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Concise report

Burden of rheumatoid arthritis among US Medicare population: co-morbidities, health-care resource utilization and costs

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Abstract

Objectives. The study aimed to assess the burden of RA among the US Medicare population (aged ≥65 years) by comparing co-morbidities, health-care resource utilization (HCRU) and costs against matched non-RA Medicare patients.

Methods. Data were obtained from the Medicare fee-for-service claims database from 2010 to 2013. RA Medicare patients were identically matched with Medicare patients without RA (controls) based on demographics. Bivariate analyses were conducted to examine differences between cohorts for co-morbidities, HCRU and costs. A generalized linear model was used to test relationships between patient-level characteristics, HCRU and costs.

Results. The study population included 115 867 RA patients and 115 867 age-, sex-, race- and region-matched non-RA controls. Mean age was 75.2 years; 79.4% were female. Co-morbidities were greater in RA *vs* non-RA patients [Charlson Co-morbidity Index (excluding RA): 1.86 *vs* 1.00; $P < 0.0001$]. All-cause annual HCRU was greater in RA *vs* non-RA patients. Total annual health-care costs were ∼3-fold higher in RA *vs* non-RA patients ($20 919 *vs* $7197, respectively; $P < 0.0001$) with the major driver of costs in the RA cohort being outpatient costs. Approximately half of the overall costs in the RA cohort were RA related ($11 587). After controlling for differences in patient characteristics and co-morbidities between cohorts, the adjusted total mean annual costs for RA patients were still more than twice those of non-RA patients ($16 374 *vs* $6712; $P < 0.0001$).

Conclusions. Among US Medicare patients, those with an RA diagnosis had a significantly greater burden of co-morbidities, HCRU and costs compared with a matched cohort without RA.

Key words: rheumatoid arthritis, elderly, burden of disease, co-morbidities, health-care resource utilization

CONCISE REPORT

Key messages

- US Medicare patients with RA had significantly greater co-morbidity burden, health-care resource utilization, and costs.
- Annual all-cause health-care costs were 3-fold higher among RA Medicare patients *vs* non-RA Medicare patients.
- Outpatient visits were the main cost driver, accounting for nearly half of the total cost.

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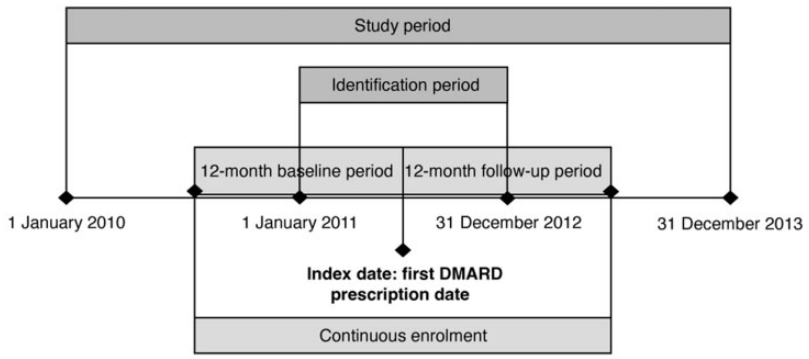
Introduction

RA is estimated to affect ∼0.2–1% of the worldwide population [1, 2]. Based on 1987 diagnostic criteria, in the US, ∼0.6% of adults (≥18 years) and ∼2.0% of individuals ≥60 years of age are affected [3, 4], resulting in 2.9 million visits to physicians related to RA in the US annually based on 2007 data [5]. However, the updated

Fig. 1 Overview of study design



2010 criteria include in their diagnosis patients previously classified as having undifferentiated arthritis; as a result, the number of patients with RA may be higher [6].

Although disease onset may occur at any age, approximately one-third of all RA patients are >65 years of age [7]. Given disease chronicity, low remission rates (estimated to be between 8.6 and 19.6% based on varying definitions of remission [8]) and the increasing size of the US elderly population [9], RA poses a significant economic burden.

