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Health Economic Consequences Related to the Diagnosis of Fibromyalgia Syndrome

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Objective. **To evaluate the use and costs of medical resources before and after a diagnosis of fibromyalgia syndrome (FMS) in a large primary care population in the UK.**

Methods. **We applied an existing data set for medical resource use among patients with a coded diagnosis of FMS. The observed quantities of 157 types of medical resource use before and after the diagnosis of FMS were multiplied by unit costs in order to calculate the cost of care (general practitioner [GP] visits, drugs, referrals, and diagnostics) within the National Health Service, excluding hospital costs. Costs before diagnosis were used in a trend analysis to predict later costs, assuming the diagnosis had never been made, and these predicted costs were compared with the observed costs after diagnosis.**

Results. **Following a diagnosis of FMS, a decrease in costs as compared with the predicted trend was observed. In the 4 years after diagnosis, the average difference between the predicted and observed cost was £66.21 per 6 months per patient. This suggests that making the diagnosis leads to savings and a decrease in resource use. The main effect was observed for tests and imaging (£24.02 per 6 months), followed by pharmaceuticals (£22.27), referrals (£15.56), and GP visits (£4.36).**

Conclusion. **Failure to diagnose a true case of FMS has its own costs, largely in excess GP visits, investigations, and prescriptions.**

The fibromyalgia syndrome (FMS) is a disorder characterized by widespread pain and fatigue and is associated with significant morbidity in both patients and their families. According to recent studies, patients with FMS are high consumers of health care services (1–5), and FMS is associated with significant productivity-related costs. The degree of disability and the number of comorbidities are strongly associated with costs (6). From a provider perspective, given the estimated prevalence of FMS of ~3.4% in women and ~0.5% in men (7), FMS is expensive and is associated with a high burden to society (8–12). The differential diagnosis of muscular pain is extensive, and, given the well-known frequency of such symptoms in the population, it is a frequent source of concern for general practitioners (GPs). Patients with FMS may repeatedly present to their GPs with various symptoms before a diagnosis of FMS is made.

There are 2 schools of thought about the diagnostic process. According to the first theory, it is possible that acquiring the label of FMS might lead to increased illness behavior, dependence on health care providers, and increased health service costs. According to the second theory, it is possible that making a definite diagnosis will reduce the number of referrals, use of multiple health care providers, and costs. If the latter hypothesis is confirmed, providers might then be legitimately concerned not only with the costs of diagnosing FMS but also with the costs of not diagnosing FMS.

To test this second hypothesis, we evaluated medical resource consumption by patients as recorded by GPs, in a large primary care population in the UK. We investigated the impact of making a diagnosis of

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FMS on the frequency of GP visits, the use of drugs, patient referrals to specialists, diagnostic tests, and the total cost of medical care (with the exception of hospital costs, which were not available in the data set) within the National Health Service (NHS). This impact can be measured by comparing the observed resource use and costs versus the forecasted trend, assuming that the diagnosis had not been made. Such forecast analyses are already common in health services research (13–17), but we are aware of only one previous study, by Hughes et al (18), in which the technique was used for FMS, based on the same sample frame as that used in the current study.

The present study builds on the earlier study by Hughes et al, in which only the effect on some general types of medical resource use following a diagnosis of FMS was described. In that study, it was shown that following a diagnosis of FMS, the use of most types of health care resources declined. The latter results were reported on an aggregate level, i.e., as the static difference in resource use between patients in whom FMS was ultimately diagnosed compared with a control group, and it was deemed impossible to translate these results into an estimate of potential savings following diagnosis, because no details on different types of resource use were reported. In the current study, we report on the cost of care before and after the diagnosis of FMS, with each subject acting as his or her own control, making use of the detailed original data set as applied by Hughes et al.

