Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Study Medications

Corticosteroid medications	Dexamethasone, betamethasone, prednisone, prednisolone, methylprednisolone, cortisone, hydrocortisone, triamcinolone
Anti-TNF medications	infliximab, adalimumab, certolizumab pegol

TNF = tumor necrosis factor

eTable 2. Prednisone-Equivalent Dosages of Systemic Corticosteroid Medications

Dose	Glucocorticoid Name
0.6 mg	Betamethasone
0.75 mg	Dexamethasone
4 mg	Methylprednisolone
4 mg	Triamcinolone
5 mg	Prednisone
5 mg	Prednisolone
20 mg	Hydrocortisone
25 mg	Cortisone

eTable 3. Definitions of Covariates Used

Measurement indicates covariates also coded as time-varying (every 6 months).

Covariates	Definition
Carotid artery disease	**ICD9 code 433.1**
Carotid artery disease	ICD9 procedure 38.12, 00.63
Hypercholesterolemia*^	ICD9 code 272.0, 272.4, 272.2
Osteoporosis*^	ICD9 code 733
Coronary artery disease	410-412, 414.0-414.9 , 414.01
Parkinsons disease	332
History of stroke^	430.x, 431.x, 433.x1, 434.x1, 435.x, 436,
Problems with balance	781.2
Falls in prior 365 days	E880-E888
DEXA scan in prior 365 days*^	CPT codes (pre-2006) 76075 and (post-2006) 77080
Serious infection w/in 183 days prior to index^	The primary hospital discharge diagnosis must be for one of the below • Meningitis – 320.x, 049.x • Encephalitis – 323.x, 054.3 • Cellulitis – 681.x, 682.x • Endocarditis – 421.x • Pneumonia – 481.x, 482.x • Pyelonephritis – 590.x • Septic arthritis – 711.0x excluding 711.08 • Osteomyelitis – 730.0x, 730.1x, 730.2x • Bacteremia – 038.x, 790.7
Opportunistic infection w/in 183 days prior to index	The primary hospital discharge diagnosis must be for infection with one of the following organisms, +/- prescription requirements as below • Aspergillus -- 117.3 or 484.6 + prescription for posaconazole, itraconazole, or voriconazole within 90 days of the diagnosis code • Blastomyces (116.0), Coccidiodes (114.x), Cryptococcus (117.5 or 321.0), Histoplasma (115.x): also require prescription for fluconazole, itraconazole, or voriconazole within 90 days of the diagnosis code • Pneumocystis (136.3) • Actinomyces (039.x) • Legionella (482.84) • Listeria (027.0) • Nocardia (defined as actinomyces) • Salmonella (003.x) • Tuberculosis: 010.x – 018.x + prescription of pyrazinamide within 90 days of diagnosis code • non-tuberculous mycobacteria: 031.x • Toxoplasma (130.x)
Pyoderma Gangrenosum w/in 183 days prior to index	ICD-9 686.01
Stool culture w/in 183 days prior to index	CPT 87045
Diabetes	250.x, 357.2, 362.0, 362.0[1-7], 366.41, 962.3, E932.3 VA:
Hypertension	401.0-401.9
Coronary artery disease^	414.01
Congestive heart failure^	428.0 as primary dx for hospitalization,
Blood transfusion w/in 183 days prior to index	36430, 36440, 36450, 36444

