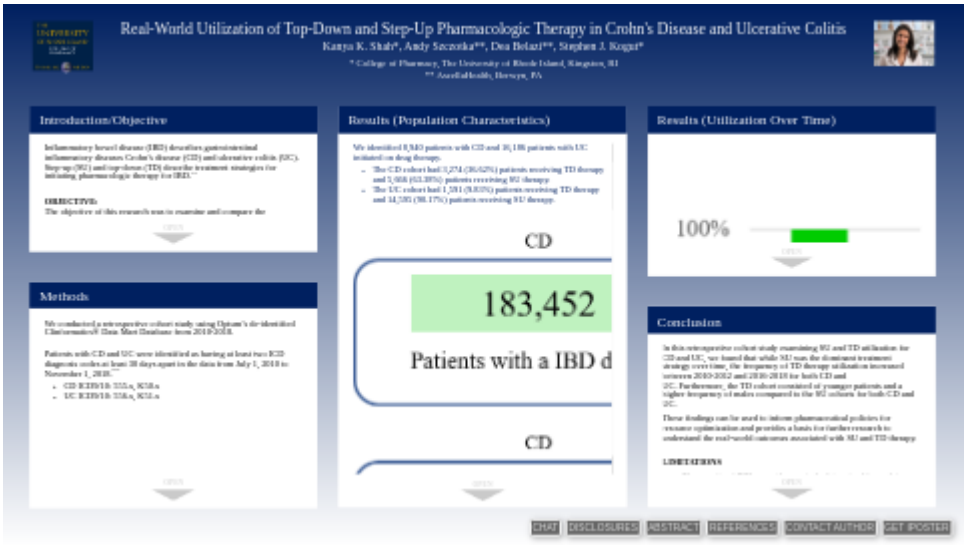
Real-World Utilization of Top-Down and Step-Up Pharmacologic Therapy in Crohn's Disease and Ulcerative Colitis



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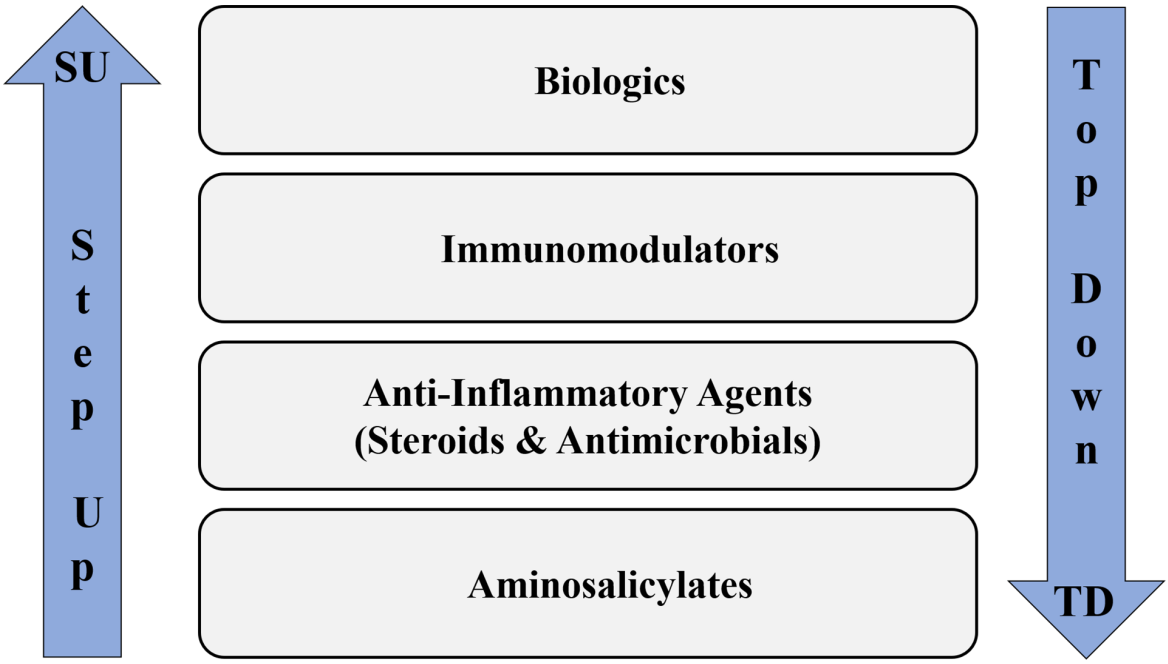
INTRODUCTION/OBJECTIVE