PATIENTS AND METHODS

Data source and patients. Hughes et al (18) investigated the burden of disease associated with FMS in "real-life" clinical practice in a large primary care population in the UK. The main focus was on the management of FMS, particularly determination of whether the time period before diagnosis is associated with increased consumption of resources. The burden of FMS was estimated by comparing the frequency in the community of selected clinical outcomes and health care resource use by patients with FMS and persons without FMS, and, among patients with FMS, by comparing the frequency of selected clinical outcomes and health care resource use prior to diagnosis and the frequency during the same time period following diagnosis.

Hughes et al based their study on the Full Feature General Practice Research Database (FF-GPRD), a collection of electronic medical records of patients who have attended >350 general practices in the UK that represents ~4.6% of the UK population. The FF-GPRD database contains longitudinal records from primary care clinics, including demographic information, lists of prescriptions, medical symptoms and diagnoses, referrals, and dates of registration and deregistration from the general practices (19). All patients in the FF-GPRD for whom a definite diagnosis of FMS was recorded in the electronic record after January 1, 1998 and who were registered at the practice for at least 2 years prior to their first diagnosis of FMS were identified as FMS cases. FMS was coded based on either International Classification of Diseases, Ninth Revision (ICD-9) Read codes or Oxford Medical Information System (OXMIS) codes. The Read and OXMIS medical codes are part of a mandatory medical terminology coding system for use in primary care in the UK. Each term identifies a symptom, sign, or diagnosis clinical concept. OXMIS codes are based on ICD-8 codes and the UK office for National Statistics operation codes, whereas Read codes are based on ICD-9 codes. Acceptable patients were determined using logical consistency checks on dates.

The date of FMS diagnosis was defined as the index date. A non-FMS control group (with 10 control subjects per case) was generated by matching subjects for index date, practice, sex, and year of birth. Rates per 100 person-years (with 95% confidence intervals [95% CIs]) of the clinical, therapeutic, and health service outcomes of interest were estimated in 6-month intervals for up to 10 years before and up to 4 years after the index date, by dividing the total number of events by the total exposure time for the respective patient cohort. The investigators determined that patients with FMS had considerably higher rates of visits, prescriptions, and testing from at least 10 years prior to diagnosis compared with controls. By the time of diagnosis, patients with FMS had 25 visits and 11 prescriptions per year compared with 12 visits and 4.5 prescriptions per year in controls. Following diagnosis, the number of visits for most symptoms and health care use markers declined, but within 2–3 years the numbers rose to levels similar to or higher than those observed at the time of diagnosis.

Medical resource use and costs. Our study builds on the results reported by Hughes et al, by translating the observed reduction in resource use into monetary values, based on a detailed assessment of all medical resource use and applying unit costs to each of the identified resource items. Moreover, in order to avoid the typical bias of a pre–post type design, we applied a trend analysis on the prediagnosis data, in order to predict the evolution of costs in case the diagnosis had not been made.

Costs were calculated based on the NHS perspective, by multiplying the numbers of units of medical resource use by the cost per unit. Hence, the cost data collection was performed in 2 steps. First, rates per 100 person-years for different types of health care services were estimated in 6-month intervals for up to 10 years before and up to 4 years after the index date. The rates were obtained by dividing the total number of events by the total exposure time for the respective patient cohort. This was done for the following services: GP visits, tests requested by the GP (62 different types of tests identified), drug prescriptions (for nonsteroidal antiinflammatory drugs, tricyclic antidepressants, selective serotonin reuptake inhibitors, and corticosteroids [78 different drugs identified]), and referrals to secondary care, divided by the type of specialist (16 different types of referrals identified).

Second, for each type of resource use, unit costs were collected from a variety of NHS sources. For laboratory tests, NHS National Reference Costs 2004 and The Royal Hospital

NHS Trust 1999 were used (20,21). For drugs, the British National Formulary 2004 was used (22), and for visits and referrals, the NHS National Reference Costs 2004 were searched (20). The weighted average unit cost of a test was £6.78, the weighted average cost of a 28-day pack of medication was £7.66, the weighted average cost of a referral was £48.41, and the weighted average cost of a GP visit was £19.

