Estimating Indirect Costs in Primary Sjögren's Syndrome

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ABSTRACT. ***Objective.*** To estimate the indirect costs associated with primary Sjögren's syndrome (pSS) compared with rheumatoid arthritis (RA) and community controls.

Methods. Data were obtained from 84 women patients with pSS as part of a study to develop a systemic activity measure, from 87 consecutive women patients with RA attending a hospital clinic, and from 96 women community controls on a general practice list. A modified economic component of the Stanford Health Assessment Questionnaire was used to assess lost productivity.

Results. Using a conservative model, the estimated total annual indirect costs (95% CI) were £7677 (£5560, £9794) for pSS, £10,444 (£8206, £12,681) for RA, and £892 (£307, £1478) for controls. Using a model that maximizes the estimates, the equivalent figures were £13,502 (£9542, £17,463), £17,070 (£13,112, £21,028), and £3382 (£2187, £4578), respectively. These were all significantly greater at $p < 0.001$ for patient groups than for the control group.

Conclusion. pSS is associated with significantly increased indirect costs equivalent to 69%–83% of that for patients with RA. This needs to be taken into account when evaluating the overall economic consequences of pSS. (J Rheumatol First Release April 1 2010; doi:10.3899/jrheum.090734)

Key Indexing Terms:
PRIMARY SJÖGREN'S SYNDROME INDIRECT COSTS PRODUCTIVITY

Primary Sjögren's syndrome (pSS) is an immune-mediated rheumatic disease in which inflammation of exocrine glands leads to dry eyes and dry mouth[1]. Patients typically also complain of fatigue and arthralgia and have reduced health-related quality of life[2].

Although symptomatic therapy is available for dry eyes and, to a degree, for dry mouth, there is no conventional disease-modifying therapy or therapy for the fatigue and other systemic features. With the continuing development of new biological therapies against a range of molecules, there is some hope that one or more of these therapies could be effective in treating this condition[3-5].

In order to justify the provision of such expensive therapies for pSS, we need to measure the economic burden associated with the disease. We have previously assessed the direct healthcare costs (the value of resources used in the diagnosis, treatment, and rehabilitation of a disease) of pSS[6]. In our current study, we report the potential indirect costs representing the value of economic productivity lost due to the disease, including both labor and other activities such as housework and childcare.

MATERIALS AND METHODS

The data from patients with pSS in our study were collected as part of a broader project to develop activity and damage measures for use in clinical trials in pSS[7,8]. The objective was to recruit a minimum of 100 patients with pSS based on a pragmatic decision that this should be achievable from the participating centers and offered a reasonable chance of meeting the scientific objectives of the main study. We recruited 114 consecutive women patients with pSS fulfilling the American-European consensus criteria (AECC)[9] between April 2003 and June 2005 from 8 UK hospitals. One patient declined to participate and 2 others, following reevaluation, did not fulfill the AECC. Of the 111 eligible patients, 81 completed and returned the study questionnaire. Three additional patients with pSS who returned data after the end of recruitment to the main study were also included, for a total of 84 patients with pSS. This was felt to be a reasonably sized convenience sample for an initial study.

For disease controls, 87 consecutive women patients with rheumatoid arthritis (RA) recruited from the Rheumatology Department at Selly Oak Hospital, Birmingham, UK, completed the questionnaire. Only 1 additional patient declined to participate.

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The study questionnaire along with a screening questionnaire on health and medication usage were posted to a convenience sample of 400 women patients on a local general practitioner's list, aged between 20 to 80 years. Ninety-six completed questionnaires were returned. As this number was comparable to the number of patients with pSS, we did not perform a second round of invitations. When we have used this approach previously[10], there were no differences in the demographics of sequential rounds of invitations.

Multi-Centre Research Ethics Committee approval was received for this study and written informed consent was obtained from all patients.

