

# Economic and Humanistic Burden of Rheumatoid Arthritis: Results From the US National Survey Data 2018–2020

Yinan Huang,<sup>1</sup>  Jieni Li,<sup>2</sup>  and Sandeep Krishna Agarwal<sup>3</sup>

**Objective.** Our objective was to estimate the economic and humanistic burden among US adults with rheumatoid arthritis (RA).

**Methods.** This study analyzed results from the Medical Expenditure Panel Survey from 2018 to 2020. Adults (aged  $\geq 18$  years) self-reporting with RA or with the presence of the *International Classification of Disease, 10th Revision* clinical modification codes were identified. Healthcare expenditures (inpatient care, outpatient care, emergency department, office visits, prescription medications, home health, and others) were measured. The Short Form 12 Health Survey physical component summary (PCS), mental component summary (MCS), activities of daily living (ADL), and instrumental ADL (IADL) were measured. Two-part models assessed the incremental increase in the health care expenditures for the RA group compared to the non-RA group. In addition, the multivariable linear regression was used to evaluate the marginal difference in PCS and MCS between those with RA and those without RA, whereas the multivariable logistic regression models were used to evaluate the association between ADL and IADL by RA status.

**Results.** Annually, 4.27 million adults with RA were identified. The two-part model showed significantly higher total annual healthcare expenditures in the RA group than non-RA group (mean \$3,382.971 [95% confidence interval (CI) \$1,816.50–\$4,949.44]). Compared to the non-RA group, the RA group was associated with lower PCS scores (mean 4.78 [95% CI 3.47–6.09]) and similarly lower MCS scores (mean  $-0.84$  [95% CI  $-2.18$  to  $0.50$ ]), as well as increased odds of requesting ADL (adjusted odds ratio [aOR] 2.02 [95% CI 1.59–2.56]) and IADL assistance (aOR 2.11 [95% CI 1.57–2.84]).

**Conclusion.** RA was associated with higher health care expenditures, particularly prescription medication costs, and was associated with suboptimal quality of life.

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune inflammatory disease characterized by inflammation across multiple joints.<sup>1,2</sup> RA is the most common form of autoimmune arthritis that affects an estimated 1.36 million adults in the United States (US).<sup>3–5</sup> Uncontrollable RA is a leading cause of long-term disability and even premature death. The clinical practice guidelines published by the American College of Rheumatology recommend the administration of conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (such as hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine), biologics, or targeted synthetic DMARDs (also known as JAK inhibitors [JAKi]) for the management of RA,<sup>6,7</sup> and these medications have been shown to improve short- and long-term outcomes in patients with RA.

RA can pose a significant economic burden to society and patients. The introduction of biologics or targeted synthetic DMARDs dramatically transformed the health outcomes for RA; however, these advanced treatments are very costly, resulting in up to \$12,500 to \$36,000 annually.<sup>8,9</sup> Because these biologics are costly, the inclusion of them could greatly increase the overall health expenditure made for RA.<sup>10,11</sup> Therefore, an up-to-date assessment of health expenditure for RA with consideration of biologics or targeted synthetic (ts) DMARDs is critically needed for payers and the patient community. On the other hand, RA also poses negative clinical impacts on the patient community. Patients with RA are likely to have a two- to three-year reduction in life expectancy than the general population, primarily due to other systemic complications from inflammation, such as pulmonary and cardiovascular diseases.<sup>12,13</sup> In addition, those with RA

<sup>1</sup>Yinan Huang, MS, PhD: School of Pharmacy, University of Mississippi, University, Mississippi; <sup>2</sup>Jieni Li, MPH, PhD: College of Pharmacy, University of Houston, Houston, Texas; <sup>3</sup>Sandeep Krishna Agarwal, MD, PhD: Baylor College of Medicine, Houston, Texas.

Author disclosures are available at <https://onlinelibrary.wiley.com/doi/10.1002/acr2.11728>.

Address correspondence via email to Yinan Huang, MS, PhD, at [yhuang9@olemiss.edu](mailto:yhuang9@olemiss.edu).

Submitted for publication October 3, 2023; accepted in revised form July 3, 2024.

also experience increased pain and a greater probability of physical and activity limitations.<sup>14–16</sup> Taken together, there is a need to assess total health expenditure for RA since the new biologics and JAKi approval, and there is also a need to provide an updated understanding of the quality of life for patients with RA.

Most economic evaluation studies that evaluate health care resource use and costs of RA are limited to payer's perspectives, are performed outside the United States.<sup>17,18</sup> Previous studies mainly evaluated difficult-to-treat RA groups,<sup>19,20</sup> or considered old data failing to account for the modern medical costs. Only two US-based cost studies have shown that RA is associated with an increased economic burden. A Medicare study showed that the annual mean costs for RA were more than two times higher than those for non-RA (RA 20,919 \$ vs non-RA \$7,197).<sup>21</sup> Another commercial claims-based study showed that the average annual cost of medical care for RA was between \$31,561 and \$33,753, and the outpatient prescription costs were the largest contributor.<sup>22</sup> However, these US studies were limited to a Medicare or commercial payer-insured population with RA. There is a dearth of data on the overall health expenditure impact in US patients with RA across all types of payers.

