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ORIGINAL ARTICLE

Health care costs and comorbidities for patients with inclusion body myositis

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ABSTRACT

Objective: This study identifies the health care costs and utilization, as well as comorbidities, in a Medicare population of inclusion body myositis (IBM) patients.

Methods: Medicare patients aged ≥65 years with a diagnosis claim for IBM were identified and matched to a cohort of non-IBM patients based on age, sex, race, calendar year and census region. Generalized linear models were used to estimate health care costs and utilization during the follow-up period.

Results: The prevalence of IBM in this population, aged ≥65 years, was 83.7 cases per 1 million patients. Mean 1 year costs for the IBM cohort ($N = 361$) were $44,838 compared to $10,182 for the matched non-IBM cohort ($N = 1805$), an excess of $34,656. IBM was significantly associated with multiple unsuspected comorbidities, including hypertension (66% vs. 22%), hyperlipidemia (47% vs. 18%) and myocardial infarction (13% vs. 2%) (all $p < .0001$).

Conclusions: IBM patients utilize more health care resources and incur higher health care costs than patients without IBM. Furthermore, IBM patients were more likely to have multiple comorbidities, including cardiovascular risk factors and events, muscle and joint pain, and pulmonary complications compared to those without IBM.

Limitations: The presence of a diagnosis code for a condition on a medical claim does not necessarily indicate the presence of the disease condition because the diagnosis code could be incorrectly entered in the database. Clinical and disease-specific parameters were not available in the claims data. Additionally, due to the observational study design, the analysis may be affected by unobserved differences between patients.

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Introduction

Inclusion body myositis (IBM) is an inflammatory autoimmune disorder of skeletal muscle, with no effective treatment, resulting in progressive limb weakness and loss of function[1–3]. It is a late-onset disease with an average onset age of 61–66 years[4–6] and delayed diagnosis, resulting in an estimated age of 65–70 years at diagnosis. IBM is an orphan disease, as defined by the US Food and Drug Administration, with published prevalence estimates of 11–117 per million[7–9].

Only a few studies have evaluated IBM-associated health care costs[10], in contrast to other forms of myositis[11,12]. IBM is generally viewed as a muscle-specific disorder without related comorbidities; however, it has been determined to be associated with autoimmune diseases, such as Sjogren's syndrome, large granular lymphocytic leukemia, viral infections and other conditions[13–17]. One study identified high rates of hypertension, diabetes, hyperlipidemia and cardiovascular disease among patients with all forms of myositis[18] but lacked IBM age-matched controls and was confounded by frequent corticosteroid use. To our knowledge, there has been no study evaluating US health care costs and utilization associated with IBM in the US Medicare population. Due to the progressive nature of IBM and lack of effective treatment, there is a substantial economic burden that has not been evaluated in prior studies. Understanding the economic burden of this patient population would help to assess the potential value of a likely new treatment. Medicare fee-for-service covers over two thirds of people over the age of 65 in the US; therefore, this is an important population to evaluate with regard to the burden of IBM. We conducted a Medicare data analysis to further understand the prevalence, health care costs, resource utilization and comorbidities for IBM patients over a 1 year period.

Methods

Study population

Data from the 100% national Medicare database from 1 January 2009 to 31 December 2013 was used for this study. Medicare is the federal health insurance program for those aged ≥65 years in the United States, as well as for

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Supplemental data for this article can be accessed here.

certain individuals aged <65 years with disabilities and/or end-stage renal disease. This study was restricted to elderly patients with fee-for-service (FFS) Medicare Part A, Part B and Part D in order to capture the complete health care costs and utilization among Medicare beneficiaries[19]. Part A covers inpatient care in hospitals, including critical access hospitals, skilled nursing facilities, hospice care and some home health care; Part B covers doctors' services and outpatient care; and Part D provides prescription drug coverage. Patients with commercial insurance, such as Medicare Advantage, were not included in the analysis. Patients were identified based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses, ICD-9 procedure codes and hospital medication billing codes. This study was approved by the institutional review board at Columbia Medical School, which waived the requirement for informed consent since the data was de-identified and only aggregate results would be reported.

