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Impact of Comorbid Conditions on Healthcare Expenditure and Work-related Outcomes in Patients With Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To evaluate the effect of comorbid conditions on direct healthcare expenditure and work-related outcomes in patients with rheumatoid arthritis (RA).

Methods. This is a retrospective analysis of the Medical Expenditure Panel Survey from 2006 to 2015 in 4967 adults with RA in the United States. Generalized linear models were used for healthcare expenditure and income, logistic models for employment status, and zero-inflated negative binomial models 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. Patients with RA with heart failure (HF) had the highest incremental annual healthcare expenditure (US$8205, 95% CI $3683–$12,726) compared to those without the condition. Many comorbid conditions including hypertension (HTN), diabetes, depression, chronic obstructive pulmonary disease, cancer, stroke, and HF reduced the chance of patients with RA aged between 18–64 years being employed. Absenteeism of employed patients with RA was significantly affected by HTN, depression, disorders of the eye and adnexa, or stroke. On average, RA patients with HF earned US$15,833 (95% CI $4435–$27,231) per year less than RA patients without HF.

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

Key Indexing Terms: comorbidity, employment, health expenditures, income, indirect cost, rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune disorder of the joints that affects approximately 0.53–0.55% of adults in the United States.[1] Comorbidity in patients with RA contributes to worsening of quality of life, premature mortality, and economic burden.[2, 3,4] In a global study, hypertension (HTN) and depression were the most prevalent comorbid conditions occurring in 40.4% and 15% of patients with RA, respectively, followed by asthma (6.6%) and cardiovascular disease (CVD; 6%).[5] While an RA patient usually has ≥ 2 comorbid conditions, few studies have addressed the effect of comorbidities on healthcare 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 patients with RA.

Most of the research into the economic effect of comorbidity in RA has been limited to a few common comorbid conditions. For example, Joyce, *et al*[7] found that the annual mean healthcare costs for an RA patient with CVD or depression in the US were approximately $2700 and $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 effect on healthcare expenditure as well as indirect costs associated with work-related outcomes.

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

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 deidentified data were used for the analyses.

Data source. We used the Household Component (HC) of the MEPS, a nationally representative survey of the noninstitutionalized, civilian US population, to estimate healthcare 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 (Supplementary Data, Detailed Methods, available with the online version of this article).

Study population. We extracted and analyzed the Full-Year Consolidated data file and the Medical Conditions file from MEPS-HC. The former file contained respondents' demographic and socioeconomic characteristics, health conditions and status, healthcare utilization, behavior, and expenditure, health insurance coverage, employment status, income, and sick leave.[10] Our sample contained adults with RA ≥ 18 years in the US irrespective of treatment received. We used the International Classification of Diseases, 9th 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 < 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 patients with RA (i.e., individuals with both ICD-9-CM code [714] and CCC [202] indicating RA were included, and patients with RA who did not report an arthritis diagnosis in the Full-Year Consolidated data file were excluded).

Outcomes. For each patient, we assessed 4 outcomes: average annual healthcare expenditure, employment status, absenteeism, and income. Annual healthcare expenditure was defined as the total payment for all health services utilized within 1 calendar year. Sources of payment included out-of-pocket 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 healthcare, 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 (aged 18–64 yrs) given that workforce participation for adults aged ≥ 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 1 calendar year as being employed.[13] For patients who were employed, absenteeism was defined as the number of workdays missed due to illness/injury. Finally, annual income was defined as the total net income of an employed patient with RA within 1 calendar year that was derived from most types of earnings including wages, salaries, commissions, and other income sources such as bonuses and interest.[10]

Both total annual healthcare expenditure and income are in US dollars (US$) in the year 2015 (the latest year when data were available). We used the Personal Consumption Expenditure Health indices as recommended by the Agency for Healthcare Research and Quality to adjust healthcare expenditure, and the Consumer Price Index to adjust income for inflation.[14]

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 a prevalence > 1% (Table 1) in our sample of patients with RA in the list of potential predictors (Table 2; Supplementary Data, available with the online version of this article). 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 effect 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 1 multivariable regression model for each of the 4 outcomes to adjust the effect of a comorbid condition for other covariates. We used the generalized linear model with a log link and γ distribution to assess the association between comorbidities among patients with RA and annual healthcare expenditure and income. To compare total annual healthcare expenditure and income between patients with RA 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 patients with RA 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 modeling and variable selection, see the Supplementary Data (available with the online version of this article).

