

Comorbidities and Extraintestinal Manifestations among Patients with Difficult-to-Treat Inflammatory Bowel Disease in Latin America

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Background

Patients with Inflammatory Bowel Diseases (IBD) can also have quality of life affected by extraintestinal manifestations (EIMs) and comorbidities.¹

The IBD prevalence is increasing in Latin America and access to treatment is heterogeneous, making it important to understand the frequency and presentation of EIMs, especially among patients with difficult-to-treat IBD (D2T-IBD).^{3,4}

Objectives

To evaluate the frequency and presentation of EIMs in patients with D2T-IBD in Latin American region (LatAM)

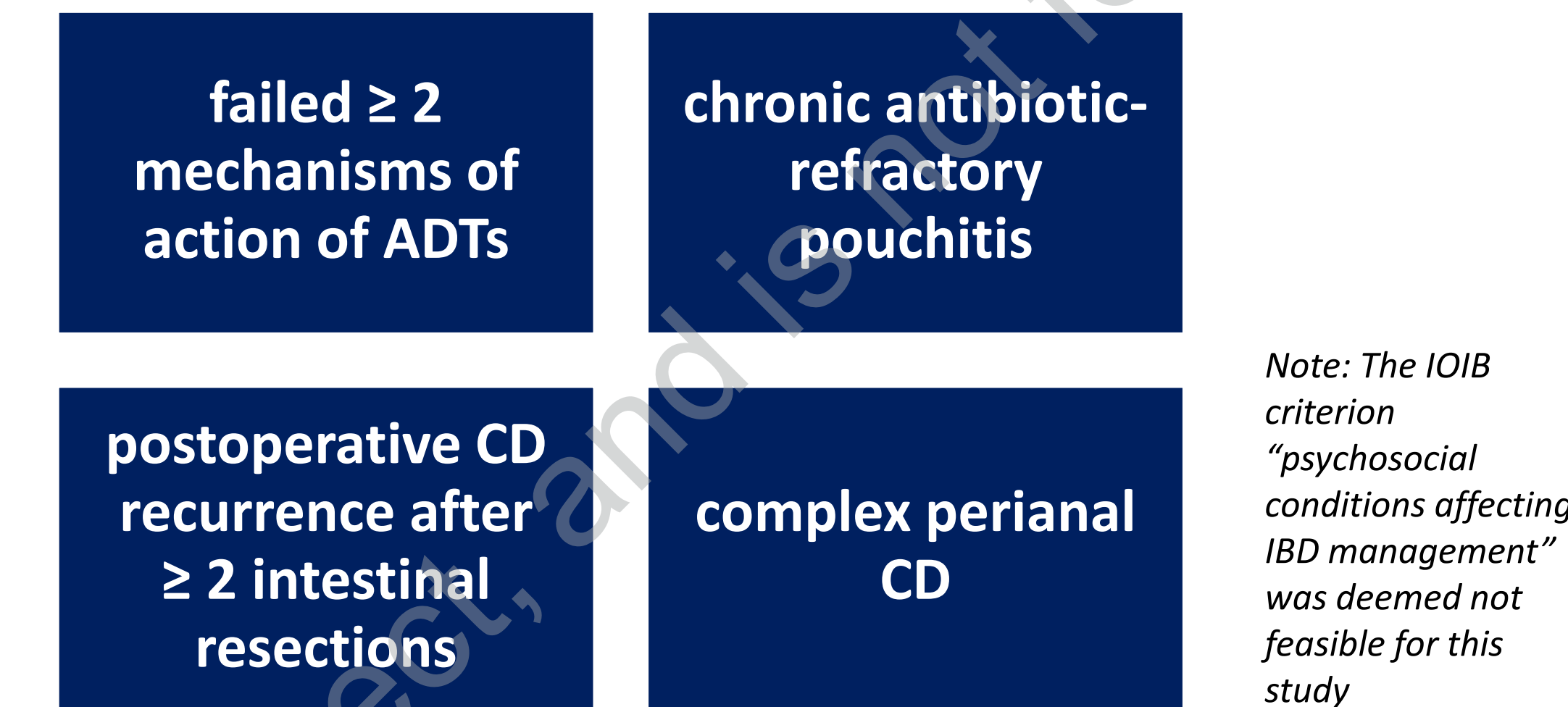
Methods

Observational study with secondary data of adult UC (ulcerative colitis), CD (Crohn's disease) or unclassified IBD patients and at least one IBD drug, from LatAM registries:

- Epidemiologic characterization of Inflammatory Bowel Disease in Latin America Multicentric Study (9 countries)
- GEDIIB - Brazilian Organization of Crohn's Disease and Colitis registry
- CEMIC - Centro de Educación Médica y Investigaciones Clínicas “Norberto Quirno”, Buenos Aires, Argentina
- HPUC - Hospital Privado Universitario de Córdoba, Argentina

Patients were classified with D2T-IBD, based on IOIBD criteria (Fig. 1).²

Figure 1. Criteria for D2T-IBD classification, according to the IOIBD consensus.²



Statistical Analysis: Comorbidities, EIMs, and other characteristics of D2T and non-D2T patients were compared with Mann-Whitney and chi-square tests (p<0.05).

Results

Of 6417 included patients, 55.7% had UC, 43.4% CD, and 0.9% had unclassified IBD.

- The median (Q1-Q3) disease duration at registry inclusion was 9 (5-15) years, and 56% were female – Table 1.
- The most frequent comorbidities were cardiovascular (17%) and endocrine (14%). Articular EIMs - arthralgia/arthritis (20%) - were the most frequent EIMs.

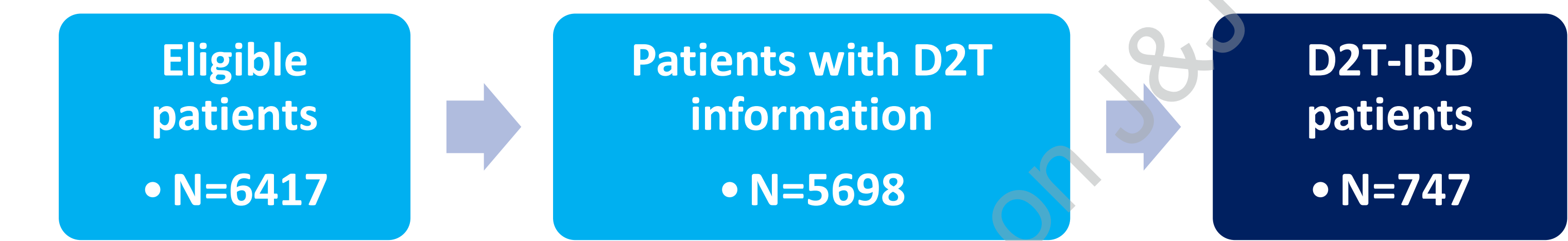
Table 1. Characteristics of all included patients, overall and by IBD type.

