SUPPLEMENTAL METHODS

Danish Health Registers

The Danish Civil Registration System contains information regarding the sex, date of birth, vital status and emigration for all Danish citizens.[1] Linkage between the Danish Civil Registration System and the Danish National Patient Registry is accomplished via unique personal identification numbers that are assigned to all Danish citizens at the time of birth or immigration. The Danish National Patient Registry captures all inpatient encounters from January 1, 1977 and all outpatient encounters dating from January 1, 1995.[2] The Danish Prescription Registry was established in 1995 and includes data regarding all prescription therapies in Denmark.[3]

Patient Selection

Patients with UC were defined based on previously published criteria utilizing International Classification of Diseases (ICD) coding (ICD-8: 536.19, 569.04; ICD-10: K51),[4] where patients were required to have at least 2 registrations or a single contact lasting 7 days or more. All patients undergoing proctocolectomy with IPAA for UC were identified using Current Procedural Terminology (CPT)/The Nordic Medico-Statistical Committee Classification of Surgical Procedures (NCSP, Supplemental Table 1). In each of these coding strategies, the index date for the study was defined as the 30 days after the final stage of surgery (to avoid misclassification of the outcome). This index date was identified using a CPT/NCSP code for an IPAA or a CPT/NCSP code for an ileostomy takedown following a CPT/NCSP code for a total abdominal colectomy or total proctocolectomy (with or without IPAA). Most patients undergo proctocolectomy and ileal pouch-anal anastomosis (IPAA) in a staged approach. To ensure that

we were capturing the index date at the latest stage of IPAA surgery, we employed the following approach. The “final stage” of surgery was defined as the last CPT/NCSP code for a pouch surgery, the fourth pouch surgery/pouch-related procedure, or two years after first pouch surgery, whichever came first. Follow-up began 30 days after the “final stage” of surgery to avoid misclassification of the outcome.

Of note, in using this definiton, the index date is conditioned on occurring within up to 2 years of follow up from the first stage of IPAA. We have estimated the probability of loss to follow-up within 2 years (by either death or emigration) to be 2.2% (1.7% - 3.1%), and we have estimted the probability of having a second stage of IPAA within 2 years of the first stage of IPAA to be 86.6% (84.9% - 88.2%). Using this approach, the error we introduce by conditioning on the future is smaller than the error present if using first stage of the IPAA as index date for all patients.

Secondary Outcomes

There are no NCSP codes that correspond with the CPT code for pouchoscopy used in prior evaluations of administrative claims (44385, 44386). Given this limitation, we evaluated the use of any lower endoscopic procedure in the post-IPAA period (Supplemental Table 1) as a proxy for pouchoscopy, comparing the use of these procedures over time and between patients with pouchitis and those without pouchitis in the first 2 years after IPAA.

SUPPLEMENTAL REFERENCES

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3. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, et al. Data Resource Profile: The Danish National Prescription Registry. Int J Epidemiol 2017;46:798-798f.
4. Singh S, Andersen NN, Andersson M, et al. Comparison of Infliximab and Adalimumab in Biologic-Naive Patients With Ulcerative Colitis: A Nationwide Danish Cohort Study. Clin Gastroenterol Hepatol 2017;15:1218-1225 e7.

Supplemental Table 1. Current Procedural Terminology and Danish Sundhedsvæsenets Klassifikations System coding for procedures related to ileal pouch-anal anastomosis

