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# SJÖGREN'S SYNDROME: A COMMUNITY-BASED STUDY OF PREVALENCE AND IMPACT

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SUMMARY

*Objective.* Using the European Community (EC) criteria for classification Vitali *et al*. Arthritis Rheum 1993;36:340–7, we report the prevalence estimates of Sjögren's syndrome (SS) from a general population and present the first population data to assess the impact of the syndrome.

*Methods.* A cross-sectional population-based survey performed on 1000 adults, aged 18–75 yr, randomly selected from a population register. Responders to the initial postal phase were invited for an interview. The five criteria measured at interview were: (1) the reporting of subjective oral symptoms lasting for >3 months; (2) the reporting of subjective ocular symptoms lasting for >3 months; (3) Schirmer-I test; (4) unstimulated salivary flow; (5) autoantibodies [Ro (SS-A), La (SS-B), rheumatoid factor (RF), antinuclear antibodies (ANA)]. SS was diagnosed if at least four of these five criteria were positive. The MOS Short-form 36 (SF-36), General Health Questionnaire (GHQ) and the Health and Fatigue Questionnaire (HFQ) were completed by subjects after the interview, and scores were compared between those with and without a diagnosis of SS.

*Results.* A total of 341 subjects completed both the postal questionnaire and home visit. A diagnosis of SS could be given to 13 subjects. After adjusting for the presence of possible bias due to non-response, our best estimate of the prevalence of SS in the study population was 33 per 1000 subjects (95% CI 22–44). The prevalence of the disorder was higher in females (38; 95% CI 27–52) and for those subjects aged ⩾55 yr (46; 95% CI 34–61). Those subjects diagnosed positively were more impaired for each of the eight dimensions of the SF-36 than those without a diagnosis, and also suffered from higher levels of depression and fatigue.

*Conclusions.* SS affects ~3–4% of adults and in the general population appears to be associated with a clinically significant impairment of a subject's health and well-being.

KEY WORDS: Sjögren's syndrome, Prevalence, Population-based survey, Cross-sectional study, Impact.

SJÖGREN'S syndrome (SS) is considered to be one of the most common autoimmune diseases with a prevalence thought to equal or exceed that of rheumatoid arthritis (RA) [1]. It is characterized by inflammation of the lachrymal and salivary glands, which then leads to well-recognized clinical features of dry eyes and dry mouth. Other exocrine glands may also be affected, causing a wider variety of complaints—coughs, pancreatic insufficiency, vaginal dryness. In isolation, SS is termed 'primary' and when in combination with another autoimmune disease it is termed 'secondary'.

Evidence of dry eyes and dry mouth is frequently found in subjects suffering from other autoimmune diseases, such as systemic lupus erythematosus (SLE) and RA. The prevalence of SS in subjects with SLE has been reported to range from 8% to >30% [2–4]. A higher level of the syndrome has been reported in subjects with RA: 31% in a Greek study [5] and 55% from Spanish data [6].

Although frequently ascertained in attenders to rheumatology [7], dental [8] and ophthalmic [9] clinics, few studies have estimated the population prevalence of SS. Those published studies report wide-ranging prevalence estimates in adults from 0.04 to 4.8% [10–15]. Furthermore, these studies have been performed on diverse populations using a restricted age range [11, 14], low initial sample size [10, 14] or low follow-up rates [15].

Studies of SS have also used a variety of classification criteria, leading to difficulties when trying to compare results. Four main criterion sets were used for the classification of SS [16–19]. Each of these criterion sets used a slightly different definition of the syndrome; one classification is based solely on objective tests [18] whereas the others also involved the presence of subjective symptoms. In response to this, the European Community criteria set [1] was developed in 1993 to standardize the definition of SS for use in research studies.

Symptoms of SS vary widely in severity. For example, within SLE or RA they may be subclinical, i.e. only a small number of subjects volunteer information on oral and ocular symptoms, which may be dismissed as of minor clinical significance [2, 3, 5]. By contrast, subjects with 'primary' SS may have major complaints, including systemic features such as Raynaud's, central nervous system (CNS) and pulmonary involvement [20–24]. Clinic sufferers have been shown to complain of increased levels of fatigue, pain and a general interference with their life [25, 26]. Although the level of SS has been measured in the general population, albeit infrequently, no previous studies have evaluated the impact of symptoms in terms of disability and quality of life on a community-based sample.