	Total N=6417		Ulcerative Colitis N=3572		Crohn's Disease N=2778	
Female sex, n (%)	3603 (56.2%)	[n=6414]	2136 (59.8%)	[n=3571]	1440 (51.7%)	[n=2786]
Disease duration (years), median (Q1-Q3)	9 (5-15)	[n=6206]	9 (5-16)	[n=3482]	9 (5-15)	[n=2668]
Country, n (%)						
Argentina	513 (8.0%)		378 (10.6%)		130 (4.7%)	
Brazil	3656 (57.0%)		1692 (47.4%)		1934 (69.4%)	
Colombia	103 (1.6%)		84 (2.4%)		18 (0.6%)	
Cuba	73 (1.1%)		51 (1.4%)		22 (0.8%)	
Dominican Republic	331 (5.2%)		130 (3.6%)		197 (7.1%)	
Ecuador	122 (1.9%)		91 (2.5%)		22 (0.8%)	
Mexico	1255 (19.6%)		953 (26.7%)		295 (10.6%)	
Peru	31 (0.5%)		15 (0.4%)		16 (0.6%)	
Puerto Rico	157 (2.4%)		43 (1.2%)		114 (4.1%)	
Uruguay	19 (0.3%)		12 (0.3%)		7 (0.3%)	
Venezuela	157 (2.4%)		123 (3.4%)		33 (1.2%)	
Extraintestinal manifestations ^{a)} , n (%)						
Articular	1552 (24.2%)		804 (22.5%)		734 (26.3%)	
Arthralgia/arthritis	1306 (20.4%)		699 (19.6%)		597 (21.4%)	
Axial articular	429 (6.7%)		187 (5.2%)		237 (8.5%)	
Sacroiliitis	120 (1.9%)		55 (1.6%)		65 (2.3%)	
Ankylosing spondylitis	331 (5.2%)		149 (4.3%)		177 (6.4%)	
Primary sclerosing cholangitis	130 (2.0%)		105 (2.9%)		25 (0.9%)	
Skin	173 (2.7%)		76 (2.1%)		94 (3.4%)	
Pyoderma gangrenosum	71 (1.1%)		36 (1.0%)		33 (1.2%)	
Erythema nodosum	101 (1.6%)		36 (1.0%)		64 (2.3%)	
Uveitis	142 (2.2%)		73 (2.0%)		69 (2.5%)	
Oral ulcers	128 (2.0%)		37 (1.1%)		91 (3.3%)	
Comorbidities not EIM ^{a)} , n (%)						
Musculoskeletal	469 (7.4%)		297 (8.5%)		166 (6.0%)	
Cardiovascular	987 (16.9%)		564 (17.6%)		415 (16.1%)	
Neurologic	105 (1.9%)		53 (1.8%)		52 (2.1%)	
Psychiatric	246 (4.6%)		103 (3.6%)		137 (5.6%)	
Skin	146 (2.7%)		53 (1.8%)		91 (3.6%)	
Hepato/Gastrointestinal	308 (5.8%)		136 (4.8%)		169 (6.9%)	
Hematologic	58 (1.1%)		27 (0.9%)		31 (1.2%)	
Urogenital	139 (2.6%)		62 (2.2%)		77 (3.1%)	
Respiratory	102 (1.9%)		46 (1.6%)		54 (2.2%)	
Endocrine	826 (14.1%)		463 (14.4%)		354 (13.7%)	
Oncology	113 (2.0%)		56 (1.8%)		56 (2.2%)	

Note: Percentages are based on total of patients except otherwise mentioned. a) more than one possible option. b) Comorbidities do not include EIM nor the following IBD complications (abdominal fistula/abscess, perianal fistula/abscess, toxic megacolon, intestinal obstruction/perforation, colorectal cancer, infection, thromboembolic events, anemia, fatigue). Q1=First quartile, Q3= Third quartile.

Of 5698 patients with D2T criteria information, 13.1% (n=747) were classified with D2T-IBD. Among patients with at least one ADT, 25.8% were D2T.

Figure 2. Patient flowchart.



- The proportion of D2T-IBD was higher among CD patients (30.2% vs 1.6% of UC patients; p<0.001) – Fig. 3.
- The most frequent D2T criteria were complex perianal disease for D2T-CD (90.5%), and failure to 2+ mechanisms of ADTs for D2T-UC (92.6%) – Fig. 4.