Study instrument and calculation of indirect costs. Lost productivity was measured using a modified version of the economic portion of the Stanford Health Assessment Questionnaire[11]. This questionnaire asks about time lost from work, etc., because of illness rather than because of a specific condition. The disease "specificity" is then quantified through differences in the means between different disease groups. Indirect costs were estimated according to the human capital approach, which attempts to value an individual's contribution to the economy and measures indirect costs in terms of time lost from work due to illness, either in the work force or unpaid work at home[12,13]. Time lost from labor market activity represented 2 components: the additional weekly hours participants reported they would be working if they were not ill and actual days patients reported missing from their current work schedule because of illness. Additional expected hours if not ill were computed separately for patients currently working, over weeks actually worked in the previous 6-month period, and for weeks not worked, as well as for patients who had not been working. Average sex-matched and age-matched wages for 2008 as published by the UK Office for National Statistics (www.statistics.gov.uk) were then multiplied by the time lost to value losses in productivity.

Time lost from unpaid labor represented the difference between the number of hours participants devoted to domestic and volunteer work and the number of hours they would have devoted if they were not ill. The associated costs were estimated using 2 methods. In the replacement cost method, estimates of the value of lost time in household work are made based on expected earnings of service workers. The alternative opportunity cost method values household work as equivalent to the amount the person might have earned in the labor market based on sex-matched and age-matched wages, assuming the patients are representative of the wider population.

Time that helpers spent accompanying the patient to hospital visits or other health services was also included and valued according to the same methodologies.

Missing values. A number of assumptions were made. Where patients did not complete the question on the number of weeks worked in a 6-month period (n = 7), the assumption was made that the whole 6-month period was worked, and that if numbers relative to hypothetical behavior if there were no health problem were missing (n = 80), that there would be no change from the current working schedule. In cases where the current amount of housework was left blank (n = 45), the assumption was made that it would be unchanged in a hypothetical no-ill-health scenario. In 7 patients, the question on current numbers of hours/week of housework in the past month was answered by the number of hours of housework/month and this was corrected before the analysis.

Statistical analysis. Demographics were expressed using means and SD. Simple and age-adjusted means were also computed with their 95% CI for components of lost productive time and for estimates of indirect costs. Comparisons between groups were calculated using nonparametric statistical tests (Mann-Whitney U test) for demographics, as well as conventional F-tests and t-tests for differences between mean productivity losses in each group, both before and after adjusting for age.

Age adjustment. Mean time losses and indirect costs were adjusted for age through linear regressions with age and dichotomous variables for patient groups as independent variables. Adjusted means were thus estimated by predicting all 3 group-specific outcomes at the mean age of controls.

RESULTS

The mean age of the 84 patients with pSS (± SD) was 60 (± 11) years; for the 87 patients with RA it was 61 (± 14) years, and for the 96 community controls, it was 51 (± 14) years. The ages of patients with RA and pSS were significantly different from controls' ages, at $p < 0.0001$. Sixty-nine of 84 patients with pSS (82%) were positive for anti-Ro and/or anti-La antibodies. Sixty-one of 87 patients with RA (70%) were rheumatoid factor-positive and 53 had erosive disease (61%). None of the controls had inflammatory arthritis or a connective tissue disorder. The pSS and RA group are predominantly of Caucasian background (pSS 95%, RA 89%) except for 4 of the patients with pSS (1 is of African Caribbean extraction and 3 of South Asian extraction), and 10 of the patients with RA who are of South Asian extraction. Individual data were not collected from the community controls. Local population data are, however, available through the 2001 UK census (www.statistics.gov.uk/census2001/profiles) and in the local area, 80% are of Caucasian background, 12% of South Asian extraction, and 3% of African Caribbean background. The mean (± SD) disease duration for the pSS group was 7 (± 7) years (time since formal diagnosis using the AECC criteria) and for the RA group, 15 (± 12) years.

Both the pSS and RA groups had a greater number of members aged over 65 (i.e., of retirement age) compared with controls (pSS 25/84, RA 36/87, controls 16/96; pSS vs RA $p = 0.113$, pSS vs controls $p = 0.037$, RA vs controls $p < 0.001$). A greater number of controls were working (either full-time or part-time) compared with both the pSS and RA groups [pSS 26/84 (31%) at an average of 26.7 hrs per week, RA 22/87 (25%) at 28.7 hrs per week, and controls 68/96 (71%) at 33.3 hrs per week; pSS vs RA $p = 0.410$, pSS vs controls $p < 0.001$, RA vs controls $p < 0.001$]. The same was found when examining full-time work only: a greater percentage of controls were employed full-time (30 hrs per week or more) compared to the other groups (15% of patients with pSS were working full-time, at an average of 35.0 hrs per week, 14% of patients with RA, at 38.5 hrs per week, and 49% of controls, at 39.0 hrs per week; pSS vs RA $p = 0.656$, pSS vs controls $p = 0.027$, RA vs controls $p = 0.127$). Four controls over age 65 were still working, as were 1 patient with pSS and 1 patient with RA.