This paper presents estimates of the prevalence of SS based on data from a population-based, cross-

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sectional survey of adults aged 18–75 yr carried out in the UK. In addition to estimating the size of the problem, we present the first population data demonstrating the impact of SS.

## METHODS

### *Study design*

The study design was a two-phase, cross-sectional survey consisting of a baseline questionnaire and subsequent home visit by a research nurse. Responders to the questionnaire were contacted by telephone and permission was sought for a home visit which involved an interview, examination and a blood test. Ethical approval was granted by the local research and ethics committee.

### *Study population*

The study population consisted of 1000 adults, aged 18–75 yr, who were randomly selected from a population register of individuals enrolled with a local general practice in the south of Manchester, UK. As general practice registers cover >95% of the population in the UK [27] and access to most other health service care is through the general practitioner, this register is therefore a convenient frame for a local population survey.

Under the conservative assumption of a minimum prevalence of 20/1000 and assuming a 75% response, this sample size would be sufficient to provide estimates with a 95% confidence interval of $\pm$ 1%. There were insufficient data from published sources to guide whether stratified sampling would be inappropriate. We chose, *a priori*, to study only two age groups: above and below 55 yr of age. Thus, the precision of the prevalence estimates in these two age groups and in the two genders would be <1%, but sufficient to provide estimates of large differences.

### *Baseline survey*

The baseline survey consisted of a self-completed postal questionnaire, labelled as a 'rheumatism survey'. This questionnaire inquired about demographic factors such as age, gender and, amongst other self-reported symptoms, contained four broad questions pertaining to symptoms of dry eyes and dry mouth. The questionnaires were mailed with pre-paid envelopes. Subjects who did not respond to the initial questionnaire were sent up to two repeat mailings at 1 month intervals. Those subjects responding to the initial mailing are referred to as 'first-time' responders, whilst those who responded only after the reminder mailings are termed the 'reluctant' responders. All responding subjects were asked whether they would be willing to participate in an in-depth home interview and examination of their eyes and mouth. Separate permission was sought for the collection of a blood sample.

### *Home visit*

The interview, carried out by a research nurse, consisted of an interviewer-administered questionnaire and an examination. Subjects were asked to report whether they had suffered from any of three specific oral and three specific ocular symptoms for a period of at least 3 months (see Table I). Information was also gathered on any disability or physician-diagnosed long-standing illness, with special emphasis on RA and SLE, and details were obtained of all current medication.

TABLE I
Criteria for the classification of Sjögren's syndrome (modified from Vitali *et al.* [1])

1. Ocular symptoms for at least 3 months

*A positive response to at least one of the three following questions:*

   a) Troublesome dry eyes every day?
   b) A recurrent sensation of sand or gravel in your eyes?
   c) Do you use artificial tears more than 3 times a day?

2. Oral symptoms for at least 3 months

*A positive response to at least one of the three following questions:*

   a) Does your mouth feel dry every day?
   b) Have you had recurrent or persistent swelling of your salivary glands as an adult?
   c) Do you frequently have to take a drink in order to swallow food?

3. Ocular test
   A positive Schirmer-I test ($\leqslant$5 mm in 5 min)
4. Oral test
   A positive unstimulated salivary flow measurement ($\leqslant$0.5 ml in 5 min)
5. Autoantibodies

*Presence of at least one of the following serum antibodies:*

   a) Antibodies to Ro/SS-A or La/SS-B antigens (value >2 U/ml)
   b) Antinuclear antibodies (dilution $\geqslant$1 in 40)
   c) Rheumatoid factor (dilution >1 in 20)

The following tests were carried out on all interviewed subjects. A Schirmer-I test was performed to measure lachrymal flow [28]. The unstimulated whole salivary flow (USF) was recorded to measure salivary function [28]. Blood samples were taken for the measurement of antibodies to Ro and La (by ELISA), antinuclear antibodies (ANA) (by indirect immunofluorescence), and rheumatoid factor (RF) (by latex) (Table I).

