0.1 (0.7)		0.2 (0.9)	0.1 (0.7)		0.1 (0.7)	0.2 (0.8)		
Median (IQR)	0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		
Midwife										
Mean (SD)	-	0.1 (0.6)	[d]	-	0.09	[d]	-	0.1 (0.8)	[d]	
Median (IQR)	-	0 (0-0)		-	0 (0-0)		-	0 (0-0)		
Social worker										
Mean (SD)	0.06 (0.6)	0.08 (0.5)		0.01 (0.1)	0.06 (0.4)	[d]	0.1 (0.9)	0.1 (0.7)		[a]
Median (IQR)	0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		
Dental hygienist										
Mean (SD)	0.03 (0.2)	0.03 (0.3)		0.04 (0.3)	0.02 (0.2)		0.02 (0.1)	0.04 (0.5)		
Median (IQR)	0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		
Psychologist										
Mean (SD)	0	0.0 (0.03)		0	0.0 (0.04)		0	0.0 (0.03)		
Median (IQR)	0	0 (0-0)		0	0 (0-0)		0	0 (0-0)		
Other										
Mean (SD)	0.6 (2.2)	0.6 (2.5)		0.4 (1.8)	0.5 (2.2)		0.8 (2.7)	0.7 (3.0)		[a]
Median (IQR)	0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		0 (0-0)	0 (0-0)		

CI: confidence interval; IQR: interquartile range; PHC: primary health care; SD: standard deviation.
[a] *p*-value shows $p<0.05$ differences between primary and associated SS based on bivariate analysis.
[b] *p*-value shows $p<0.001$ differences between primary and associated SS based on bivariate analysis.
[c] *p*-value shows $p<0.05$ differences between male and female sex based on bivariate analysis.
[d] *p*-value shows $p<0.001$ differences between male and female sex based on bivariate analysis.

lower prevalence of symptoms in this cohort from Madrid could be explained by the fact that these SS patients were mainly followed at the hospital level by rheumatology or internal medicine departments instead of their PHC professionals, which could have conditioned the patients to less communication with the latter about their SS-related symptoms. Finally, looking at the significant differences by sex concerning the symptoms and comorbidities present in SS patients and in line with previous studies, males were more affected by diabetes, heart diseases and malignant neoplasms, while females suffered more from lupus, fibromyalgia, osteoporosis and depression (30, 31).

- Use of PHC services

The intensity of PHC utilisation reveals the existence of unmet needs regarding the management and treatment of SS. However, the percentage of cases in our population that used PHC services and their mean annual consultations were lower than those observed by Birt *et al.* (16). This diminished proportion could be attributed to the period in disease development of the patients studied, since Birt *et al.* analysed the time interval of a year immediately after diagnosis, when patients register a high number of medical encounters attributable to the necessity of pre-management evaluation involving different medical tests (37). In contrast, most of our patients were not recently diagnosed; therefore, having lived with the disease over several years, they could have acquired the knowledge and experience to decide which approaches they should follow, avoiding consulting a professional.

Associated SS patients made a statistically significant higher use of PHC

Table VII. Factors associated with the utilisation of PHC services by patients with SS.

