TITLE

Impact of comorbid conditions on health care expenditure and work-related outcomes in patients with rheumatoid arthritis

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Rheumatoid Arthritis; Comorbidity; Health Expenditures; Employment; Income; Indirect Cost

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CONFLCITS OF INTEREST

No conflict of interest to declare.

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RUNNING HEAD

Comorbid conditions and their costs in RA

ABSTRACT

Objective. To evaluate the impact of comorbid conditions on direct health care expenditure and work-related outcomes in patients with rheumatoid arthritis (RA).

Methods. This was a retrospective analysis of the Medical Expenditure Panel Survey from 2006 to 2015 in 4,967 adult RA patients in the USA. Generalised linear models were used for health care expenditure and income, logistic model for employment status, and zero-inflated negative binomial model for absenteeism. Thirteen comorbid conditions were included as potential predictors of direct cost and work-related outcomes. The models were adjusted for sociodemographic factors including sex, age, region, marital status, race/ethnicity, income, education and smoking status.

Results. RA patients with heart failure had the highest incremental annual health care expenditure (US$8,205; 95% CI, US$3,683-US$12,726) compared to those without the condition. Many comorbid conditions including hypertension, diabetes, depression, obstructive pulmonary disease, cancer, stroke and heart failure reduced the chance of RA patients aged between 18-64 years being employed. Absenteeism of employed RA patients was significantly affected by hypertension, depression, disorders of the eye and adnexa or stroke. On average, an RA patient with heart failure earned US$15,833 (95% CI, US$4,435-US$27,231) per year less than an RA patient without heart failure.

Conclusions. Comorbid conditions in RA patients were associated with higher annual health care expenditure, lower likelihood of employment, higher rates of absenteeism and lower income. Despite its low prevalence, heart failure was associated with the highest incremental health care expenditure and the lowest likelihood of being employed compared to other common comorbid conditions.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disorder of the joints that affects approximately 0.53% to 0.55% of adults in the United States (US)[1]. Comorbidity in RA patients contributes to worsening of quality of life, premature mortality and economic burden[2-4]. In a global study, hypertension and depression were the most prevalent comorbid conditions occurring in 40.4% and 15% of RA patients, respectively, followed by asthma (6.6%) and cardiovascular disease (CVD; 6%)[5]. While an RA patient usually has two or more comorbid conditions, few studies have addressed the impact of comorbidities on health care expenditure[6]. Much less has been done to examine the indirect costs related to reduced workforce participation/employment, increased absenteeism and lost income caused by comorbidities in RA patients.

Most of the research into the economic impact of comorbidity in RA has been limited to a few common comorbid conditions. For example, Joyce, et al[7] found that the annual mean health care cost for an RA patient with CVD or depression in the US was about $2,700 or $821 higher than that for an RA patient without CVD or depression, respectively. However, these results cannot be generalized because many RA-related comorbid conditions other than CVD and depression were not adjusted for in the cost estimations. Prevalent comorbid conditions in RA such as chronic obstructive pulmonary disease (COPD) may also be associated with significantly higher costs[8]. It is unclear which comorbid conditions have the largest impact on health care expenditure as well as indirect costs associated with work-related outcomes.

Using data collected in the Medical Expenditure Panel Survey (MEPS)[9] from 2006 through 2015, we aimed to examine the impact of a wide range of comorbid conditions in RA patients, adjusted for sociodemographic factors, on direct costs in terms of total health care expenditure, and indirect costs in terms of employment status, absenteeism and

income.

MATERIALS AND METHODS

This study received approval from the Melbourne School of Population and Global Health Human Ethics Advisory Group at the University of Melbourne (Ethics ID: 1851014.1). Patients' written informed consent was waived as only publicly available de-identified data were used for the analyses.

Data source. We used the Household Component (HC) of the Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the non-institutionalized, civilian US population, to estimate health care usage and expenditure[10]. We pooled MEPS-HC data collected over 10 calendar years (2006-2015) to increase the power of statistical analyses. The 2015 MEPS-HC is the latest version of MEPS-HC data available at the time of our study (see the Supplementary document for more information).