We assessed the impact of SS on three aspects of health: (i) psychological distress; (ii) fatigue; (iii) health status. Levels of psychological distress were measured using the 12-item General Health Questionnaire (GHQ) [29] which identifies symptoms of depression and anxiety of a recent onset. There are four categories of response to each item, yielding a total GHQ score between 12 and 48. The severity of fatigue was measured (score 14–56) using the Health and Fatigue Questionnaire (HFQ) [30]. The Medical Outcome Study Short Form-36 (SF-36) [31] was used to measure health status in eight 'dimensions': physical functioning, social functioning, role limitation due to physical problems, role limitation due to emotional problems, mental health, vitality, pain and general perceptions of health. The items for each dimension are summed and then transformed to a scale of 0 (worst possible health status) to 100 (best possible health status).

*Analysis*

*Case definition*. Table I shows the five criteria used in the classification of SS. Subjects who had at least four positive criteria out of the possible five were classified as positive for SS. A further refinement to the classification of SS was made dependent on the subjects' autoantibody status, i.e. subjects with positive autoantibodies were classified as having 'autoimmune' SS.

*Presence of positive criteria in the diagnosis of Sjögren's syndrome.* The number of subjects classified as positive for each of the individual criteria and those who satisfied the criteria for SS was calculated for the interviewed population. This analysis was repeated separately for males and females, and across two age groups ($<55$ yr, $\geqslant 55$ yr).

*Estimated population prevalence of Sjögren's syndrome.* Inevitably, in a survey which contains a fairly lengthy questionnaire and relatively invasive tests, there will not be complete data on the whole study population. Firstly, 384 (38%) of the targeted study population did not reply to the initial or reminder postal questionnaires and thus did not provide information on even the broad eye and mouth symptoms. The prevalence of such symptoms may be different in those who did and did not respond. Secondly, not all of those subjects who responded to the questionnaire agreed to participate in a home visit and thus data on detailed symptoms and test results are lacking. Clearly, those subjects examined may be selectively different in their likelihood of having SS from those not examined.

Such differences between the groups may introduce important selection bias and affect the calculation of the prevalence estimates. Therefore, to take account of such bias, we based the calculations of our prevalence estimates on a series of assumptions (Table II). The aim of these assumptions was to give a range of estimates in which the true population prevalence was likely to fall.

These assumptions resulted in four prevalence estimates which allowed for the influence of questionnaire non-response and/or home visit non-participation. Each of these prevalence estimates refers to the expected number of subjects who would be classified as having SS in the target study population ($n = 1000$). Confidence intervals for these estimated rates, at the 95% level, were calculated using the exact binomial distribution and represent the range in which the estimated prevalence would lie had all subjects in the target population sample been interviewed. Estimates were also calculated separately across gender and age ($<55$ yr, $\geqslant 55$ yr). All analyses were carried out using the STATA statistical software package [32].

*Impact of Sjögren's syndrome.* Scores from the GHQ, HFQ and the eight dimensions of the SF-36 were compared in those subjects classified with SS and those not given a positive classification ('non-cases'). The percentage of subjects suffering from a long-term illness, disability or having a physician's diagnosis of either RA or SLE was calculated for the two groups.

TABLE II
Assumptions used in the calculation of prevalence estimates

*Questionnaire response*

a. The frequencies of the broad oral and ocular symptoms in those not responding to the postal questionnaire were the same as all those subjects responding in the age ($</\geqslant 55$ yr) and gender groups (Assumes no questionnaire response bias)
b. The frequencies of the broad oral and ocular symptoms in those not responding to the postal questionnaire were the same as in the 'reluctant responders' in the age ($</\geqslant 55$ yr) and gender groups, i.e. those subjects who responded only after a reminder (Assumes questionnaire response bias)

*Home visit participation*

c. The estimated participation rate in the home visit within the questionnaire non-responders is the same as the questionnaire responders and the frequencies of Sjögren's syndrome in subjects not participating, within each broad symptom category, were the same as in those who participated (Assumes no non-participation bias)
d. The estimated participation rate in the home visit within the questionnaire non-responders is the same as the questionnaire responders and the frequency of Sjögren's syndrome for subjects not participating was nil (Assumes maximum non-participation bias)