Patients were assigned to IBM and non-IBM cohorts. Those included in the IBM cohort were aged ≥65 years and had ≥2 outpatient IBM diagnoses (ICD-9-CM code: 359.71) on different dates ≥7 days apart or ≥1 inpatient or emergency room (ER) diagnosis of IBM during the identification period (1 January 2010–31 December 2012)[10]. This definition aimed to minimize the number of patients misdiagnosed with IBM[20]. The first observed IBM diagnosis date during the identification period was designated as the index date. Patients were excluded from the IBM cohort if they had a diagnosis of hereditary muscular dystrophy during the study period.

Control patients did not have an IBM diagnosis during the study period and were matched to case (IBM) patients with identical age, sex, race, calendar year and census region. Matched controls were assigned the same index date as the paired IBM patients for the analyses. To reduce the probability of misclassifying a misdiagnosed case of IBM, control patients were also excluded if they had any of the following diagnoses during the study period: hereditary muscular dystrophy, chronic inflammatory demyelinating polyneuritis, symptomatic inflammatory myopathy, Sjogren's disease, dermatomyositis, polymyositis, myotonic disorders, periodic paralysis or other myopathies. For both cohorts, patients were required to have continuous medical and pharmacy benefits for 12 months pre-index date (baseline period) and post-index date (follow-up period). After applying the inclusion and exclusion criteria, all eligible controls were selected randomly and matched to IBM patients at a 1:5 ratio.

Prevalence analysis

IBM prevalence among patients aged ≥65 years from 1 January 2009 to 31 December 2013 was calculated by selecting patients who had ≥2 outpatient IBM diagnoses on different dates ≥7 days apart or ≥1 inpatient or ER diagnosis of IBM during the identification period. The number of patients identified with an IBM diagnosis was divided by the total number of unique enrollees in the Medicare population. Prevalence was reported as IBM cases per million patients.

Health care utilization and costs, and comorbidities

During the 12 months preceding the index date, age, race, sex, US geographical region, health care costs and resource utilization, Charlson comorbidity index (CCI) score[21], chronic disease score (CDS)[22], and comorbid conditions were captured. During the 1 year follow-up period, health care costs and resource utilization were evaluated for all services from Medicare, including inpatient visits, ER visits, outpatient office visits, all outpatient (office and ER) visits, durable medical equipment (DME) claims, skilled nursing facility (SNF) visits, home health agency (HHA) visits, hospice care and Part D prescriptions. Costs were adjusted to the 2014 medical care component of the Consumer Price Index. Health care utilization was reported as the mean number of visits and claims and dichotomously as whether the patient had a visit or not.

Statistical analysis

All study variables were examined descriptively. Numbers and percentages were provided for dichotomous and polychotomous variables. Means and standard deviations were provided for continuous variables; *p* values were calculated from chi-square and *t*-tests for categorical and continuous variables, respectively.

Generalized linear models were used to estimate the health care costs and utilization. Log-transformation and gamma distribution were applied based on the distribution and presence of heteroskedasticity. Log link was chosen, as this has been found to best specify the relationship between cost and explanatory variables[23]. Gamma distribution was used after a modified Park test was conducted to determine the appropriate distribution[23]. In these models, the dependent variables were total health care costs, including inpatient, ER, outpatient office, total outpatient, DME, SNF, HHA, hospice and pharmacy costs. Statistical analyses were performed using Statistical Analysis System (SAS) Version 9.3 (Cary, NC, USA).

Results

Inclusion body myositis prevalence in patients aged ≥65 years

There were 2551 cases of IBM among 30,473,220 Medicare patients from 1 January 2009 to 31 December 2013 identified for inclusion, resulting in an estimated prevalence of 83.7 per million individuals aged ≥65 years (95% confidence interval [CI]: 80.5–87.0).

Demographics

After applying additional inclusion and exclusion criteria, largely to ensure continued medical and pharmacy benefits during the 1 year study period, 361 patients were assigned to an IBM cohort and 1805 non-IBM patients were assigned to a matched non-IBM cohort (Figure 1). The mean age in both cohorts was 75.8 years; 52.4% of the population were men and 92.8% of patients were Caucasian (Table 1).