RESULTS

Descriptive statistics. There were 4967 adult patients with RA

Table 1. RA-related comorbidities as potential predictors of healthcare 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

ICD-9-CM: International Classification of Diseases, 9th revision, Clinical Modification; RA: rheumatoid arthritis.

Table 2. Descriptive statistics on the sociodemographic and comorbid conditions.[a]

	Unweighted	Weighted[b]
Sex		
Female	3454 (69.6)	3.0 (64.9)
Male	1513 (30.4)	1.6 (35.1)
Age, yrs, mean (SD)	59.8 (14.5)	60.9 (15.2)
Age, yrs		
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	1046 (21.1)	0.92 (19.8)
55–64	1305 (26.3)	1.2 (24.8)
> 64	1889 (38.0)	2.0 (41.9)
Region		
Northeast	712 (14.3)	0.76 (16.3)
Midwest	948 (19.1)	0.98 (21.0)
South	2174 (43.8)	1.9 (41.8)
West	1133 (22.8)	0.97 (20.9)
Marital status		
Married	2290 (46.1)	2.4 (50.5)
Unmarried	2677 (53.9)	2.3 (49.5)
Race/ethnicity		
White	2259 (45.5)	3.1 (67.2)
Black	1330 (26.8)	0.68 (14.6)
Hispanic	535 (10.8)	0.28 (6.0)
Other	843 (17.0)	0.57 (12.3)
Family income level		
Poor/negative	1312 (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	1283 (25.8)	1.3 (28.9)
High income	992 (20.0)	1.3 (27.6)
Insurance coverage		
Uninsured	551 (11.1)	0.42 (9.0)
Any private	2124 (42.8)	2.4 (51.7)
Public only	2292 (46.1)	1.8 (39.2)
Education		
High school not completed	1621 (32.6)	1.2 (25.3)
High school completed	1883 (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		
Nonsmoker	3835 (77.2)	3.6 (77.0)
Smoker	1132 (22.8)	1.1 (23.0)
Comorbid conditions[c]		
Hypertension	3166 (63.7)	2.9 (62.2)
Lipid metabolism disorders	2316 (46.6)	2.2 (47.3)
Diabetes	1379 (27.8)	1.2 (25.1)
Depression	1009 (20.3)	0.93 (20.0)
Eye and adnexa disorders	837 (16.8)	0.84 (18.1)
Asthma	827 (16.6)	0.69 (14.8)
COPD	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		
2006–2007	416 (8.4)	0.42 (9.1)
2008–2009	1086 (21.9)	1.0 (22.3)
2010–2011	1096 (22.1)	1.0 (22.5)
2012–2013	1200 (24.2)	1.1 (23.1)
2014–2015	1169 (23.5)	1.1 (22.9)

Values are expressed as n (%) unless otherwise indicated. [a] The sample patient population was 4967, representing approximately 4.68 million US adult RA patients. [b] Number of patients are in millions. [c] Comorbidities were selected based on a prevalence of > 1%. COPD: chronic obstructive pulmonary disease; RA: rheumatoid arthritis.

from 2006 to 2015 (Table 2). Most patients with RA in the weighted sample were women (64.9%), aged ≥ 55 years (66.7%), White (67.2%), and nonsmokers (77.0%). The most prevalent chronic comorbid conditions were HTN (62.2%), followed by disorder of lipid metabolism (47.3%), diabetes mellitus (DM; 25.1%), and depression (20.0%). The least common comorbid conditions were stroke (6.2%), heart failure (HF; 3.0%), and peptic ulcer (1.2%). Patients with RA with no comorbid conditions accounted for 14.6% of the RA population.