In addition, the burden of disability and pain in patients with RA has negatively impacted patient function and quality of life. Health-related quality-of-life (HRQoL) measures, such as the Short Form 6 (SF-6), have been widely used in randomized clinical trial assessments of patients with RA receiving treatment.<sup>23–25</sup> Several real-world studies also evaluated HRQoL measures in patients with RA, but these studies are limited to non-US settings. There is a lack of US data on the assessment of HRQoL in RA.<sup>26–30</sup> Using the Medical Expenditure Panel Survey (MEPS) data, this study aimed to estimate the healthcare expenditure for RA in the United States from 2018 through 2020 and then compared the expenditure for patients with RA versus individuals without RA. This study also evaluated the HRQoL among patients with RA as compared to adults without RA using MEPS data.

## PATIENTS AND METHODS

**Data source and study design.** This observational study was a retrospective, cross-sectional design using data from the MEPS from 2018 through 2020 to examine the economic and humanistic burden of RA. The MEPS is an annual US nationally representative survey involving families and individuals regarding data on their sociodemographic characteristics, medical conditions, and health service use and expenditure.<sup>31</sup> Sponsored by the Agency for Healthcare Research and Quality and the Centers for Disease Control and Prevention, the MEPS samples a panel of approximately 14,000 households of the US noninstitutionalized population selected to participate. The MEPS involves oversampling for racial and ethnic minority individuals, for example, oversampling for Hispanic people and Black people, to

generate unbiased national estimates. The MEPS included four data components: household component (HC) files, medical provider condition (MPC) files, insurance component, and nursing home component.<sup>32</sup> MEPS involves a complex, multistage, and stratified sampling design, and to derive the national representative generalizability, the survey weights are assigned to address nonresponses and unequal probabilities of selection into MEPS respondents. Specifically, the MEPS data use files involve the survey design variables and sampling weight variables to generate the weighted estimates and derive national estimates, ensuring the robustness of these estimates.

Basically, as a reflection of the MEPS survey design, these variables include the person estimation weight (PERWT02F), sampling strata (VARSTR), and primary sampling unit (VARPSU). These variables relate to sampling weights and help to generate national representative estimates. In addition, to help increase the precision of national estimates, oversampling for specific subgroups was implemented in MEPS data. For example, racial and ethnic minority groups (such as Asian, Black, and Hispanic persons) might be selected in the oversampling process, making the results generalizable to represent an improved precision of estimates for specific subgroups of a population. More information about the survey design and data availability in MEPS is available on the Agency for Healthcare Research and Quality website.<sup>32</sup>

In this study, we used the HC and MPC files. Specifically, the HC and MPC were merged together to obtain information about the participants' sociodemographics, medical conditions, health care use, costs, and quality-of-life measures. The full-year consolidated HC files, as primary person-level files, provide information on sociodemographics (including demographics, education, income, and insurance) as well as health care use and costs (ie, prescriptions and inpatient care). To supplement the HC files, the MPC is an event-level file that includes information on MEPS participants' medical conditions, including diagnoses and procedures, which were collected on the dates of their medical visits from the health care providers. We did not consider other components, such as the insurance component and nursing home component, because these components are not related to the scope of this study.

Recent three-year data of HC and MPC files (2018–2020) were pooled to analyze the economic and humanistic burdens of RA. Next, data from the three-year MPC files were linked to the HC files using the common identifier variable DUID. DUID, also known as dwelling unit ID, is composed of seven digit number and identifies uniquely each participant in the survey. Specifically, in the pooled analyses, a pooled linkage file including variables of stratum (STRA9619) and primary sampling unit (PSU9619) was included from the HC-036 file. Such survey design variables were further incorporated into the analyses along with sampling weight variables to derive national estimates. As recommended by the US Department of Health and Human Services, because the data

were deidentified and publicly available, the exemption from review and informed consent by the institutional review board at the University of Mississippi, was issued.

**Study sample.** This analysis included adults aged 18 or above who had a self-reported type of arthritis diagnosis (value 1 = RA) from the HC and/or an *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnosis of RA (ICD-10-CM codes for RA: M05) from the MPC.<sup>33</sup> The non-RA comparator group consists of all remaining individuals aged 18 or above.

**Direct and indirect economic burden of RA.** From the MEPS event files, total all-cause health care costs were the aggregate expenditure associated with any health care services. Accordingly, total healthcare expenditure was calculated by adding the costs related to inpatient, outpatient, emergency department, prescription medications, dental, home health, and other services (such as ambulance, equipment, and glasses). Of note, expenditure estimates in the HC are the actual amount paid either by the patients or by the payers for the health care services rendered rather than the cost of services received by the providers. All cost variables were inflated to 2023 US-dollar value using the Consumer Price Index for medical care listed by the Bureau of Labor Statistics.<sup>34</sup>

**Humanistic burden of RA.** The humanistic burden of RA was measured in terms of quality-of-life questionnaire administered, including the Short Form 12 Health Survey (SF-12). In the SF-12, there are two subitems indicating physical and mental health status. Specifically, from the full-year consolidated file, the SF-12 included a physical component summary (PCS) and a mental component summary (MCS). Both PCS and MCS values range from 0 to 100, with an average score of 50 and SD of 10, and the higher values represent better physical or mental quality-of-life measures.

In addition, for the humanistic burden, the activities of daily living (ADL) and instrumental ADL (IADL) were considered as measures for autonomy and self-dependence. Specifically, two health status variables, including ADL and IADL, were used. Information about ADL and IADL was available in the health status variable section of the MEPS full-year consolidated HC files. Those questions related to ADL and IADL were initially asked at the household level to ascertain the need of functional impairment among the family members.