Variables	ExpB	Robust SE	95% CI	*p*
Atrial fibrillation/flutter	1.59	0.07	1.47-1.73	[b]
Sterile saline solutions	1.33	0.18	1.01-1.74	[a]
Corticosteroids	1.26	0.04	1.19-1.34	[b]
Type II diabetes	1.22	0.04	1.14-1.31	[b]
Hypertension	1.19	0.03	1.13-1.26	[b]
Opioids	1.19	0.04	1.12-1.27	[b]
Solid malignant neoplasm	1.19	0.05	1.09-1.30	[b]
Coronary heart disease	1.16	0.07	1.04-1.30	[a]
Dry mouth	1.16	0.03	1.09-1.22	[b]
Associated SS	1.15	0.04	1.08-1.22	[b]
Fatigue	1.14	0.03	1.09-1.20	[b]
Dry vagina	1.14	0.04	1.07-1.22	[b]
Joint pain, swelling or stiffness	1.13	0.04	1.05-1.2	[a]
Dry skin	1.12	0.12	0.91-1.37	
COPD	1.11	0.05	1.02-1.20	[a]
Biologic DMARDs	1.11	0.05	1.01-1.21	[a]
Obesity	1.1	0.04	1.03-1.17	[a]
Purpura	1.10	0.05	1.01-1.19	[a]
Muscle pain, myalgia or fibromyalgia	1.10	0.03	1.04-1.16	[a]
Lymphadenopathy	1.09	0.04	1.01-1.17	[a]
High risk level by AMG	1.09	0.01	1.06-1.1	[b]
Depression	1.09	0.03	1.03-1.15	[a]
Raynau	1.08	0.07	0.96-1.22	
Male sex	1.08	0.05	0.98-1.18	
Dysphagia	1.06	0.04	0.99-1.14	
Arthritis	1.06	0.03	1.00-1.12	[a]
Dry eye	1.04	0.03	0.99-1.10	
Osteoporosis	1.03	0.03	0.97-1.09	
Cough	1.02	0.03	0.97-1.08	
Non-steroidal anti-inflammatory and anti-rheumatic product	1.01	0.03	0.96-1.07	
Hypothyroidism	1.01	0.03	0.96-1.07	
Xerophthalmia treatment	1.01	0.03	0.96-1.06	
Age (years)	1.01	0.00	1.01-1.01	[b]
Time from diagnosis	0.99	0.00	0.99-1.00	
Lipid disorder	0.99	0.03	0.94-1.04	
Conventional immuno-suppressive drugs and non-biologic DMARDs	0.99	0.03	0.93-1.05	
Xerostomia treatment	0.99	0.04	0.92-1.07	
Spanish	0.99	0.04	0.91-1.07	
Vasculitis	0.47	0.04	0.35-0.63	[b]

A hurdle negative binomial regression model was performed by setting as the dependent variable the total number of contacts with the PHC system and considering as covariates all the clinical and demographic variables collected from our 4,778 SS patients.
Akaike information criterion (AIC) = 7.47.
AMG: adjusted morbidity groups; CI: confidence interval; COPD: chronic obstructive pulmonary dsease; DMARDs: disease-modifying anti-rheumatic drugs; ExpB: exponentiation of B; SE: standard error.
[a] p-value <0.05; [b] p-value <0.001.

services than pSS patients, owing to the coexistence of an additional autoimmune disorder that makes their disease more complex, requiring greater care needs. To our knowledge, this is the first study that stratifies the use of PHC services by SS type, whereas only a few studies describe the use of healthcare resources by pSS subjects (15, 17, 19). Our pSS population registered a mean of 18.6 total PHC contacts in a year, notably higher than the 4.4 outpatient visits of a Swedish population (19) but closer to the 14.6 office visits described for a United States population (17), and meaningfully lower than the 17 physician visits per 6 months in a German population (15). However, data from these other studies should be interpreted with caution since some results may be overestimated, as they could include other healthcare professionals outside those in PHC. All the differences among studies could be due to the distinct populations analysed or to the variability in the design and characteristics of the healthcare systems in each country.

The variety of health professionals seen by SS patients emphasises the multidisciplinary approach required by this disease. The most contacted provider was the GP, which emphasises the gatekeeping core strategy of the Spanish national healthcare system (38). In comparison with the outcomes from a US cohort that has a mixture of health plans (39), our population almost doubled the proportion of SS patients who visited the GP (16). Unexpectedly, a German study described similar GP results to ours (15), considering that Germany adheres to an open access healthcare system and not to a gatekeeping program (40); the GP elevated rate in Germany might be explained by the elevated volume of overall visits described in that study. Interestingly, the average number of GP consultations from SS patients in our study exceeded the 9.7 mean number of visits reported in another Madrid study analysing individuals with chronic diseases (41).