Statistical analysis. Each item of resource use (n = 157) was considered as an "event." For the analysis and estimation of the rates of events over time, the number of events and the number of exposed subjects were assessed per 6-month time period. The study time frame ranged from 10 years before and up to 4 years after the index date. Thus, the time to event (TTE) ranged from −10 to +4 years, in 6-month time intervals.

Using 3 sequential variations of similar Poisson log-linear regression models, the event rates of the different outcomes (drug prescriptions, referrals, etc.) were estimated and extrapolated. In the first type of analyses, log-linear regression models were constructed, with the number of patients with a specific event as a dependent variable and the TTE as a class-type independent variable. Because the TTE is entered as a class variable, such models allow for separate number-of-event estimates (+95% CI) at each time interval, i.e., the estimated mean number of events equals the true number of events at this time interval. As offset variables for these models (and the other 2 variations), the natural logarithm of the number of exposed patients was obtained. One can consider this offset variable as the denominator in the event rate formula, as follows: event rate = number of events/number of exposed subjects for that time interval, where the number of events can be estimated by the model. One can thus present the event rates with 95% CIs simply by dividing the number of estimated events and the estimated upper and lower limits of the 95% CI, respectively, by the number of exposed subjects for the corresponding time interval.

In the second Poisson model, the number of events (dependent variable) was estimated by including the TTE as a linear effect instead of a class effect, i.e., the number of events was correlated with the TTE value (range −10 to +4); the quadratic (x^2) and cubic (x^3) effects of TTE were also included. Such a setup models the number of events over time, trying to determine the best fitted curvature based on the linear, quadratic, and cubic effects to allow for maximum flexibility. As a consequence, the estimated event rate at a given TTE time interval does not necessarily agree fully with the true observed event rate. The aim of such models, however, is to estimate the general trend of event rates over time.

In an effort to assess the resource use pattern that could be expected if the diagnosis of fibromyalgia was never made, we then used a third model in which we extrapolated the number of events that occurred after the index date, with the assumption that the diagnosis of FMS was never made. This model again included the TTE as a linear effect but without higher-order terms (quadratic or cubic) and was constructed based only on the data from 4 years before diagnosis.

In summary, the first form of regression model provides exact estimates per time point, permitting an estimate of the mean. The second regression model attempts to use time as a linear predictor. This smoothes out any differences (peaks) between time points that might be attributable to random error. The third model was constructed to assess the impact of the diagnosis: what would the outcome be if the diagnosis was not made? Hence, this model extrapolates beyond the time of diagnosis, using only prediagnosis data (23).

The usually large peak of events during the index date period (6 months before the index date up to the index date), which would not have been witnessed if the diagnosis was not made, was excluded from the trend analysis. Note that due to the log-linear nature of the models, the extrapolated event rates follow an exponential curvature. The models assess the number of events linearly in a log-transformed scale. To assess the number of events, exponentiation of the estimations was performed.

The above-described procedure was repeated for all 157 items (GP visits, 68 laboratory tests, 72 drugs, and 16 referrals); hence, 157 observed and predicted trends were produced. By multiplying the observed and predicted trends in resource use by the unit cost of each resource item, the observed and predicted trends in costs were then calculated. The impact of making the diagnosis on the costs of a specific item was calculated as the difference between the predicted trend and the observed trend in costs. In a secondary analysis, we assumed that the level of resource use before diagnosis would simply be continued (no increase) if no diagnosis would be made. Thus, the predicted curve would be a horizontal line.

RESULTS

In total, between 1998 and the end of March 2003, 2,260 new diagnoses of FMS were recorded in the GPRD. Of the 2,260 diagnoses, 81.3% of the cases were in women, and the mean age of the patients was 49 years.

