Segmentation of Ontario Physicians Treating Crohn's Disease for the Purposes of Sales and Marketing

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Introduction

Crohn's disease (CD) is a chronic inflammatory autoimmune disease centralized in the gastrointestinal (GI) tract which is also accompanied by other systematic effects on the patient. Symptoms include abdominal pain, problems with bowel movements, fever and fatigue, and can range from mild to severely debilitating. Genome-wide association studies have identified that CD is caused by both genetic and environmental factors (Baumgart et al., 2016). Behaviours such as smoking, poor diet and antibiotic consumption are more likely to trigger the onset of disease, but sex, age and ethnicity influence disease characteristics as well. These findings are especially important for Western countries such as Canada, where there is high incidence of CD, with the prevalence still increasing. (Ranjbar et al., 2015)

Treatment guidelines for CD begin with the assessment of disease severity. In patients with CD of any severity, treatment is recommended to begin with antibiotics to induce or maintain remission. For the treatment of mild to moderate CD, corticosteroids and aminosalicylates or other immunosuppressants are recommended next. Treatment for patients with moderate to severe CD or patients with high risk of poor prognosis begin with Anti-TNF biologics as their first-line therapy. Two anti-TNF medications that are the current standard of care are infliximab and adalimumab. TNF-α is an inflammatory molecule and its malfunctioning is associated with the pathogenesis of various autoimmune diseases (Parameswaran and Patial, 2011). These anti-TNF therapies work to block the pathways of TNF-α to reduce inflammation (Panaccione et al., 2019). As a second line therapy for this patient group, the current treatment guidelines recommend the prescription of non-anti-TNF biologics, vedolizumab and ustekinumab for the induction and maintenance of remission.

The objective of this paper is to identify patterns in prescribing habits of physicians treating CD in Ontario for the purposes of targeted pharmaceutical marketing strategies. Meta-analyses have identified numerous factors affecting physician prescribing habits including personal attributes such as their experience, specialty, industry associations and financial incentives, preferred information sources and influence from other key opinion leaders (KOLs). (Davari et al., 2018) For example, a notable pattern research has identified is a statistically significant relationship between a physician's industry associations and the administration of that company's medications (Davari et al., 2018). Furthermore, research has shown that male physicians receive more payments from industry, in turn leading them to prescribe more brand name medications than female physicians (Watane et al., 2021) In addition, prescribing habits are also influenced by patients' attributes, such as their personal and families' preferences and expectations, severity of illness and tolerance of the medications. Lastly, prescribing habits can also be affected by additional factors such as cost of the medication, cost of biosimilars, practice guidelines or logistical constraints.

This analysis was done on data collected by IQVIA between 2019-2021 on 303 gastroenterologists in Ontario. Variables included the full name of the physician, primary specialty, special interests, address, city, province, postal code, office type, primary language of office, gender, medical school graduation year, status, prescribed product, date and average RX volume; redundant features and features with too much missingness were excluded from analysis. Through the identification of certain patterns, this study aims to construct unique physician personas.

Summary of Data

Table 1, **Table 2,** and **Table 3** outline the categorical and continuous variables of interest for our analysis. This includes gender, office type, product, address and graduation year. These variables were chosen for further analysis due to all groups having an adequate sample size (n > 24). While address was not directly used, additional variables were created from it, as it was observed that most activity originated from urban areas, where there is likely a high concentration of teaching hospitals

and influential physicians (**Supplementary Figures 1-5**). Additional variables, publishing activity, research status (coauthor, supervisor or neither), involvement in medical conferences, author on CD treatment guidelines, KOL status and approximate age were created based on adapting original variables and literature searches. While some groups had a sample size below 30 resulting in the potential for misleading results, inferences could still be drawn. Variables in **Table 1,2 and 3** with high missingness of data or sample sizes below 5 were omitted from any analysis.