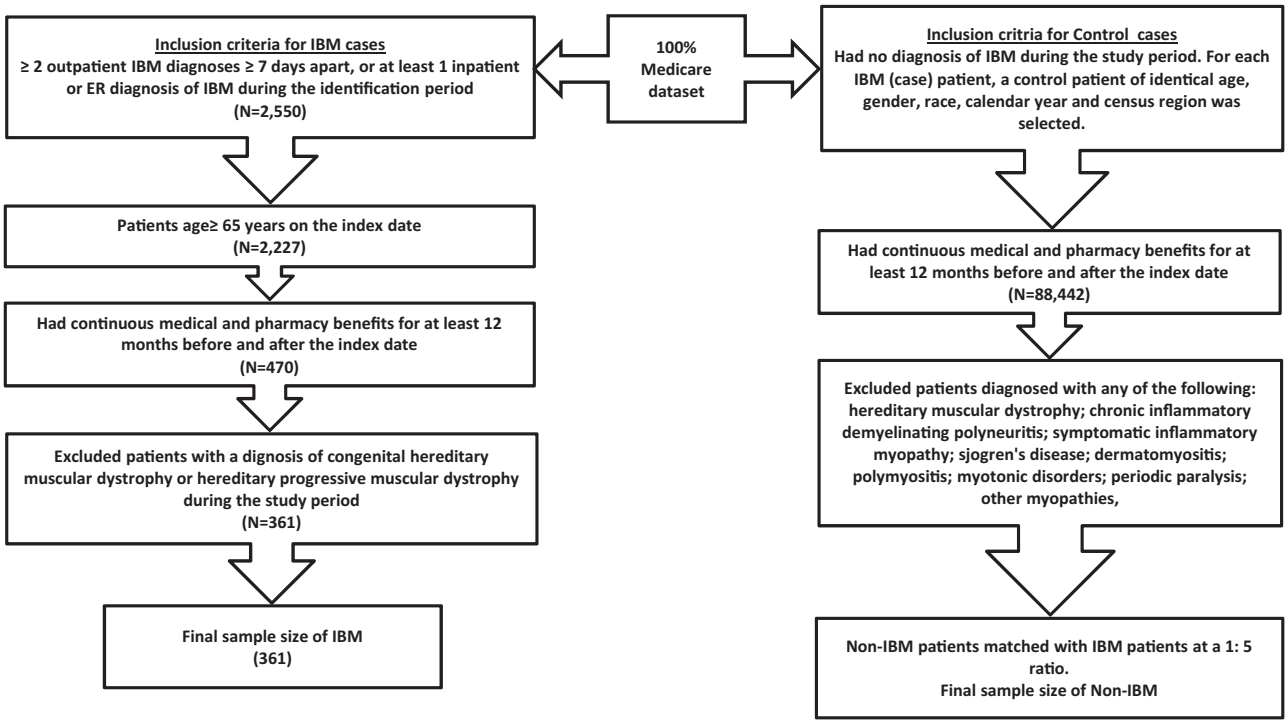

Figure 1. Patient selection criteria. Abbreviation. IBM, inclusion body myositis.

Table 1. Pre-index demographic characteristics of the IBM and non-IBM cohorts.

	IBM		Non-IBM	
	(*N* = 361)		(*N* = 1805)	
	N/Mean	%/SD	*N*/Mean	%/SD
Age (years; mean/SD)	75.8	6.3	75.8	6.3
Age group (years)				
65–69	63	17.5	315	17.5
70–74	106	29.4	530	29.4
75–79	92	25.5	460	25.5
80–84	60	16.6	300	16.6
≥85	40	11.1	200	11.1
Sex				
Male	189	52.4	945	52.4
Female	172	47.7	860	47.7
Race				
White	335	92.8	1,675	92.8
Black	20	5.5	100	5.5
Other	6	1.7	30	1.7
US geographic location				
Northeast	62	17.2	310	17.2
North Central	130	36.0	650	36.0
South	99	27.4	495	27.4
West	70	19.4	350	19.4
Comorbidity index				
Charlson Comorbidity Index score (Mean/SD)*	1.09	1.72	0.53	1.35

Abbreviations. IBM, inclusion body myositis; SD, standard deviation.
*The Charlson Comorbidity Index score contains 19 categories of comorbidity and predicts the 10 year mortality. Higher scores indicate greater comorbidity.

Table 2. Health care costs for IBM and non-IBM cohorts in the 1 year follow-up period.

Health Care Costs (Mean)	IBM (*N* = 361)	Non-IBM (*N* = 1805)	*p* value*
Inpatient Stay Cost	$18,639	$2701	.0030
ER Visit Cost	$606	$140	<.0001
Office Visit Cost	$9736	$3330	<.0001
Outpatient Cost (ER + Office)	$10,341	$3470	<.0001
DME Cost	$2361	$239	.0010
SNF Cost	$6148	$684	.0090
HHA Cost	$2875	$391	<.0001
Hospice Cost	$482	$319	.5770
Part D Prescriptions Pharmacy Cost	$3991	$2378	<.0001
Total Cost	$44,838	$10,182	<.0001

Abbreviations. DME, durable medical equipment; ER, emergency room; HHA, home health agency; IBM, inclusion body myositis; SNF, skilled nursing facilities.
*p value <.05 is significant.