Figure 1 shows an example (complete blood count) of a resource use trend analysis. The figure represents the ten 6-month periods before, and the four 6-month periods after the index date. Based on this difference in predicted and observed resource use, the difference in costs related to the diagnosis was calculated as explained in Patients and Methods. Table 1 shows an example of such a calculation for the item "complete blood count." The right column of the table shows the net costs (in British pounds) per patient-year, presented per 6-month period after diagnosis. Similar tables for all 157 items are available upon request. Summing the savings (or extra costs) for all 157 items led to a total estimate of the economic impact of making the diagnosis, with the exclusion of hospital costs.

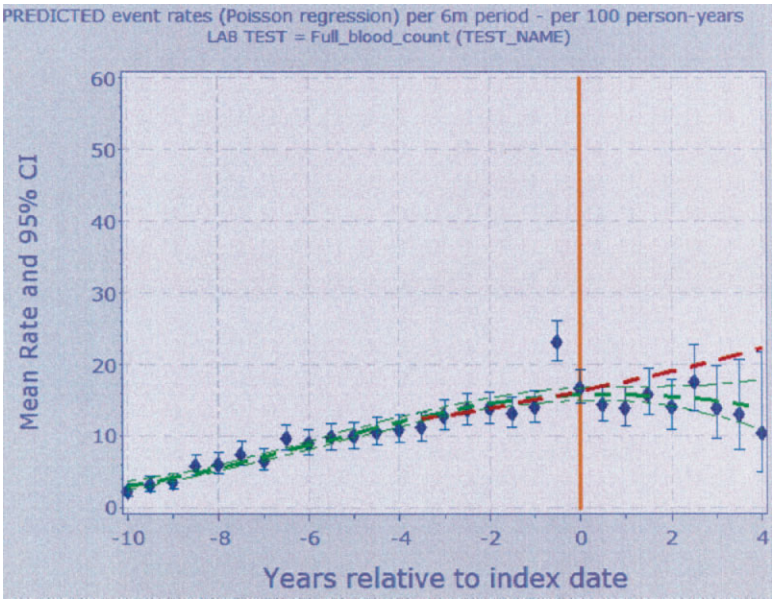

Figure 1. Example of a trend analysis (for the item "complete blood count"). The x-axis represents the 10 periods of 6 months before and the 4 periods of 6 months after the index date. The predicted event rates are represented by the broken red line, starting at period −4. The observed event rates are represented by the broken green line. 95% CI = 95% confidence interval.

The economic impact of making a diagnosis of FMS is presented schematically in Figure 2. The 157 items were grouped in 4 categories, as follows: tests, referrals, GP visits, and drugs. The use of tests clearly decreased from the index date, leading to increasing savings per 6-month period, when comparing the observed trend versus the predicted trend. By the end of the fourth period, the predicted savings were almost £60 per 6-month period. For drugs, by the end of the fourth period the predicted savings were ± £65 per 6 months. For patient referrals, by the end of the fourth year the predicted savings were more than £25 per 6 months. Finally, for GP visits, a different trend was observed, with extra costs in the first three 6-month periods. By the end of the fourth period, the predicted savings were ± £15 per 6 months.

In order to obtain an average estimate of the savings after the index date, the results over the eight

Table 1. Example of calculating the cost impact of making the diagnosis of fibromyalgia syndrome*

Six-month period after diagnosis	Real observed resource use, no. per 100 patient-years	Predicted resource use, no. per 100 patient-years	Real observed cost, £ per patient per year	Predicted cost, £ per patient per year	Difference between observed and predicted cost, £ per patient per year†
0.5	15.85	16.94	0.65	0.68	−0.03
1	15.82	17.61	0.67	0.78	−0.10
1.5	15.69	18.31	0.68	0.88	−0.20
2	15.48	19.05	0.66	1.01	−0.34
2.5	15.19	19.80	0.63	1.15	−0.52
3	14.82	20.59	0.57	1.31	−0.74
3.5	14.39	21.42	0.50	1.49	−0.99
4	13.90	22.27	0.42	1.69	−1.28

* Calculations are based on the item "complete blood count" (complete blood count − unit cost = £2.33).
† Negative net costs are savings; small differences may occur between reported figures in the last column and simple calculation of the difference between the predicted cost and the observed cost, due to rounding.