**Conceptual framework of study variables.** The independent covariates were selected based on the literature and consideration of the MEPS data availability.<sup>20–22</sup> The socio-demographic information available on the HC, including age, sex, self-reported race and ethnicity, education, marital status,

family income (as a percentage of the poverty line by the federal standard), census region, and insurance status are included as covariates. In addition, to adjust for the individual's comorbidity profile, the Elixhauser index score, which was computed including the weighted information of 30 different comorbidities, was also used as a covariate. The Elixhauser scale was used as a categorical variable and was then categorized as 0, 1, 2, and 3.

**Statistical analysis.** Descriptive analyses (chi-square tests and *t*-tests) accounting for the complex weighted survey design were used to compare the characteristics between RA and non-RA groups. In addition, *t*-tests were used to compare the healthcare expenditures between RA and non-RA groups.<sup>35</sup> The average expenditure for specific health care expenditures (inpatient, outpatient, emergency department visits, and other medical services) were also compared using *t*-tests. In addition, the quality-of-life measures were compared between RA and non-RA groups using *t*-tests.

A two-part model (TPM) adjusting for the covariates was used to analyze the incremental overall healthcare expenditures between RA and non-RA groups. The TPM is a common approach in analyzing expenditure variables because it can handle discrete, continuous dependent outcome variables and address the issue of excessive zero expenditure variables and related positive skewness. In the first part of the TPM, a probit logistic regression model was used to estimate the probability of having a positive expenditure versus having a zero expenditure. Next, conditional on the nonzero expenditure, in the second part, a generalized linear model (GLM) was specified to estimate the incremental healthcare expenditure between RA and non-RA groups. The specification of the GLM involves (1) the modified Park test to determine the appropriateness of the family distribution and (2) the Pregibon link test to verify the link function. Here, the modified Park test found that the current data follow a Poisson family distribution, whereas the Pregibon link test confirmed that the suitable link function is the log link function. Stata (StataCorp) was used to find the best-fitting TPM.

For the analyses of quality-of-life measures, multivariable linear regression was used to compare the SF-12 PCS and MCS between patients with RA and the non-RA groups. In addition, multivariate logistic regression, adjusting for baseline characteristics, was used to evaluate the adjusted odds of seeking assistance for ADL and IADL between RA and non-RA groups. All other analyses were conducted in SAS statistical software version 9.4 (SAS Institute, Inc). We set a statistical significance level at  $P < 0.05$ .

## RESULTS

**Patient characteristics.** From the national survey between 2018 and 2020, there was a total of 1,296 unweighted

patients diagnosed with RA identified, nationally representing an annual weighted estimate of 4.27 million patients with RA (95% confidence interval [CI] 3.84–4.69). The comparative group included 63,378 unweighted individuals without RA, representing a weighted estimate of 249,835,278 (95% CI 237,052,031–262,618,524) patients annually.

Most patient demographics characteristics, including age category, sex, race, education, marital status, family income, and insurance, differed significantly between RA and non-RA groups. The details of study sample characteristics are available in Table 1.

**Health care expenditures.** From the unadjusted analyses, the mean unadjusted total healthcare expenditure for RA (\$24,068 [95% CI \$20,627.49–\$27,508.25]) was higher than that

for the non-RA group (\$8,381.19 [95% CI \$8,120.12–\$8,642.27]). The mean unadjusted hospital inpatient care–related health care expenditures for RA (\$3,389.84 [95% CI \$2,507.16–\$4,272.53]) were also higher than that for the non-RA group (\$1,772.58 [95% CI \$1,656.38–\$1,888.78]). Table 2 shows a more detailed unadjusted comparison of health care expenditure between RA and non-RA groups, stratified by different types of health care services. Overall, most of the health care expenditures were used for prescription medications, the inpatient setting, and office-based visits.

Table 3 shows the incremental health care expenditure in patients with RA by health care service. After adjusting for all covariates, the total healthcare expenditure for RA was \$3,382.97 (95% CI \$1,816.50–\$4,949.44;  $P < 0.0001$ ) higher than that for non-RA. In adjusted analyses, the average

**Table 1.** Characteristics of adults with RA and without RA, Medical Expenditure Panel Survey, 2018 to 2020\*

Characteristic	RA group		Non-RA group		P value
	Weighted frequency	%	Weighted frequency	%	
Age, y					<b>&lt;0.0001</b>
18–49	657,532	15.41	134,427,722	52.90	
50–64	1,694,651	39.72	61,425,571	24.17	
≥65	1,914,377	44.87	53,981,985	21.24	
Sex					<b>&lt;0.0001</b>
Male	1,320,392	30.95	121,619,937	48.68	
Female	2,946,168	69.05	128,215,341	51.32	
Race					<b>&lt;0.0001</b>
Hispanic	639,688	14.99	41,361,934	16.56	
White	2,659,357	62.33	155,901,180	62.40	
Black	657,354	15.41	29,734,760	11.90	
Other <sup>a</sup>	310,161	7.27	22,837,404	9.14	
Region					0.1476
Northeast	2,084,043	16.282	129,214,986	17.24	
Midwest	2,603,034	20.34	153,968,589	20.54	
South	5,187,612	40.53	281,726,489	37.59	
West	2,924,992	22.85	184,595,769	24.63	
Education					<b>&lt;0.0001</b>
No degree	1,153,933	27.05	56,487,587	13.82	
GED/high school graduation	2,208,697	51.77	109,793,987	21.80	
Associate's/bachelor's degrees	511,441	11.99	52,247,809	44.32	
Master's degree or higher	392,488	9.20	31,305,896	20.07	
Marital status					<b>&lt;0.0001</b>
Married	2,192,243	51.38	128,251,095	51.33	
Widowed/divorced/separated	1,657,544	38.85	48,265,504	19.32	
Single/never married	416,772	9.77	73,318,679	29.35	
Family income					<b>&lt;0.0001</b>
Poor/near poor	998,174	23.49	34,812,095	13.934	
Low income	649,761	15.23	30,001,718	12.01	
Middle income	1,083,738	25.4007	71,073,750	28.45	
High income	1,534,887	35.97	113,947,715	45.61	
Insurance					<b>&lt;0.0001</b>
Private	2,189,125	51.31	172,080,799	68.88	
Public	2,024,038	47.44	58,645,163	23.47	
Uninsured	53,396	1.25	19,109,316	7.65	
Number of Elixhauser comorbidities					<b>&lt;0.0001</b>
0–1	1,139,173	26.70	191,302,105	76.57	
2.0–3.0	1,516,743	35.55	40,031,040	16.02	
≥4	1,610,644	37.75	18,502,133	7.41	