Intravenous iron w/in 183 days prior to index^	J1439, J1756, J2916
Parenteral nutrition w/in 183 days prior to index^	S9364', 'S9365', 'S9366', 'S9367', 'S9368', 'B4164', 'B4168', 'B4172', 'B4176', 'B4178', 'B4180', 'B4185', 'B4189', 'B4193', 'B4197', 'B4199', 'B4220', 'B4222', 'B4224', 'B5000', 'B5100', 'B5200'
	ICD 9: Parenteral infusion of concentrated nutritional substances 99.15
Anemia from iron deficiency or NOS w/in 183 days prior to index*^	280.9
Bowel Resection	17.31, 17.34, 45.61, 45.62, 45.71, 45.74, 46.02, 46.04, 48.41, 48.42, 48.43, 48.49, 48.5, 48.51, 48.52, 48.59, 48.62-69
Ostomy	46.1x, 46.2x, 46.3x
Proctectomy Ileostomy (inpatient)	'4840','4842','4843','4850','4851','4852','4849','4859'
Proctectomy Ileostomy (outpatient)	'44155','44156','45121','44211'
Fistula w/in 365 & 56 days prior to index*^ "procedures for fistula drainage or seton placement in the prior 365 days "	ICD 9 dx: intestinal fistula 569.81, anal fistula 565.1; '5374', CPT: 46280, 46285
Malnutrition	263.0, 263.1, 263.8, 263.9
Electrolyte abnormality	276.1, 276.8
Small bowel follow-through exam w/in 365 & 56 days prior to index*^	CPT codes: 74250, 74245
Other nutritional anemia (e.g. B12) w/in 183 days prior to index^	281.9

Colonoscopy or sigmoidoscopy w/in 365 & 56 days prior to index*^	CPT codes: '44388', '44389', '44390', '44391', '44392', '44393',
	  '44394', '45378', '45379', '45380', '45381',
	  '45382', '45383', '45384', '45385', '45386', 'G0105', 'G0121',
	  sigmoidoscopy: 45330, 45331, 45332, 45334

CT or MRI scan of abdomen/pelvis w/in 365 & 56 days prior to index*^	74176, 74177, 74178
C difficile w/in 183 & 56 days prior to index^	ICD9 code 008.45
Quinolone Rx w/in 183 days prior to index*^	
Metronidazole Rx w/in 183 days prior to index*^	
Other Antibiotic Rx w/in 183 days prior to index*^	
Herpes Antiviral Rx w/in 183 days prior to index^	acyclovir, valacyclovir, famciclovir
Antifungal Rx w/in 183 days prior to index^	VA drug class AM700
Mesalamine Rx w/in 183 days prior to index*^	
AZA/6MP Rx w/in 183 days prior to index*^	
Methotrexate Rx w/in 183 days prior to index^	
Narcotics Rx (excluding Belladonna/Opium) w/in 183 days prior to index*^	Dihydrocodeine Fentanyl Hydrocodone Hydromorphone Meperidine Morphine Oxycodone Oxymorphone Pentazocine Propoxyphene Tapentadol Tramadol

PPI Rx w/in 183 days prior to index*^	esomeprazole, pantoprazole, lansoprazole, rabeprazole, omeprazole, dexlansoprazole, prilosec, prevacid, nexium, kapidex, zegerid, dexilant, protonix, aciphex
Benzodiazepine Rx w/in 183 days prior to index*^	
Bisphosphonate Rx w/in 183 days prior to index*^	ZOLEDRONIC ACID, etidronate, alendronate, risedronate, tiludronate
High dose Vitamin D Rx w/in 183 days prior to index	VA drug class VT500
Statins Rx w/in 183 days prior to index*^	atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin, lipitor, zocor, mevacor
Fibrates Rx w/in 183 days prior to index^	fenofibrate, gemfibrozil
Prednisone use in 183 days prior to index*	
Budesonide use in 183 days prior to index*	
Number of non-IBD medication classes taking during 183 days prior to index*^	(excl IM600, GA400, MS190)
Hypovolemia or dehydration	276.52, 276.51

eTable 4. Population Characteristics at Cohort Entry for all Included Covariates
All covariates are assessed over the 12 months prior to enrollment. Standardized mean differences between new anti-TNF and prolonged corticosteroid (CS) users before (raw) and after (adjusted) baseline propensity weighting (weighted).