Physicians' publishing activity, research status and whether they have presented at conferences before was determined by their google scholar and other online pages. Next, the approximate ages of the physicians were calculated based on their year of graduation. These variables were created as personal opinions, interests and preferences influence prescribing habits. Lastly, this study assessed the influence of the physicians through checking if they are on the CD treatment guidelines. For physicians that were on treatment guidelines, worked in teaching hospitals and published two or more times from 2019 to 2021, they were determined as KOLs.

Methods

To identify different physician segments within the data set, a general exploratory analysis was performed. The primary focus of this analysis was to search for segment-specific trends in the volume of prescriptions written by physicians, and also in the proportions by which the physicians prescribed each drug. This study analyzed the prescribing patterns while splitting the data three ways; only first-line biologics, only second line biologics or all 4 biologics from the dataset

Physician personas were identified through the creation of plots that segmented physicians by either one or two variables which were included in the supplemented data set. Literature on differences in physician prescribing habits was consulted to aid in the selection of the segmenting variables for some visuals. To potentially elucidate less well-known physician segments, numerous groups were also created by selecting segmenting variables arbitrarily. For example, it is known that clinician decision-making can be impacted by their gender (Champagne-Langabeer and Hedges, 2011; Mishra et al., 2020), and thus numerous segments were created which included physician gender as a segmenting variable. However, a factor such as degree of publishing activity is not commonly cited in literature as a potential influencer of physician prescribing trends, but it was still included in our analysis as a variable which could segment the clinicians in the data set. Through this method, 3 physician segments were found to include a compelling trend in regard to overall prescription volume or proportion. In terms of what was considered a 'compelling trend', this group loosely defined it as a group of segmented physicians that showed prescribing volumes or proportions which clearly deviated (visually) from the other segments. Statistical tests were not run due to the small sample size of some groups.

After the identification of the 3 physician segments, 3 personas were subsequently created in an attempt to personify the identified segments and ultimately, provide potentially useful leads for a pharmaceutical company's marketing and sales team.

Identified Segments and Corresponding Personas

In addition to identifying potential physician segments as it relates to prescribing habits for CD, this study also made attempts to elucidate why these trends existed amongst the segmented physicians. It is impossible to clearly understand and identify the exact reasons which influence the observed trends, but through literature searches and inference, some factors could be identified which may be of use to a marketing or sales team.

Segment 1: Older, Female, Pediatric Gastroenterologist, "Kelly"

The first segment that was identified was related to older, female physicians who do not actively publish and work at children's hospitals. During our research, it was clear that this segment prescribes a much higher proportion of adalimumab for their patients relative to infliximab, while the opposite is true for their actively publishing counterparts (**Figure 1**). In an attempt to understand some factors which may contribute to these observed trends, literature on anti-TNF biologics for moderate-severe pediatric CD was consulted. Interestingly, studies have concluded that infliximab and adalimumab have comparable efficacy in both the youth and adult populations (Kestens et al., 2013; Narula et al., 2016). In addition to this, studies have found non-significant differences in patient response to therapy rate and clinical remission rate across the therapies (Kestens et al., 2013; Narula et al., 2016). Thus, it is not likely that exposure to more research about these biologics is the cause of the difference in prescribing habits. However, it is known that patient preference can also impact clinician decision making when it comes to these therapies, and so if there is some fundamental difference in the patient population treated by non-publishing physicians, this may potentially explain some of the trends observed regarding this segment.

Moreover, other factors which could offer some insight into this trend is physician age and gender. As can been seen in **Figure 2**, there appears to be a trend showing that older, female physicians are prescribing more adalimumab and less infliximab than their younger colleagues (male or female). The exact reason for this is unclear, but when we combine our findings from **Figure 1** and **Figure 2**, it appears that older, female pediatricians who do not publish tend to favour adalimumab much more than infliximab. Ultimately, we believe more research into this segment and their characteristics would be required.

Until then, we believe these findings can act as a useful preliminary signal for marketing teams to follow-up on. Our persona for this segment will be Kelly, an older pediatric gastroenterologist who focuses more on practice than research and prioritizes providing patient-centric care. Kelly enjoys her profession but she often finds herself sticking to therapies she trusts and knows well, even when an alternative confers similar efficacy and safety profiles. Since Kelly isn't an active follower of the newest research in her field, she tends to stick to treatment guideline recommendations and will consult key opinion leaders if she is faced with a particularly difficult case.