Average annual healthcare expenditure. Patients with RA with HTN, DM, depression, disorders of the eye and adnexa, COPD, cancer, myocardial infarction (MI), osteoporosis, stroke, or HF had statistically significant higher average annual healthcare expenditure compared to those without the condition. For instance, the average annual healthcare expenditure for patients with RA with HTN was 1.23 times (95% CI 1.06–1.43) that for patients with RA without HTN (Table 3). HF had the strongest relative effect on the annual healthcare expenditure with a mean ratio of 1.75 (95% CI 1.38–2.22) compared to patients without the condition.

Patients with RA without health insurance had less direct costs compared to patients with RA with only public health insurance (mean ratio 0.52, 95% CI 0.43–0.62; Table 3). Compared to patients with RA without any high school qualifications, patients with RA with a bachelor's or other degree on average spent more on direct health care. Average annual healthcare expenditure for patients with RA living in the Midwest region was 1.26 times (95% CI 1.03–1.55) that of patients with RA living in the West region, with no significant differences for patients with RA in the Northeast or South region compared to the West region. Smokers spent annually 20% less on healthcare services compared to nonsmokers (mean ratio 0.80, 95% CI 0.67–0.95).

HF was the most expensive comorbid condition with an incremental average annual healthcare expenditure of $8205 (95% CI $3683–$12,726) compared to patients without the

Table 3. Multivariable GLM results for total annual healthcare expenditure in patients with RA.

	Mean Ratio, (95% CI)[a]	Mean Difference, 2015 US$ (95% CI)[b]
Hypertension	1.23 (1.06–1.43)*	2343 (605–4079)*
Lipid metabolism disorders	0.95 (0.83–1.09)	535 (–1993 to 923)
Diabetes	1.24 (1.08–1.43)*	2603 (813–4393)*
Depression	1.40 (1.21–1.61)**	4235 (2167–6301)**
Eye and adnexa disorders	1.22 (1.05–1.42)*	2407 (440–4373)*
Asthma	1.09 (0.92–1.28)	968 (–961 to 2896)
COPD	1.46 (1.26–1.69)**	4972 (2633–7311)**
Cancer	1.32 (1.13–1.53)**	3372 (1322–5423)*
Myocardial infarction	1.60 (1.27–2.01)**	6511 (2699–10,323)*
Osteoporosis	1.27 (1.05–1.53)*	2925 (318–5531)*
Stroke	1.47 (1.19–1.82)**	5150 (1764–8536)*
Heart failure	1.75 (1.38–2.22)**	8205 (3683–12,726)**
Sex (ref: male)		
Female	1.13 (0.99–1.30)	
Age	1.00 (0.99–1.01)	
Region (ref: West)		
Northeast	1.19 (0.97–1.46)	
Midwest	1.26 (1.03–1.55)*	
South	1.06 (0.90–1.25)	
Insurance coverage (ref: public only)		
Any private	0.97 (0.84–1.13)	
No insurance	0.52 (0.43–0.62)**	
Education (ref: high school not completed)		
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 (ref: nonsmoker)		
Smoker	0.80 (0.67–0.95)*	

[a] Values are the exponential form of the β coefficients for a covariate, which represents the multiplier factor for the outcome when the covariate increases by 1; the reference for each comorbidity is absence of the condition. [b] Values are the average marginal effect for a comorbidity compared to absence of the condition, holding all other covariates at the average values. * $P < 0.05$. ** $P < 0.001$. COPD: chronic obstructive pulmonary disease; GLM: generalized linear model; RA: rheumatoid arthritis.

condition (Table 3, Supplementary Figure 1, available with the online version of this article). Patients with RA with HTN (the most prevalent comorbidity) had an incremental average annual healthcare expenditure of $2343 (95% CI $605–$4079) compared to those without HTN (Table 3).