Pharmacological therapy is considered the mainstay of treatment for RA [10, 11]; however, despite an abundance of treatment options, elderly patients with RA are less likely to be prescribed DMARDs, including MTX, AZA, LEF, SSZ, HCQ, gold and minocycline, than younger patients [12, 13]. This may be explained by the perception that DMARDs can have greater propensity for adverse events in this patient population. Additionally, elderly patients may fear trying new treatments [12].

Co-morbidities associated with RA [14] are likely to further impact clinical problems, associated health-care resource utilization (HCRU), and direct and indirect costs [15]. In the US, total annual health costs (including direct and indirect costs) among the overall RA patient population have been estimated at up to $19.3 billion (in 2005 US dollars) [16]. However, additional data on the clinical and economic impact of RA in the US are required, especially in the elderly population, to provide better information for health-care and health policy decision-making for this growing patient group.

The aim of this retrospective cohort analysis was to establish the burden of RA in the US Medicare population (≥65 years old) by comparing co-morbidities, HCRU and associated costs with a matched non-RA Medicare cohort.

Methods

Study design and sample population

Patient-level data for this observational, retrospective cohort analysis were obtained from the anonymized Medicare fee-for-service (FFS) claims database. Data were collected between 1 January 2010 and 31 December 2013 for two cohorts (aged ≥65 years) of Medicare beneficiaries, comprising an RA cohort and a matched cohort without RA. Patients were included in the RA cohort if they had made at least two RA-related medical claims [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 714.xx] ≥7 days apart, and had continuous health plan enrolment with FFS medical and pharmacy benefits for the 12-month pre-index (baseline) period until the end of the 12-month post-index (follow-up) period. The index date was defined as the date of the patient's first pharmacy claim for a DMARD. Each RA cohort patient was matched (1:1) with a patient without RA [i.e. no diagnosis of RA (ICD-9-CM code 714.xx) during the study period] of identical age, sex and race, who was from the same US region, and had continuous FFS health plan enrolment with medical and pharmacy benefits for the 12-month baseline period and the 12-month follow-up period (Fig. 1). These control patients were assigned the same index date as the case patients with whom they were matched.

Baseline data

Patient demographic characteristics were obtained at the index date. Co-morbid conditions were assessed throughout the 12 months pre-index date (baseline period). Overall co-morbidity was measured using the Charlson Co-morbidity Index (CCI) Score, which assigns a weight ranging from one to six according to disease severity for 19 conditions [17]. In addition, the Deyo-modified CCI was used to allow ICD-9-CM diagnosis codes to contribute to the score [18]. The Chronic Disease Score was developed by Von Kroff and colleagues, and is an aggregate co-morbidity measure, which is based on current medication use and serves as an indicator of a patient's morbidity and overall health. The Chronic Disease Score ranges from 0 to 36, and the higher the score, the more likely that the patient will be hospitalized and/or die. In this study, pharmacy claims were used to determine the Chronic Disease Score [19]. Additionally, the severity index for RA (SIFRA®) score, which ranges from 0 to 128.5 and was

assessed by an expert Delphi panel of six board-certified, clinically active rheumatologists, was used exclusively to measure RA severity through medical records [20–22]. Using associated scores from the Delphi panel, a severity index for RA was created by calculating the weighted sum, which was then verified by its estimation power for health-care outcomes and utilization [20]. Using claims data, 39 indicators, including laboratory, extra-articular manifestations, surgical history and medication, are included. Co-morbidities in the RA cohort (primary and secondary diagnosis) based on the first three digits of ICD-9-CM diagnosis codes were compared with the corresponding rates for the non-RA cohort, and the top 10 non-bone- and joint-related co-morbidities were reported.