CPT code	Definition	NCSP Code
44153	Legacy code, colectomy without proctectomy	
44157	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, includes loop ileostomy, and rectal mucosectomy, when performed	(K) JFH 30 (K) JFH 33
44158	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed	
44211	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileoanal anastomosis, creation of ileal reservoir (S or J), with loop ileostomy, includes rectal mucosectomy, when performed	(K) JFH 31 (K) JFH 34
44227	Laparoscopy, surgical, closure of enterostomy, large or small intestine, with resection and anastomosis	
44620	Closure of enterostomy, large or small intestine	(K) JFG 00 (K)JFG00A (K) JFG 10 (K) JFG 10A
44625	Closure of enterostomy, large or small intestine; with resection and anastomosis other than colorectal	(K) JFG 20 (K) JFG 20A
44626	Closure of enterostomy, large or small intestine; with resection and colorectal anastomosis (eg, closure of Hartmann type procedure)	(K) JFG 23 (K) JFG 26 (K) JFG 29 (K) JFG 30 (K) JFG 33
45113	Proctectomy, partial, with rectal mucosectomy, ileoanal anastomosis, creation of ileal reservoir (S or J), with or without loop ileostomy	(K) JGB 50 (K) JGB 60 (K) JGB 61
44385	Pouchoscopy	
	Colonoscopy	(K) UJF 32
	Colonoscopy with biopsy	(K) UJF 35
	Flexible sigmoidoscopy	(K) UJF 42
	Flexible sigmoidoscopy with biopsy	(K) UJF 45
	Peranal enteroscopy	(K) UJF 82
	Peranal enteroscopy with biopsy	(K) UJF 85
44386	Pouchoscopy with biopsy	
46712	IPAA revision via the combined abdominoperineal approach	(K) JFG 53
45136	IPAA excision	(K) JFG 73

Current Procedural Terminology (CPT); The Nordic Medico-Statistical Committee Classification of Surgical Procedures (NCSP)

Supplemental Table 2. Specific coding utilized in the identification of patients treated with anti-tumor necrosis factor alpha therapy, corticosteroid therapy, and those patients experiencing an inflammatory bowel disease-related hospitalization

Exposure	Codes
IBD-related hospitalization	Inpatient contact (c_pattype=0) with A-diagnosis of ICD-10: DK50, DK51 or B-diagnosis of DK50, DK51 and A-diagnosis of one the following
Abdominal pain	ICD-10: DR100, DR101, DR102C, DR103
Nausea and vomiting	ICD-10: DR11
Non-infectious gastroenteritis	ICD-10: DK529+A-H (excl. DK529B1)
Rectal- or anal bleeding	ICD-10: DK625A+B
Fistula	ICD-10: DK603-605, DK316E, DK632, DN822-825+DN828F
Abscess	ICD-10: DK610-14, DK630, DK650A, DK650G, DK650H, DL023C
Stenosis	ICD-10: DK264A-E, DK566+F+G
Ileus and sub-ileus	ICD-10: DK566C, DK567
Corticosteroids	ATC: H02AB
Anti-Tumor Necrosis Factor-alpha	ATC: L04AB , SKS: B0HJ18A

Abbreviations: ATC Anatomic Therapeutic Classification, ICD-10 International Classification of Diseases version 10, NCSP The Nordic Medico-Statistical Committee Classification of Surgical Procedures, SKS Sundhedsvæsenets Klassifikations System (classification system used for documentation of clinical and administrative matters in the Danish health care system).

Supplemental Table 3. International Classification of Diseases coding for extraintestinal manifestations

Diagnostic Group	**Diagnoses**	**ICD-8**	**ICD-10**
Arthritis/arthralgia	Psoriatic Arthritis	696.09	M07
	Rheumatoid Arthritis	712.00, 712.10, 712.19, 712.29, 712.38, 712.39, 712.59	M05
	Ankylosing Spondylitis	712.49	M45
	Sacroiliitis	726	M43.2
Osteoporosis	Osteoporosis	723	M80-M82
Primary Sclerosing Cholangitis	Primary Sclerosing Cholangitis	575	K83.0
Non-alcoholic Fatty Liver Disease	Non-alcoholic Fatty Liver Disease	573	K76.0
Dermatologic Manifestations	Erythema Nodosum	695.2	L52
	Pyoderma Gangrenosum	686	L88
	Psoriasis	696.09, 696.10, 696.19	L40
Ocular Lesions	Conjunctivitis	360	H10
	Uveitis	364	H20
	Episcleritis		H15
Apthous Stomatitis	Apthous Stomatitis	528	K12.0
Thromboembolic Events	PulmonaryEembolism	450	J84
	Deep Venous Thrombosis	453	I82.4

Supplemental Table 4. Demographic characteristics of patients undergoing proctocolectomy with ileal pouch-anal anastomosis between 1996 and 2018, evaluated by time period of ileal pouch-anal anastomosis