	Crohn's Disease		SMD		Ulcerative Colitis		SMD	
	TNF	CS	Raw	Weighted	TNF	CS	Raw	Weighted
Age (%)			0.5539	0.2745			0.3766	0.2335
[18,35)	323 (36.9)	179 (20.8)			98 (34.3)	216 (22.1)		
[35,50)	223 (25.5)	150 (17.5)			62 (21.7)	190 (19.4)		
[50,65)	202 (23.1)	280 (32.6)			63 (22.0)	296 (30.3)		
[65,70)	77 (8.8)	102 (11.9)			32 (11.2)	103 (10.5)		
[70,75)	25 (2.9)	60 (7.0)			17 (5.9)	67 (6.9)		
[75,80)	16 (1.8)	38 (4.4)			9 (3.1)	46 (4.7)		
[80,85)	5 (0.6)	34 (4.0)			3 (1.0)	41 (4.2)		
[85,110)	4 (0.5)	16 (1.9)			2 (0.7)	18 (1.8)		
Race (%)			0.1780	0.1801			0.1019	0.0749
Black	115 (13.1)	84 (9.8)			20 (7.0)	95 (9.7)		
Other	26 (3.0)	18 (2.1)			9 (3.1)	33 (3.4)		
Unknown	61 (7.0)	95 (11.1)			30 (10.5)	104 (10.6)		
White	673 (76.9)	662 (77.1)			227 (79.4)	745 (76.3)		
Calendar year at index date (%)			0.5546	0.0069			0.7245	0.1247
2007	35 (4.0)	116 (13.5)			8 (2.8)	100 (10.2)		
2008	57 (6.5)	123 (14.3)			8 (2.8)	106 (10.8)		
2009	80 (9.1)	100 (11.6)			15 (5.2)	113 (11.6)		
2010	84 (9.6)	110 (12.8)			23 (8.0)	138 (14.1)		
2011	112 (12.8)	93 (10.8)			29 (10.1)	120 (12.3)		
2012	135 (15.4)	108 (12.6)			35 (12.2)	121 (12.4)		
2013	152 (17.4)	111 (12.9)			70 (24.5)	130 (13.3)		
2014	220 (25.1)	98 (11.4)			98 (34.3)	149 (15.3)		
Male (%)	765 (87.4)	779 (90.7)	0.1045	0.1019	262 (91.6)	919 (94.1)	0.0953	0.0348
Anemia by iron deficiency = yes (%)	65 (7.4)	54 (6.3)	0.0452	0.1071	20 (7.0)	57 (5.8)	0.0473	0.0274
Problems with balance = yes (%)	1 (0.1)	5 (0.6)	0.0795	0.0035	2 (0.7)	7 (0.7)	0.002	0.0100
Blood transfusion = yes (%)	3 (0.3)	3 (0.3)	0.0011	0.0086	2 (0.7)	11 (1.1)	0.0449	0.0502
Congestive heart failure = yes (%)	5 (0.6)	16 (1.9)	0.1047	0.0591	1 (0.3)	22 (2.3)	0.0432	0.0953
Coronary artery disease = yes (%)	43 (4.9)	73 (8.5)	0.1437	0.1006	20 (7.0)	97 (9.9)	0.1056	0.1076
Colonoscopy or sigmoidoscopy (%)			0.1735	0.1966			0.204	0.2704
none	564 (64.5)	558 (65.0)			169 (59.1)	530 (54.2)		

