The Economic Burden of Thromboembolic Events Among Patients With Inflammatory Bowel Disease

Juliana Setyawan,[1] Andres Yarur,[2] Fan Mu,[3] Miriam L Zichlin,[3] Emma Billmyer,[3] Nathaniel Downes,[3] Hongbo Yang,[3] Nassir Azimi,[4] Vibeke Strand[5]

[1]Arena Pharmaceuticals, Inc., San Diego, CA, USA; [2]Division of Gastroenterology and Hepatology, Medical College of Wisconsin, Milwaukee, WI, USA; [3]Analysis Group Inc., Boston, MA, USA; [4]Sharp Grossmont Hospital, La Mesa, CA, USA; [5]Division of Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto, CA, USA.

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BACKGROUND

- Inflammatory bowel diseases (IBD) have been associated with a higher risk of thromboembolic events (TE)[1-3]
- While there have been studies on the economic impact of TE among patients undergoing surgery or those with malignancies, less is known about the economic burden of TE among patients with IBD, especially after the introduction of novel therapeutic agents

OBJECTIVE

- To estimate the healthcare costs associated with TE among patients with IBD
  - TE included deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), and ischemic stroke (IS)

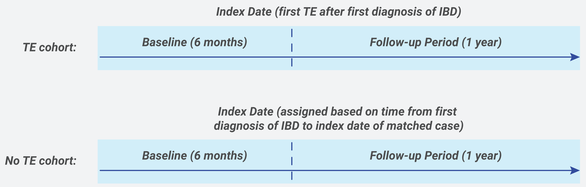
METHODS

DATA SOURCE

- This was a retrospective cohort study of IBM MarketScan® Commercial Claims and Encounters (CCAE) and Medicare Supplemental and Coordination of Benefits Databases: 2014-2018
  - These databases include both employer-paid (e.g., active employees, early retirees, Consolidated Omnibus Budget Reconciliation Act [COBRA] continuations, and dependents) and employer-sponsored Medicare supplemental healthcare encounters
  - Data contain enrollment history, dates of service, claims for medical (e.g., professional and institutional services) and pharmacy services, and demographic variables (e.g., age, sex, and geographic region)

STUDY DESIGN

Figure 1. Study Timeline



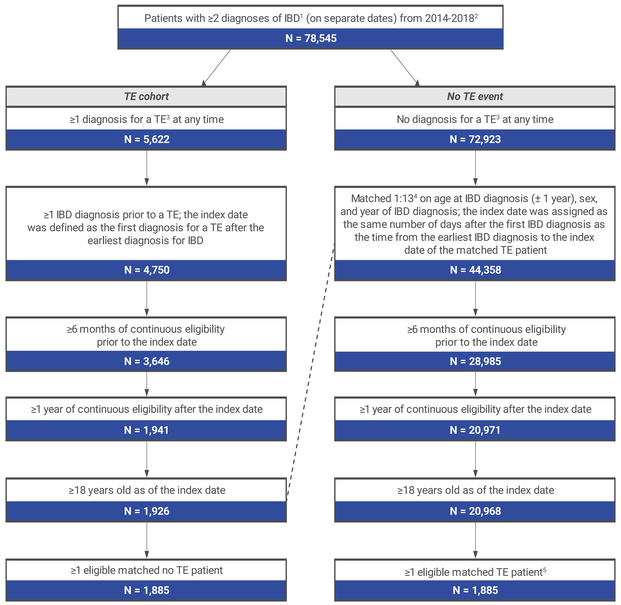
- Baseline period
  - Defined as 6 months prior to the index date
- Index Date
  - *TE cohort*: the index date was defined as the first diagnosis of a TE after the first diagnosis for IBD
  - *No TE cohort*: the index date was assigned so that the time from the first diagnosis of IBD and the index date was the same as the corresponding period of the matched TE patient
- Follow-up period
  - Defined as 1 year following the index date (inclusive)
- See **Figure 2** for details on Sample Selection

STATISTICAL ANALYSIS

- Baseline characteristics were summarized and compared between the TE cohort and the no TE cohort
  - Statistical comparisons were conducted using the Wilcoxon signed-rank test for continuous variables and McNemar's test for dichotomous variables
- Outcomes included all-cause healthcare costs and TE-related costs (i.e., cost of medical visits with diagnosis of TE) in the 30-day and 1-year periods following the index date
  - Unadjusted statistical comparisons of costs were conducted using the Wilcoxon signed-rank test
  - Adjusted costs were estimated using generalized estimating equations with a Tweedie distribution, and adjusted for age, sex, index year, healthcare plan type, baseline comorbidities and conditions of interest, and immune-mediated disease (IMD) and non-IMD medications that patients were receiving during the baseline period