Study population. We extracted and analyzed the Full-Year Consolidated data file and the Medical Conditions file from MEPS-HC. The former file contained respondent's demographic and socioeconomic characteristics; health conditions and status; health care utilization, behavior and expenditure; health insurance coverage; employment status, income and sick leave[10]. Our sample contained adult RA patients aged 18 years or older living in the US irrespective of treatment received. We used the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes as recorded in the Medical Conditions file to identify patients with RA and comorbidities. These ICD-9-CM codes were derived only from self-reported conditions by professional coders with an error rate less than 2.5%[11]. MEPS aggregates clinical homogenous and similar ICD-9-CM codes into a Clinical Classification Code (CCC). To enhance case ascertainment, we used both ICD-9-CM code and CCC to identify RA patients, i.e. we included individuals with both ICD-9-CM code (714)

and CCC (202) indicating RA, and excluded RA patients who did not report arthritis diagnosis in the Full-Year Consolidated data file.

Outcomes. For each patient, we assessed four outcomes: average annual health care expenditure, employment status, absenteeism and income. Annual health care expenditure was defined as the total payment for all health services utilized within one calendar year. Sources of payment included out-of-pocket (OOP) payments, Medicare, Medicaid, private insurance and entitled government benefits. Health services consisted of visits to physicians or medical providers supervised by physicians, hospital outpatient and emergency department (ED) visits, inpatient hospital stays, prescription medicines, dental visits, home health care, and other medical expenses such as vision aids, medical supplies and equipment. MEPS did not record payments from over-the-counter medications and alternative care services so these were not included in our analyses.

To examine indirect costs, we analyzed employment status, absenteeism (days of sick leave) and net income. Both analyses of employment status and absenteeism were restricted to working-age adults (ages 18-64 years) given that workforce participation for adults age ≥ 65 years in MEPS was small (< 5%). The respondent's employment status was recorded in each interview round, where employment was defined as having work with payment in wages, salary or commission, or in kind[12]. Consistent with previous research in RA and work-related outcomes, we classified respondents who indicated employment at any round of interviews within one calendar year as being employed[13]. For patients who were employed, absenteeism was defined as the number of work days missed due to illness/injury. Finally, annual income was defined as the total net income of an employed RA patient within a calendar year, which was derived from most types of earnings, including wages, salaries, commissions and other income sources such as bonuses and interest[14].

Both total annual health care expenditure and income are in US-dollars (USD) in year

2015 (the latest year when data were available). We used the Personal Consumption Expenditure Health indices as recommended by the AHRQ to adjust health care expenditure and the Consumer Price Index (CPI) to adjust income for inflation[15].

Explanatory variables. Potential predictors in our models include comorbidities and sociodemographic variables. Comorbidities in our study sample were identified based on ICD-9-CM codes. As there are a very large number of RA-related comorbidities reported in the literature, we included only comorbidities with prevalence greater than 1% (Table 1) in our sample of RA patients in the list of potential predictors (see Table 2 or the Supplementary document). Income level in a specific year was based on family household income as a percentage of the federal poverty line (FPL; national level) for that year, with poor people defined as having an income <100% FPL, near poor as ≥100% and <125% FPL, low-income as ≥125% and <200% FPL, middle income as ≥200% to <400% FPL, and high income as ≥400% of FPL[10]. In the analysis of the impact of comorbidities on employment and income, we excluded income level from the list of potential predictors because of reverse causation[13].

Statistical analysis. We used person-level weights[10] in both descriptive and inferential statistics to address the disproportionate sampling of certain minority groups. We developed one multivariable regression model for each of the four outcomes to adjust the effect of a comorbid condition for other covariates. We used the generalized linear model (GLM) with a log link and gamma distribution to assess the association between comorbidities among RA patients and annual health care expenditure and income. To compare total annual health care expenditure and income between RA patients with and without a comorbid condition, we calculated average marginal effects, holding all else at the average values. We used the logistic regression model to examine the association between comorbidities among RA patients and being employed. Given that the observed days of sick leave consisted of excess zeros (> 60% of all observations), we used the zero-inflated negative binomial model to examine the

association between comorbidities and days of sick leave. For further details of statistical modelling and variable selection, see the Supplementary document.

RESULTS

Descriptive statistics. There were 4,967 adult patients with RA from 2006 to 2015 (Table 2). Most RA patients in the weighted sample were women (64.9%), aged 55 years or older (66.7%), white (67.2%) and non-smokers (77.0%). The most prevalent chronic comorbid conditions were hypertension (62.2%), followed by disorder of lipid metabolism (47.3%), diabetes (25.1%) and depression (20.0%). The least common comorbid conditions were stroke (6.2%), heart failure (3.0%) and peptic ulcer (1.2%). RA patients with no comorbid conditions accounted for 14.6% of the RA population.