Table 1 sets out the components used in constructing the different estimates of total indirect costs for each of the 3 groups. The numbers given are for the number of hours over a period of 12 months. The 3 main components are loss of time from work, loss of time that would have been spent doing household or voluntary work, and time spent by another individual ("helper") assisting the person obtaining healthcare services (e.g., accompanying them to a hospital appointment).

Time lost from work also has a number of components. At its simplest is sickness absence from the existing work

Table 1. Time component (in annualized hours) of lost productivity. Data are yearly values (95% CI).

	Controls, n = 96	pSS, n = 84	RA, n = 87
Paid work			
Missed hours of paid work within current schedule	22.5 (6.9, 38.1)	35.8 (-3.3, 74.9)	35.4 (–6.2, 76.9)
Loss of regular paid hours from current weekly schedule	16.4 (–13.9, 46.6)	434.4 (278.5, 590.2)*	444.3 (293, 595.5)*
Maximum loss in paid hours for weeks not currently worked for workers†	171.6 (98.7, 244.4)	58.2 (21.3, 95.1)*	33.4 (5.2, 61.6)*
Loss of paid hours for nonworkers	11.9 (–11.7, 35.6)	362.1 (205.8, 518.5)*	371.8 (223.2, 520.3)*
Unpaid work			
Housework time loss	35.1 (–3.7, 74)	146.3 (70.2, 222.4)**,***	401.7 (275.3, 528.1)*
Outside help			
Helper's missed hours of paid work	1.6 (–0.3, 3.4)	10.5 (2.3, 18.7)**	14.5 (1.3, 27.6)**

† Assuming that weeks were not worked because of ill health. * Significant difference from controls, $p < 0.001$. ** Significant difference from controls, $p < 0.05$. *** Significant difference from patients with RA; pSS: primary Sjögren's syndrome; RA: rheumatoid arthritis.

schedule ("missed hours of paid work within current schedule"). Individuals with ill health, however, may also reduce the total number of hours they choose or are able to work during their working week ("loss of regular paid hours from current weekly schedule") and/or reduce the number of weeks they work in a year ("maximum loss in paid hours for weeks not currently worked"). In addition, some individuals who would have otherwise worked do not do so ("loss of paid hours for nonworkers").

In Table 2 we have used these data on time lost to construct 3 estimates of the cost of time lost from work using published age-matched and sex-matched average UK wages available from the Office of National Statistics. In the most conservative approach (low estimate), we combined "sickness" absence with self-reported reductions in hours worked due to ill health within the individual's existing work schedule, for those individuals who were employed. In the intermediate estimate, we added to this the estimated costs of time lost from work by those not employed who would have lost work time had it not been for their ill health. Finally, in the high estimate, we also included the costs associated with those who were employed reducing the number of weeks worked in a year because of ill health.

In order to calculate estimates of total indirect costs we added to the low, intermediate, and high estimates of paid work losses the cost estimates of loss of household/volun-

Table 2. Cumulative indirect annualized costs (£) of lost productivity (based on 2008 age-specific and sex-specific wage except where indicated). Data are yearly values (95% CI).