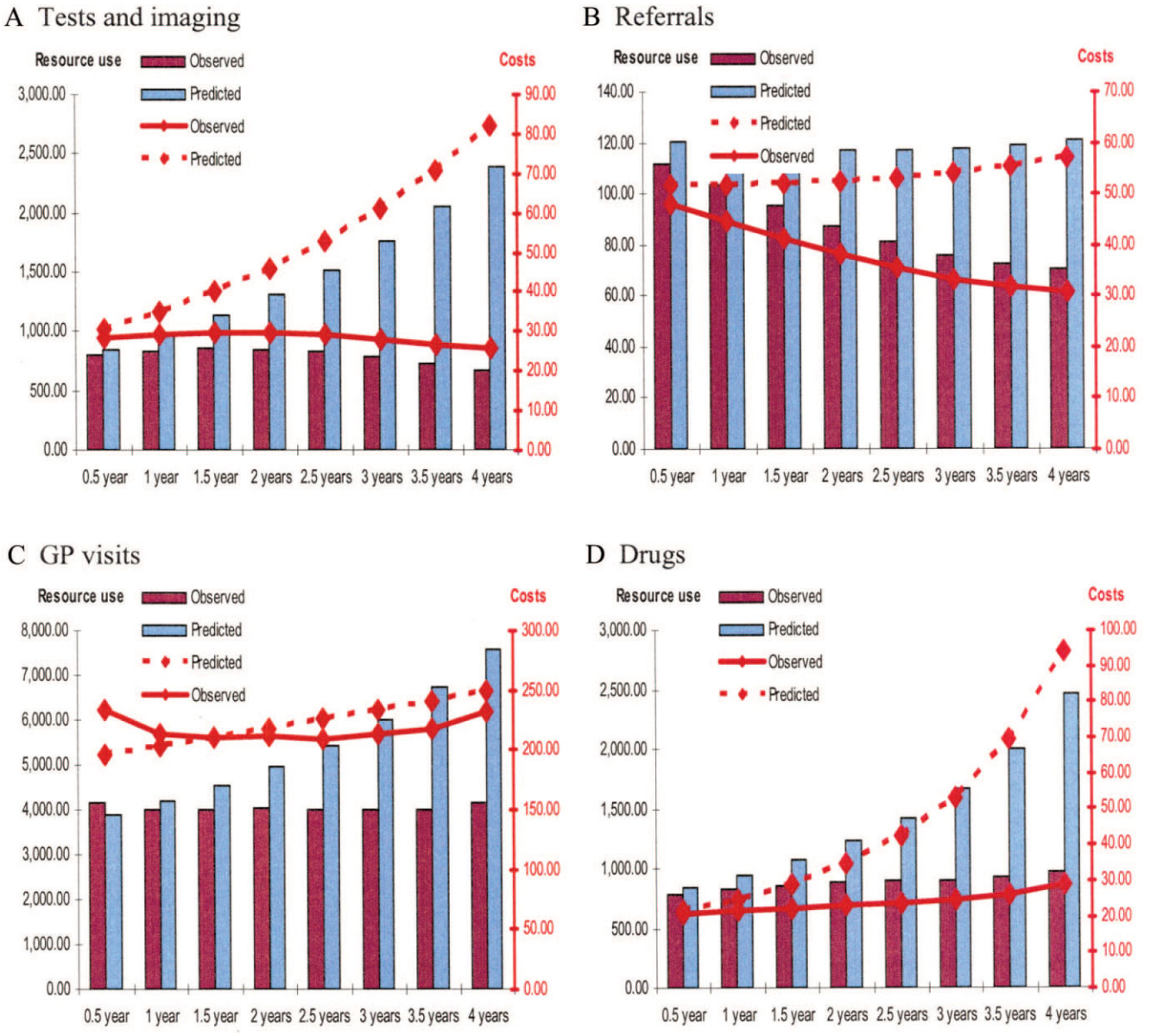

Figure 2. Impact on National Health Service resources and expenses (in British pounds) of making a diagnosis of fibromyalgia syndrome. **A,** Tests and imaging. **B,** Referrals. **C,** General practitioner (GP) visits. **D,** Drugs. Bars show the mean per 100 patient-years. Red lines show the predicted and observed costs per 6-month period after diagnosis. Costs refer to total direct medical costs with the exclusion of hospital costs.

6-month periods following the index date were averaged, as presented in Table 2. The sum of the averages led to a final average savings of £66.2 per 6 months or £132.4 per patient per year.

The savings were highest for tests, followed by drugs and referrals. The savings on GP visits were, however, small. The secondary analysis, assuming that resource use before the index date would be continued without further increase, led to a smaller difference between predicted and observed costs, as expected (Table 2).

DISCUSSION

The outcomes of this comparison between real observed medical resource use following the diagnosis of

Table 2. Average differences between predicted and observed costs per patient per 6-month period*

Six-month period after diagnosis	Laboratory tests	Medications	Referrals	GP visits	Total cost*
Base case analysis					
0.5	2.22	0.80	3.79	−38.44	−31.63
1	5.59	3.14	6.98	−10.13	5.59
1.5	10.26	6.70	10.53	0.40	27.88
2	16.34	11.60	14.18	6.28	48.39
2.5	23.94	18.78	17.70	16.69	77.11
3	33.14	28.93	20.95	20.76	103.79
3.5	44.03	43.44	23.87	23.34	134.68
4	56.66	64.81	26.46	15.94	163.87
Average	24.02	22.27	15.56	4.36	66.21
Secondary analysis†					
0.5	−1.54	0.74	3.43	−20.39	−17.76
1	−2.54	3.02	6.98	0.34	7.79
1.5	−2.98	6.50	10.62	3.29	17.42
2	−2.88	11.31	14.10	1.58	24.11
2.5	−2.28	18.39	17.16	4.41	37.68
3	−1.29	28.44	19.64	0.90	47.69
3.5	−0.04	42.82	21.45	−4.11	60.12
4	1.25	64.06	22.58	−19.09	68.79
Average	−1.54	21.91	14.49	−4.13	30.73