Employment. Among patients with RA aged 18–64 years (n = 3078), those with HTN, depression, COPD, cancer, osteoporosis, stroke, or HF were significantly less likely to be employed than patients without the condition (Table 4). HF had the strongest effect on the likelihood of employment (OR 0.08, 95% CI 0.02–0.29). There was no significant difference in the chance of being employed between patients with RA with and without DM, disorders of the eye and adnexa, asthma, peptic ulcers, disorders of lipid metabolism, or osteoporosis.

Older patients with RA were less likely to be employed than younger patients with RA patients (OR 0.98, 95% CI 0.96–0.99; Table 4). Female patients with RA also had a lower chance of being employed compared with male patients with RA. Private health insurance was a strong indicator for a higher chance of employment compared to public health insurance. Patients with RA without any health insurance had a higher chance of being employed than patients with RA 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 patients with RA aged 18–64 years (n = 1466), HTN, depression, disorders of the eye and adnexa or stroke had a statistically significant effect on absenteeism (Table 5), with stroke having the strongest effect. The rate of absenteeism of employed patients with RA 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 patients with RA with HTN, depression, or disorders of the eye and adnexa, respectively.

Absenteeism was significantly higher in employed patients with RA 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.

Table 4. Multivariable logistic regression results for employment status in patients of working age (18–64 yrs) with RA.

	OR (95% CI)[a]
Hypertension	0.69 (0.51–0.92)*
Lipid metabolism disorders	1.01 (0.78–1.32)
Diabetes	0.85 (0.61–1.18)
Depression	0.47 (0.34–0.63)**
Eye and adnexa disorders	0.83 (0.54–1.27)
Asthma	1.06 (0.72–1.54)
COPD	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 (ref: male)	
Female	0.70 (0.52–0.95)*
Age	0.98 (0.96–0.99)*
Marital status (ref: unmarried)	
Married	0.78 (0.59–1.04)
Race/ethnicity (ref: White)	
Black	0.86 (0.63–1.17)
Hispanic	1.27 (0.87–1.87)
Other	0.89 (0.62–1.29)
Insurance coverage (ref: public only)	
Any private	10.35 (7.35–14.57)**
No insurance	3.43 (2.30–5.123
Education (ref: high school not completed)	
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 (ref: nonsmoker)	
Smoker	0.91 (0.66–1.26)

[a] The OR is the exponential form of the β coefficient, which represents the multiplier factor for the odds of being employed when the covariate increases by 1; the reference for each comorbidity is the absence of the condition. * $P < 0.05$. ** $P < 0.001$. COPD: chronic obstructive pulmonary disease; RA: rheumatoid arthritis.

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. HF 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 DM (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 $4435–27,231) for HF, $11,437 (95% CI $5977–$16,899) for COPD, and $5816 (95% CI $1415–$10,218) for DM (Table 6; Supplementary Figure 2, available with the online version of this article).

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

DISCUSSION

In this study we investigated the influence of 13 comorbid conditions in patients with RA and found varying effects of different comorbidities on healthcare expenditure and work-related outcomes. In line with the study by Deb, *et al*[15], which found that RA patients with depression had higher healthcare expenditure compared to those without depression ($14,752 vs $10,541 per patient/yr), we found that the increase in direct cost for depression was $4235 per RA patient per year. While our study also showed that RA patients with depression had a lower likelihood of being employed, the rate of absenteeism was higher for those with depression compared with those without depression among those who were employed.