\*GED, graduate equivalent degree; RA, rheumatoid arthritis. Significance at  $P < 0.05$  has been bolded.

<sup>a</sup>Others included non-Hispanic and Asian only or non-Hispanic and other races or multiple races.

**Table 2.** Health care expenditures between patients with RA and patients without RA by health care service, Medical Expenditure Panel Survey, 2018 to 2020\*

Type of health care expenditure	RA group			Non-RA group		
	Mean, \$	95% CI, \$	%	Mean, \$	95% CI, \$	%
Total	24,068	20,627.49–27,508.25	100	8,381.19	8,120.12–8,642.27	100
Hospital inpatient	3,389.84	2,507.16–4,272.53	14.08	1,772.58	1,656.38–1,888.78	21.15
Office-based visits	4,872.76	3,236.83–6,508.68	20.25	2,125.41	2,045.12–2,205.670	25.36
Outpatient	1,351.24	958.40–1,744.08	5.61	738.55	673.39–803.71	8.81
Emergency department	133.40	81.43–185.37	0.55	50.79	47.57–54.01	0.61
Prescription medication	9,884.83	7,827.56–11,942.09	41.07	1,923.34	1,812.70–2,033.98	22.95
Dental	599.77	458.65–740.89	2.49	430.42	412.58–448.27	5.14
Home health and others <sup>a</sup>	1,610.42	1,138.93–2,081.91	6.69	406.91	358.85–454.98	4.86
Total, excluding prescription medications <sup>b</sup>	14,183.00	11,503.22–16,862.87	58.92	6,457.85	6,236.63–6,679.08	77.05

\*CI, confidence interval; RA, rheumatoid arthritis.

<sup>a</sup>Includes glasses, ambulance, and equipment.

<sup>b</sup>Calculated as the total health care expenditure minus prescription medication expenditures; significance at  $P < 0.05$  has been bolded.

expenditures of prescription medication in RA were \$2,319.15 (95% CI \$1,408.39–\$3,229.90;  $P < 0.001$ ) higher than that for the non-RA group. Additionally, no significant differences for other types of expenditures were identified in this study.

**Quality-of-life measures.** Table 4 shows the quality-of-life measures in patients with RA versus patients without RA. The average PCS score was 31.31 (95% CI 30.00–32.62) for those with RA as compared to 39.05 (95% CI 38.63–39.46) for those without RA. Patients with RA had an average MCS score

**Table 3.** Incremental health care expenditures in patients with RA by health care service: Medical Expenditure Panel Survey, 2018 to 2020\*

Type of healthcare expenditure	Incremental expenditure, \$	95% CI, \$	<i>P</i> value
Total	3,382.97	1,816.50 to 4,949.44	<b>&lt;0.001</b>
Hospital inpatient	-136.19	-528.13 to 255.75	0.494
Office-based outpatient visits	686.60	-208.03 to 1,581.23	0.132
Outpatient	104.19	-119.44 to 327.83	0.359
Emergency department	27.62	-3.11 to 58.36	0.078
Prescription medication	2,319.15	1,408.39 to 3,229.90	<b>&lt;0.001</b>
Dental	68.31	-50.26 to 186.89	0.257
Home health and others <sup>a</sup>	56.12	-71.52 to 183.76	0.387

\*CI, confidence interval; RA, rheumatoid arthritis. Significance at  $P < 0.05$  has been bolded.

<sup>a</sup>Includes glasses, ambulance, and equipment.

**Table 4.** Health-related quality of life in RA, Medical Expenditure Panel Survey, 2018 to 2020\*

Type of health-related quality of life	RA group		Non-RA group	
	Mean	95% CI	Mean	95% CI
SF-12 PCS	31.31	30.00–32.62	39.05	38.63–39.46
SF-12 MCS	40.87	39.54–42.21	40.62	40.18–41.06
ADL, %				
Seeking help for ADL <sup>a</sup>				
Yes	9.60	7.57–11.63	1.75	1.60–1.91
No	90.40	88.37–92.43	98.25	98.09–98.40
Seeking help for IADL <sup>b</sup>				
Yes	14.92	12.33–17.52	3.06	2.87–3.25
No	85.08	82.48–87.67	96.94	96.75–97.13

\*ADL, activities of daily living; CI, confidence interval; IADL, instrumental activities of daily living; MCS, mental component summary; PCS, physical component summary; RA, rheumatoid arthritis; SF-12, Short Form 12.

<sup>a</sup>ADL includes activities for independent self-care (such as walking, dressing, eating, and bathing).