Outcomes measures

During the 12-month follow-up period, all-cause (both cohorts) and RA-related (RA cohort only) HCRU was estimated for ambulatory (physician office and outpatient) visits, emergency department (ED) visits, inpatient admissions, length of stay (LOS) and prescription fills; these were considered RA-related if the claim had a primary or secondary diagnosis of RA or involved use of any RA-related medication, including CSs, NSAIDs or DMARDs. Similarly, all-cause (both cohorts) and RA-related (RA cohort only) health-care costs were estimated for ambulatory and ED visits, inpatient admissions and pharmacy visits. In addition, total (medical plus pharmacy) costs as paid by health plans were also estimated. All costs were adjusted for inflation to 2013 US dollars using the annual medical care component and drug cost component of the Consumer Price Index.

Analysis

All patient variables, including age, sex, race, region and baseline co-morbidity index scores, as well as all-cause HCRU, and costs over the 12-month follow-up period, were compared between the RA and non-RA cohorts. The benefit of treatment on the risk of disease(s) of interest, HCRU, and costs were also determined.

Bivariate comparisons were conducted to examine the differences between the RA and non-RA cohorts in co-morbidities, HCRU, and costs. For dichotomous and polychotomous variables, *P*-values were calculated using the χ^2 test, and for continuous variables *P*-values were calculated using an unpaired *t*-test.

A generalized linear model (GLM) was used to test the relationships between patient-level characteristics, HCRU and costs. The dependent variables included patients with total HCRUs, including inpatient, outpatient, ED, office, and pharmacy visits. Independent variables included all patient demographic characteristics (age, sex, race and region), baseline co-morbidities (CCI, individual co-morbidities), and the cohort variable (RA or non-RA Medicare). In addition, negative binomial and logistic regressions were used to model HCRU measures.

To estimate total costs, $\log_{10}$-transformation and GLMs were applied, depending on the distribution and presence of heteroscedasticity. In these models, the dependent variables included the costs of inpatient, outpatient, ED and office visits, and pharmacy use.

Results

Clinical characteristics and demographics

In total, 3 156 628 Medicare beneficiaries were identified in the study period (from 1 January 2011 to 31 December 2013). Of these, 2 924 894 were excluded because they were aged <65 years, had no continuous health enrolment plan or had no diagnosis of RA during the study period, resulting in a total sample size of 231 734 patients (115 867 patients in the RA Medicare cohort and 115 867 matched patients in the non-RA Medicare cohort; Fig. 2). Mean (S.D.) patient age was 75.2 (6.36) years; 79.4% were women; 86.4% were Caucasian; and 41.3% resided in the Southern region of the US (Table 1).

Co-morbidity burden

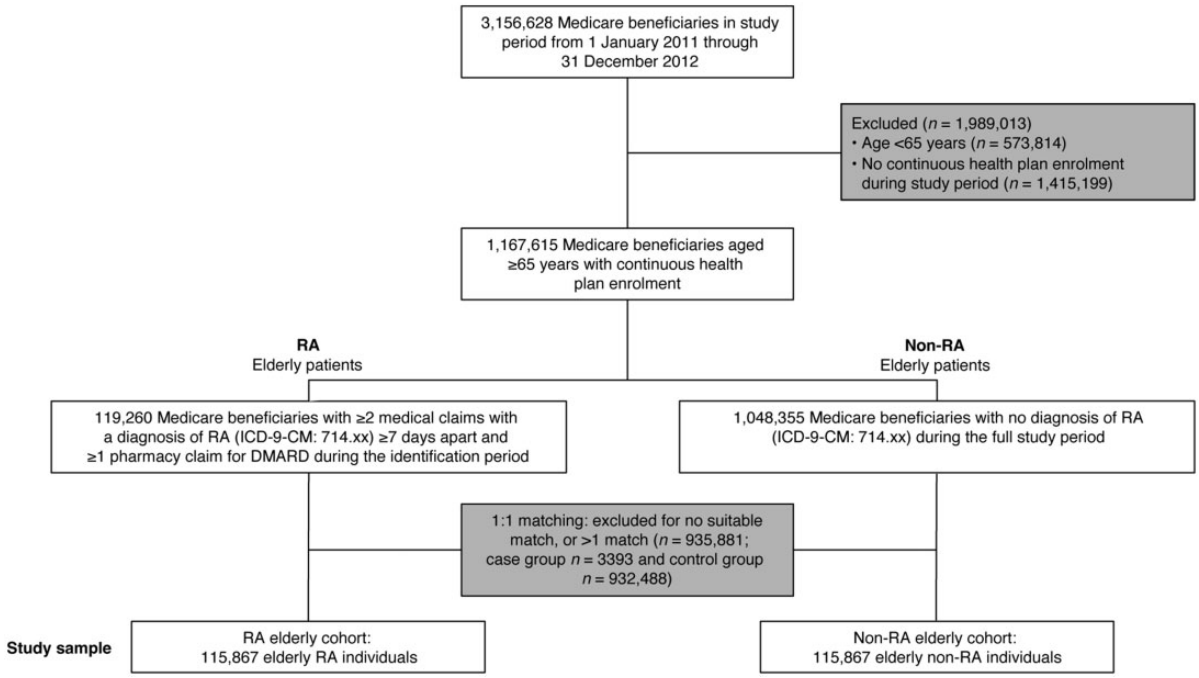
Compared with the non-RA cohort, the RA cohort had significantly greater overall co-morbidities [CCI score (excluding RA) 1.86 *vs* 1.00; $P < 0.0001$; Table 1]. Likewise, the chronic disease score (8.50 *vs* 5.54; $P < 0.0001$) and severity index for RA (19.43 *vs* 0.51; $P < 0.0001$) were significantly higher in the RA cohort *vs* the non-RA cohort (Table 1).