Average annual health care expenditure. RA patients with hypertension, diabetes, depression, disorders of the eye and adnexa, COPD, cancer, myocardial infarction, osteoporosis, stroke or heart failure had statistically significant higher average annual health care expenditure compared to those without the condition. For instance, the average annual health care expenditure for RA patients with hypertension was 1.23 times (95% CI, 1.06-1.43) that for RA patients without hypertension (Table 3). Heart failure had the strongest relative impact on the annual health care expenditure with a mean ratio of 1.75 (95% CI, 1.38-2.22) compared to patients without the condition.

RA patients without health insurance had less direct costs compared to RA patients with only public health insurance (mean ratio, 0.52; 95% CI, 0.43-0.62) (Table 3). Compared to RA patients without any high school qualifications, RA patients with a bachelor's or other degree on average spent more on direct health care. Average annual health care expenditure for RA patients living in the Midwest region was 1.26 times (95% CI, 1.03-1.55) that for RA patients living in the West region, with no significant differences for RA patients in the Northeast or South region compared to the West region. Smokers spent annually 20% less

money on health care services compared to non-smokers (mean ratio, 0.80; 95% CI, 0.67-0.95).

Heart failure was the most expensive comorbid condition with an incremental average annual health care expenditure of $8,205 (95% CI, $3,683-$12,726) compared to patients without the condition (Table 3; Supplementary Figure S1). RA patients with hypertension (the most prevalent comorbidity) had an incremental average annual health care expenditure of $2,343 (95% CI, $605-$4,079) compared to those without hypertension.

Employment. Among RA patients aged 18-64 years (n=3,078), those with hypertension, depression, COPD, cancer, osteoporosis, stroke or heart failure were significantly less likely to be employed than patients without the condition (Table 4). Heart failure had a strongest impact on the likelihood of employment (odds ratio, 0.08; 95% CI, 0.02-0.29). There was no significant difference in the chance of being employed between RA patients with and without diabetes, disorders of the eye and adnexa, asthma, peptic ulcers, disorders of lipid metabolism or osteoporosis.

Older RA patients were less likely to be employed than younger RA patients (odds ratio, 0.98; 96% CI, 0.96-0.99) (Table 4). Female RA patients also had a lower chance of being employed compared with male RA patients. Private health insurance was a strong indicator for a higher chance of employment compared to public health insurance. RA patients without any health insurance had a higher chance of being employed than RA patients with only public insurance. Patients with high school completed or any degrees had a higher chance of employment compared to patients who had not completed high school.

Absenteeism. In employed RA patients ages 18-64 years (n=1,466), hypertension, depression, disorders of the eye and adnexa or stroke had a statistically significant impact on absenteeism (Table 5), with stroke having a strongest impact. The rate of absenteeism of

employed RA patients with stroke was 2.15 times (95% CI, 1.03, 4.47) that of those without stroke. This rate was 1.30 (95% CI, 1.00-1.69), 1.44 (95% CI, 1.05-1.97) and 1.51 (95% CI, 1.03-2.21) for RA patients with hypertension, depression or disorders of the eye and adnexa, respectively.

Absenteeism was significantly higher in employed RA patients living in the Midwest region compared to those living in the West. Patients with a high income took fewer days of sick leave compared to those with an income under the poverty line. Older and married patients had a higher chance of absenteeism being unobserved (i.e. having extra no sick leave days) compared to younger and unmarried patients, respectively.

Income. Heart failure was associated with the largest reduction in annual income (mean ratio, 0.59; 95% CI, 0.36-0.97) (Table 6). This was followed by COPD (mean ratio, 0.71; 95% CI, 0.59-0.85) and diabetes (mean ratio, 0.85; 95% CI, 0.75-0.96).

Compared to patients without the condition, the mean decrease in income per patient per year was $15,833 (95% CI, $4,435-$27,231) for heart failure, $11,437 (95% CI, $5,977-$16,899) for COPD, and $5,816 (95% CI, $1,415-$10,218) for diabetes (Table 6; Supplementary Figure S2).

Sex, insurance coverage and education had a significant association with income (Table 6). Females RA patients had a 25% decrease in average income compared with male RA patients. Average income of RA patients with private health insurance was 2.05 times that of RA patients with only public health insurance.

DISCUSSION

In this study we investigated the influence of thirteen comorbid conditions in RA patients and found varying impact of different comorbidities on health care expenditure and work-related

outcomes. In line with the study by Deb et al[16] which found that RA patients with depression had higher health care expenditure compared to those without depression ($14,752 versus $10,541 per patient per year), we found that the increase in direct cost for depression was $4,235 per RA patient per year. While our study also showed that RA patients with depression had a lower likelihood of being employed, among those who were employed, the rate of absenteeism was higher for those with depression compared with those without depression.