Figure 3. Proportion of D2T-IBD

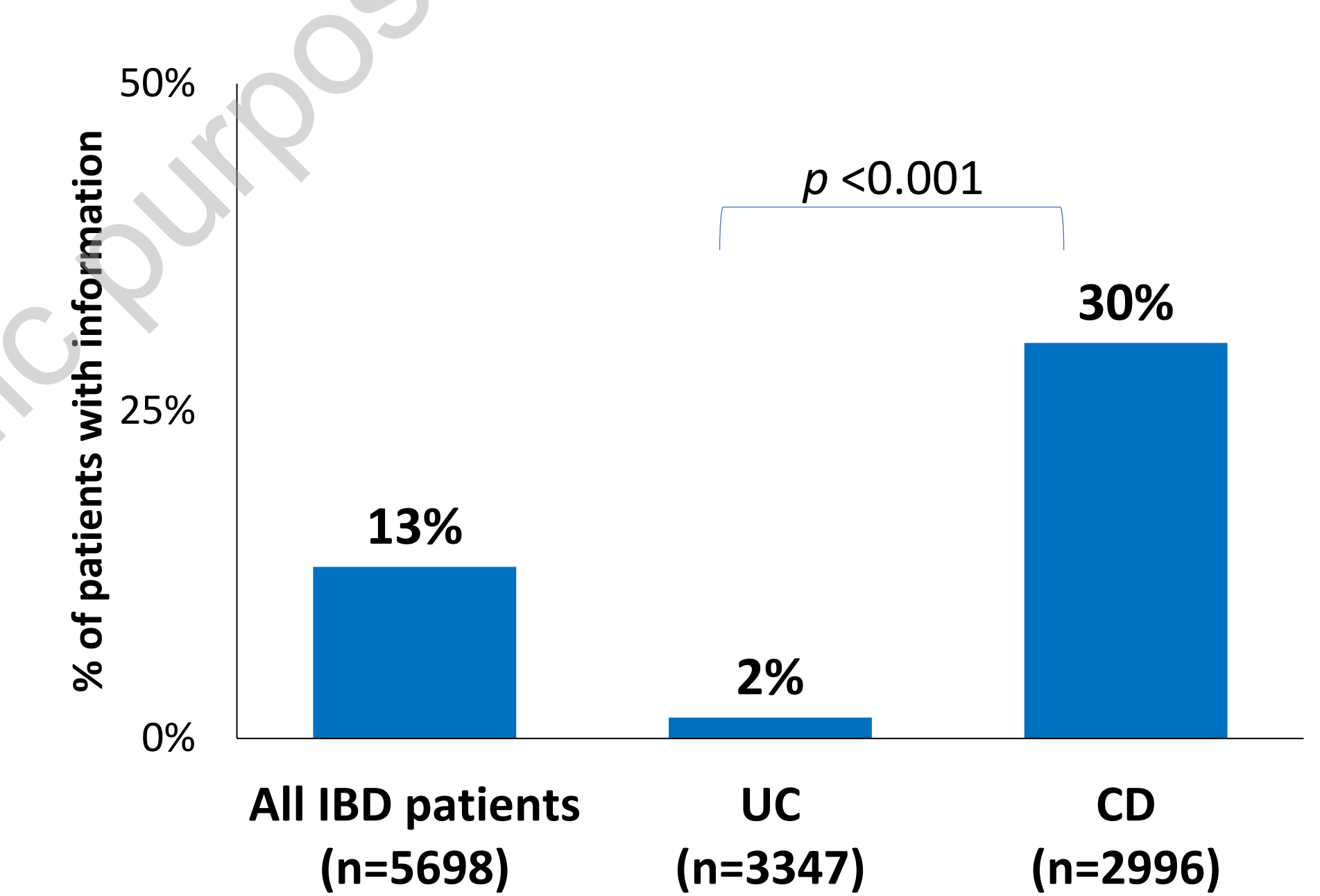
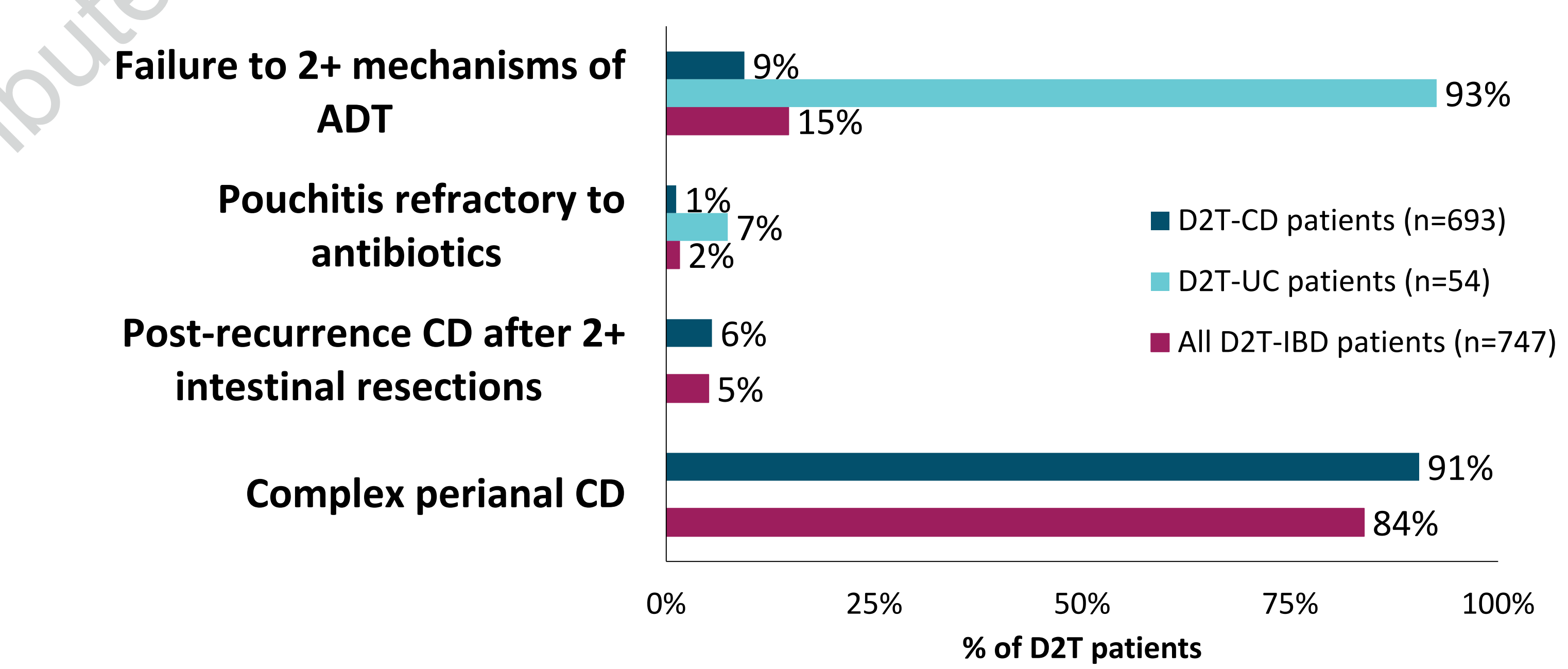