<sup>b</sup>IADL includes mental skills required to live within the community, such as shopping and medication management, using the phone, paying bills, and doing housework.

of 40.87 (95% CI 39.54–42.21), and patients without RA had an average MCS score of 40.62 (95% CI 40.18–41.06). In addition, a higher proportion of patients with RA sought help for ADL (9.60% [95% CI 7.57%–11.63%]), whereas only 1.75% (95% CI 1.60%–1.91%) of patients without RA sought help for ADL. Seeking help for IADL was among 14.92% (95% CI 12.33%–17.52%) of patients with RA, whereas it was among only 3.06% (95% CI 2.87%–3.25%) of patients without RA.

Results from the multivariable logistic regression analysis for PCS and MCS between RA and non-RA groups are presented in Table 5. It showed that the adjusted marginal effects of PCS for RA were 4.78 (95% CI 6.09–3.47;  $P < 0.001$ ) units less with reference to individuals without RA. However, the adjusted marginal difference of MCS was similar for RA and non-RA (–0.84, 95% CI –2.19 to 0.50;  $P = 0.216$ ).

Table 5 also presents the multivariable logistic regression results of seeking help with ADL and IADL between RA and non-RA groups. As shown in Table 5, compared to individuals without RA, individuals with RA were 2.02 times (95% CI 1.59–2.56;  $P < 0.001$ ) more likely to seek help for ADL. In addition, individuals with RA were associated with 2.11 times (95% CI 1.57–2.84;  $P < 0.001$ ) higher likelihood of seeking help for IADL than individuals without RA.

**Table 5.** Adjusted analysis of health-related quality of life between RA and non-RA groups, Medical Expenditure Panel Survey, 2018 to 2020\*

Health-related quality of life	Adjusted marginal difference <sup>a</sup>		
	Parameter estimate	95% CI	P value
SF-12 PCS			
RA status			
Yes	–4.78	–6.09 to –3.47	<b>&lt;0.0001</b>
No	1 (reference)		
SF-12 MCS			
RA status			
Yes	–0.84	–2.19 to 0.50	0.2164
No	1 (reference)		
ADL			
RA status			
Yes	2.02 <sup>b</sup>	1.59 to 2.56	<b>&lt;0.0001</b>
No	1 (reference) <sup>b</sup>		
IADL			
RA status			
Yes	2.11 <sup>b</sup>	1.57 to 2.84	<b>&lt;0.0001</b>
No	1 (reference) <sup>b</sup>		

\*ADL includes activities for independent self-care (such as walking, dressing, eating, and bathing). IADL includes mental skills required to live within the community, such as shopping and medication management, using the phone, paying bills, and doing housework. Significance at  $P < 0.05$  has been bolded. ADL, activities of daily living; aOR, adjusted odds ratio; CI, confidence interval; IADL, instrumental activities of daily living; MCS, mental component summary; PCS, physical component summary; RA, rheumatoid arthritis; SF-12, Short Form 12.

<sup>a</sup>Calculated using ordinary least square methods.

<sup>b</sup>Values are aORs, calculated using multivariable logistic regression models.

## DISCUSSION

This is the largest study evaluating the expenditure and quality of life for patients with RA compared to all other populations, providing insights into the economic and humanistic burden among RA patients. Using nationally representative data sets, this cross-sectional study had three key findings on the burden of RA. First, the average unadjusted healthcare expenditure for patients with RA can be up to \$24,069 annually, significantly higher than that for patients without RA. After adjusting for patients’ sociodemographics and comorbidities, patients with RA spent \$3,382.97 more in healthcare expenditures than patients without RA. Second, a significant proportion of health care costs for RA were spent on prescription medications, followed by the inpatient setting. Thirdly, patients with RA were more likely to have suboptimal quality-of-life outcomes compared to patients without RA, as measured by PCS, ADL, and IADL.

Our current findings show that the RA group had \$3,382.971 more in adjusted marginal overall healthcare expenditure than the non-RA group. Previous literature found the cost burden associated with RA in the United States to be lower than our findings.<sup>8</sup> A Medicare study by Chen et al.<sup>22</sup> reported annual healthcare costs of \$20,919 in patients with RA. The difference in medical expenditures associated with RA observed in this study can be explained by two reasons. First, the study by Chen et al.<sup>22</sup> evaluated data that were limited to an earlier time period (2010–2013), before the approval of new JAKi and non-tumor necrosis factor inhibitor biologics in recent years. The more frequent administration of these expensive biologics or new JAKi in recent study years can explain the increase in the health care expenditure for RA. In addition, biologics have increased in price over time for a variety of reasons not directly related to drug costs but more administrative issues with the medications. Second, the differences in healthcare expenditures can also be attributed to the discrepancy in the population studied. This present study evaluated healthcare expenditure data from a nationwide sample of all types of insurance enrollees and uninsured population, which is different from the study of Chen et al.<sup>22</sup> who used Medicare claims data. However, the total estimates of healthcare expenditure of this current study are generally consistent with a recent systematic review.<sup>36</sup> A systematic review of 12 studies by Hresko et al.<sup>8</sup> showed that the medical care costs associated with RA range from \$12,509 to \$36,053.