In another study, Joyce et al[7] assessed medical and pharmacy claims across the US from 2001-2005 and found that the adjusted annual total health care costs in RA patients with and without CVD (myocardial infarction, angina pectoris, stroke, revascularization procedure, or angioplasty) were $14,145 and $11,404, respectively. Our study focused specifically on myocardial infarction, stroke and heart failure and found that all three comorbidities were associated with greater health care expenditure with an incremental health care expenditure of $6,511, $5,150 and $8,205 per patient per year, respectively. We also assessed the effect of these cardiovascular conditions on indirect costs and found that RA patients with either stroke or heart failure were less likely to be employed compared to those without the condition. RA patients with stroke missed more workdays, and heart failure was associated with lower income. Despite its low prevalence in our cohort of RA patients, heart failure was associated with the highest incremental average annual health care expenditure and the greatest incremental loss of income compared to other comorbid conditions.

It was surprising that the presence of some chronic conditions such as heart failure, COPD and diabetes did not significantly influence absenteeism. One explanation for this might be that the severity of the RA disease and symptoms themselves rather than the presence of comorbid condition is the major determinant of absenteeism. For instance, RA patients were 53% less likely to be employed than people without RA, but once RA patients

were employed their missed workdays were not significantly different from those of people without RA[13, 17]. Ozminkowski et al[17] argued that the severity of disease symptoms was a potential confounder in the relationship between comorbidity and absenteeism based on the observation that employed RA patients have less severe symptoms than unemployed RA patients. Therefore, employed RA patients remain in the workforce and their absenteeism is not affected by other comorbid conditions. As disease severity was not recorded in MEPS, we were not able to examine its effect, and this is an area of future research.

Examining the full economic cost of common comorbidities will assist in the identification of RA patients at risk of increased financial burden and work productivity loss[18]. Hypertension, diabetes, depression, COPD, cancer, osteoporosis, stroke and heart failure comorbidities were associated with increased medical costs but also negatively influenced employment, absenteeism and/or income for RA patients. For many of the conditions (e.g. diabetes, COPD, stroke and heart failure) characterized by high systemic and chronic inflammation, increased health care expenditure might be due to complications arising from comorbidities contributing to increased ED visits, hospitalization and health care utilization[8]. In other conditions such as depression and osteoporosis, comorbidities may indicate functional disability, and consequently reduce workforce participation and income earnings[19]. Our findings provided both direct and indirect cost perspectives to comorbidities in RA, and suggested that many comorbid conditions are likely to impact health care spending and work productivity, highlighting the dual financial hardships arising from comorbidities. While substantial work on the influence of direct and indirect cost on treatment adherence has been published, relatively few studies have measured the additional costs associated with comorbidities[20-22]. It is increasingly recognized that the management of RA is more complicated for patients with comorbidities, but high medical costs that may also consume household income will disadvantage RA patients with comorbidities in achieving

disease remission and better patient outcomes[23]. Effective control and prevention of comorbidities can significantly ease the economic burden of comorbidities in RA patients.

Surprisingly, average health care expenditure in RA patients who were current smokers was only 0.80 times that of non-smoker RA patients. A possible explanation might be that RA patients who smoke might value their health less than RA patients who do not smoke and therefore are less likely to utilise and spend money on health care. For example, patients with poor health behaviour such as smoking had lower health literacy, which is associated with less use of preventive health care services[24, 25]. Additionally, smoking was found to be associated with reduced quality of life[26]. It is unclear whether this was because smokers valued their health less than non-smokers, or because smoking increased the disease severity which reduced quality of life, independent of comorbidities. Another explanation for higher health care expenditure in non-smokers is that this group of patients may contain a considerable number of former smokers who stopped smoking because of disease severity and substantially had higher health care expenditure compared to the current smokers. Unfortunately, MEPS does not contain information about history of smoking status and therefore we were not able to stratify our analyses by former and current smokers.

To our knowledge, our study is the first to investigate the influence of a wide range of comorbid conditions on health care expenditure and work-related outcomes of RA patients using a nationally representative sample. We also chose to investigate both direct and indirect costs to better understand the societal economic burden for RA patients. We used advanced statistical modelling techniques and showed the marginal effect of each comorbid condition on health care expenditure and income. By quantifying the increased risk of being unemployed and having sick leave, and increased health care cost and reduced income in patients with a comorbid condition, our findings have strong implications for

rheumatologists, health care professionals and patients on the benefits of prevention of comorbidities and adherence to treatment for RA.