w/in 56 days prior	123 (14.1)	78 (9.1)			52 (18.2)	140 (14.3)		
w/in 57-365 days prior	188 (21.5)	223 (26.0)			65 (22.7)	307 (31.4)		
C. difficile (%)			0.0406	0.0865			0.085	0.0729
none	858 (98.1)	844 (98.3)			276 (96.5)	928 (95.0)		
w/in 56 days prior	8 (0.9)	5 (0.6)			4 (1.4)	15 (1.5)		
w/in 57-365 days prior	9 (1.0)	10 (1.2)			6 (2.1)	34 (3.5)		
CT scan or MRI (%)			0.1840	0.0880			0.0968	0.1255
none	692 (79.1)	733 (85.3)			264 (92.3)	880 (90.1)		
w/in 56 days prior	97 (11.1)	54 (6.3)			10 (3.5)	35 (3.6)		
w/in 57-365 days prior	86 (9.8)	72 (8.4)			12 (4.2)	62 (6.3)		
Diabetes = yes (%)	80 (9.1)	101 (11.8)	0.0856	0.0210	31 (10.8)	137 (14.0)	0.0966	0.0467
DEXA scan = yes (%)	56 (6.4)	66 (7.7)	0.0502	0.0709	12 (4.2)	64 (6.6)	0.1046	0.0914
Dehydration = yes (%)	19 (2.2)	30 (3.5)	0.0797	0.0477	16 (5.6)	58 (5.9)	0.0147	0.0931
Falls = yes (%)	16 (1.8)	29 (3.4)	0.0973	0.0450	7 (2.4)	25 (2.6)	0.0071	0.1079
Fistula (%)			0.2314	0.0605			0.0952	<0.0001
none	804 (91.9)	833 (97.0)			285 (99.7)	976 (99.9)		
w/in 56 days prior	36 (4.1)	9 (1.0)			0 (0.0)	1 (0.1)		
w/in 57-365 days prior	35 (4.0)	17 (2.0)			1 (0.3)	0 (0.0)		
Hypercholesterolemia = yes (%)	140 (16.0)	184 (21.4)	0.1393	0.1479	63 (22.0)	283 (29.0)	0.1597	0.049
Hypertension = yes (%)	175 (20.0)	265 (30.8)	0.2511	0.1439	75 (26.2)	322 (33.0)	0.1479	0.0306
IV iron = yes (%)	6 (0.7)	5 (0.6)	0.0131	0.0003	4 (1.4)	2 (0.2)	0.1342	0.0069
Small bowel follow through (%)			0.0478	<0.0001			<0.0001	<0.0001
none	801 (91.5)	744 (86.6)			285 (99.7)	957 (98.0)		
w/in 56 days prior	19 (2.2)	31 (3.6)			0 (0.0)	3 (0.3)		
w/in 57-365 days prior	55 (6.3)	84 (9.8)			1 (0.3)	17 (1.7)		
Stool culture = yes (%)	9 (1.0)	27 (3.1)	0.1484	0.0805	13 (4.5)	65 (6.7)	0.0918	0.0198
Osteoporosis = yes (%)	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
Opportunistic infection = yes (%)	0 (0.0)	0 (0.0)	-	-	2 (0.7)	3 (0.3)	-	-
Parenteral nutrition = yes (%)	1 (0.1)	1 (0.1)	0.0006	0.0021	0 (0.0)	0 (0.0)	-	-
Serious infection = yes (%)	38 (4.3)	27 (3.1)	0.0632	0.0041	8 (2.8)	33 (3.4)	0.0336	0.0251
Bowel resection = yes (%)	6 (0.7)	2 (0.2)	0.0670	0.0219	0 (0.0)	1 (0.1)	0.0453	<0.0001
Nutritional anemia = yes (%)	3 (0.3)	3 (0.3)	0.0011	0.1081	1 (0.3)	4 (0.4)	0.0097	0.0446
Electrolyte disorders = yes (%)	19 (2.2)	39 (4.5)	0.1318	0.0334	16 (5.6)	52 (5.3)	0.012	0.0334
Benzodiazepine Rx = yes (%)	105 (12.0)	127 (14.8)	0.0818	0.1791	29 (10.1)	145 (14.8)	0.1426	0.1650
Bisphosphonate Rx = yes (%)	14 (1.6)	37 (4.3)	0.1604	0.0495	1 (0.3)	27 (2.8)	0.1959	0.1446
Statin = yes (%)	95 (10.9)	149 (17.3)	0.1873	0.0786	48 (16.8)	261 (26.7)	0.2425	0.0548
High dose vitamin D Rx = yes (%)	110 (12.6)	96 (11.2)	0.0432	0.192	25 (8.7)	97 (9.9)	0.0408	0.0816
Weight loss or malnutrition = yes (%)	11 (1.3)	11 (1.3)	0.0021	0.1429	5 (1.7)	7 (0.7)	0.0936	0.0356
Antibiotic Rx = yes (%)	102 (11.7)	91 (10.6)	0.0338	0.1136	15 (5.2)	116 (11.9)	0.2386	0.0331
Herpes antiviral Rx = yes (%)	18 (2.1)	15 (1.7)	0.0228	0.0895	6 (2.1)	25 (2.6)	0.0306	0.0076
Comorbidity score (%)			0.1775	0.0547			0.1765	0.1126