* Total cost means direct medical costs with the exclusion of hospital costs. All values are British pounds. GP = general practitioner.
† Predicted cost function = horizontal line (i.e., no further increase in costs assumed).

FMS in a UK general practice population and predicted resource use, assuming that the diagnosis had not been made, confirm the hypothesis that the act of diagnosis does lead to cost savings. The largest contribution comes from the decrease in the number of diagnostic tests after diagnosis, followed by the savings in medication costs. The cumulative savings pattern over time is linear, pointing to constant savings over time. For drugs, the trend of the net cost impact is more exponential, but the absolute differences are slightly lower compared with the trend for tests. For patient referrals, the trend is comparable with that observed for tests but is far weaker. Finally, for GP visits, a different trend was observed, with extra costs (negative savings) in the first three 6-month periods.

What we are observing is the considerable burden of investigations and/or referrals that occur prior to diagnosis, presumably instigated as doctors and patients continue to search for answers. However, the act of diagnosis reduces this burden, although it does not reduce GP attendance. This is perhaps not surprising; one would expect a confident diagnosis to reduce the incidence of further diagnostic tests and referrals, but a diagnosis, by itself, would not be expected to reduce symptoms and/or disability and hence the need for medical care.

Our study builds on the results reported by Hughes et al (18) by translating the observed reduction in resource use into monetary values, based on a detailed assessment of all medical resource use and applying unit costs to each of the 157 identified resource items. The use of a control group was not required for that purpose, because the goal was to forecast the expected expenditures for the patients if FMS had not been diagnosed.