Figure 4. Proportion of D2T patients by D2T-IBD criteria.



About 41% of D2T patients had at least one comorbidity other than EIM or IBD complication.

- D2T patients had statistically more male patients (55%), IBD family history (5.5%), non-current smokers (93%), and were younger at diagnosis [median: 26 (21-37) years] – Table 2.

Most frequent EIMs among D2T patients:

- arthralgia/arthritis, erythema nodosum, uveitis, and oral ulcers

Most frequent Comorbidities not EIMs, among D2T patients:

- Psychiatric, hepato/gastrointestinal, urogenital and musculoskeletal

Table 2. Characteristics of D2T and non-D2T patients.

	Total (N=5698)		D2T patients (N=747)		Non-D2T patients (N=4951)		p-value ^{a)}
Age at IBD diagnosis (years), median (Q1-Q3)	33 (24-46)	[n=5499]	26 (21-37)	[n=719]	35 (25-48)	[n=4780]	<0.001
Disease duration (years), median (Q1-Q3)	9 (5-15)	[n=5502]	10 (6-16)	[n=722]	9 (5-15)	[n=4780]	<0.001
Years until IBD diagnosis, median (Q1-Q3)	0 (0-1)	[n=5296]	0 (0-2)	[n=682]	0 (0-1)	[n=4614]	<0.001
Female sex, n (%)	3183 (55.9%)	[n=5696]	338 (45.2%)		2845 (57.5%)	[n=4949]	<0.001
Family history (1 st grade) of IBD, n (%)	57 (2.0%)	[n=2816]	11 (5.4%)	[n=203]	46 (1.8%)	[n=2613]	0.002 *
Current smokers, n (%)	639 (11.8%)	[n=5436]	52 (7.4%)	[n=699]	587 (12.4%)	[n=4737]	<0.001
Private referral institution, n (%)	2385 (63.0%)	[n=3786]	305 (73.3%)	[n=416]	2080 (61.7%)	[n=3370]	<0.001
Pharmacological class ^{b)} , n (%)							--
Steroids	1609 (28.2%)		204 (27.3%)		1405 (28.4%)		
Salicylates	3874 (68.0%)		251 (33.6%)		3623 (73.2%)		
Immunomodulators	2444 (42.9%)		479 (64.1%)		1965 (39.7%)		
Advanced Drug Therapy	2426 (42.6%)		621 (83.1%)		1805 (36.5%)		