The most common non-bone- and joint-related diagnoses in both cohorts were cardiovascular system related, with 76.4% of patients in the RA cohort and 44.8% in the non-RA cohort experiencing essential hypertension (ICD-9-CM:401), 66.4 and 41.7%, experiencing disorders of lipid metabolism (ICD-9-CM:272), 27.5 and 14.5% experiencing ischemic heart disease (ICD-9-CM:414.9), and 21.0 and 9.6% experiencing peripheral vascular disease (ICD-9-CM:443.9), respectively. Other common co-morbidities included: general symptoms (ICD-9-CM:780; code includes sleep disturbances and fatigue) in 50.3 and 24.3%; symptoms involving the respiratory system and other chest symptoms (ICD-9-CM:786) in 48.1 and 22.1%; and other disorders of the soft tissues (ICD-9-CM:729) in 45.4 and 17.4%, respectively. Furthermore, across the 10 most common co-morbidities in both groups, the relative risk of the co-morbidity was significantly greater for the RA cohort *vs* the non-RA cohort ($P < 0.0001$; Table 1).

Health-care resource utilization and costs

Compared with the non-RA cohort, mean annual all-cause HCRU, including percentage of patients with inpatient/ED visits, outpatient visits and pharmacy visits (as well as the mean number of these visits in the 1-year follow-up period), were all significantly greater

Fig. 2 Patient attrition scheme



($P < 0.0001$) for the RA cohort than the non-RA cohort (Fig. 3). For example, in the RA cohort there were 0.96 inpatient/ED visits during the 1-year follow-up overall, whereas in the non-RA cohort there were 0.40 visits ($P < 0.0001$; Fig. 3). Moreover, RA-related HCRU was a major driver of the overall HCRU in each case (Fig. 3). The mean (S.D.) inpatient LOS per visit was also significantly greater in the RA cohort compared with the non-RA cohort [4.38 (16.2) *vs* 0.97 (4.92) days, respectively; $P < 0.0001$], with the mean LOS specifically related to RA in the RA cohort being 2.66 (10.77) days.

Mean annual total health-care costs were ~3-fold higher for the RA cohort compared with the non-RA cohort ($20 919 *vs* $7197, respectively; $P < 0.0001$), and more than half of the total costs were related to RA ($11 587; Fig. 4). Among the RA cohort, the main driver for increased costs was outpatient costs, followed by inpatient costs and then pharmacy costs. Mean annual all-cause outpatient costs were $9022 in the RA cohort *vs* $2607 in the non-RA cohort ($P < 0.0001$), and more than half ($4719) of the outpatient costs in the RA cohort were RA related (Fig. 4).