The number of contacts with the nurse was expected to be higher and similar to that of the GP, in line with the strategy for the care of patients with chronic diseases in the Community of Madrid (32). In terms of this strategy, SS patients were equally expected to show increased needs for social assistance, inconsistent with the low number of contacts with the social worker we observed. Administrative personnel were the third most frequently contacted professional, which indicates the presence of an important bureaucratic workload in addition to consultations related to actual care (42).

Because one of the main signs of SS syndrome is related to the dryness of the oral cavity, good dental hygiene and regular visits to a dentist are especially important (43). However, our population had far fewer dental provider contacts than the majority of previous studies (14, 15, 19), which is explained by the notably low occurrence of dry mouth in our population and because public dental coverage in Spain is poor and most of the procedures are not covered, so patients resort to the private sector (44).

Consistent with other most common symptoms and comorbidities suffered by SS patients, studies highlight the elevated number of visits to ophthalmologists and rheumatologists (14, 45). These specialists were not analysed in our study, as they are secondary care professionals. At the PHC level, subjects with ocular ailments are attended by the GP, nurse and administrative personnel, who might give a referral to the ophthalmologist if it is deemed necessary. A similar situation occurred for patients with rheumatic afflictions, involving the physiotherapist, who was the fourth most frequently visited physician in our population. Finally, and contrary to the high prevalence of depression reported in our population, only a few patients attended the psychologist, possibly due to the stigmatised perception of mental illnesses causing these patients to avoid seeking help, or perhaps owing to the difficult access to public PHC psychological services in Spain, causing many people to opt for private health insurance (46).

- Factors associated with PHC service utilisation

Predisposing factors associated with a greater utilisation of PHC services were associated SS, a higher AMG risk level and older age, consistent with the profile of a more complex patient who requires more healthcare assistance (13, 16). Interestingly, although we found significant differences between sexes for other variables analysed in this study, we discovered that SS males and females made a similar use of PHC resources.

Dry mouth was found to be the symptom that most influenced the use of services, consistent with the high prevalence of patients with this ailment and the relatively low prescription of xerostomia treatment within our population. The second symptom that most often promoted visits to PHC was fatigue, which was the most common affliction in our population and therefore, it frequently becomes the most disturbing symptom of the disease, in addition to the lack of certainty on the effectiveness of its treatment approaches, increasing the number of times these patients visit a GP (15). As expected, suffering from the other most common SS symptoms reported in our population, including dry vagina, joint and/or muscle pain, purpura and lymphadenopathy, encouraged patients to enlist the aid of the PHC system to reduce their discomfort and achieve a better quality of life (11, 47).

Atrial fibrillation was the comorbidity most commonly linked to higher PHC resource utilisation, in accordance with its previous association with substantial healthcare utilisation and economic burden (48), which is explained by a reduction in the quality of life, functional status and cardiac performance of these patients and because treatment with anticoagulants usually requires continuous follow-up involving close clinical monitoring, regular analytical monitoring and frequent dose adjustment (49). Additionally, patients with type II diabetes, hypertension, solid malignant neoplasms, coronary heart disease, COPD, obesity, depression and osteoarthritis demand a high burden of healthcare, including annual reviews, personalised care plans, treatment intensification, monitoring, and daily clinical and social care of disease-related complications (11, 14, 15).

The use of sterile saline solutions was highly associated with a greater mean number of contacts per year with PHC, rather than tear and saliva substitutes, which are commonly used to treat the prevalent eye and mouth dryness typical of SS subjects and which were indicative of above average numbers of physician visits in the study by Westhoff *et al*. (15). This could be because sterile saline solution is usually used to alleviate eye symptoms, while most tear substitutes are not covered by the public health system, and the patient has to pay for them in full. We also found an association with corticosteroids, opioids and biologic DMARDs, but the correlation was weaker.

Limitations and strengths

The principal limitation of our study is the lack of consensus for standardised diagnostic criteria for SS, which have changed over the years among the 2002 AECG criteria (22), the 2012 ACR criteria (23) and/or the 2016 ACR/EULAR classification criteria (24). To overcome the disparities in definitions, resulting in an important strength of this study, all identified SS cases were validated and confirmed by a specialist physician who accessed the hospital and primary care public electronic medical records.