Inflammatory bowel disease (IBD) describes gastrointestinal inflammatory diseases Crohn's disease (CD) and ulcerative colitis (UC). Step-up (SU) and top-down (TD) describe treatment strategies for initiating pharmacologic therapy for IBD.[1-4]

OBJECTIVE:
The objective of this research was to examine and compare the utilization of SU and TD prescribing patterns in patients with CD and UC using Optum claims data from 2010-2012 to 2016-2018.



We defined step-up (SU) therapy as beginning IBD treatment with anti-inflammatory agents (aminosalicylates, steroids, and antimicrobials) and progressing to immunomodulatory agents and biologics.[5-7]

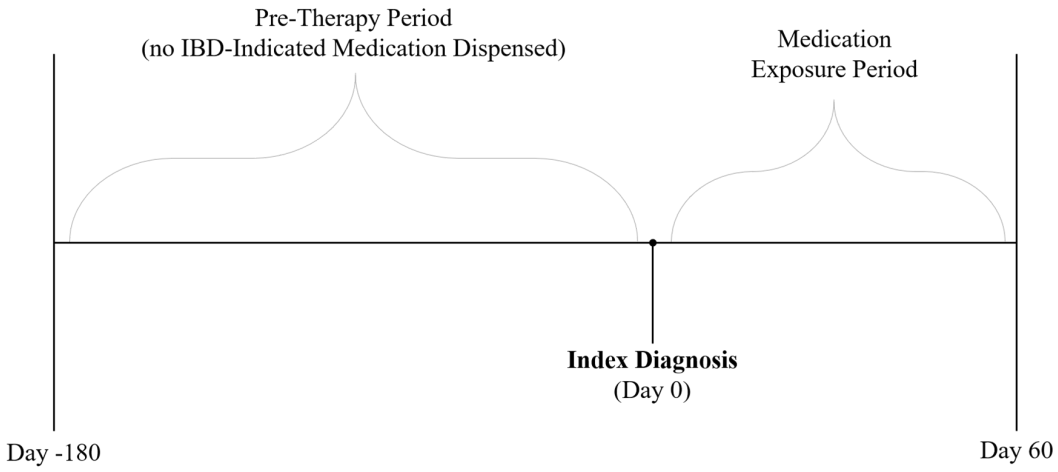
We defined top-down (TD) therapy as initiating with biologic or immunomodulatory agents and using aminosalicylate and anti-inflammatory agents as a secondary therapy.[5-7]

METHODS

We conducted a retrospective cohort study using Optum's de-identified Clinformatics® Data Mart Database from 2010-2018.

Patients with CD and UC were identified as having at least two ICD diagnosis codes at least 30 days apart in the data from July 1, 2010 to November 1, 2018.[8-12]