Segment 2 - Younger Gastroenterologist Working in an Office, "Cathy"

For the next segment that was identified, it was clear that female physicians working in offices were the only group to prescribe more vedolizumab than ustekinumab (proportionally) when segmenting the physician population by office type and gender (**Figure 3**). Males working in offices, and also males and females working in clinics or hospital offices all prescribed more ustekinumab than vedolizumab (**Figure 3**). This suggests the observed trend could be attributable to both the factors of office type and gender. This, for example, could be related to the type of patient referred to these offices and/or gender influence on prescribing habits. Since the pharmacokinetic and pharmacodynamic properties of these second line therapies differ, some patients may be more responsive to one therapy over another; vedolizumab is preferable for patients who struggle with other comorbidities, such as hepatitis B or C (Shim et al., 2018). It could be possible that for an unclear reason, a greater number of patients who are better suited for vedolizumab are being treated by this physician segment. Additionally, research that considered gender differences in clinician prescribing practices among older adults found that female physicians were more likely to take a careful and conservative approach to prescribing for their patients (Mishra et al., 2020). To make an inference from this finding, it may be possible that patients experiencing more comorbidities fitting the treatment of vedolizumab prefer a physician who is more careful and patient-centric. This may be the cause of the high prescription of female physicians prescribing vedolizumab.

Additionally, our group determined that physician age and gender corresponded with a clear trend regarding second line therapy prescriptions. Specifically, and as can be seen in **Figure 4**, younger female physicians are prescribing much more Vedolizumab relative to their older colleagues. This could be related to the methods by which physicians are trained and the medications they are most commonly exposed to, but nonetheless this trend could function as a potential signal for marketing teams to follow-up on.

Our persona for this category will be Cathy, a younger gastroenterologist working in an office that is surrounded by a local population which has a high prevalence of disease (e.g. obesity). Many of Cathy's patients have existing comorbidities which accompany their CD. Due to this, and the fact that Cathy was predominantly exposed to vedolizumab during her gastroenterology training, Cathy often finds herself prescribing vedolizumab for a second line therapy rather than ustekinumab.

Segment 3 - Young Pediatric Gastroenterologist, "Polly"

Our third identified segment consisted of younger physicians who worked at youth hospitals. This segment displayed a clear increase in the proportion of their prescriptions being for infliximab when considering all 4 CD-specific drugs in our data set (**Figure 5**). Due to this increase in infliximab prescriptions, an expected decreasing trend in adalimumab prescriptions for these young doctors was also observed. This trend was quite interesting considering that doctors of any age who do not work at children's hospitals seem to prescribe a relatively constant proportion of infliximab and adalimumab (**Figure 5**). This suggests that the trend which defined this segment could be attributable to both the physician's age, and the different needs of pediatric patients relative to adults.

As mentioned, both infliximab and adalimumab have proven to be similarly efficacious (Narula et al., 2016). However, other factors are considered when clinicians decide which anti-TNF therapy to prescribe, and it is possible that these factors could explain why younger doctors treating youth are prescribing more infliximab. For example, adalimumab is required to be taken every two weeks whereas Infliximab is only required to be taken every 8 weeks after the first three doses (at 0, 2 and 6 weeks) (Abbvie, 2022; Janssen, 2022). Thus, it is possible that adalimumab could increase caregiver burden as parents would be required to take their children to the hospital every two weeks as opposed to 8. These subtle differences and patient preferences could explain some of the observed trends for this segment. Moreover, since this trend is emphasized in younger doctors (those who graduate later), it is possible that younger doctors are exposed to more infliximab during their training and are thus more likely to prescribe it to their patients. This group believes research into gastroenterologist training could provide some useful insights as to why younger physicians seem to prefer infliximab over adalimumab.