Our study has some limitations. Our results are specific to the US population and may not be generalized to other health care settings. This was a retrospective cross-sectional data analysis and it was unclear whether RA was diagnosed before the occurrence of the comorbid conditions included as independent variables. In our study cohort, only 116 RA patients reported no comorbid condition in the first assessment and at least one comorbid condition in the next assessment. Given this small sample and more than 20 potential confounding factors captured in our study cohort and many other confounding factors not measured in MEPS, for example cholesterol and blood pressure as risk factors of myocardial infarction and stroke, it was difficult to determine the causal relationship between RA and the development of co-morbidities. We were therefore not able to determine the true causal relationship between the comorbidities in RA patients and the outcomes of interest or the direction of association. Because the MEPS data structure was complex, we were only able to select the models based on univariable analyses, and therefore our final models might not be the best parsimonious models. In addition, MEPS is based on patient self-reported data which is subjected to recall bias. Further, in the context of health insurance in the US, we did not consider Medicare Part D, particularly for patients over 65 years of age, as a factor of health care expenditure or work-related outcomes. However, the majority of patients in our sample were under 65 years of age and therefore the impact of the absence of adjusting our models for Medicare Part D on our findings would be small. Another limitation in interpretation of the statistical outputs in our analysis is that MEPS did not record type of employment (e.g. full-time, part-time) or type of job (manual, non-manual), which may modify the effects of sex and comorbidity on absenteeism and income. For example, women are more likely than men to work part-time, and this might explain our observation that women were more likely to be absent from work,

although this was not statistically significant. Another example is that stroke might have a greater impact on absenteeism and income among those with a manual job, but this was not adjusted for in our analysis.

In conclusion, we showed that up to 12 comorbid conditions were associated with increased average annual health care expenditure for RA patients, among which heart failure had a strongest impact. Hypertension, depression, COPD, cancer, osteoporosis, stroke or heart failure was associated with lower likelihood of being employed in working-age RA patients, with heart failure having the largest negative effect. Among employed working-age RA patients, hypertension, depression, disorders of the eye and adnexa and stroke were associated with a higher rate of absenteeism. RA patients with diabetes, COPD or heart failure earned less than those without the condition, where heart failure led to a substantial reduction in annual income. Rheumatologists should work with other health professionals to prevent and appropriately manage comorbidities, and therefore potentially avoid downstream costs and financial hardships for RA patients.

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Table 1. Rheumatoid arthritis related comorbidities as potential predictors of health care expenditure and work-related outcomes.

Condition	**ICD-9-CM codes**
Asthma	493
Cancer	140-239
Chronic obstructive pulmonary disease	491, 492, 496
Depression	311
Diabetes	250
Disorders of the eye and adnexa	360-379
Disorders of lipid metabolism	272
Heart failure	428
Hypertension	401
Myocardial infarction	410, 412
Osteoporosis	733
Peptic ulcer	531, 532, 533, 534
Stroke	430, 431, 432, 433, 434, 436, 437, 438

Table 2. Descriptive statistics on the sociodemographic and comorbid conditions variables.*

Variable	**Un-weighted**	**Weighted†**
Sex, n (%)		
Female	3,454 (69.6)	3.0 (64.9)
Male	1,513 (30.4)	1.6 (35.1)
Age, mean (SD)	59.8 (14.5)	60.9 (15.2)
Age, n (%)		
18-24	53 (1.1)	0.059 (1.3)
25-34	212 (4.3)	0.17 (3.7)
35-44	462 (9.3)	0.40 (8.6)
45-54	1,046 (21.1)	0.92 (19.8)
55-64	1,305 (26.3)	1.2 (24.8)
64+	1,889 (38.0)	2.0 (41.9)
Region, n (%)		
Northeast	712 (14.3)	0.76 (16.3)
Midwest	948 (19.1)	0.98 (21.0)
South	2,174 (43.8)	1.9 (41.8)
West	1,133 (22.8)	0.97 (20.9)
Marital status, n (%)		
Married	2,290 (46.1)	2.4 (50.5)
Unmarried	2,677 (53.9)	2.3 (49.5)
Race/ethnicity, n (%)		
White	2,259 (45.5)	3.1 (67.2)
Black	1,330 (26.8)	0.68 (14.6)
Hispanic	535 (10.8)	0.28 (6.0)
Other	843 (17.0)	0.57 (12.3)