*Prevalence estimates*

| | |
|---|---|
| Crude estimates | Assumptions a and c |
| Estimates adjusted for non-response to questionnaire | Assumptions b and c |
| Estimates adjusted for non-participation to home visit | Assumptions a and d |
| Estimates adjusted for both non-response to questionnaire and non-participation to home visit | Assumptions b and d |

## RESULTS

*Study population*

Results of the response to the baseline survey and home visit have been published elsewhere [33] and are also represented schematically in Fig. 1. In summary, of the 1000 subjects mailed a baseline survey, a completed questionnaire was returned by 616, 38% of whom responded only after at least one reminder. The response to the baseline survey was higher in females than in males (65% *vs* 59%; $P = 0.04$) and those aged $\geqslant 55$ yr (73% *vs* 58%; $P < 0.0001$). The frequency of broad dry eyes (DE) and mouth (DM) symptoms

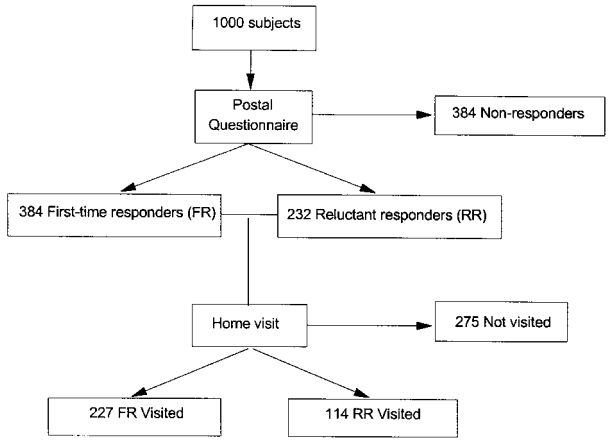


FIG. 1.—Schematic diagram of the study population.

reported at initial contact, overall, and by gender and age, is presented in Table III. A significantly higher proportion of 'first-time' responders reported both symptoms of dry eyes (27% *vs* 19%; $P = 0.02$) and of dry mouth (26% *vs* 19%; $P = 0.04$) compared to those subjects who responded only after a reminder questionnaire.

A successful interview was carried out in 341 (55%) subjects who responded to the baseline survey. Those subjects willing to be examined were more likely to report the presence of dry eye (30% *vs* 17%; $P = 0.0001$) and mouth symptoms (27% *vs* 19%; $P = 0.03$) at initial contact than those who refused to participate further. In addition, those interviewed were also more likely to report the presence of any ache or pain in the month prior to the baseline survey, specifically back, neck and shoulder pain.

*Presence of positive criteria in the diagnosis of Sjögren's syndrome*

Overall, 28% of those interviewed reported having at least one of the specific ocular symptoms for $>3$ months and a slightly lower figure (24%) reported suffering from at least one of the specific oral symptoms. Both ocular and oral symptoms were more prevalent in females and those over the age of 55 yr. An abnormal USF (Table I) was recorded in 93 subjects (27%) and was, again, more frequent in females and subjects $\geqslant 55$ yr. The prevalence of a positive Schirmer-I test was lower at 21% with the percentage being higher for males and the older subjects. Sixteen per cent of subjects ($n = 56$) tested positive for the presence of at least one of the three required serum autoantibodies. The majority of these subjects ($n = 32$) tested positive for anti-Ro and/or anti-La antibodies, 23 had positive ANA and 11 were positive for RF. A higher prevalence was seen in the older subjects, but there was little difference between the genders (Table IV).

Only 13 subjects (3%) had four or more positive criteria and thus satisfied our definition of SS, with none suffering from any of the disorders noted within the classification exclusion criteria [1]. This proportion was higher in females (4.8%) than males (2.6%), and in those aged $\geqslant 55$ yr (5.0%) compared with those aged $<55$ yr (3.2%). A higher proportion was found in the 227 'first-time' questionnaire responders (4.4%) who participated in the follow-up compared with 114 'reluctant' responders (2.6%). Of the 13 subjects classified as positive for SS, six also satisfied the criteria for autoimmune SS; only one of these was male and there were equal numbers across the age groups (Table IV).