- CD ICD9/10: 555.x, K50.x
- UC ICD9/10: 556.x, K51.x



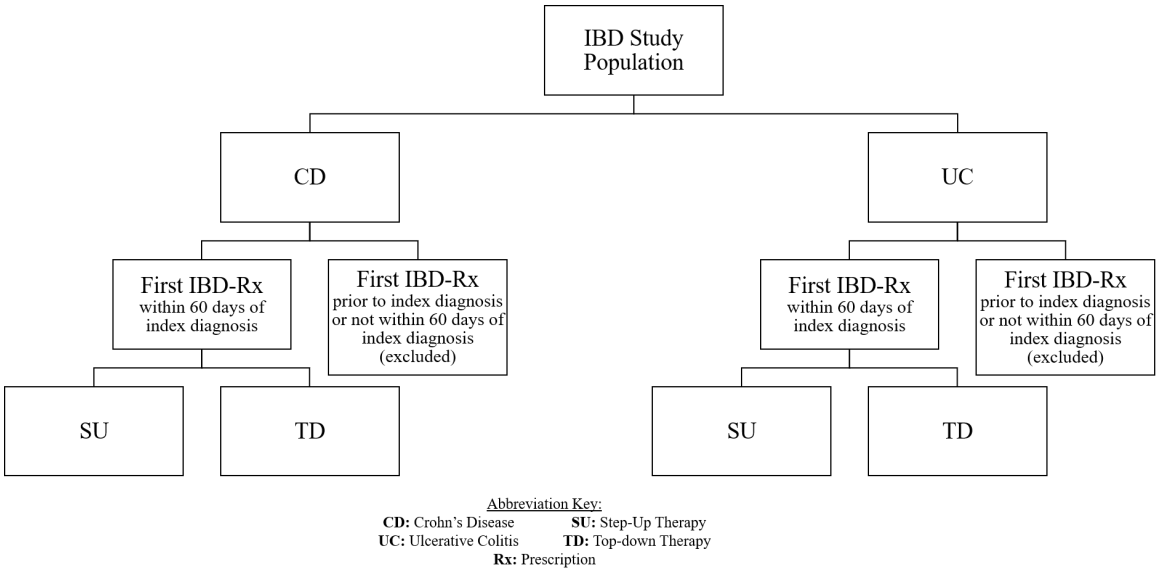
The index diagnosis was the first ICD code occurrence of IBD in the claims data from 2010 to 2018. Prior to the index diagnosis date, patients were required to have evidence of enrollment without an IBD-indicated medication dispensed for six months.

Patients newly initiated on pharmacologic therapy were identified as having:

- An IBD-indicated medication dispensed in the 60-day period after index diagnosis, and
- A six-month period prior to index diagnosis without an IBD-indicated medication dispensed.

Exclusion Criteria:

- Missing Data
- Patients not newly initiated on therapy
- Incomplete eligibility for the 240-day study period
- Have comorbidities treated with IBD-indicated biologics.



Abbreviation Key:
CD: Crohn's Disease **SU:** Step-Up Therapy
UC: Ulcerative Colitis **TD:** Top-down Therapy
Rx: Prescription

Patients were categorized into the SU or TD cohort based on drugs dispensed in the medication exposure period.

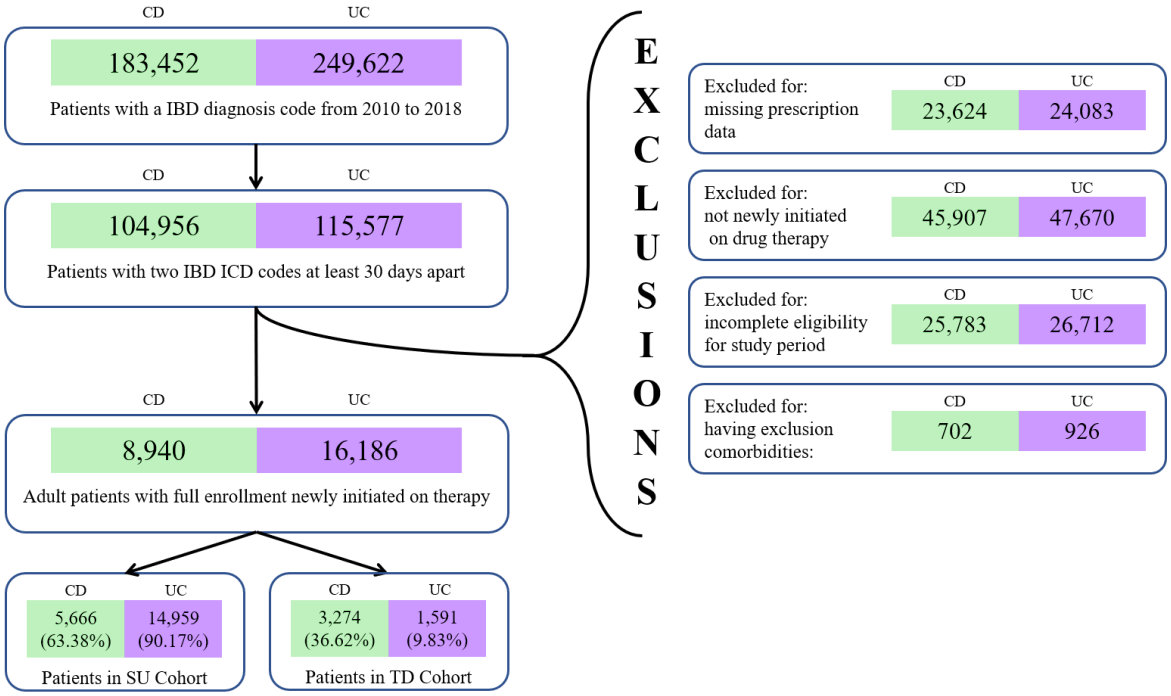
Medications Filled in the 60-Day Exposure Period		Cohort Assigned
SU Medications	TD Medications	
X		SU
	X	TD
X	X	TD