Variable	Un-weighted	Weighted†
Family income level, n (%)		
Poor/negative	1,312 (26.4)	0.86 (18.6)
Near poor	483 (9.7)	0.37 (8.0)
Low income	897 (18.1)	0.79 (16.9)
Middle income	1,283 (25.8)	1.3 (28.9)
High income	992 (20.0)	1.3 (27.6)
Insurance coverage, n (%)		
Uninsured	551 (11.1)	0.42 (9.0)
Any private	2,124 (42.8)	2.4 (51.7)
Public only	2,292 (46.1)	1.8 (39.2)
Education, n (%)		
High school not completed	1,621 (32.6)	1.2 (25.3)
High school completed	1,883 (37.9)	1.8 (39.5)
Bachelor's degree	415 (8.4)	0.49 (10.5)
Postgraduate	213 (4.3)	0.27 (5.9)
Other degree	835 (16.8)	0.88 (18.9)
Smoking status, n (%)		
Non-smoker	3,835 (77.2)	3.6 (77.0)
Smoker	1,132 (22.8)	1.1 (23.0)
Comorbid conditions, n (%) ‡		
Hypertension	3,166 (63.7)	2.9 (62.2)
Disorders of lipid metabolism	2,316 (46.6)	2.2 (47.3)
Diabetes	1,379 (27.8)	1.2 (25.1)
Depression	1,009 (20.3)	0.93 (20.0)
Disorders of the eye and adnexa	837 (16.8)	0.84 (18.1)

Variable	Un-weighted	Weighted†
Asthma	827 (16.6)	0.69 (14.8)
Chronic obstructive pulmonary disease	654 (13.2)	0.62 (13.3)
Cancer	595 (12.0)	0.68 (14.7)
Myocardial infarction	402 (8.1)	0.41 (8.8)
Osteoporosis	346 (7.0)	0.34 (7.3)
Stroke	298 (6.0)	0.29 (6.2)
Heart failure	156 (3.1)	0.14 (3.0)
Peptic ulcer	67 (1.3)	0.056 (1.2)
No comorbid conditions	724 (14.6)	0.68 (14.6)
Number of comorbid conditions, mean (SD)	2.4 (1.7)	2.4 (1.8)
Year, n (%)		
2006/2007	416 (8.4)	0.42 (9.1)
2008/2009	1,086 (21.9)	1.0 (22.3)
2010/2011	1,096 (22.1)	1.0 (22.5)
2012/2013	1,200 (24.2)	1.1 (23.1)
2014/2015	1,169 (23.5)	1.1 (22.9)

* The sample patient population was 4,967, representing approximately 4.68 million U.S. adult RA patients.

† Number of patients are in millions.

‡ Comorbidities were selected based on a prevalence of greater than 1%.

Table 3. Multivariable GLM results for total annual health care expenditure in patients with rheumatoid arthritis.

Variable	**Mean ratio, (95% CI)***	**Mean difference, 2015 USD (95% CI)†**
Hypertension	1.23 (1.06, 1.43)‡	2,343 (605, 4,079)‡
Disorders of lipid metabolism	0.95 (0.83, 1.09)	535 (-1,993, 923)
Diabetes	1.24 (1.08, 1.43)‡	2,603 (813, 4,393)‡
Depression	1.40 (1.21, 1.61)§	4,235 (2,167, 6,301)§
Disorders of the eye and adnexa	1.22 (1.05, 1.42)‡	2,407 (440, 4,373)‡
Asthma	1.09 (0.92, 1.28)	968 (-961, 2,896)
Chronic obstructive pulmonary	1.46 (1.26, 1.69)§	4,972 (2,633, 7,311)§
Cancer	1.32 (1.13, 1.53)§	3,372 (1,322, 5,423)‡
Myocardial infarction	1.60 (1.27, 2.01)§	6,511 (2,699, 10,323)‡
Osteoporosis	1.27 (1.05, 1.53)‡	2,925 (318, 5,531)‡
Stroke	1.47 (1.19, 1.82)§	5,150 (1,764, 8,536)‡
Heart failure	1.75 (1.38, 2.22)§	8,205 (3,683, 12,726)§
Sex (Male as reference)		
Female	1.13 (0.99, 1.30)	
Age	1.00 (0.99, 1.01)	
Region (West as reference)		
Northeast	1.19 (0.97, 1.46)	
Midwest	1.26 (1.03, 1.55)‡	
South	1.06 (0.90, 1.25)	
Insurance coverage (Public only as reference)		
Any private	0.97 (0.84, 1.13)	
No insurance	0.52 (0.43, 0.62)§	