Although several types of healthcare services contributed to the higher incremental total healthcare expenditures in RA, this study found that a major proportion of the total healthcare expenditure in the group of patients with RA was attributable to prescription medications. The adjusted prescription medication expenditure was \$2,319.146 (95% CI \$1,408.392–\$3,229.901), significantly higher than that for the non-RA group. In consistent, previous literatures also showed that the costs of biologic DMARD prescriptions are the main contributor to the total healthcare expenditure in the RA population.<sup>36–39</sup>

This study also found that patients with RA reported lower PCS scores compared to patients without RA. This is consistent with other studies, which found that patients with RA have poorer quality of life than the general US population.<sup>27,29,40–42</sup> A systematic review and meta-analysis by Matcham et al.<sup>40</sup> found that patients with RA have a significantly reduced HRQoL, with an SF-36 based PCS score of 34.1 (95% CI, 22–46.1) and an MCS score of 45.6 (95% CI, 30.3–60.8) by pooling mean HRQoL scores from 31 studies. The study by Gerhold et al.<sup>42</sup> also found that both physical and mental health scores were reported as remarkably lower in patients with RA than in the general population. RA is a progressive, inflammatory autoimmune arthritis involving multiple joints, potentially leading to joint damage and physical limitation, and the reduced PCS in RA can be explained by multiple factors, such as disease activity, physiologic disturbance,<sup>27,29,41</sup> and other RA-related comorbidities.<sup>43</sup> Moreover, although our study only found that patients with RA had numerically lower MCS scores than their counterparts without RA, more research is needed because it has been reported earlier that mental health problems, such as depression, were commonly observed in patients with RA.<sup>44</sup>

Furthermore, this study also found that patients with RA were more likely to seek help for ADL (such as bathing or dressing) than the non-RA group. RA is a chronic inflammatory disease affecting multiple joints, implicating the risk of progressive joint damage.<sup>45</sup> Apart from the joint pain as the main symptom, clinically, RA also involves other physical features, such as joint swelling and stiffness, which these components may contribute to patients' impaired motor function.<sup>46</sup> A recent US national study found that more than 36% of patients with RA had physical activity limitations, with difficulty in common ADLs, such as walking, leisure activities, or attending social events.<sup>47</sup> As a consequence, patients with RA were found to experience a reduction in work productivity,<sup>48</sup> physical function disability,<sup>30</sup> and even reduced life expectancy.<sup>49</sup> Effective patient-centered interventions, such as appropriate joint exercise, should be strengthened to improve patients' physical activity and joint mobility. In addition, the reduced cognitive ability in patients with RA has also been well documented in the literature.<sup>50–55</sup> Indeed, as high as two-thirds of patients with RA exhibit some sort of cognitive dysfunction because of multiple factors, including age, disease activity, and other coexisting underlying comorbidities.<sup>50</sup> This might explain why patients with RA had reduced odds of performing IADL, an indicator of early cognitive decline, compared to individuals without RA.

Our findings have implications for health policy and clinical practice, particularly regarding the prioritization of healthcare resources for RA management. First, for clinicians, the data on HRQoL in patients with RA offer unique patient perspectives about the impact of the disease of RA and allow clinicians to detect unfavorable disease progression. In addition, in clinical practice, it may be beneficial to assess humanistic outcomes,

such as HRQoL and functional limitations, to inform treatment strategies for RA. More importantly, these present findings show that patients with RA have suboptimal HRQoL, as measured by ADL and IADL, compared to non-RA controls. Hence, this highlights the need to prioritize functional outcome improvement, such as physical independence, the ability to perform daily tasks, and mobility, in patients with RA. Second, our findings are noteworthy and can inform significant economic burdens in RA versus non-RA in the US setting, which the majority of healthcare expenditures in RA were attributable to prescription medications. Payers, providers, and managed care professionals may consider minimizing the hurdles to payment coverage for these specialty drugs to facilitate access to biologics for RA.

The key strength of this study is its use of the MEPS, with rich information from national-level participants. Through multilevel probability sampling approaches, the election of the study sample in the MEPS involves oversampling of racial and ethnic minority individuals; therefore, the results are generalizable to all adult patients with RA across the United States. In addition, this is the first study involving national-level data to examine the functional limitations between patients with RA and adults without RA regarding the help needed for ADL and IADL. Another strength of this study is its methodologic rigor. This study used the TPM to analyze healthcare expenditures among the RA population. In addition, this national-level data-based study applied a strong conceptual framework for covariate adjustment.

Nevertheless, this study had some limitations, and some of them were inherent to MEPS data. First, study results were limited to noninstitutionalized populations because the MEPS data did not include those from institutionalized settings. Second, this is a cross-sectional design, and therefore causality cannot be established. Thirdly, a variety of demographics and clinical characteristics have been included in the models for confounding adjustment; however, some data variables are not available in the MEPS data, such as the type of RA, duration of RA, and disease severity. The lack of this RA-related clinical information might introduce unmeasured variable bias, which further limits the explanation of these findings. Fourthly, because of the recall bias of study respondents, the MEPS-based analyses may have issues of underreporting or overreporting. Fifthly, the information related to the cost of different types of treatments was lacking; therefore, the cost estimate was based on the overall healthcare expenditures. Sixthly, because of the data availability, this study examined RA costs using MEPS data from 2018 to 2020, which did not capture the impact of the new RA treatment and management practices available after 2020.

In this population survey, we found that RA is a chronic progressive disease with substantial economic and humanistic burden as compared to the general population. These national-level data found that most RA-related health expenditures were due to prescription medication administration and hospital inpatient services. In addition, patients with RA have suboptimal HRQoL

compared to controls without RA. Prescribers should evaluate the HRQoL impact in prescribing treatment to adults with RA. Managed care professionals and payers should be aware of the high expenditures of RA due to high-cost prescription medications.

## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr Huang has 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 conception and design.** All authors

**Acquisition, analysis and interpretation of data.** Huang, Li

**Drafting of the manuscript.** Huang

## REFERENCES

- Smolen JS, Aletaha D, Barton A, et al. Rheumatoid arthritis. *Nat Rev Dis Primers* 2018;4:18001.
- Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: a review. *JAMA* 2018;320(13):1360–1372.
- Finckh A, Gilbert B, Hodkinson B, et al. Global epidemiology of rheumatoid arthritis. *Nat Rev Rheumatol* 2022;18(10):591–602.
- Almutairi KB, Nossent JC, Preen DB, et al. The prevalence of rheumatoid arthritis: a systematic review of population-based studies. *J Rheumatol* 2021;48(5):669–676.
- Almutairi K, Nossent J, Preen D, et al. The global prevalence of rheumatoid arthritis: a meta-analysis based on a systematic review. *Rheumatol Int* 2021;41(5):863–877.
- Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2021;73(7):924–939.
- Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Ann Rheum Dis* 2023;82(1):3–18.
- Hresko A, Lin TC, Solomon DH. Medical care costs associated with rheumatoid arthritis in the US: a systematic literature review and meta-analysis. *Arthritis Care Res (Hoboken)* 2018;70(10):1431–1438.
- Lexchin J. Affordable biologics for all. *JAMA Netw Open* 2020;3(4):e204753.
- Michaud K, Messer J, Choi HK, et al. Direct medical costs and their predictors in patients with rheumatoid arthritis: a three-year study of 7,527 patients. *Arthritis Rheum* 2003;48(10):2750–2762.
- Harrold LR, Peterson D, Beard AJ, et al. Time trends in medication use and expenditures in older patients with rheumatoid arthritis. *Am J Med* 2012;125(9):937.e9–937.e15.
- Alamanos Y, Drosos AA. Epidemiology of adult rheumatoid arthritis. *Autoimmun Rev* 2005;4(3):130–136.
- Kim JW, Suh CH. Systemic manifestations and complications in patients with rheumatoid arthritis. *J Clin Med* 2020;9(6):2008–2012.
- Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. *Arch Phys Med Rehabil* 2014;95(5):986–995.e1.
- Vuong TD, Wei F, Beverly CJ. Absenteeism due to functional limitations caused by seven common chronic diseases in US workers. *J Occup Environ Med* 2015;57(7):779–784.
- Theis KA, Murphy L, Hootman JM, et al. Social participation restriction among US adults with arthritis: a population-based study using the International Classification of Functioning, Disability and Health. *Arthritis Care Res (Hoboken)* 2013;65(7):1059–1069.
- Tatangelo M, Tomlinson G, Paterson JM, et al. Health care costs of rheumatoid arthritis: a longitudinal population study. *PLoS One* 2021;16(5):e0251334.
- Hamuryudan V, Direskeneli H, Ertenli I, et al. Direct and indirect health-care costs of rheumatoid arthritis patients in Turkey. *Clin Exp Rheumatol* 2016;34(6):1033–1037.
- Roodenrys NMT, Welsing PMJ, van der Goes MC, et al. Healthcare utilization and economic burden of difficult-to-treat rheumatoid arthritis: a cost-of-illness study. *Rheumatology (Oxford)* 2021;60(10):4681–4690.
- Grabner M, Boytsov NN, Huang Q, et al. Costs associated with failure to respond to treatment among patients with rheumatoid arthritis initiating TNFi therapy: a retrospective claims analysis. *Arthritis Res Ther* 2017;19(1):92–103.
- Chen CI, Wang L, Wei W, et al. Burden of rheumatoid arthritis among US Medicare population: co-morbidities, health-care resource utilization and costs. *Rheumatol Adv Pract* 2018;2(1):rky005.
- Johnson K, Karos R, Avalos-Reyes E, et al. Total cost of care for patients with rheumatoid arthritis [abstract]. *Arthritis Rheumatol* 2020;72(suppl 10). <https://acrabstracts.org/abstract/total-cost-of-care-for-patients-with-rheumatoid-arthritis/>. Accessed August 11, 2023.
- Strand V, Rentz AM, Cifaldi MA, et al. Health-related quality of life outcomes of adalimumab for patients with early rheumatoid arthritis: results from a randomized multicenter study. *J Rheumatol* 2012;39(1):63–72.
- Strand V, Schiff M, Tundia N, et al. Effects of upadacitinib on patient-reported outcomes: results from SELECT-BEYOND, a phase 3 randomized trial in patients with rheumatoid arthritis and inadequate responses to biologic disease-modifying antirheumatic drugs. *Arthritis Res Ther* 2019;21(1):263–272.
- Schiff M, Takeuchi T, Fleischmann R, et al. Patient-reported outcomes of baricitinib in patients with rheumatoid arthritis and no or limited prior disease-modifying antirheumatic drug treatment. *Arthritis Res Ther* 2017;19(1):208–217.
- Taylor PC, Fautrel B, Piette Y, et al. Treat-to-target in rheumatoid arthritis: a real-world study of the application and impact of treat-to-target within the wider context of patient management, patient-centricity and advanced therapy use in Europe. *RMD Open* 2022;8(2):e002658.
- Goma SH, Razek MRA, Abdelbary NM. Impact of rheumatoid arthritis on the quality of life and its relation to disease activity. *Egypt Rheumatol Rehabil* 2019;46(4):304–312.
- Martinez R, Pinjatela R, Balen D. Quality of life in patients with rheumatoid arthritis - a preliminary study. *Acta Clin Croat* 2019;58(1):157–166.
- Bai B, Chen M, Fu L, et al. Quality of life and influencing factors of patients with rheumatoid arthritis in Northeast China. *Health Qual Life Outcomes* 2020;18(1):119–128.
- Ji J, Zhang L, Zhang Q, et al. Functional disability associated with disease and quality-of-life parameters in Chinese patients with rheumatoid arthritis. *Health Qual Life Outcomes* 2017;15(1):89–95.
- Cohen JW, Cohen SB, Banthin JS. The Medical Expenditure Panel Survey: a national information resource to support healthcare cost research and inform policy and practice. *Med Care* 2009;47(7 suppl 1):S44–S50.
- Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey. Accessed August 11, 2023. <https://meps.ahrq.gov/mepsweb/>