Health care costs and utilization

In the 1 year post-index period, patients in the IBM cohort incurred mean costs of $44,838 compared to $10,182 for matched non-IBM patients ($p < .0001$), an excess of $34,656. The main cost driver for the IBM cohort was inpatient hospitalizations with a mean cost of $18,639, which accounted for 41.6% of the total mean costs (Table 2). The most common hospitalization discharge diagnoses during the follow-up period were myopathies, including IBM (11.9%), septicemia (11.0%) and unspecified pneumonia (6.2%) for IBM patients. The IBM cohort had significantly higher health care resource utilization during the 1 year post-index period compared to the non-IBM cohort, including inpatient hospitalization, ER visits, outpatient visits, DME use, SNF admissions, HHA use and pharmacy claims (all p values <.0001) except for hospice care (1.7% vs. 1.1%) ($p = .3940$; Table 3).

Comorbidities

During the 1 year follow-up period, IBM patients had significantly more comorbid conditions as measured by mean CCI scores (IBM: 2.0 vs. non-IBM: 0.6, $p < .0001$) and mean CDS

scores (7.0 vs. 5.7, $p < .0001$). Specific comorbid diagnoses among IBM versus non-IBM patients are shown in Table 4. Statistically significant increases associated with IBM were found across multiple disease categories. Most notably, these included cardiovascular risk factors (IBM vs. non-IBM: hyperlipidemia 46.8% vs. 17.8%; hypertension 65.9% vs. 22.3%; diabetes mellitus 33.8% vs. 10.4%; $p < .0001$ for all) and cardiovascular events (IBM vs. non-IBM: myocardial infarction 12.5% vs. 2.4%; congestive heart failure: 17.2% vs. 4.5%). Muscle pain (myalgia and myositis, unspecified 28.3% vs. 0.8%; $p < .0001$) and joint pain (arthralgia 15.2% vs. 4.1%; $p < .0001$) were also observed among more IBM patients than non-IBM patients. Dysphagia (24.9% vs. 1.3%; $p < .0001$) and associated pulmonary complications (pneumonia 10.5% vs. 1.8%; aspiration pneumonia 5.8% vs. 0.3%; both $p < .0001$) were also more common in IBM patients than non-IBM patients, as were anemia (31.6% vs. 7.0%), fatigue (19.1% vs. 3.4%), depression (14.4% vs. 3.2%) and insomnia (5.3% vs. 0.6%; all $p < .0001$).

Because corticosteroid and other immunosuppressant medications could potentially confound the association of IBM with comorbidities (e.g. hypertension and diabetes resulting from prednisone use), a subgroup analysis restricted to patients with no history of immunosuppressant medications listed in Supplementary Table 1 (IBM: $N = 198$; non-IBM: $N = 1536$) was conducted. In this subgroup, the differences

Table 3. Health care utilization for IBM and non-IBM cohorts in the 1 year follow-up period.

Health Care Utilization	IBM ($N = 361$)	Non-IBM ($N = 1805$)	p value*
Any Inpatient Stay	63.4%	12.1%	<.0001
Any ER Visit	47.1%	15.6%	<.0001
Any Outpatient Visit	96.7%	49.8%	<.0001
Any Part D Prescriptions Pharmacy Visit	99.7%	95.1%	<.0001
Any DME Visit	64.5%	20.2%	<.0001
Any SNF Visit	23.8%	3.4%	<.0001
Any HHA Visit	38.5%	7.4%	<.0001
Any Hospice Visit	1.7%	1.1%	.3940
Length of Inpatient Stays per patient (mean)	7.91	0.97	<.0001
# ER Visits per patient (mean)	0.91	0.25	<.0001
# Outpatient Visits per patient (mean)	11.20	3.13	<.0001
# Part D Prescriptions Pharmacy Visits per patient (mean)	29.17	21.39	<.0001

Abbreviations. DME, durable medical equipment; ER, emergency room; HHA, home health agency; IBM, inclusion body myositis; SNF, skilled nursing facilities.
*p value <.05 is significant.