*Estimated prevalence of Sjögren's syndrome*

Estimated prevalence rates of SS, overall and for the subgroup who had evidence of autoimmunity, using the assumptions described in Table II, are presented in Table V. The denominator used throughout was based on the target mailed population of 1000. Adjusting for non-response to the questionnaire alone reduced the prevalence estimates by very little (35/1000 compared with 33/1000). When we assumed maximum non-participation bias, the estimated prevalence rate decreased by 40% (35/1000 compared with 21/1000). The additional effect of adjusting for non-response, as well as non-examination, was relatively small (21/1000 compared to 18/1000). The prevalence estimates calculated were similar for those subjects with and without positive autoantibodies (Table V).

Table VI reports the prevalence of SS separately for gender and age groups. The calculated crude rates were highest for females (41/1000) and those aged $\geqslant 55$ yr (49/1000). Subjects with SS were more likely to be female (69% *vs* 55%) and older (median age 54 yr *vs* 48 yr) compared with the non-cases, although neither of these differences were statistically significant. Using information collected at interview, we were able to assess whether other co-morbidities or prescribed therapies could have caused the symptoms and signs of sicca syndrome. Of the 13 subjects classified with SS, none reported suffering from chronic anxiety or thyroid problems, although two reported they have been diagnosed as diabetic by their GP, both of whom tested positive for the presence of autoantibodies.

TABLE III
Number (%) of subjects reporting dry eye and dry mouth symptoms at recruitment: overall, by gender, age and responder group

| | | Gender | | Age | |
|---|---|---|---|---|---|
| | Overall ($n = 616$) | Males ($n = 292$) | Females ($n = 324$) | $<55$ yr ($n = 422$) | $\geqslant 55$ yr ($n = 194$) |
| All responders | | | | | |
| Dry eyes* | 141 (24%) | 61 (21%) | 80 (26%) | 87 (21%) | 54 (30%) |
| Dry mouth† | 137 (23%) | 64 (22%) | 73 (24%) | 87 (21%) | 50 (27%) |
| First-time responders | | | | | |
| Dry eyes | 99 (27%) | 41 (25%) | 58 (29%) | 59 (25%) | 40 (32%) |
| Dry mouth | 95 (26%) | 44 (27%) | 51 (26%) | 58 (24%) | 37 (29%) |
| Reluctant responders | | | | | |
| Dry eyes | 42 (19%) | 20 (17%) | 22 (21%) | 28 (16%) | 14 (27%) |
| Dry mouth | 42 (19%) | 20 (17%) | 22 (21%) | 29 (17%) | 13 (24%) |

*Data on broad ocular symptoms are missing for 27 subjects (14 first-time/13 reluctant responders).
†Data on broad oral symptoms are missing for 26 subjects (13 first-time/13 reluctant responders).

TABLE IV
Number (%) of examined subjects with positive criteria: overall, by gender and age

| | Gender | | Age | | |
|---|---|---|---|---|---|
| Criteria | Males | Females | <55 yr | ⩾55 yr | Total |
| Oral symptoms | 40 (26%) | 57 (30%) | 56 (25%) | 41 (34%) | 97 (28%) |
| Abnormal USF | 36 (24%) | 57 (30%) | 44 (20%) | 49 (41%) | 93 (27%) |
| Ocular symptoms | 25 (16%) | 56 (30%) | 46 (21%) | 35 (29%) | 81 (24%) |
| Positive Schirmer-I | 37 (24%) | 33 (17%) | 38 (17%) | 32 (27%) | 70 (21%) |
| Presence of autoantibodies | 23 (15%) | 33 (17%) | 31 (14%) | 25 (21%) | 56 (16%) |
| Sjögren's syndrome* | 4 (2.6%) | 9 (4.8%) | 7 (3.2%) | 6 (5.0%) | 13 (3.8%) |
| 'Autoimmune' Sjögren's syndrome† | 1 (0.7%) | 5 (2.6%) | 3 (1.4%) | 3 (2.5%) | 6 (1.8%) |

*Sjögren's syndrome diagnosed as at least four positive criteria out of a possible five.
†Autoimmune Sjögren's syndrome diagnosed as at least four positive criteria out of a possible five, including positive test for autoantibodies.