Overall pharmacy costs (calculated from Medicare Part D) were significantly greater in the RA cohort ($5794) than the non-RA cohort ($2449; $P < 0.001$). However, among the RA cohort, pharmacy costs accounted for the smallest proportion of the total costs, with an even smaller proportion ($2670 out of $5794) related to RA (Fig. 4). The cost of biologics [calculated from pharmacy (Medicare Part D) plus medical (Medicare Part B) claims] accounted for the majority of drug-related costs [calculated from pharmacy (Medicare Part D) plus medical (Medicare Part B) claims] observed in all RA patients ($2836 out of $3331).

After controlling for differences in patient characteristics and co-morbidities, the adjusted mean annual total costs for the RA cohort remained more than twice those observed in the non-RA cohort ($16 374 *vs* $6712, respectively; $P < 0.0001$; Table 2).

Discussion

Given the high and growing prevalence of RA in the elderly population, it is important to establish its age- and disease-specific clinical and economic burden to successfully aid health-care decision-making and cost containment in this vulnerable population.

The significantly higher incidence of co-morbidities associated with RA has previously been reported among adult RA patients [23–28]; however, to our knowledge this is the first study to examine co-morbidities, HCRU and costs specifically in the RA Medicare population in a real-world setting. The results of this retrospective cohort study indicated that RA Medicare patients have a significantly higher prevalence of non-bone- and joint-related co-morbidities, including a higher incidence of cardiovascular co-morbidities, such as hypertension, disorders of lipid metabolism, ischemic heart disease and peripheral vascular disease, as well as symptoms involving the respiratory system, in comparison with a matched non-RA cohort.

Table 1 Baseline demographic and clinical characteristics for patients with and without RA