The main weakness of our study is related to the limited number of observations both before and after the point of diagnosis. For comparison, Twine et al (13), in an analysis of GP referrals to breast cancer specialists, applied monthly data over a 6-year time period. Miller and Martin (14) applied monthly data as well, over a period of 8 years, to predict the use of health care services in patients with schizophrenia. Ocana-Riola (16) used data from an earlier publication with 90 time points to predict cancer rates in Spain. Someya et al (15) used 30 yearly data points to predict inpatient care for schizophrenia. Unfortunately, only 6 monthly data points were available from GPRD for our analysis.

Therefore, we looked at a period of up to 4 years before diagnosis. This timing of 4 years before the index date was chosen based on the fact that most event rates started increasing at or beyond that time. Using a longer period before the index date would put too much emphasis on the earlier periods and hence on the "flat-line" (steady, low event rate at earlier stages), which would lead to underestimating the extrapolated

event rates after the index date. Moreover, the usually large peak of events during the index period (6 months before the index date up to the index date), which would not have been witnessed if the diagnosis was not made, was excluded from the trend analysis. Indeed, including these events would inflate the extrapolated event rates after the index date and thus would lead to an overestimation of event rates. One could consider excluding an even longer peak from the analysis (e.g., 1 year before diagnosis), but such an approach might wrongly ignore the growth of event rates before diagnosis. Regardless, a longer period of observation after the point of diagnosis could help in better understanding the long-term consequences of the diagnosis.

Obviously, the obtained savings are temporary. In fact, as explained by Hughes et al (18), following diagnosis, the number of visits for most symptoms and health care use markers declined, but within 2–3 years the number rose to levels at or above those at the time of diagnosis. In order to produce a conservative estimate of the potential savings, we conducted a secondary analysis, assuming that the predicted costs would not increase further if a diagnosis was not made. This analysis resulted in a savings per 6 months of ~50% of the base case result. It may fairly be stated that this may be considered a "worst case" result.

Hospital and home care were not taken into account in this study, because these types of costs are not available within the GPRD; including them may have reinforced our results. In the same way, losses of productivity could not be analyzed and would probably have widened the differential costs. Another point of concern may be the risk of misdiagnosis by the GP. Patients were selected if the GP filled in a code (ICD-9 or OXMIS) of FMS in the patient's record. GPs may have wrongly assigned such a code for some patients. It is possible that such cases would lead to less savings after diagnosis. Hence, our results are conservative in that regard.

It is also noteworthy that 0.93% of the study population had a diagnosis of systemic lupus erythematosus, and 5.22% of the study population had a diagnosis of rheumatoid arthritis. These conditions may well influence the patients' management and bias our results. However, there was no difference in this prevalence before and after the diagnosis of FMS; therefore, we expect that this will not have an influence on the observed differences between medical management before and after diagnosis. Another complexity in this regard is that current management guidelines in FMS are not based on high-quality evidence (7), and the cost-effectiveness of care is not well established. Finally, caution should be observed before generalizing the results to other health care systems, given the central role of the GP in the organization of health care in the UK. We are currently undertaking a similar analysis in Spain, Portugal, Italy, Germany, and France to address this issue.

In conclusion, our findings offer support for the hypothesis that an earlier diagnosis of FMS can avoid referral costs and investigations, leading to a net savings for the health care sector. Other studies are needed to confirm this.

AUTHOR CONTRIBUTIONS

Dr. Taïeb had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study design. Annemans, Wessely, Caubère, Taïeb.
Acquisition of data. Caubère, Taïeb.
Analysis and interpretation of data. Annemans, Wessely, Spaepen, Caekelbergh.
Manuscript preparation. Annemans, Wessely, Le Lay, Taïeb.
Statistical analysis. Annemans, Spaepen, Caekelbergh.

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