The main remarkable strength of this study is the utilisation of SIERMA, a population registry that records all the SS cases identified within a well-defined geographic area covered by both PHC and hospital care in a population of approximately 6 million people in the Community of Madrid. SS patients who have not been followed by the Madrid Public Health Service were not identified in our study. However, this proportion of cases would have been extremely low, as the Spanish National Health System offers coverage to nearly the totality of the population, and more than 95% of the Community of Madrid population visited their PHC centre at least once (50).

Finally, although this study included a large cohort of SS patients, analysis by sex resulted in a small number of men for comparison. Studying a larger sample size of men will allow us to obtain more precise results. However, this study is one of the few that disaggregates the analysis of numerous variables present in SS patients by sex.

Implications

The diagnostic delay in patients with SS remains a critical problem, resulting in a reduction in their quality of life, which implies a greater utilisation of medication and healthcare services, leading to higher expenses for the sanitary system.

The present study provides quality information on the utilisation of PHC services and the associated factors of its use in a wide cohort of SS patients in the Community of Madrid. The health services of GPs are widely used, but health professionals related to nursing, physiotherapy, dentistry or psychology should have more prominence in the management and follow-up of these patients.

Our results will help to design novel-oriented healthcare strategies and policies at the PHC level to make an earlier diagnosis possible, to optimise the

management of the illness, and to improve the quality of life of SS patients.

Conclusions

The use of PHC services in patients with SS was very high and was mainly associated with AMG risk level and ageing, some glandular and extra-glandular symptoms, substantial comorbidities and various treatments. The evidence provided about PHC utilisation could enable us to understand the disease burden, recurrent costs, and, ultimately, unmet needs. This knowledge could be harnessed to distribute medical goods and services in a more effective and efficient manner, prioritising the welfare of SS patients. As a result, PHC healthcare policies could be designed to improve the early diagnosis and quality of life of SS individuals and to reduce the significant healthcare costs associated with this disease.

Acknowledgments

We would like to thank the professionals of the Primary Care Research Unit of the Primary Care Management of Madrid for their methodological support. Additionally, this work could not have been accomplished without the collaboration of all professionals involved in the HARMONICSS project, especially Isabelle Bos, Jesper Dros, Sytske Wiegersma, John Paget and Robert Verheij, researchers from the Netherlands Institute for Health Services Research, as well as Jenny Inga Díaz, President of the Spanish Sjögren's Syndrome Patient Association.