Table 4. Comorbidities identified during the 1 year follow-up period.

Comorbid Conditions		IBM ($N = 361$)		Non-IBM ($N = 1805$)		p value*
		N	%	N	%	
Cardiovascular	Hypertension	238	65.9	402	22.3	<.0001
	Hyperlipidemia	169	46.8	321	17.8	<.0001
	Diabetes with or without complication	122	33.8	165	10.4	<.0001
	Congestive heart failure	62	17.2	81	4.5	<.0001
	Cerebrovascular disease	47	13.0	61	3.4	<.0001
	Myocardial infarction	45	12.5	43	2.4	<.0001
	PVD	38	10.5	58	3.2	<.0001
Joint/Muscle/Bone	Myalgia and myositis, unspecified	102	28.3	14	0.8	<.0001
	Arthralgia	55	15.2	74	4.1	<.0001
	Rheumatic disease	53	14.7	10	0.6	<.0001
	Osteoarthritis	61	16.9	102	5.7	<.0001
	Osteoporosis	49	13.6	53	2.9	<.0001
	Rheumatoid arthritis	17	4.7	7	0.4	<.0001
	Accidental falls	10	2.8	5	0.3	<.0001
	SLE	2	0.6	1	0.1	.0201
	Scleroderma	1	0.3	0	0.0	.0253
Swallowing/Pulmonary	Dysphagia	90	24.9	24	1.3	<.0001
	COPD	74	20.5	116	6.4	<.0001
	Pneumonia	38	10.5	32	1.8	<.0001
	Aspiration pneumonia	21	5.8	5	0.3	<.0001
	Choking	1	0.3	3	0.2	.6544
Hematology/Oncology	Anemia	114	31.6	126	7.0	<.0001
	Non-skin malignancy	32	8.9	78	4.3	.0003
	Metastatic solid tumor	6	1.7	11	0.6	.0385
	Other lymphoid leukemia	1	0.3	0	0.0	.0253
Cognitive	Fatigue	69	19.1	61	3.4	<.0001
	Depression	52	14.4	58	3.2	<.0001
	Insomnia	19	5.3	11	0.6	<.0001
	Dementia	8	2.2	18	1.0	.0522
Organs	Peptic ulcer disease	8	2.2	8	0.4	.0003
	Renal disease	28	7.8	84	4.7	.0151
	Mild liver disease	17	4.7	17	0.9	<.0001
	Moderate/severe liver disease	1	0.3	5	0.3	1
Infectious	AIDS/HIV	2	0.6	1	0.1	.0201
Eyes	Macular degeneration	0	0.0	1	0.1	.6546
	Cataracts	6	1.7	27	1.5	.8139

Abbreviations. COPD, chronic obstructive pulmonary disease; IBM, inclusion body myositis; PVD, peripheral vascular disease; SLE, systemic lupus erythematosus.
*p value <.05 is significant.

in comorbidities remained statistically significant and there were little, if any, changes in the magnitude of difference (Supplementary Table 2).

Discussion

This study analyzed the health care costs, resource utilization and comorbidities associated with IBM from 361 patients and 1805 matched controls from the 100% FFS Medicare database of 30,473,220 patients from 1 January 2009 to 31 December 2013. We found that, in the 1 year period following the study inclusion date, Medicare costs were $44,838 for patients with IBM compared to $10,182 for matched patients without a diagnosis of IBM. Thus, the mean excess 1 year costs associated with IBM were $34,656.

Our study is one of a few studies that have estimated the health care costs and utilization for IBM patients. In a study using the MarketScan claims database, higher costs were observed for IBM patients compared to non-IBM patients[10]. A previous study estimated costs for a combined cohort of patients with other forms of myositis (not including IBM), and determined annual costs for newly diagnosed patients at $16,319 compared to a matched control group of $4926, for an excess of $11,393[12]. Of that myositis cohort, 92% of patients were aged <65 years. However, in the current study of IBM, all patients were aged ≥65 years, and the mean age was 76 years. The significantly higher costs associated with IBM in this study, compared to other forms of myositis in the previous study, may be due to the effects of this chronic disorder in an older-age population. The results of this study determined a significantly higher rate of health care utilization in the IBM cohort compared to the non-IBM cohort, similar to the previous study in other forms of myositis[12].