Note: Percentages based on total of patients except otherwise mentioned [n]. a) p-values from Mann-Whitney test, for quantitative variables, and chi-square test for qualitative variables, except * Fisher-exact test. b) more than one possible option. D2T= Difficult to treat, IBD= Inflammatory Bowel Disease, Q1=First quartile, Q3= Third quartile.

Table 3. EIMs and other comorbidities of D2T and non-D2T patients.

	Total (N=5698)	D2T patients (N=747)	Non-D2T patients (N=4951)	p-value ^{a)}
Extraintestinal manifestations ^{b)} , n (%)				
Articular	1337 (23.5%)	207 (27.7%)	1130 (22.8%)	0.003
Arthralgia/arthritis	1130 (19.8%)	183 (24.5%)	947 (19.1%)	0.001
Axial articular	364 (6.4%)	49 (6.6%)	315 (6.4%)	0.837
Sacroiliitis	106 (1.9%)	13 (1.7%)	93 (1.9%)	0.762
Ankylosing spondylitis	279 (5.0%)	36 (4.8%)	243 (5.0%)	0.859
Primary sclerosing cholangitis	116 (2.0%)	10 (1.3%)	106 (2.1%)	0.148
Skin	149 (2.6%)	30 (4.0%)	119 (2.4%)	0.010
Pyoderma gangrenosum	56 (1.0%)	8 (1.1%)	48 (1.0%)	0.819
Erythema nodosum	91 (1.6%)	22 (3.0%)	69 (1.4%)	0.002
Uveitis	123 (2.2%)	25 (3.3%)	98 (2.0%)	0.017
Oral ulcers	114 (2.0%)	34 (4.6%)	80 (1.6%)	<0.001
Any comorbidities not EIM ^{b, c)} , n (%)	2134 (40.9%)	289 (41.3%)	1845 (40.8%)	0.799
Musculoskeletal	401 (7.2%)	35 (4.7%)	366 (7.5%)	0.005
Cardiovascular	842 (16.1%)	96 (13.7%)	746 (16.5%)	0.064
Neurologic	73 (1.5%)	8 (1.2%)	65 (1.5%)	0.514
Psychiatric	191 (4.0%)	49 (7.7%)	142 (3.5%)	<0.001
Skin	128 (2.6%)	24 (3.6%)	104 (2.5%)	0.082
Hepato/Gastrointestinal	250 (5.3%)	47 (7.4%)	203 (5.0%)	0.011
Hematologic	48 (1.0%)	9 (1.4%)	39 (0.9%)	0.291
Urogenital	106 (2.2%)	28 (4.4%)	78 (1.9%)	<0.001
Respiratory	86 (1.8%)	10 (1.6%)	76 (1.9%)	0.620
Endocrine	702 (13.5%)	96 (13.7%)	606 (13.4%)	0.815
Oncology	99 (1.9%)	17 (2.5%)	82 (1.9%)	0.249
Other	293 (5.8%)	43 (6.4%)	250 (5.7%)	0.468

Note: Percentages are based on total of patients. a) p-values from chi-square test, b) more than one possible option. c) Comorbidities do not include EIM nor the following IBD complications (abdominal fistula/abscess, perianal fistula/abscess, toxic megacolon, intestinal obstruction/perforation, colorectal cancer, infection, thromboembolic events, anemia, fatigue). D2T= Difficult to treat, IBD= Inflammatory Bowel Disease.