RESULTS

Figure 2. Sample Selection of Patients With IBD With and Without TE



IBD, inflammatory bowel disease; TE, thromboembolic event.
[1]Patients were not allowed to have a diagnosis of any of the following immune-mediated diseases prior to their first IBD diagnosis: ankylosing spondylitis, atopic dermatitis, multiple sclerosis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis, and systemic lupus erythematosus.
[2]Qualifying diagnoses for autoimmune disorders were identified on the inpatient and/or outpatient services claims datasets. All patients were required to have eligibility data.
[3]TE included deep vein thrombosis, pulmonary embolism, myocardial infarction, and ischemic stroke.
[4]Matching between the TE cohort and no TE cohort was done with 1:13 ratio to keep as many eligible patients with TE as possible.
[5]For TE patients with >1 eligible matched no TE patient, 1 no TE patient was randomly selected.

PATIENT CHARACTERISTICS

- There were 1,885 matched pairs (**Figure 2** and **Table 1**)
  - Mean age 58.9 years
  - 52.6% female
- Patients with IBD who experienced a TE had more comorbidities compared to patients with IBD who did not experience a TE (e.g., Charlson comorbidity index [1.2 vs 0.5]; cardiovascular disease [61.3% vs 47.6%]; both *P*<0.0001) (**Table 1**)
- The most common TE was DVT (47.1%), followed by IS (25.8%), MI (17.2%), and PE (15.8%)

COSTS

- In both unadjusted and adjusted results, patients with IBD who experienced a TE had statistically higher healthcare costs in the 30-day and 1-year periods relative to patients with IBD who did not experience a TE (adjusted total cost difference: 30-day $20,784; 1-year $44,630; both *P*<0.0001) (**Table 2**)
  - Total cost differences were largely driven by differences in inpatient costs (adjusted inpatient cost difference: 30-day $18,386; 1-year $30,753, both *P*<0.0001) (**Table 2**)
  - TE-related costs were $20,036 and $25,311 in the 30-day and 1-year period, respectively

Table 1. Demographics and Clinical Characteristics Among Patients With IBD Measured During the Baseline Period and on Index Date

	TE cohort (N = 1,885)	No TE cohort (N = 1,885)	*P*-value
Age on index date, mean ± SD	58.9 ± 15.5	58.9 ± 15.5	0.0052
Sex, n (%)			
Female	991 (52.6)	991 (52.6)	-
Index year, n (%)			
2014	331 (17.6)	338 (17.9)	0.3853
2015	649 (34.4)	657 (34.9)	0.5395
2016	504 (26.7)	485 (25.7)	0.1579
2017	401 (21.3)	405 (21.5)	0.6464
Healthcare plan type, n (%)			
Plans with capitation	189 (10.0)	207 (11.0)	0.3332
Plans without capitation	1,674 (88.8)	1,662 (88.2)	0.5392
Unknown	22 (1.2)	16 (0.8)	0.3304
Charlson comorbidity index, mean ± SD	1.2 ± 1.8	0.5 ± 1.0	<0.0001
Conditions of interest, n (%)			
Cancer	301 (16.0)	196 (10.4)	<0.0001
Cardiovascular disease[1]	1,155 (61.3)	897 (47.6)	<0.0001
Chronic kidney disease	180 (9.5)	68 (3.6)	<0.0001
Chronic obstructive pulmonary disease	201 (10.7)	82 (4.4)	<0.0001
Diabetes			
Type 1	40 (2.1)	16 (0.8)	0.0011
Type 2	374 (19.8)	250 (13.3)	<0.0001
Fracture (hip or leg)	24 (1.3)	9 (0.5)	0.0071
Peripheral vascular disease	217 (11.5)	92 (4.9)	<0.0001
Pregnancy[2]	16 (1.6)	14 (1.4)	0.6831
Common classes of drug use, n (%)			
Non-IMD drugs			
Hormone replacement therapies[2]	60 (6.1)	64 (6.5)	0.7127
Testosterone replacement therapies[2]	31 (3.5)	24 (2.7)	0.3452
Oral contraceptives[2]	61 (6.2)	70 (7.1)	0.3705
IMD drugs			
Biologics	168 (8.9)	159 (8.4%)	0.5913
JAK inhibitors	0	0	-
Non-biologic immunomodulators	354 (18.8)	308 (16.3)	0.0433
5-aminosalicyclic-acid derivative agents	781 (41.4)	816 (43.3)	0.2467
Glucocorticoids	693 (36.8)	404 (21.4)	<0.0001
NSAIDs	235 (12.5)	204 (10.8)	0.1141