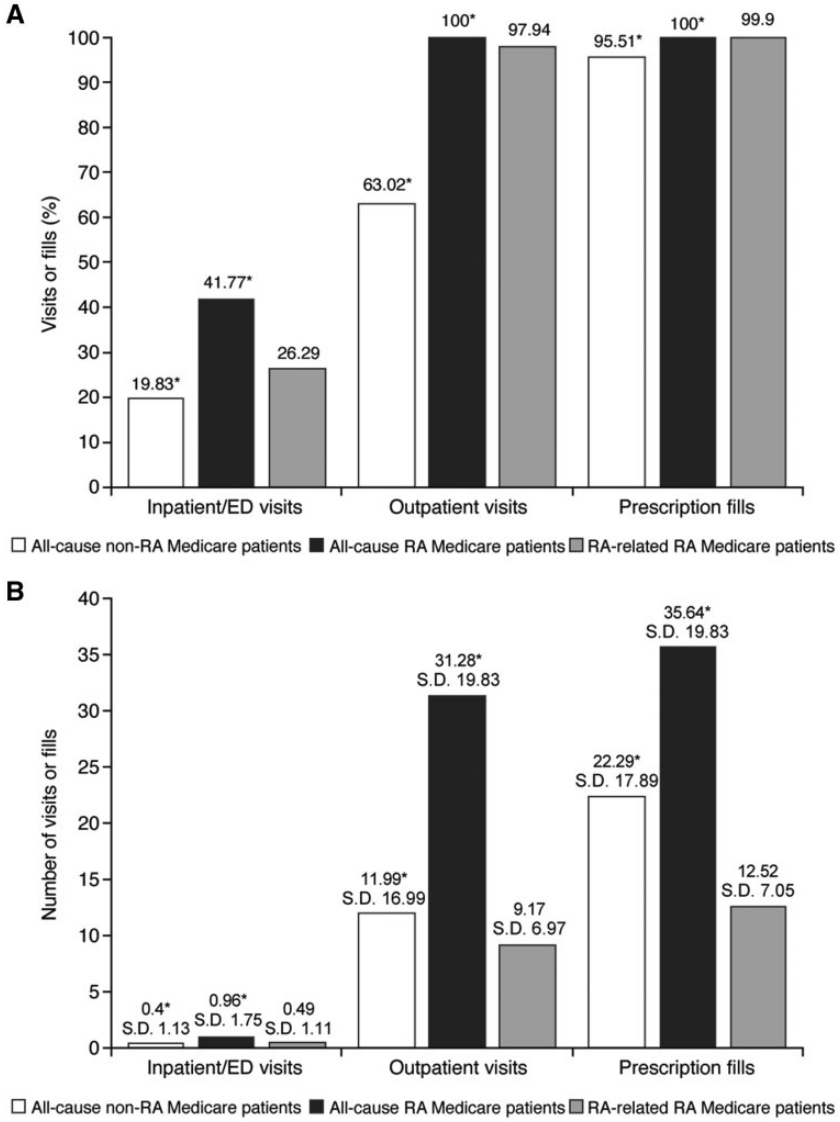
Demographic/clinical characteristics	Control group (non-RA) (n = 115 867)	Case group (RA) (n = 115 867)	P-value	RR (95% CI)
Age, mean (S.D.), years	75.2 (6.4)	75.2 (6.4)	–	–
65–69 years, n (%)	25 653 (22.1)	25 653 (22.1)	–	–
70–74 years, n (%)	34 891 (30.1)	34 891 (30.1)	–	–
75–79 years, n (%)	26 083 (22.5)	26 083 (22.5)	–	–
≥80 years, n (%)	29 240 (25.2)	29 240 (25.2)	–	–
Sex, n (%)				
Male	23 896 (20.6)	23 896 (20.6)	–	–
Female	91 971 (79.4)	91 971 (79.4)	–	–
Race, n (%)				
White	100 160 (86.4)	100 160 (86.4)	–	–
Black	8709 (7.5)	8709 (7.5)	–	–
Asian	1816 (1.6)	1816 (1.6)	–	–
Hispanic	2970 (2.6)	2970 (2.6)	–	–
North American	604 (0.5)	604 (0.5)	–	–
Other	1608 (1.4)	1608 (1.4)	–	–
Geographical location, n (%)				
Northeast	19 639 (16.9)	19 639 (16.9)	–	–
Midwest	28 334 (24.5)	28 334 (24.5)	–	–
South	47 877 (41.3)	47 877 (41.3)	–	–
West	19 777 (17.1)	19 777 (17.1)	–	–
Other	240 (0.2)	240 (0.2)	–	–
Baseline co-morbid conditions, mean (S.D.)				
CCI (excluding RA)	1.00 (1.77)	1.86 (2.02)	<0.0001	–
Chronic disease score	5.54 (3.68)	8.50 (3.66)	<0.0001	–
Severity index for RA (SIFRA)	0.51 (1.94)	19.43 (15.60)	<0.0001	–
Common baseline non-bone- and joint-related diagnoses, n (%)				
Essential hypertension (ICD-9-CM: 401)	51 897 (44.79)	88 565 (76.44)	<0.0001	1.71 (1.69, 1.72)
Disorders of lipid metabolism (ICD-9-CM:272)	48 346 (41.73)	76 934 (66.40)	<0.0001	1.59 (1.58, 1.60)
General symptoms (ICD-9-CM:780)	28 136 (24.28)	58 218 (50.25)	<0.0001	2.07 (2.05, 2.09)
Symptoms involving respiratory system (ICD-9-CM:786)	25 634 (22.12)	55 782 (48.14)	<0.0001	2.18 (2.15, 2.20)
Other disorders of soft tissues (ICD-9-CM:729)	20 101 (17.35)	52 550 (45.35)	<0.0001	2.61 (2.58, 2.65)
Cataract (ICD-9-CM:366)	22 212 (19.17)	43 122 (37.22)	<0.0001	1.94 (1.91, 1.97)
Other unspecified anemias (ICD-9-CM:285)	13 121 (11.32)	36 882 (31.83)	<0.0001	2.81 (2.76, 2.86)
Diseases of esophagus (ICD-9-CM:530)	15 212 (13.13)	35 859 (30.95)	<0.0001	2.36 (2.32, 2.40)
Acquired hypothyroidism (ICD-9-CM:244)	16 859 (14.55)	33 528 (28.94)	<0.0001	1.99 (1.96, 2.02)
Diabetes mellitus (ICD-9-CM:250)	22 162 (19.13)	32 748 (28.26)	<0.0001	1.48 (1.46, 1.50)
Baseline RA-related therapies, n (%)				
NSAIDs	25 746 (22.2)	45 958 (39.7)	<0.0001	–
CSs	147 (0.1)	31 246 (27.0)	<0.0001	–
DMARDs (including biologics)	3131 (2.7)	101 876 (87.9)	<0.0001	–