TABLE V
Estimated prevalence rates per 1000 subjects (95% CI*) for Sjögren's syndrome ('autoimmune' and 'non-autoimmune')

| | Sjögren's syndrome | 'Autoimmune' Sjögren's syndrome | 'Non-autoimmune' Sjögren's syndrome |
|---|---|---|---|
| Crude | 35 (25,48) | 16 (9,26) | 19 (12,30) |
| Adjusted for non-response to questionnaire | 33 (23,46) | 16 (9,26) | 18 (11,28) |
| Adjusted for non-participation to home visit | 21 (13,32) | 10 (5,18) | 11 (6,20) |
| Adjusted for non-response and non-participation | 18 (11,28) | 8 (3,16) | 10 (5,18) |

*95% CI (calculated using the exact binomial distribution).

TABLE VI
Estimated prevalence rates per 1000 subjects (95% CI*) for Sjögren's syndrome: by gender and age group

| | Gender | | Age | |
|---|---|---|---|---|
| | Males | Females | <55 yr | ⩾55 yr |
| Crude | 25 (16,37) | 41 (30,55) | 31 (21,44) | 49 (37,64) |
| Adjusted for non-response | 24 (15,36) | 38 (27,52) | 30 (20,43) | 46 (34,61) |
| Adjusted for non-examination | 14 (8,23) | 27 (18,39) | 17 (10,27) | 31 (21,44) |
| Adjusted for non-response and non-examination | 13 (7,22) | 21 (13,32) | 15 (8,25) | 27 (18,39) |

*95% CI (calculated using the exact binomial distribution).

Additionally, four subjects also reported taking antidepressants or diuretics, both medications known to be associated with sicca symptoms.

*Impact of Sjögren's syndrome*

Summary statistics for the GHQ, HFQ and the eight dimensions of the SF-36 are presented in Table VII. Higher levels of depression/anxiety and fatigue were evident in those 13 subjects classified as SS compared with the 328 who were non-cases. Subjects classified with SS had significantly lower median scores for each of the eight dimensions of the SF-36, indicating a greater impact on health status.

Overall, 190 (55%) of the subjects interviewed reported suffering from a long-term illness or disability. The percentage was lower in the non-cases (54%) than those diagnosed with SS (69%). A diagnosis of RA or SLE was reported by 11 subjects (two SS, nine non-cases).

## DISCUSSION

This study presents the findings from a population-based survey of the prevalence of SS and is the first to assess the impact of the syndrome in the general population. We have demonstrated that SS is relatively common in the general population compared with other autoimmune rheumatological disorders: RA 1% [34] and SLE 0.03% [35], and has a significant impact on perceived health and well-being.

Allowing for the presence of possible questionnaire non-response generated a best estimate for the prevalence of SS at 33/1000 individuals (95% CI 23–46). A more conservative, minimum prevalence estimate of 18/1000 individuals (95% CI 11–28) was calculated by additionally assuming maximum non-participation at the second stage of the study. Approximately half of the positive subjects appeared to have 'autoimmune' SS characterized by the presence of ANA, RF or antibodies to Ro or La. Comparison between our results and those from other population surveys has been hampered by methodological problems, such as the use of differing classification criteria sets, differing ages of subjects studies and the failure of other studies to take non-response bias into account (Table VIII). However, our results confirm previous reports that SS is particularly common in elderly females.

TABLE VII
Difference in 'quality of life' measures between subjects diagnosed with Sjögren's syndrome and those not given a diagnosis

| Median (IQR) | Sjögren's syndrome ($n = 13$)* | Non-cases ($n = 328$)* | Mann–Whitney $P$ value |
|---|---|---|---|
| SF-36 dimension† | | | |
| Physical functioning | 38 (25–75) | 90 (65–100) | 0.0192 |
| Bodily pain | 31 (17–41) | 72 (41–84) | 0.0006 |
| General mental health | 52 (44–68) | 76 (60–88) | 0.0514 |
| General health perceptions | 34 (15–61) | 67 (50–82) | 0.0024 |
| Vitality | 33 (18–43) | 55 (40–75) | 0.0027 |
| Physical role limitation | 0 (0–0) | 100 (25–100) | 0.0001 |
| Emotional role limitation | 0 (0–100) | 100 (33–100) | 0.0006 |
| Social functioning | 38 (25–63) | 88 (63–100) | 0.0013 |
| General Health Questionnaire‡ | 28 (26–33) | 23 (20–26) | 0.0028 |
| Health and Fatigue Questionnaire‡ | 36 (34–40) | 29 (27–35) | 0.005 |

*Owing to missing data, the scores for each group may not be based on the total number within the group.
†Low score indicates a more severe problem.
‡High score indicates a more severe problem.