In another study, Joyce, *et al*[7] assessed medical and pharmacy claims across the US from 2001 to 2005 and found that the adjusted annual total healthcare costs in patients with RA with and without CVD (MI, angina pectoris, stroke, revascularization procedure, or angioplasty) were $14,145 and $11,404, respectively. Our study focused specifically on MI, stroke, and HF, and found that all 3 comorbidities were associated with greater healthcare expenditure with an incremental healthcare expenditure of $6511, $5150, and $8205 per patient per year, respectively. We also assessed the effect of these cardiovascular conditions on indirect costs and found that patients with RA with either stroke or HF were less likely to be employed compared to those without those conditions. RA patients with stroke missed more workdays, and HF was associated with lower income. Despite its low prevalence in our cohort of patients with RA, HF was associated with the highest incremental average annual healthcare 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 HF, COPD, and DM 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 conditions is the major determinant of absenteeism. For instance, patients with RA were 53% less likely to be employed than people without RA, but once patients with RA were employed, their missed workdays were not significantly different from those of people without RA.[13,16] Ozminkowski, *et al*[16] argued that the severity of disease symptoms was a potential confounder in the relationship between comorbidity and absenteeism based on the observation that employed patients with RA have less severe symptoms than unemployed patients with RA. Therefore, employed patients with RA 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 should be an area of future research.

Examining the full economic cost of common comorbidities will assist in the identification of patients with RA at risk of increased financial burden and work productivity loss.[17] HTN, DM, depression, COPD, cancer, osteoporosis, stroke, and HF

Table 5. Multivariable zero-inflated negative binomial regression results for absenteeism in employed patients of working age (18–64 yrs) with RA.

	Zero-inflation Component OR (95% CI)[a]	Count Component IRR (95% CI)[b]
Hypertension	0.38 (0.12–1.19)	1.30 (1.00–1.69)*
Lipid metabolism disorders	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)*
Eye and adnexa disorders	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)
COPD	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 to > 1,000)[c]	1.06 (0.58–1.93)
Osteoporosis	< 0.001 (< 0.001 to > 1,000)[c]	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 to > 1,000)[c]	0.86 (0.20–3.80)
Peptic ulcer	< 0.001 (< 0.001 to > 1,000)[c]	0.52 (0.10–2.73)
Sex (ref: male)		
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 (ref: West)		
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)
Marital status (ref: unmarried)		
Married	4.70 (1.40–15.73)*	1.23 (0.97–1.56)
Race/ethnicity (ref: White)		
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 (ref: poor/negative)		
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 (ref: public only)		
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 (ref: high school not completed)		
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 (ref: nonsmoker)		
Smoker	< 0.001 (< 0.001 to > 1,000)[c]	0.85 (0.65–1.12)

[a] The OR is the exponential form of the β coefficient, which represents the multiplier factor for the odds of having undetected sick leave when the covariate increases by 1; the reference for each comorbidity is absence of condition. [b] The IRR is the exponential form of the b coefficient, which represents the multiplier factor for the expected days of sick leave when the covariate increases by 1; the reference for each comorbidity is absence of condition. [c] 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. * $P < 0.05$. COPD: chronic obstructive pulmonary disease; IRR: incidence rate ratio; RA: rheumatoid arthritis.

comorbidities were associated with increased medical costs but also negatively influenced employment, absenteeism, and/or income for patients with RA. For many of the conditions (e.g., DM, COPD, stroke, HF) characterized by high systemic and chronic inflammation, increased healthcare expenditure might be due to complications arising from comorbidities contributing to increased ED visits, hospitalization, and healthcare utilization.[8] In other conditions such as depression and osteoporosis, comorbidities may indicate functional disability, and consequently reduce workforce participation and income earnings.[18] Our findings provided both direct and indirect cost perspectives to comorbidities in RA, and suggested that many comorbid conditions are likely to affect healthcare spending and work productivity, highlighting the dual financial hardships

Table 6. Multivariable GLM results for income in patients with RA.