References

1. ANDRÉ F, BÖCKLE BC: Sjögren's syndrome. *J Dtsch Dermatol Ges* 2022; 20(7): 980-1002. https://doi.org/10.1111/ddg.14823
2. JONSSON R: Disease mechanisms in Sjögren's syndrome: what do we know? *Scand J Immunol* 2022; 95(3): e13145. https://doi.org/10.1111/sji.13145
3. PSIANOU K, PANAGOULIAS I, PAPANASTASIOU AD *et al*.: Clinical and immunological parameters of Sjögren's syndrome. *Autoimmun Rev* 2018; 17(10): 1053-64. https://doi.org/10.1016/j.autrev.2018.05.005
4. STEFANSKI A-L, TOMIAK C, PLEYER U *et al*.: The diagnosis and treatment of Sjögren's syndrome. *Dtsch Arztebl Int* 2017; 114(20): 354-61. https://doi.org/10.3238/arztebl.2017.0354
5. QIN B, WANG J, YANG Z *et al*.: Epidemiology of primary Sjögren's syndrome: a systematic review and meta-analysis. *Ann Rheum Dis* 2015; 74(11): 1983-9. https://doi.org/10.1136/annrheumdis-2014-205375
6. ALANI H, HENTY JR, THOMPSON NL, JURY E, CIURTIN C: Systematic review and meta-analysis of the epidemiology of polyautoimmunity in Sjögren's syndrome (secondary Sjögren's syndrome) focusing on autoimmune rheumatic diseases. *Scand J Rheumatol* 2018; 47(2): 141-54. https://doi.org/10.1080/03009742.2017.1324909
7. BARRIO-CORTES J, LÓPEZ-RODRÍGUEZ JA, GÓMEZ-GASCÓN T *et al*.: Prevalence and comorbidities of Sjögren's syndrome patients in the Community of Madrid: A population-based cross-sectional study. *Joint Bone Spine* 2023; 90(4): 105544. https://doi.org/10.1016/j.jbspin.2023.105544
8. NEGRINI S, EMMI G, GRECO M *et al*.: Sjögren's syndrome: a systemic autoimmune disease. *Clin Exp Med* 2022; 22(1): 9-25. https://doi.org/10.1007/s10238-021-00728-6
9. VIVINO FB, BUNYA VY, MASSARO-GIORDANO G *et al*.: Sjögren's syndrome: An update on disease pathogenesis, clinical manifestations and treatment. *Clin Immunol* 2019; 203: 81-121. https://doi.org/10.1016/j.clim.2019.04.009
10. SJÖGREN'S SYNDROME FOUNDATION. Sjögren's Foundation Accomplishes 5-Year Breakthrough Goal. https://sjögrens.org/about-us/history/breakthrough-goal
11. MIYAMOTO ST, VALIM V, FISHER BA: Health-related quality of life and costs in Sjögren's syndrome. *Rheumatology* (Oxford) 2021; 60(6): 2588-601. https://doi.org/10.1093/rheumatology/key370
12. SEGHIERI C, LUPI E, TZIOUFAS AG *et al*.: Patient-reported experience and health-related quality of life in patients with primary Sjögren's syndrome in Europe. *Clin Exp Rheumatol* 2021; 39 (Suppl. 133): S123-30. https://doi.org/10.55563/clinexprheumatol/vsv60z
13. CALLAGHAN R, PRABU A, ALLAN RB *et al*.: Direct healthcare costs and predictors of costs in patients with primary Sjögren's syndrome. *Rheumatology* (Oxford) 2007; 46(1): 105-11. https://doi.org/10.1093/rheumatology/kel155
14. SEGAL B, BOWMAN SJ, FOX PC *et al*.: Primary Sjögren's syndrome: health experiences and predictors of health quality among patients in the United States. *Health Qual Life Outcomes* 2009; 7: 46. https://doi.org/10.1186/1477-7525-7-46
15. WESTHOFF G, DÖRNER T, ZINK A: Fatigue and depression predict physician visits and work disability in women with primary Sjögren's syndrome: results from a cohort study. *Rheumatology* (Oxford) 2012; 51(2): 262-9. https://doi.org/10.1093/rheumatology/ker208