TABLE VIII
Prevalence estimates of Sjögren's syndrome in other studies

| Study | Setting | Classification criteria | Pop[n] | Female:male | Age range (yr) | Prevalence (per 1000) |
|---|---|---|---|---|---|---|
| Whaley *et al.* [10] | Glasgow, UK | 'Definite' KCS* + xerostomia | 122 | 1:0.4 | 81–93 | 33 (35F/28M) |
| Drosos *et al.* [11] | Ioannina, Greece | Greek [19] | 62 | 1:1.1 | 67–95 | 48 (100F/0M) |
| Jacobsson *et al.* [12] | Malmö, Sweden | Copenhagen [18] | 705 | Not stated | 52–75 | 27 |
| Zhang *et al.* [13] | Beijing, China | Copenhagen [18]<br>San Diego [16] | 2066 | 1:0.4 | 16–60 | 8 (11F/2M)<br>3 |
| Hochberg *et al.* [14] | Salisbury, USA | KCS + xerostomia + presence of AA† | 2341 | Not stated | 65–84 | 0.4 |
| Dafni *et al.* [15] | Aitoloakarnania, Greece | Vitali [1] | 837 | All female | 18+ | 6 |

*KCS–keratoconjunctivitis sicca.
†AA–autoantibodies.

For the first time, we have shown that complaints of fatigue and depression, commonly reported in clinic populations with SS [36, 37], are also present in community-based samples. The link between SS and such conditions as fibromyalgia and chronic fatigue syndrome (CFS) has been well documented [25, 36, 38]. Features of fibromyalgia have been reported in patients diagnosed with SS [36] and sicca symptoms have been described as one of the commonest manifestations of CFS [38]. In addition to this increased level of morbidity, community subjects with SS appeared to have significantly poorer health status compared with non-cases.

In our cross-sectional survey, clearly we cannot establish cause and effect with respect to symptoms of dry eyes and mouth, and complaints of fatigue, depression and poor health status. Confounders such as smoking or medication may also have influenced our results, although there was no overall difference demonstrated between those with or without SS with respect to these variables. In addition to the difficulty of establishing a temporal relationship, the comparisons of these measures were based on only 13 subjects suffering from the syndrome under investigation. Whatever the reason, the burden of ill health suffered by subjects with SS appears to be substantial and warrants further investigation in a larger sample using a prospective study design.

There are certain limitations to our study, the most important of which is that only 34% of the original target population agreed to participate in both phases of the study. First, a low response rate to participation in a home visit appears to have introduced selection bias; the presence of subjective oral and ocular symptoms was higher in those interviewed than those not interviewed. Differences were also found in the prevalence of these symptoms between the 'first-time' and 'reluctant' responders. To take account of this, we introduced a series of assumptions similar to those employed in similar population surveys [39, 40]. Chief amongst these is to assume that the non-responders are likely to be closer to 'reluctant' responders than 'first-time' responders in their symptom prevalence. It is obviously difficult to verify this. However, the data comparing (i) 'first-time' with 'reluctant' responders and (ii) interview participants with non-interviewed participants do go some way to supporting these assumptions. Therefore, we feel that the estimates calculated give a realistic range in which the true population prevalence lies, although the confidence

intervals are artificially narrow as they are calculated assuming that a classification was available for all 1000 subjects in the population.

Second, we were unable to apply the European classification criteria exactly as proposed by the authors [1]. The reasons for this have been discussed elsewhere [33], but briefly relate to problems with standardization of techniques in patients' homes, and the impracticality of performing certain tests in the field setting. It was also not feasible to use the classification tree form of the European criteria [1] because lip biopsy, one of the early nodes in the tree, was considered unethical in a community survey. The effect of these methodological limitations would lower our reported prevalence estimates. Hence, our results should be regarded as minimum estimates of the frequency of SS in the general population.

In conclusion, SS is a relatively common complaint in the community which often goes unrecognized. We have presented an undiagnosed group of subjects who have considerable unmet health care needs, particularly relating to the recognition and management of associated disability.

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