CCI: Charlson co-morbidity index; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; RR: relative risk.

As expected based on the higher incidence of co-morbidities, HCRU was significantly higher in the RA Medicare cohort than in the non-RA Medicare cohort, resulting in nearly 3-fold higher annual health-care costs, with RA-related costs accounting for slightly more than half of the total costs in the RA cohort. Significant differences between the RA Medicare cohort and the non-RA Medicare cohort were observed across medical (outpatient and inpatient/ED) and pharmacy costs. Increased pharmacy costs in the RA cohort might be expected given the recent greater understanding of RA disease pathogenesis and corresponding development of targeted biologic and non-biologic synthetic DMARD treatments [29]. For example, a 2008 analysis of prescribing patterns identified an increase in biologic use in the US from 3% of RA patients in 1999 to 26% of RA patients in 2006 [30]. Importantly, this increased use of biologics appears to have translated into an increase in the proportion of patients achieving disease remission [8, 31].

Although the increase in remission rates is encouraging, it is possible that the cost of biologics would be a

FIG. 3 Percentage of all-cause and RA-related visits during the 1-year follow-up (A) and mean (S.D.) number of all-cause and RA-related visits during the 1-year follow-up (B)

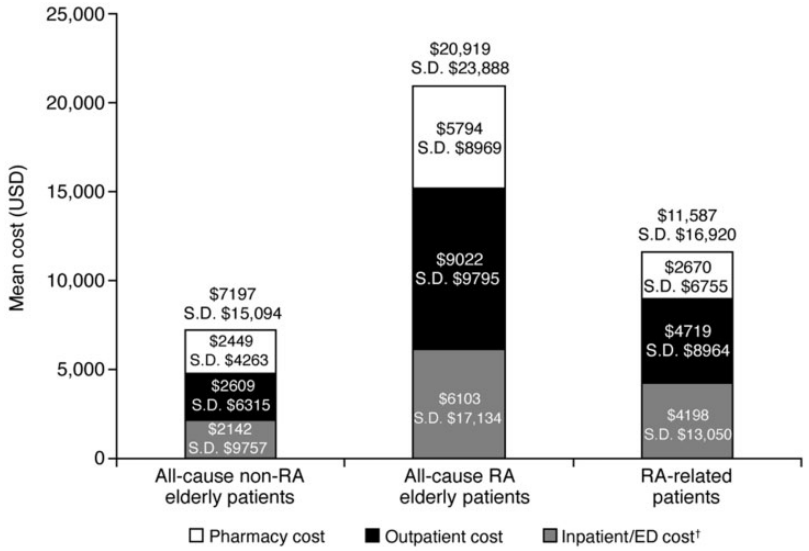


*All *P*-values between all-cause non-RA Medicare patients and all-cause RA Medicare patients were <0.0001. ED: emergency department.

significant concern for health-care budget-holders, and their use may be discouraged without adequate information on disease burden and treatment patterns in the real-world setting. In the present study, pharmacy costs accounted for only 23% ($2670) of the overall RA-related costs, with the major driver of costs being medical costs (outpatient costs represented 41% and inpatient/ED costs represented 36% of overall RA-related costs). In addition, in this real-world study, the cost of biologics across the overall RA cohort (e.g. infliximab, etanercept, adalimumab, golimumab, certolizumab, abatacept, anakinra, rituximab and tocilizumab) accounted for less than a quarter of the overall difference in costs between the RA and non-RA cohort. Moreover, pharmacy costs represented a smaller proportion of the total RA-related costs than they did in the total overall cost in the RA cohort (23 *vs* 27%). Instead, the largest component of increased overall costs within the RA Medicare cohort was outpatient costs.