Variable	Mean ratio, (95% CI)*	Mean difference, 2015 USD (95% CI)†
Education (High school not completed as reference)		
High school completed	1.07 (0.93, 1.24)	
Bachelor degree	1.56 (1.21, 2.01)‡	
Postgraduate degree	1.36 (0.98, 1.89)	
Other degree	1.33 (1.12, 1.59)‡	
Smoking status (Non-smoker as reference)		
Smoker	0.80 (0.67, 0.95)‡	

* Values are the exponential form of the beta coefficients for a covariate, which represents the multiplier factor for the outcome when the covariate increases by one; Reference for each comorbidity is absence of the condition.

† Values are the average marginal effect for a comorbidity compared to absence of the condition, holding all other covariates at the average values.

‡ $P < 0.05$

§ $P < 0.001$

Table 4. Multivariable logistic regression results for employment status in working-age patients (ages 18-64 years) with rheumatoid arthritis.

Variable	**OR (95% CI)***
Hypertension	0.69 (0.51, 0.92)†
Disorders of lipid metabolism	1.01 (0.78, 1.32)
Diabetes	0.85 (0.61, 1.18)
Depression	0.47 (0.34, 0.63)‡
Disorders of the eye and adnexa	0.83 (0.54, 1.27)
Asthma	1.06 (0.72, 1.54)
Chronic obstructive pulmonary disease	0.53 (0.35, 0.82)†
Cancer	0.46 (0.27, 0.79)†
Myocardial infarction	0.60 (0.36, 1.01)
Osteoporosis	0.55 (0.30, 0.99)†
Stroke	0.48 (0.26, 0.89)†
Heart failure	0.08 (0.02, 0.29)‡
Peptic ulcer	0.74 (0.19, 2.78)
Sex (Male as reference)	
Female	0.70 (0.52, 0.95)†
Age	0.98 (0.96, 0.99)†
Marital status (Unmarried as reference)	
Married	0.78 (0.59, 1.04)
Race/ethnicity (White as reference)	
Black	0.86 (0.63, 1.17)
Hispanic	1.27 (0.87, 1.87)
Other	0.89 (0.62, 1.29)

Variable	OR (95% CI)*
Insurance coverage (Public only as reference)	
Any private	10.35 (7.35, 14.57)‡
No insurance	3.43 (2.30, 5.123
Education (High school not completed as reference)	
High school completed	1.43 (1.01, 2.03)†
Bachelor degree	2.46 (1.37, 4.42)†
Postgraduate degree	2.56 (1.36, 4.83)†
Other degree	1.79 (1.20, 2.67)†
Smoking status (Non-smoker as reference)	
Smoker	0.91 (0.66, 1.26)

* The odds ratio (OR) is the exponential form of the beta coefficient, which represents the multiplier factor for the odds of being employed when the covariate increases by one; Reference for each comorbidity is the absence of the condition.

† $P < 0.05$

‡ $P < 0.001$

Table 5. Multivariable zero-inflated negative binomial regression results for absenteeism in employed working-age patients (ages 18-64 years) with rheumatoid arthritis.

Variable	Zero-inflation component OR (95% CI)*	Count component IRR (95% CI)†
Hypertension	0.38 (0.12, 1.19)	1.30 (1.00, 1.69)‡
Disorders of lipid metabolism	0.42 (0.10, 1.70)	0.83 (0.62, 1.11)
Diabetes	2.96 (0.59, 14.95)	1.08 (0.77, 1.51)
Depression	1.14 (0.35, 3.72)	1.44 (1.05, 1.97)‡
Disorders of the eye and adnexa	0.25 (0.03, 2.02)	1.51 (1.03, 2.21)‡
Asthma	0.00 (0.00, 0.00)	1.19 (0.86, 1.64)
Chronic obstructive pulmonary disease	0.00 (0.00, 0.00)	1.40 (0.92, 2.15)
Cancer	0.86 (0.22, 3.27)	1.39 (0.88, 2.21)
Myocardial infarction	<0.001 (<0.001, >1,000)§	1.06 (0.58, 1.93)
Osteoporosis	<0.001 (<0.001, >1,000)§	0.61 (0.35, 1.08)
Stroke	1.93 (0.17, 21.40)	2.15 (1.03, 4.47)‡
Heart failure	<0.001 (<0.001, >1,000)§	0.86 (0.20, 3.80)
Peptic ulcer	<0.001 (<0.001, >1,000)§	0.52 (0.10, 2.73)
Sex (Male as reference)		
Female	1.01 (0.43, 2.37)	1.11 (0.85, 1.45)
Age	1.11 (1.04, 1.19)‡	1.00 (0.99, 1.01)
Region (West as reference)		
Northeast	0.59 (0.16, 2.21)	1.05 (0.71, 1.55)
Midwest	0.81 (0.26, 2.52)	1.40 (1.00, 1.97)‡
South	0.65 (0.23, 1.86)	1.25 (0.89, 1.76)