SU Medications[3,4]	TD Medications[3,4]
Aminosalicylates	Immunomodulators
Balsalazide Mesalamine Olsalazine Sulfasalazine	Azathioprine Cyclosporine Mercaptopurine Methotrexate Tacrolimus
Corticosteroids	Biologics
Budesonide Betamethasone Cortisone Dexamethasone Hydrocortisone Methylprednisolone Prednisone Prednisolone Triamcinolone	Adalimumab Certolizumab pegol Golimumab Infliximab Natalizumab Tofacitinib Ustekinumab Vedolizumab
Antimicrobial	
Ciprofloxacin Metronidazole	

RESULTS (POPULATION CHARACTERISTICS)

We identified 8,940 patients with CD and 16,186 patients with UC initiated on drug therapy.

- The CD cohort had 3,274 (36.62%) patients receiving TD therapy and 5,666 (63.38%) patients receiving SU therapy.
- The UC cohort had 1,591 (9.83%) patients receiving TD therapy and 14,595 (90.17%) patients receiving SU therapy.

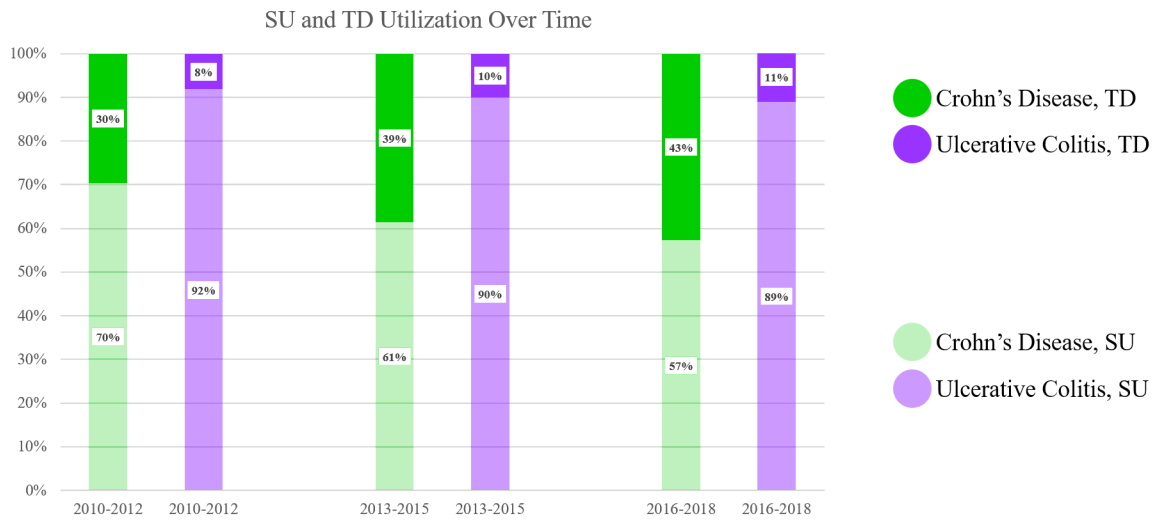


Age and sex were significantly different between treatment strategies for both CD and UC.

- TD cohort had a slightly higher percentage of males in both CD and UC (54.1%; 54.9%, respectively, $p<0.001$).
- TD cohort had a lower mean age for CD and UC (TD: 34.8, 39.8 years, SU: 44.1, 46.6 years, respectively, $p<0.001$).