IMD, immune-mediated disease; JAK, Janus kinase; NSAIDs, nonsteroidal anti-inflammatory drugs; SD, standard deviation.
[1]Cardiovascular disease included atherosclerosis, atrial fibrillation, heart failure, hyperlipidemia, and hypertension.
[2]The proportions of patients with pregnancy, hormone replacement therapies, and oral contraceptives were reported out of the total number of females in each cohort. The proportion of patients with testosterone replacement therapies was reported out of the total number of males in each cohort.

Table 2. Adjusted Cost Differences Among Patients With IBD During the 30-day and 1-year Period Post TE

	30-day period post TE				1-year period post TE			
	TE cohort (N = 1,885)	No TE cohort (N = 1,885)	Cost difference	*P*-value	TE cohort (N = 1,885)	No TE cohort (N = 1,885)	Cost difference	*P*-value
All-cause healthcare costs (2019 USD)								
Total costs	22,669.19	1,885.69	20,783.50	<0.0001	67,054.32	22,424.45	44,629.87	<0.0001
Medical costs	21,432.85	1,077.54	20,355.31	<0.0001	53,801.21	12,768.85	41,032.36	<0.0001
Inpatient	18,600.66	214.51	18,386.15	<0.0001	34,290.42	3,537.36	30,753.05	<0.0001
Outpatient	1,978.50	749.18	1,229.32	<0.0001	17,108.01	8,556.66	8,551.35	<0.0001
Emergency department	987.44	39.55	947.89	<0.0001	2,806.23	631.19	2,175.04	<0.0001
Pharmacy costs	1,199.14	750.77	448.37	<0.0001	13,663.06	9,367.11	4,295.95	<0.0001

IMD, immune-mediated disease; TE, thromboembolic event.

LIMITATIONS

- Limitations that are inherent to retrospective observational studies using claims data include:
  - Data contain only diagnostic and procedure codes recorded for reimbursement purposes and may be subject to coding errors or data omissions
  - Patients may not have used the recorded medication as prescribed after filling a prescription
  - Confounding adjustments can only account for factors that are observable and recorded in the database
- This study was conducted in a commercially insured US population. Therefore, the results might not be generalizable to the elderly and Medicaid populations, which have different clinical and severity profiles than the commercially insured population
- Recently approved treatments for IBD may be underrepresented since the data cut spans 2014-2018

CONCLUSIONS

- Among patients with IBD, TEs are associated with substantial economic burden within the 30-day and 1-year periods after the event
- TE risk reduction in patients with IBD could lead to lower economic burden in addition to better clinical outcomes

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DISCLOSURES:
AY serves as a paid consultant for Arena, Prometheus Bioscience, and Takeda; **FM, MLZ, EB, ND** and **HY** are employees of Analysis Group, which received consultancy fees from Arena to conduct this analysis; **NA**: is a member of the Delphi panel for Arena; Astra Zeneca – Speaker's Bureau; Daiichi Sankyo – Advisory Committee/Board Member, Speaker's Bureau; Gilead – Advisory Committee/Board Member, Speaker's Bureau; Janssen – Advisory Committee/Board Member, Speaker's Bureau; **JS**: is an employee of Arena; **VS**: has received consultancy fees from Abbvie, Amgen, Arena, Astra Zeneca, Bayer, Blackrock, Bioventus, BMS, BI, Celltrion, Concentric Analgesics, Crescendo / Myriad Genetics, EMD Serono, Equillium, Eupraxia, Flexion, Galapagos, Genentech / Roche, Gilead, GSK, Horizon, Ichnos, Inmedix, Janssen, Kiniksa, Kypha, Lilly, Merck, MiMedx, MyoKardia, Novartis, Pfizer, Regeneron, Samsung, Samumed, Sandoz, Sanofi, Scipher, Servier, Setpoint, Tonix, and UCB; **VS** has served on Advisory Boards for Abbvie, Amgen, AstraZeneca, Bayer, BMS, BI, Celltrion, Crescendo, EMD Serono, Galapagos, Genentech/Roche, GSK, Horizon, Ichnos, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, and UCB.

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