	Controls, n = 96	pSS, n = 84	RA, n = 87
Paid work			
Cost of paid losses (low estimate)	540 (69, 1012)	6155 (4091, 8218)*	6462 (4378, 8547)*
Cost of paid work losses (intermediate estimate)	705 (–29, 1439)	10,840 (6843, 14,836)*	11,465 (7479, 15,451)*
Cost of paid work losses (high estimate)	2937 (1795, 4079)	11,612 (7652, 15,572)*	11,887 (7935, 15,839)*
Unpaid work			
Housework loss (replacement cost)	330 (–35, 696)	1376 (660, 2093)**,***#	3780 (2590, 4969)*
Housework loss (opportunity cost)	423 (–58, 904)	1745 (814, 2675)**,***	4982 (3393, 6571)*
Outside help			
Cost of helper's missed paid work	22 (–4, 48)	146 (31, 261)**#	201 (19, 384)**
Total indirect costs			
Low estimate for paid work + housework loss (replacement) + cost of helper's missed paid work	892 (307, 1478)	7677 (5560, 9794)*††	10,444 (8206, 12,681)*
Low estimate for paid work + housework loss (opportunity) + cost of helper's missed paid work	985 (325, 1645)	8046 (5868, 10,223)*†	11,645 (9193, 14,097)*
Intermediate estimate for paid work + housework loss (replacement) + cost of helper's missed paid work	1057 (248, 1866)	12,362 (8365, 16,359)*	15,446 (11,523, 19,369)*
Intermediate estimate for paid work + housework loss (opportunity) + cost of helper's missed paid work	1150 (286, 2014)	12,730 (8714, 16,747)*	16,648 (12,639, 20,657)*
High estimate for paid work + housework loss (replacement) + cost of helper's missed paid work	3289 (2125, 4454)	13,134 (9189, 17,079)*	15,868 (11,994, 19,743)*
High estimate for paid work + housework loss (opportunity) + cost of helper's missed paid work	3382 (2187, 4578)	13,502 (9542, 17,463)*	17,070 (13,112, 21,028)*

* Significant difference from controls, $p < 0.001$. ** Significant difference from controls, $p < 0.05$. *** Significant difference from RA patients, $p < 0.001$. † Significant difference from RA patients, $p < 0.05$. †† Significant difference from RA patients, $p < 0.05$ only after age adjustment with regard to controls. Not significant compared with controls after age adjustment with regard to controls. pSS: primary Sjögren's syndrome; RA: rheumatoid arthritis.

tary work and the calculated costs associated with the loss of helpers' time from work. Two options are given for the costs associated with the loss of household work. The first (replacement cost) is based on the wages of household workers (e.g., cost of hiring a cleaner) and the second (opportunity cost) is based on the UK average wage using the assumption that had the individual not had ill health, he or she would have had the opportunity to be employed for these hours.

This approach generates 6 models of increasing estimated total indirect costs. Using the conservative model ("low estimate"), the estimated total annual indirect costs (95% CI) were £7677 (£5560, £9794) for pSS, £10,444 (£8206, £12,681) for RA, and £892 (£307, £1478) for controls. Using a model that maximizes the estimates, the equivalent figures were £13,502 (£9542, £17,463), £17,070 (£13,112, £21,028), and £3382 (£2187, £4578), respectively.

All 6 estimates of mean indirect costs for both pSS and RA groups were substantially greater than in controls, with a significant difference at $p < 0.001$. The mean estimated values for pSS were 69%–83% of those for patients with RA. At the intermediate and high estimates, these did not reach statistical difference between the pSS and RA groups, while for the low estimates, there was a modest statistical difference at $p < 0.05$ using the opportunity cost method to estimate household work loss (Table 2).

The control group was younger than the 2 patient groups. Although we excluded recruitment of controls at the "extremes" of age (under 20 or over 80 years), we did not specifically set out to recruit an age-matched sample. Using linear regression analysis, however, adjusted means were estimated for the patient groups' variables at the mean age of controls. Using this approach, all the total indirect cost estimates for pSS and RA groups remained significantly different from controls at $p < 0.0001$ and the only difference from the results using the unadjusted means was between the lowest estimate in the pSS and RA groups, which became significant at $p < 0.05$ using this approach (data not shown).

DISCUSSION

Cost-of-illness studies provide valuable information for decision makers in allocating healthcare resources. This is particularly relevant to cost-benefit analysis of expensive biological therapies.

We have previously published the only analysis to date of direct healthcare costs in patients with pSS[6]. The direct costs of pSS were estimated at two-thirds to four-fifths of the direct healthcare costs of the comparator RA group. We have now extended this approach through an estimate of the indirect costs of pSS, i.e., the costs of time lost from productive activity by the patients and their helpers as a result of ill health, presumed to result from the condition.

In our study, we used self-reported patient data using the Health Economic component of the Health Assessment Questionnaire[11]. It is legitimate to question the accuracy of self-reported data and this is a potential limitation of the study. Nevertheless, when formally compared, patient-reported data have been shown to generate results similar to health insurance data[14].