This data also allowed for a prevalence estimate of 84 per million during the study period for a population aged ≥65 years. Previous general population estimates of IBM prevalence in the United States and Europe have ranged from 11 to 117 per million[7–9] but are limited by small sample size and geographic region. Previous age-based prevalence estimates were 29 per million people aged ≥45 years in Connecticut[7] and 35 per million people aged ≥50 years in Western Australia[24].

We also identified a number of statistically significant IBM-associated comorbidities that appear to have been unrecognized in past studies. In particular, it appears that patients with IBM are at an increased risk of cardiovascular disease compared to matched non-IBM patients, as indicated by associations with hypertension, diabetes, dyslipidemia, myocardial infarction and congestive heart failure. The prevalences of hypertension (65.9%) and diabetes (25.2%) found here are remarkably similar to previous prevalence estimates found in a cohort of approximately 65 patients in Southern Australia (65% and 24%, respectively)[18]. Our study observed increased cardiovascular comorbidities among IBM patients, similar to the Capkun *et al.* study[10]. Additionally, several previous studies identified increased cardiovascular risks in those with dermatomyositis and polymyositis[25–29], including altered lipid levels in untreated patients[30,31], increased prevalence of diabetes and hypertension[32], and common subclinical cardiac inflammation[33]. One previous study of 51 patients with IBM identified frequent cardiac abnormalities but lacked a control group for comparison[34]. More generally, the association of cardiovascular risk factors and disease with inflammatory and autoimmune diseases has been increasingly recognized[35,36]. We believe that the high frequency of cardiovascular comorbidities observed in the population could have several explanations. First, the study population is made up of elderly patients (≥65 years), and they are prone to cardiovascular conditions. Moreover, IBM patients presenting with myalgia may not be compliant with cardiovascular medications, such as statins, because they can cause muscle pain in some patients[37,38]. This can worsen cardiovascular conditions like hyperlipidemia. Some IBM patients may be managed with corticosteroids which can also lead to cardiovascular conditions like hypertension[39]. Finally, there is the possibility that IBM patients who have more contact with health care services are investigated more thoroughly, thereby increasing the frequency of diagnosis of these comorbidities. Other intriguing comorbid associations were anemia and malignancy, the latter of which seemed principally due to hematological malignancy. IBM has previously been associated with large granular lymphocytic leukemia, which includes anemia as a manifestation[14].

Although claims data is valuable for the efficient and effective examination of health care outcomes, treatment patterns, resource utilization and costs, claims data is collected for the purpose of payment and not research. Therefore, certain limitations are associated with claims data use. The presence of a diagnosis code for a condition on a medical claim does not necessarily indicate the presence of the disease condition because the diagnosis code could be incorrectly entered in the database. Certain information is not readily available in claims data that could influence study outcomes, such as clinical and disease-specific parameters. Additionally, due to the observational study design, the analysis may be affected by unobserved differences between patients. The database includes only Medicare FFS enrollees and patients aged ≥65 years; therefore, patients with commercial insurance plans or who were aged <65 years were not included in this study.

Conclusions

In summary, this study suggests that marginal annual health costs for patients with IBM aged ≥65 years in the first year after the study inclusion date are higher than those of non-IBM patients. Multiple previously unrecognized comorbidities may contribute to health costs, including cardiovascular disease, muscle and joint pain, and pulmonary complications. As IBM is a progressive disease in an elderly population, the associated annual marginal cost of IBM may be greater in subsequent years. These results shed light on the economic burden of IBM within the US Medicare population, and we believe they can inform patients and health care providers' decisions regarding IBM patient management. Furthermore, we recommend future studies using electronic medical

records in combination with claims data. This would be helpful in further exploring the clinical characteristics and economic burden associated with IBM, in addition to validating IBM studies that use claims data.

Transparency

Declaration of funding

This study was funded by Novartis Pharmaceuticals Corporation.

Author contribution

A.K., S.A.G., N.A. and O.B. were responsible for the study concept and design. A.K., S.A.G., N.A., K.J. and O.B. were responsible for data interpretation and writing and revision of manuscript.

Declaration of financial/other relationships

S.A.G has disclosed that he is a consultant to Novartis Pharmaceuticals Corporation. A.K. has disclosed that she is an employee of STATinMED Research which is a consultant to Novartis Pharmaceuticals Corporation. N.A. and K.J have disclosed that they are employees of Novartis Pharmaceuticals Corporation. O.B. has disclosed that he has no significant relationships with or financial interests in any commercial companies related to this study or article.

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