Variable	Zero-inflation component OR (95% CI)*	Count component IRR (95% CI)†
Marital status (Unmarried as reference)		
Married	4.70 (1.40, 15.73)‡	1.23 (0.97, 1.56)
Race/ethnicity (White as reference)		
Black	0.20 (0.02, 1.84)	1.07 (0.77, 1.49)
Hispanic	0.38 (0.11, 1.28)	0.78 (0.53, 1.16)
Other	0.52 (0.17, 1.64)	0.80 (0.57, 1.13)
Income level (Poor/negative as reference)		
Near poor	0.12 (0.00, 8.89)	1.12 (0.63, 1.99)
Low income	0.20 (0.03, 1.29)	0.92 (0.60, 1.40)
Middle income	0.42 (0.10, 1.83)	0.77 (0.51, 1.18)
High income	0.38 (0.08, 1.78)	0.63 (0.40, 0.98)‡
Insurance coverage (Public only as reference)		
Any private	0.30 (0.06, 1.41)	1.19 (0.82, 1.71)
No insurance	2.42 (0.56, 10.39)	0.88 (0.57, 1.36)
Education (High school not completed as reference)		
High school completed	1.57 (0.40, 6.18)	0.93 (0.67, 1.29)
Bachelor degree	0.68 (0.12, 4.01)	0.71 (0.45, 1.10)
Postgraduate degree	3.37 (0.43, 26.66)	1.15 (0.65, 2.04)
Other degree	1.30 (0.23, 7.28)	1.16 (0.79, 1.70)
Smoking status (Non-smoker as reference)		
Smoker	<0.001 (<0.001, >1,000)§	0.85 (0.65, 1.12)

* The odds ratio (OR) is the exponential form of the beta coefficient, which represents the multiplier factor for the odds of having undetected sick leave when the covariate increases by one; Reference for each comorbidity is absence of condition.

† The incidence rate ratio (IRR) is the exponential form of the beta coefficient, which represents the multiplier factor for the expected days of sick leave when the covariate increases by one; Reference for each comorbidity is absence of condition.

‡ $P < 0.05$

§ Very small positive values of OR and lower limit of the 95% CI, and very large value of the upper limit of the 95% CI.

Table 6. Multivariable GLM results for income in patients with rheumatoid arthritis.

Variable	**Mean ratio, (95% CI)***	**Mean difference, 2015 USD (95% CI)†**
Diabetes	0.85 (0.75, 0.96)‡	-5,816 (-10,218, -1,415)‡
Asthma	1.03 (0.83, 1.27)	1,027 (-7,615, 9,670)
Chronic obstructive pulmonary disease	0.71 (0.59, 0.85)§	-11,437 (-16,899, -5,977)§
Heart failure	0.59 (0.36, 0.97)‡	-15,833 (-27,231, -4,435)‡
Peptic ulcer	0.83 (0.49, 1.39)	-6,799 (-23,629, 10,029)
Sex (Male as reference)		
Female	0.75 (0.67, 0.84)§	
Marital status (Unmarried as reference)		
Married	1.01 (0.89, 1.15)	
Insurance coverage (Public only as reference)		
Any private	2.05 (1.70, 2.47)§	
No insurance	1.11 (0.87, 1.42)	
Education (High school not completed as reference)		
High school completed	1.07 (0.87, 1.31)	
Bachelor degree	1.82 (1.43, 2.31)§	
Postgraduate degree	1.92 (1.46, 2.53)§	
Other degree	1.36 (1.07, 1.73)‡	
Smoking status (Non-smoker as reference)		
Smoker	0.92 (0.81, 1.04)	

* Values are the exponential form of the beta coefficients for a covariate, which represents the multiplier factor for the outcome in patients with the comorbid condition or certain level of a categorical variable compared to the reference; Reference for each comorbidity is absence of the condition.

† Values are the average marginal effect for a comorbidity compared to absence of the condition, holding all other covariates at the average values.

‡ $P < 0.05$

§ $P < 0.001$