16. BIRT JA, TAN Y, MOZAFFARIAN N: Sjögren's syndrome: managed care data from a large United States population highlight real-world health care burden and lack of treatment options. *Clin Exp Rheumatol* 2017; 35(1): 98-107.
17. PERERA S, MA L, PUNWANEY R *et al*.: Clinical and cost burden of primary Sjögren's syndrome: descriptive analysis using a US administrative claims database. *J Health Econ Outcomes Res* 2018; 5(2): 150-61. https://doi.org/10.36469/9807
18. HUANG Y-T, LU T-H, CHOU P-L *et al*.: Diagnostic delay in patients with primary Sjögren's syndrome: a population-based cohort study in Taiwan. *Healthcare* (Basel) 2021; 9(3): 363. https://doi.org/10.3390/healthcare9030363
19. WESTERLUND A, KEJS AMT, BEYDOGAN H *et al*.: Primary Sjögren's syndrome: a retrospective cohort study of burden of illness in Sweden. *Rheumatol Ther* 2021; 8(2): 955-71. https://doi.org/10.1007/s40744-021-00314-y
20. GOULES A V, EXARCHOS TP, FOTIADIS DI *et al*.: The clinical and technical impact of the HarmonicSS project. *Clin Exp Rheumatol* 2021; 39 (Suppl. 133): S17-9. https://doi.org/10.55563/clinexprheumatol/u7knfy
21. Community of Madrid: Creation of the Information system on rare diseases in Madrid (SIERMA). *Official Gazette of the Community of Madrid* 2015; 571: 349-52. http://www.madrid.org/wleg_pub/servlet/Servidor?opcion=VerHtml&nmnorma=9000
22. VITALI C, BOMBARDIERI S, JONSSON R *et al*.: Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; 61(6): 554-8. https://doi.org/10.1136/ard.61.6.554
23. SHIBOSKI SC, SHIBOSKI CH, CRISWELL LA *et al*.: American College of Rheumatology classification criteria for Sjögren's syndrome: a data-driven, expert consensus approach in the Sjögren's International Collaborative Clinical Alliance cohort. *Arthritis Care Res* (Hoboken) 2012; 64(4): 475-87. https://doi.org/10.1002/acr.21591
24. SHIBOSKI CH, SHIBOSKI SC, SEROR R *et al*.: 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: a consensus and data-driven methodology involving three international patient cohorts. *Arthritis Rheumatol* 2017; 69(1): 35-45. https://doi.org/10.1002/art.39859
25. MONTERDE D, VELA E, CLÈRIES M: [Adjusted morbidity groups: A new multiple morbidity measurement of use in Primary Care]. *Aten Primaria* 2016; 48: 674-82. https://doi.org/10.1016/j.aprim.2016.06.003
26. Spanish Ministry of Health, Consumption and Social Welfare: Report of the project on population stratification by adjusted morbidity groups (AMG) in the National Health System (2014-2016). 2018. https://www.sanidad.gob.es/organizacion/sns/planCalidadSNS/pdf/informeEstratificacionGMASNS_2014-2016.pdf
27. ARIAS-LÓPEZ C, RODRIGO VAL MP, CASAÑA FERNÁNDEZ L *et al*.: [Validity of predictive power of the Adjusted Morbidity Groups (AMG) with respect to others population stratification tools.]. *Rev Esp Salud Publica* 2020; 94.
28. DEB P, NORTON EC: Modeling health care expenditures and use. *Annu Rev Public Health* 2018; 39: 489-505. https://doi.org/10.1146/annurev-publhealth-040617-013517
29. SHIBOSKI CH, DANIELS TE: Historical background, classification, and diagnostic criteria. In: PRICE EJ, TAPPUNI AR (Eds.): Oxford Textbook of Sjögren's Syndrome. Oxford Textbooks in Rheumatology, 2021. https://doi.