0	621 (71.0)	534 (62.2)			197 (68.9)	608 (62.2)		
1	171 (19.5)	191 (22.2)			63 (22.0)	206 (21.1)		
2-3	70 (8.0)	110 (12.8)			22 (7.7)	126 (12.9)		
4+	13 (1.5)	24 (2.8)			4 (1.4)	37 (3.8)		
AZA/ 6MP Rx = yes (%)	283 (32.3)	326 (38.0)	0.1177	0.1613	100 (35.0)	336 (34.4)	0.0121	0.1082
Budesonide use = yes (%)	46 (5.3)	442 (51.5)	1.1936	0.1841	13 (4.5)	139 (14.2)	0.3366	0.1944
Fibrates Rx = yes (%)	20 (2.3)	34 (4.0)	0.0963	0.0563	2 (0.7)	19 (1.9)	0.1092	0.0876
Methotrexate Rx = yes (%)	23 (2.6)	13 (1.5)	0.0784	0.0947	1 (0.3)	8 (0.8)	0.0616	0.0783
Metronidazole Rx = yes (%)	176 (20.1)	187 (21.8)	0.0407	0.0801	43 (15.0)	233 (23.8)	0.2241	0.0309
Narcotics Rx = yes (%)	348 (39.8)	364 (42.4)	0.0529	0.0864	81 (28.3)	375 (38.4)	0.2146	0.0295
Quinolone Rx = yes (%)	139 (15.9)	168 (19.6)	0.0963	0.0826	31 (10.8)	188 (19.2)	0.2367	0.1394
Pyoderma Gangrenosum = yes (%)	3 (0.3)	2 (0.2)	0.0205	0.0032	0 (0.0)	3 (0.3)	0.0785	<0.0001
Prednisone use = yes (%)	239 (27.3)	401 (46.7)	0.4095	0.2805	120 (42.0)	792 (81.1)	0.8777	0.1407
PPI Rx = yes (%)	310 (35.4)	382 (44.5)	0.1854	0.1621	95 (33.2)	407 (41.7)	0.1751	0.1042
Number of non-IBD med classes during 183 days prior (%)			0.3522	0.2117			0.5069	0.1641
0-3	306 (35.0)	175 (20.4)			108 (37.8)	172 (17.6)		
4-6	219 (25.0)	218 (25.4)			72 (25.2)	242 (24.8)		
7-10	168 (19.2)	219 (25.5)			52 (18.2)	245 (25.1)		
10+	182 (20.8)	247 (28.8)			54 (18.9)	318 (32.5)		
Number of IBD hospitalization days = none (%)	803 (91.8)	759 (88.4)	0.1143	0.0584	270 (94.4)	828 (84.7)	0.3200	0.0469
Number of non IBD hospitalizations = 1+ (%)	63 (7.2)	87 (10.1)	0.1042	0.0913	20 (7.0)	96 (9.8)	0.1022	0.0397
First drug that qualified patient into steroids or anti-TNF cohorts (%)			-	-			-	-
Adalimumab	699 (79.9)	0 (0.0)			206 (72.0)	0 (0.0)		
Prednisone	0 (0.0)	343 (39.9)			0 (0.0)	825 (84.4)		
Infliximab	120 (13.7)	0 (0.0)			79 (27.6)	0 (0.0)		
Budesonide	0 (0.0)	516 (60.1)			0 (0.0)	152 (15.6)		
Certolizumab Pegol	56 (6.4)	0 (0.0)			1 (0.3)	0 (0.0)		

TNF = new anti-TNF users; CS = prolonged CS users