	Year of surgery										All	
	1996-2000		2001-2005		2006-2010		2011-2014		2015-2018			
	N	%	N	%	N	%	N	%	N	%	N	%
All	320	100.0	381	100.0	431	100.0	353	100.0	179	100.0	1,664	100.0
Sex												
Female	145	45.3	180	47.2	206	47.8	166	47.0	71	39.7	768	46.2
Male	175	54.7	201	52.8	225	52.2	187	53.0	108	60.3	896	53.8
Age at surgery												
less than 35	193	60.3	200	52.5	192	44.5	166	47.0	96	53.6	847	50.9
35 or above	127	39.7	181	47.5	239	55.5	187	53.0	83	46.4	817	49.1
Duration of UC prior to colectomy (median, quartile range)	2.0	4.7	2.2	5.2	2.4	6.6	2.5	8.0	1.7	6.1	2.2	6.1
Corticosteroid use in the year prior to IPAA	141	44.1	169	44.4	151	35.0	113	32.0	49	27.4	623	37.4
IBD-related hospitalization in the year prior to IPAA	289	90.3	322	84.5	316	73.3	220	62.3	101	56.4	1,248	75.0
Extraintestinal manifestations (in the 5 years prior to IPAA)	24	7.5	38	10.0	31	7.2	37	10.5	29	16.2	159	9.6

Ileal pouch-anal anastomosis (IPAA), ulcerative colitis (UC)

Supplemental Table 5. Percentage of patients with a diagnosis of Crohn's disease within the first two years after ileal pouch-anal anastomosis, overall and evaluated by time period of index surgery

	Cumulative Incidence of CD in the First 2 Years after IPAA	**95% CI**
Overall	7.4%	(6.2%-8.7%)
1996-2000	7.6%	(5.1%-11.1%)
2001-2005	8.2%	(5.9%-11.5%)
2006-2010	8.0%	(5.8%-11.0%)
2011-2014	4.9%	(3.1%-7.7%)
2015-2018	8.4%	(5.2%-13.6%)

Supplemental Table 6. Percentage of patients undergoing lower endoscopic procedures during the first two years after ileal-pouch anal anastomosis, evaluated by time period of index surgery

	Proportion of Patients	**(95% CI)**
1996-2000	17.4%	13.6%-22.0%
2001-2005	30.7%	26.3%-35.6%
2006-2010	44.6%	40.0%-49.5%
2011-2014	48.1%	42.9%-53.4%
2015-2018	62.3%	55.2%-69.4%

Supplemental Table 7. Development of pouchitis within the first two years after ileal pouch-anal anastomosis, evaluated by time period of index surgery and stratified by age at the time of surgery

	Adjusted HR (95% CI)
Patients Age 18-34	
1996-2000	Reference
2001-2005	1.10 (0.81 – 1.50)
2006-2010	1.42 (1.06 – 1.92)
2011-2014	1.61 (1.19 – 2.19)
2015-2018	1.81 (1.27 – 2.56)
Patients Age 35 and above	
1996-2000	Reference
2001-2005	0.98 (0.68 –1.42)
2006-2010	1.25 (0.89 –1.77)
2011-2014	1.23 (0.87 –1.77)
2015-2018	1.32 (0.86 –2.01)

*Adjusted for sex, year of surgery, age and socioeconomic index

Supplemental Table 8. Comparison of criteria used to diagnose pouchitis, evaluated by time period

	Diagnosis method			
	ICD-10 code		Antibiotic Use (ATC code)	
	N	%	N	%
All	500	63.7	285	36.3
Time Period				
1996-2000	86	67.2	42	32.8
2001-2005	98	59.8	66	40.2
2006-2010	135	64.0	76	36.0
2011-2014	110	59.8	74	40.2
2015-2016	71	72.4	27	27.6

Anatomic Therapeutic Classification (ATC), International Classification of Diseases (ICD)

Supplemental Table 9. Evaluation of the impact of clinical factors on the risk of pouchitis within the first two years after ileal pouch-anal anastomosis for ulcerative colitis

	Adjusted HR* (95% CI)
IBD-related hospitalization in the year prior to IPAA	1.16 (0.97 – 1.39)
Corticosteroid use in the year prior to IPAA	1.01 (0.87 – 1.18)
Extraintestinal manifestations diagnosed in the 5 years prior to IPAA	1.40 (1.11 – 1.74)

*Adjusted for sex, year of surgery, age, socioeconomic index

Supplemental Figure 1. Cumulative incidence of pouchitis among all patients undergoing ileal pouch-anal anastomosis, analyzed over years of available follow-up