33. Curtis JR, Xie F, Zhou H, et al. Use of ICD-10 diagnosis codes to identify seropositive and seronegative rheumatoid arthritis when lab results are not available. *Arthritis Res Ther* 2020;22(1):242–250.
34. Lee H, Sparks JA, Lee SB, et al. Validation of serostatus of rheumatoid arthritis using ICD-10 codes in administrative claims data. *Pharmacoepidemiol Drug Saf* 2023;32(5):586–591.
35. US Bureau of Labor Statistics. Consumer Price Index. Updated June 11, 2024. Accessed November 26, 2022. <https://www.bls.gov/cpi/>
36. Ding Q, Shiltz D, Hossami D, et al. The economic burden of biologic disease-modifying antirheumatic drugs in rheumatoid arthritis patients in the United States. *Expert Rev Pharmacoecon Outcomes Res* 2022; 22(8):1231–1241.
37. Park T. Health care utilization and expenditures among adults with rheumatoid arthritis using specialty pharmaceuticals. *Res Social Adm Pharm* 2019;15(6):724–729.
38. Brkic A, Diamantopoulos AP, Haavardsholm EA, et al. Exploring drug cost and disease outcome in rheumatoid arthritis patients treated with biologic and targeted synthetic DMARDs in Norway in 2010–2019 - a country with a national tender system for prescription of costly drugs. *BMC Health Serv Res* 2022;22(1):48–62.
39. Erath A, Dusetzina SB. Assessment of expected out-of-pocket spending for rheumatoid arthritis biologics among patients enrolled in Medicare part D, 2010–2019. *JAMA Netw Open* 2020;3(4): e203969.
40. Matcham F, Scott IC, Rayner L, et al. The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2014;44(2):123–130.
41. Katchamart W, Narongroeknawin P, Chanapai W, et al. Health-related quality of life in patients with rheumatoid arthritis. *BMC Rheumatol* 2019;3(1):34–41.
42. Gerhold K, Richter A, Schneider M, et al. Health-related quality of life in patients with long-standing rheumatoid arthritis in the era of biologics: data from the German biologics register RABBIT. *Rheumatology (Oxford)* 2015;54(10):1858–1866.
43. An J, Nyarko E, Hamad MA. Prevalence of comorbidities and their associations with health-related quality of life and healthcare expenditures in patients with rheumatoid arthritis. *Clin Rheumatol* 2019; 38(10):2717–2726.
44. Deb A, Dwibedi N, LeMasters T, et al. Burden of depression among working-age adults with rheumatoid arthritis. *Arthritis* 2018;2018: 8463632.
45. Metsios GS, Stavropoulos-Kalinoglou A, Sandoo A, et al. Vascular function and inflammation in rheumatoid arthritis: the role of physical activity. *Open Cardiovasc Med J* 2010;4(1):89–96.
46. Kauranen K, Vuotikka P, Hakala M. Motor performance of the hand in patients with rheumatoid arthritis. *Ann Rheum Dis* 2000;59(10): 812–816.
47. Gikaro JM, Xiong H, Lin F. Activity limitation and participation restriction in osteoarthritis and rheumatoid arthritis: findings based on the National Health and Nutritional Examination Survey. *BMC Musculoskelet Disord* 2022;23(1):647–655.
48. Sullivan PW, Ghushchyan V, Huang XY, et al. Influence of rheumatoid arthritis on employment, function, and productivity in a nationally representative sample in the United States. *J Rheumatol* 2010;37(3): 544–549.
49. Norton S, Sacker A, Dixey J, et al; Early Rheumatoid Arthritis Study. Trajectories of functional limitation in early rheumatoid arthritis and their association with mortality. *Rheumatology (Oxford)* 2013;52(11): 2016–2024.
50. Vitturi BK, Nascimento BAC, Alves BR, et al. Cognitive impairment in patients with rheumatoid arthritis. *J Clin Neurosci* 2019;69:81–87.
51. Oláh C, Schwartz N, Denton C, et al. Cognitive dysfunction in autoimmune rheumatic diseases. *Arthritis Res Ther* 2020;22(1):78–84.
52. Chaurasia N, Singh A, Singh IL, et al. Cognitive dysfunction in patients of rheumatoid arthritis. *J Family Med Prim Care* 2020;9(5):2219–2225.
53. Meade T, Manolios N, Cumming SR, et al. Cognitive impairment in rheumatoid arthritis: a systematic review. *Arthritis Care Res (Hoboken)* 2018;70(1):39–52.
54. Pankowski D, Wytrychiewicz-Pankowska K, Janowski K, et al. Cognitive impairment in patients with rheumatoid arthritis: a systematic review and meta-analysis. *Joint Bone Spine* 2022;89(3):105298.
55. Gwinnutt JM, Toyoda T, Jeffs S, et al. Reduced cognitive ability in people with rheumatoid arthritis compared with age-matched healthy controls. *Rheumatol Adv Pract* 2021;5(2):rkab044.