We have generated a hierarchy of estimates based on a series of assumptions. The lowest estimate is based on the hours lost from the existing schedule of weeks actually worked, while the highest estimate assumes that weeks not worked are a consequence of ill health. It is evident from Tables 1 and 2 that the indirect costs due to these chronic diseases do not result primarily from increased absenteeism from current work schedules, but rather from a lower probability of holding a job and from reduced work schedules due to illness for those who do have a job.

We have also used 2 estimates of the cost of housework — the lowest based on the costs of hiring a (lower-paid) worker to do the housework (replacement cost) and the higher by valuing the cost of housework at the average wage for the population (opportunity cost). These differing assumptions make a substantial difference for the resulting estimates of total indirect costs (control group: lowest £892, highest £3382; pSS: lowest £7677, highest £13,502; RA: lowest £10,444, highest £17,070). As with the direct costs, the indirect costs associated with pSS are approximately two-thirds to four-fifths (69%–83%) of those for RA.

We have no other studies in pSS to compare these data with but we do have information from other studies in RA[14-23] and in systemic lupus erythematosus (SLE)[12,13]. There are some methodological issues — we have referred to the self-reported nature of the data in most studies (but also evidence that this does appear comparable to independent data sources). The simplest assumption to make for the cost of time lost from work is to use average wages for the general population (human capital approach). This may overestimate real costs from a societal (as opposed to an employer) perspective because in the absence of full employment, if a patient with chronic disease stops working, after a period of time a new employee will take over the patient's role (friction costs method). Short-term sickness absence may be covered by coworkers or by the worker upon return to work. In addition, different studies are likely to use different average costs and this will also be dependent on the country where the study took place.

The number of participants in these studies was also variable — in most studies the numbers ranged from 62 to 383 individuals[14,15,17-21,23]. One study involved 1063 participants[17] and another that used a national registry had 4351 participants[22].

As a consequence of these variations, these different studies generate a wide variation in the estimated annual indirect costs for patients with RA. In order to discuss these studies, we have converted the following data into euros using a conversion rate of £1 = €1.2 = American $1.5 = Canadian $2.

A number of studies, mainly using the friction costs method, estimate the indirect costs of RA at €561 to 3162[14,17,22,23]. Other studies, using the human capital approach but taking a conservative approach to indirect costs, focusing on sick leave and work loss, estimate the indirect costs at €2470 to 5965[14,16,21]. The studies that are most comparable in methodology to our study and include a broader definition of indirect costs generate estimates ranging from €7833 to €10,900[19,20,22,23]. The methodology is generally comparable to that used to generate the "lower estimate" in this study and the figure of €12,532 (£10,444) for the patients with RA in this study is similar to the figure of €10,750 from a previous study of 121 patients with RA[23]. These issues are reviewed in more detail in other studies[14,23].

Because the RA group was recruited primarily as a comparator group to the pSS group, we recruited only women with RA. We might expect that older women with RA would, in general, have lower indirect costs than younger men with RA and, therefore, that our estimates in this study for the RA group would be comparable with the lower estimates in the literature. This was not the case, however, and this might suggest that we have overestimated the indirect costs in this study for the RA group and, by extension, for the pSS group. This should at least be considered when using the data in our study.

Data from SLE are also available from the tri-nation study of healthcare costs in Canada, the USA, and the UK[12,13]. Like pSS, SLE is also a disease of women — 95% of the participants in the tri-nation study were women. SLE is also a disease of younger women (mean age in the UK group in the tri-nation study was 41 years compared with 60 years for the pSS group in this study).

Using an approach equivalent to the "low estimate" (but not including the modest costs associated with time lost by helpers), the annual indirect cost for patients with SLE converted to euros for UK patients was €7617 (replacement cost method for nonlabor market activity) or €9002 (opportunity cost method for nonlabor market activity). These are very similar to the equivalent data for patients with pSS in this study (€9213 and €9655, respectively).

Clearly, in comparing indirect costs associated with different diseases, the demographic profile of the condition will have a major influence. A condition principally affecting young men of working age will have different indirect costs from a condition affecting retired men or women in their 80s. What is particularly interesting in our study is that despite these perceptions, the relative indirect costs of pSS are, with the limitations set out above, of a similar order of magnitude to those of RA and data from SLE. In our view, therefore, if novel therapies are shown to be effective in pSS, the data in this study, subject to more detailed evaluation, may support the use of such therapies on cost-effectiveness grounds as well.

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