	CD		UC	
	SU	TD	SU	TD
n (row %)	5,666 (63.4)	3,274 (36.6)	14,959 (90.2)	1,591 (9.8)
Age (SD)	44.1 (19.6)	34.9 (18.1)	46.6 (18.8)	39.82 (18.5)
Sex				
Male (column %)	2,723 (48.1)	1,771 (54.2)	7,264 (49.8)	874 (54.9)
Female	2,941 (51.9)	1,502 (45.9)	7,327 (50.2)	717 (45.1)

RESULTS (UTILIZATION OVER TIME)



The rate of TD therapy utilization was higher in 2016-2018 than 2010-2012 for both CD (42.7%; 29.6%, respectively) and UC (11.4%; 8.17%, respectively; $p < 0.0001$ for both comparisons).

CONCLUSION

In this retrospective cohort study examining SU and TD utilization for CD and UC, we found that while SU was the dominant treatment strategy over time, the frequency of TD therapy utilization increased between 2010-2012 and 2016-2018 for both CD and UC. Furthermore, the TD cohort consisted of younger patients and a higher frequency of males compared to the SU cohorts for both CD and UC.

These findings can be used to inform pharmaceutical policies for resource optimization and provides a basis for further research to understand the real-world outcomes associated with SU and TD therapy.

LIMITATIONS

- The severity of IBD cannot be precisely determined from claims data. The CD and UC treatment guidelines recommend both SU and TD therapy options for patients with moderate/severe disease who are at a high risk of disease progression, relapse, and disease complications (stricture and fistula development), but only recommend SU therapy options for patients with mild/low-risk disease.[3,4]
- Data relating to geographic location, race, or other social determinants of health were not included in our analysis but may influence SU and TD therapy choices.
- Medications/Biologics distributed through specialty channels that bypass community pharmacies may not have been completely recorded in the database.
- Prescriber bias: Prescribing practices and conventions may vary by factors unmeasured in the data source and uncontrolled in our study.
- Misdiagnosis and reporting bias may be present in this study as a result of relying on ICD coding to determine IBD diagnosis and index diagnosis date.

DISCLOSURES

This was an unfunded study completed as Kanya Shah's MS thesis project. Dr. Shah is supported by an educational grant provided to the URI College of Pharmacy by Ascella Health

ABSTRACT

Real-World Utilization of Top-Down and Step-Up Pharmacologic Therapy in Crohn's Disease and Ulcerative Colitis

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Objective

Drug treatment strategies for Crohn's disease (CD) and ulcerative colitis (UC) include step-up (SU) and top-down (TD) therapy. SU therapy initiates with oral anti-inflammatory agents, while TD therapy initiates with biologics or immunomodulators. This research examined the utilization of TD and SU therapy in CD and UC over time using claims data.

Methods

We conducted a retrospective cohort study using Optum's de-identified Clinformatics® Data Mart Database data from 2010 through 2018. Patients with at least two separate diagnosis codes for CD or UC were included. TD or SU treatment strategies were assigned based on the first drug prescribed for CD or UC filled after a six-month period without a CD- or UC-indicated drug claim and within 60-days of the first diagnosis. Gender and age were assessed during the year of index diagnosis. Additionally, we compared the proportion of TD or SU therapy used during 2010-2012 and 2016-2018. Statistical significance of differences in TD or SU therapy according to age, gender and time periods were assessed with chi-squared tests and t-tests.

Results

We identified 8,940 CD and 16,186 UC patients initiated on drug therapy. The CD cohort had 3,274 (36.62%) patients receiving TD therapy and 5,666 (63.38%) patients receiving SU therapy. The UC cohort had 1,591 (9.83%) patients receiving TD therapy and 14,595 (90.17%) patients receiving SU therapy. Age and gender were significantly different ($p<0.001$) between treatment strategies for both CD and UC, with the TD cohort having a higher percentage of males (54.12%; 54.93%, respectively) and a lower mean age (TD: 34.8[SD:18.1], 39.8[18.5]; SU: 44.1[19.6], 46.6[18.8], respectively). The rate of TD therapy utilization was higher in 2016-2018 than 2010-2012 for both CD (42.7%; 29.6%, respectively) and UC (11.4%; 8.17%, respectively; $p<0.0001$ for both comparisons).

Conclusion

We found the frequency of TD therapy utilization has increased between 2010-2012 and 2016-2018. These findings can inform policies for resource optimization.

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