Similar to the present study, a study conducted by Wolfe *et al*. [32] in 1986 found medical costs to be the biggest driver of costs among patients with severe RA, although in their study, conducted before the availability of biologics, a majority (66%) of direct medical costs were found to be attributable to inpatient hospitalization costs. The reason for this outcome is likely to stem from surgical treatment to relieve severe pain and improve the function of severely deformed joints, management of medication side-effects, and the management of severe co-morbidities such as cardiovascular events [33]. As shown in the

Fig. 4 Mean annual all-cause and RA-related health-care costs in the Medicare population



*All *P*-values between all-cause non-RA Medicare patients and all-cause RA Medicare patients were <0.0001. †ED visits accounted for all-cause $107 and RA-related $37 in the RA Medicare cohort and $51 in the non-RA Medicare cohort. ED: emergency department.

Table 2 Generalized linear model-adjusted follow-up all-cause health-care utilization and costs

All-cause follow-up health-care costs, $	Control group (non-RA)	S.E.	Case group (RA)	S.E.	*P*-value
Inpatient/ED cost	1602	5	3973	12	<0.001
Outpatient cost	2091	6	7109	22	<0.001
Pharmacy cost	2523	8	4928	16	<0.001
Total cost (inpatient, outpatient, pharmacy)	6712	21	16 374	51	<0.001
RA-related drug cost (based on Jcode and NDC)	104	0	3080	10	<0.001
Biologics-related drug costs (based on Jcode and NDC)	15	0	3103	11	<0.001

ED: emergency department; Jcode: Healthcare Common Procedure Coding System Level II codes mainly used for infusions, injections, that is, drugs that are not given orally; NDC: National Drug Code.

present study, patients with RA have a higher rate of co-morbidities, including a higher incidence of cardiovascular events, than patients without RA.

Overall, the present study shows that HCRU is significantly greater among RA patients compared with non-RA patients. In addition, there is a relatively high total cost for care, including the cost of biologics. These results highlight the importance of RA from a societal perspective, and we hope that they will be useful for future research, including cost-effectiveness analyses.

A strength of this study is that it reflects real-world management patterns in a large cohort of RA Medicare patients, but studies based on claims data may have some limitations. Firstly, the population included in this analysis was limited only to FFS enrollees, meaning that the cohort may not be representative of the full Medicare population. Secondly, the costs for medical services reimbursed by insurers other than Medicare paid solely by beneficiaries out of pocket may not be captured, thereby potentially underestimating the cost burden. In the study, outpatient costs rather than pharmacy costs were considered the main driver for the economic burden of RA; however, the reason for the outpatient visit is not known, and it cannot be discounted that some of the outpatient costs might be attributed to attendance for the administration of injectable biologics. Furthermore, it is also possible that i.v. RA biologics could be covered under medical benefits instead of pharmacy benefits, meaning that the cost of prescription fills could have been underestimated. Finally, there is a potential for inaccuracies in assigning RA and capturing co-morbidities, as the presence of an ICD-9-CM diagnosis code on a medical claim may not automatically indicate the presence of disease.

Conclusion

Among US Medicare patients, RA diagnosis is associated with a significantly greater burden of co-morbidities, HCRU and costs when compared with a matched cohort of non-RA Medicare patients. The annual all-cause health-care costs in Medicare RA patients were 3-fold higher than those of the cohort without RA; this difference was mainly attributed to increased outpatient costs, which accounted for nearly half of the total cost. When considering RA-related costs alone, outpatient visits remained a major driver of costs, with pharmacy costs representing only 23% of the total RA-related costs.

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