	Mean Ratio, (95% CI)[a]	Mean Difference, 2015 US$ (95% CI)[b]
Diabetes	0.85 (0.75–0.96)*	−5816 (−10,218 to −1415)*
Asthma	1.03 (0.83–1.27)	1027 (−7615 to 9670)
COPD	0.71 (0.59–0.85)**	−11,437 (−16,899 to −5977)**
Heart failure	0.59 (0.36–0.97)*	−15,833 (−27,231 to −4435)*
Peptic ulcer	0.83 (0.49–1.39)	−6799 (−23,629 to 10,029)
Sex (male as reference)		
Female	0.75 (0.67–0.84)**	
Marital status (ref: unmarried)		
Married	1.01 (0.89–1.15)	
Insurance coverage (ref: public only)		
Any private	2.05 (1.70–2.47)**	
No insurance	1.11 (0.87–1.42)	
Education (ref: high school not completed)		
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 (ref: nonsmoker)		
Smoker	0.92 (0.81–1.04)	

[a] Values are the exponential form of the β 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; the reference for each comorbidity is absence of the condition. [b] Values are the average marginal effect for a comorbidity compared to absence of the condition, holding all other covariates at the average values. * $P < 0.05$. ** $P < 0.001$. COPD: chronic obstructive pulmonary disease; GLM: generalized linear model; RA: rheumatoid arthritis.

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.[19,20,21] 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.[22] Effective control and prevention of comorbidities can significantly ease the economic burden of comorbidities in patients with RA.

Surprisingly, average healthcare expenditure in patients with RA who were current smokers was only 0.80 times that of nonsmoker patients with RA. A possible explanation might be that patients with RA who smoke might value their health less than patients with RA who do not smoke and therefore are less likely to utilize and spend money on health care. For example, patients with poor health behavior such as smoking had lower health literacy, which is associated with less use of preventive healthcare services.[23,24] Additionally, smoking was found to be associated with reduced quality of life.[25] It is unclear whether this was because smokers valued their health less than nonsmokers, or because smoking increased the disease severity, which reduced quality of life, independent of comorbidities. Another explanation for higher healthcare expenditure in nonsmokers is that this group of patients may contain a considerable number of former smokers who stopped smoking because of disease severity and subsequently had higher healthcare 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 healthcare expenditure and work-related outcomes of patients with RA using a nationally representative sample. We also chose to investigate both direct and indirect costs to better understand the societal economic burden for patients with RA. We used advanced statistical modeling techniques and showed the marginal effect of each comorbid condition on healthcare expenditure and income. By quantifying the increased risk of being unemployed and having sick leave, and increased healthcare cost and reduced income in patients with a comorbid condition, our findings have strong implications for rheumatologists, healthcare 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 healthcare settings. This was a retrospective cross-sectional data analysis and it was unclear whether RA was diagnosed before the occurrence of the comorbid conditions that were included in the models as independent variables. In our study cohort, only 116 patients with RA reported no comorbid condition in the first assessment and at least 1 comorbid condition in the next assessment.

Given this small sample and > 20 potential confounding factors captured in our study cohort and many other confounding factors not measured in MEPS (e.g., cholesterol and blood pressure as risk factors of MI and stroke), it was difficult to determine the causal relationship between RA and the development of comorbidities. We were therefore not able to determine the true causal relationship between the comorbidities in patients with RA 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 are subject to recall bias. Further, in the context of health insurance in the US, we did not consider Medicare Part D, particularly for patients > 65 years, as a factor of healthcare expenditure or work-related outcomes. However, the majority of patients in our sample were < 65 years and therefore the effect 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 or part time) or type of job (manual or nonmanual), 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 effect on absenteeism and income among those with manual jobs, 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 healthcare expenditure for patients with RA, among which HF had the strongest effect. HTN, depression, COPD, cancer, osteoporosis, stroke, or HF were associated with lower likelihood of being employed in working-age patients with RA, with HF having the largest negative effect. Among employed working-age patients with RA, HTN, depression, disorders of the eye and adnexa, and stroke were associated with a higher rate of absenteeism. Patients with RA with DM, COPD, or HF earned less than those without the condition, with HF leading 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 patients with RA.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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