

## **Supplementary file 1**

Additional information on materials and methods:

### 1. EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI).

This instrument has been developed recently to assess the key symptoms of pSS patients – dryness, pain and fatigue <sup>1</sup>. A single 0-10 numerical scale is used to assess each of these symptoms. The ESSPRI score is a global measure of the severity of the symptoms experienced by the patients and is defined as the mean of the domain scores of dryness, limb pain and (somatic) fatigue. The EULAR sicca score (EULAR-SS), a measure of overall severity of dryness experienced by the patients, is defined as  $(2 \times \text{oral dryness} + \text{ocular dryness})/3$ .

### 2. Profile of fatigue and discomfort

To quantify fatigue levels in pSS, all pSS patients completed the Profile of fatigue and discomfort (ProFAD) questionnaire <sup>2</sup>. The ProFAD is the first patient-reported outcome tool designed specifically for PSS patients <sup>3</sup>. The ProFAD was originally designed with 64 questions to assess different 'facets' of symptoms commonly experienced by PSS patients. However, this was considered burdensome and a shorter version has been developed with 19 questions, each reflecting a single 'facet' of the longer version <sup>2</sup>. Each item is scored on an 8 point (0-7) likert scale and an average is taken for the domain score. There are 6 questions in this instrument which assess somatic and mental fatigue along with a visual analogue score, ranging from 0 for absent to 100 for worst imaginable perceived fatigue levels. A score of above 2.0 and

1.8 are considered significant for the somatic fatigue and mental fatigue domains, respectively <sup>3,4</sup>.

### 3. Epworth Sleepiness Scale (ESS)

This instrument assesses daytime somnolence in 8 typical situations such as watching TV or as a passenger in a car <sup>5</sup>. Patients are asked to score on a scale of 0, 'would never doze off' to 3, 'high chance of dozing off' for each of these situations. The total ESS score is the sum of the score for each situation. A score of 10 or above indicates significant daytime somnolence. A score of  $\geq 8$  and  $<10$  indicates moderate daytime somnolence.

### 4. Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item (7 items per subscale) measure of anxiety (HADS-A) and depression (HADS-D) <sup>6</sup>. The HADS was specifically developed for use in physical illness by excluding items related to somatic symptoms. Each subscale has a maximum score of 21, with a score of 8-10 considered 'borderline' and a score of over 10 "definite" case of generalised anxiety disorder or major depressive state respectively.

### ***Assessment of health-related quality of life***

#### *EuroQuol-5 Dimension health measure (EQ-5D)*

The EQ-5D is a standardised measurement of health related – quality of life. Five different dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) are assessed <sup>7</sup> ([www.euroqol.org](http://www.euroqol.org)). Each dimension can be scored by 3 possible responses; 1- no problems, 2-

some/moderate problems and 3-severe problems. From here, each patient score is converted into a health status, which ranges from -1 to 1, with 1 being full health. Patients scoring lower than 0 are considered to have significantly bad health or disabled. This assessment tool also includes a visual analogue score for how good or bad the individual perception of his or her health on a 0-100 scale, with 0 being 'worst imaginable health state' and 100 being 'best imaginable health state'.

### ***Assessment of PSS disease activity***

*EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI).*

All PSS subjects were assessed for disease activity using the ESSDAI<sup>8</sup>. This index consists of 12 domains of disease activity in PSS; constitutional, lymphadenopathy, glandular, articular, cutaneous, pulmonary, renal, muscular, peripheral nervous system, central nervous system, haematological and biological. Each domain was selected according to its organ specific relevance to disease activity based on clinical experience, literature review and previous work of a panel of SS experts. For each domain, a score between 0 = 'no activity' to 3 = 'high activity' is given, with the exception of the constitutional, glandular and biological domains which a score of 0-2 is given. Each domain is then weighted according to its contribution to the overall disease activity in the original derivation datasets. The sum of each weighted domain score gives the total score.

### ***Community controls cohort***

The Newcastle Fatigue Interest Group (led by co-corresponding author JLN) has acquired a bank of community control data that has been developed through a number of research studies to investigate the pathogenesis of fatigue in a range of chronic diseases including primary biliary cirrhosis<sup>9</sup>, chronic fatigue syndrome<sup>10</sup>, primary Sjögren's syndrome and idiopathic thrombocytopenia. The cohort was created through advertisement in the local community (Newcastle upon Tyne, UK) inviting people who are generally healthy to participate in research into the autonomic nervous system. In addition, participants when completing symptom assessment tools including are asked to invite a friend of similar age and sex who are healthy and does not have chronic disease to complete the same measures which include the COMPASS. This approach has provided a resource of 596 subjects from which the matched controls for this study were drawn. This community cohort did not undergo full medical examination. Therefore, it is possible that a proportion of the cohort may have underlying medical conditions that predispose to autonomic symptoms.

#### References:

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