org/10.1093/med/9780198806684.003.0002
30. BRUNO KA, MORALES-LARA AC, BITTENCOURT EB *et al*.: Sex differences in comorbidities associated with Sjögren's disease. *Front Med* (Lausanne) 2022; 9: 958670. https://doi.org/10.3389/fmed.2022.958670
31. PU J, GAO R, ZHUANG S *et al*.: Gender difference of primary Sjögren's syndrome in a Chinese cohort: why do women suffer more? [Preprint] *Res Squ* 2023. https://doi.org/10.21203/rs.3.rs-2683911/v1
32 Madrid Regional Ministry of Health. Care strategy for patients with chronic diseases in the Community of Madrid. 2013. http://www.madrid.org/bvirtual/bvcm017570.pdf
33. BRETOS-AZCONA PE, SÁNCHEZ-IRISO E, CABASÉS HITA JM: Tailoring integrated care services for high-risk patients with multiple chronic conditions: a risk stratification approach using cluster analysis. *BMC Health Serv Res* 2020; 20(1): 806. https://doi.org/10.1186/s12913-020-05668-7
34. MAHONEY EJ, SPIEGEL JH: Sjögren's disease. *Otolaryngol Clin North Am* 2003; 36(4): 733-45. https://doi.org/10.1016/s0030-6665(03)00024-0
35. MÆLAND E, MIYAMOTO ST, HAMMENFORS D *et al*.: Understanding fatigue in Sjögren's syndrome: outcome measures, biomarkers and possible interventions. *Front Immunol* 2021; 12: 703079. https://doi.org/10.3389/fimmu.2021.703079
36. KOSLOW M, KIVITY S, VISHNEVSKIA-DAI V *et al*.: Unexplained cough: it is time to rule out Sjogren's syndrome. *Clin Rheumatol* 2018; 37(5): 1215-22. https://doi.org/10.1007/s10067-018-3987-4
37. VITALI C, MINNITI A, PIGNATARO F, MAGLIONE W, DEL PAPA N: Management of Sjögren's syndrome: present issues and future perspectives. *Front Med* (Lausanne) 2021; 8: 676885. https://doi.org/10.3389/fmed.2021.676885
38. KRINGOS D, BOERMA W, HUTCHINSON A *et al*.: Building primary care in a changing Europe: Case studies. Copenhagen (Denmark): European Observatory on Health Systems and Policies 2015.
39. FORREST CB: Primary care in the United States: primary care gatekeeping and referrals: effective filter or failed experiment? *BMJ* 2003; 326(7391): 692-5. https://doi.org/10.1136/bmj.326.7391.692
40. REIBLING N, WENDT C: Gatekeeping and provider choice in OECD healthcare systems. *Current Sociology* 2012; 60: 489-505. https://doi.org/10.1177/0011392112438333
41. BARRIO-CORTES J, CASTAÑO-REGUILLO A, BECA-MARTÍNEZ MT, BANDEIRA-DE OLIVEIRA M, LÓPEZ-RODRÍGUEZ C, JAIME-SISÓ A: Chronic diseases in the geriatric population: morbidity and use of primary care services according to risk level. *BMC Geriatr* 2021; 21(1): 278. https://doi.org/10.1186/s12877-021-02217-7
42. CASAJUANA J, GÉRVAS CAMACHO JJ, UPF: La renovación de la atención primaria desde la consulta. Madrid, Springer Healthcare Ibérica, 2012.
43. MARSHALL LL, STEVENS GA: Management of Primary Sjögren's syndrome. *Consult Pharm* 2018; 33(12): 691-701. https://doi.org/10.4140/tcp.n.2018.691
44. European Observatory on Health Systems and Policies. Spain: Country Health Profile 2021.
45. ALBRECHT K, DÖRNER T, REDEKER I *et al*.: Comorbidity and health care utilisation in persons with Sjögren's syndrome: a claims data analysis. *Clin Exp Rheumatol* 2020; 38 (Suppl. 126): S78-84.
46. PALACIOS RUIZ AJ: [The profession of clinical psychology: The current issue and the challenges ahead]. *Asoc Esp Neuropsiq* 2004; 91: 139-47.
47. LACKNER A, FICJAN A, STRADNER MH *et al*.: It's more than dryness and fatigue: The patient perspective on health-related quality of life in Primary Sjögren's syndrome - A qualitative study. *PLoS One* 2017; 12(2): e0172056. https://doi.org/10.1371/journal.pone.0172056
48. DESHMUKH A, IGLESIAS M, KHANNA R *et al*.: Healthcare utilization and costs associated with a diagnosis of incident atrial fibrillation. *Heart Rhythm O2* 2022; 3(5): 577-86. https://doi.org/10.1016/j.hroo.2022.07.010
49. MARTÍNEZ-RUIZ M, BALLESTEROS-MERINO M, SÁNCHEZ-LÓPEZ AB *et al*.: [Use of new oral anticoagulants in primary care: Quality of prescription.]. *Rev Clin Med Fam* 2017; 10: 18-28.
50. ESTEBAN-VASALLO MD, DOMÍNGUEZ-BERJÓN MF, ASTRAY-MOCHALES J *et al*.: Epidemiological usefulness of population-based electronic clinical records in primary care: estimation of the prevalence of chronic diseases. *Fam Pract* 2009; 26(6): 445-54. https://doi.org/10.1093/fampra/cmp062