Our persona for this category will be Polly, a pediatrician working in a busy teaching hospital. Some of the parents at her clinic struggle to take time off from their responsibilities, and prefer to minimize the number of visits. This may be due to any number of factors, including socioeconomic struggles, time constraints, or restrictive disabilities. Additionally, it can be mentally and physically strenuous on children to regularly be subject to IV and subcutaneous injections; it is not uncommon for parents and practitioners to be faced with a frightened child. Polly deals with young patients suffering from Crohn's disease. In order to avoid a more frequent injection schedule, she will opt to prescribe infliximab over adalimumab for the younger patient.

Limitations

There are several limitations to the analysis of this data. These limitations include factors relating to the physicians' personal attributes, the patients' attributes and morbidities, and financial and regulatory factors of each treatment.

In certain segments, the sample size was extremely small and therefore conclusions drawn could be considered questionable. For example, research has identified physicians' personal interests and specialties as an influencing factor. In this dataset, there were 15 interests that only had 1 physician and 247 of the 303 physicians answered "NULL" to that question. Due to the high missingness of data in that variable, it was excluded from all analyses.

Another limitation is the lack of knowledge about all the personal factors influencing the physicians' prescribing decisions. This data set is limited to the analysis of the physicians' research history, type of office, specialty and approximate industry experience but lacks detailed information about their industry associations and financial incentives. For example, there are numerous infliximab and adalimumab products. The pricing and reimbursement of each product would also affect the physicians' choices. Adding onto this, physicians may have different financial incentives due to their industry connections. Due to this, while segments may be identified based on available data, prescribing habits could be influenced by factors completely unrelated to drug efficacy in the patient.

Conclusion

Despite limitations with the dataset, external sources of data were imported to analyze and segment gastroenterologists in Ontario. Three personas were constructed. Kelly represented older, female, pediatric gastroenterologists who rarely stray from recommendations in treatment guidelines and usually stick to medications they are comfortable with. Cathy represents younger gastroenterologists working in offices whose patients often present with comorbidities in addition to their CD. Finally, Polly represents physicians who opt to prescribe drugs that better match the desired convenience of her patients.

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Appendix

Table 1. Categorical variables of interest of the 303 physicians

Variable	Count (percent)
Gender	
Male	220 (72.61%)
Female	83 (27.39%)
Office Type	
Hospital/Office	104 (34.32%)
Office	120 (39.60%)
Clinic	76 (25.08%)
Other	3 (0.99%)
Language	
English	301 (99.34%)
French	2 (0.66%)
Product*	
Adalimumab	82,901 (25.89%)
Golimumab	7,755 (2.42%)
Infliximab	138,063 (43.13%)
Ustekinumab	57,572 (17.98%)
Vedolizumab	33,852 (10.57%)
Interest	
Anesthesia	1 (0.33%)
Cardiology	2 (0.66%)
Clinician Investigator	5 (1.65%)
Critical Care Medicine	1 (0.33%)
Emergency Medicine	1 (0.33%)
Endocrinology & Metabolism	1 (0.33%)
Family Medicine	4 (1.32%)
General Surgery	1 (0.33%)
Genetics	1 (0.33%)
Hematology	1 (0.33%)
Hepatology	11 (3.63%)
Infectious Diseases	1 (0.33%)
Internal Medicine	2 (0.66%)
Microbiology	1 (0.33%)
No Primary Interest	247 (81.52%)
Nuclear Medicine	1 (0.33%)
Nutrition	3 (0.99%)
Oncology	1 (0.33%)
Orthopedic Surgery	1 (0.33%)

Palliative Care	1 (0.33%)
Pediatric Gastroenterology	14 (4.62%)
Pharmacology & Toxicology	1 (0.33%)
Psychiatry	1 (0.33%)
Works at Teaching Hospital	
Yes	53 (17.50%)
No	250 (82.51%)
Age Treated	
Youth	24 (7.92%)
Mixed	279 (92.10%)

*Proportions and counts between drug categoricals determined by aggregating total Rx. volume

Table 2. Continuous variables for the 303 physicians

Variable	Median	Mean (SD)	[Min, Max]	IQR
Graduation Year	2000	1998 (10.57)	[1965, 2015]	(1992, 2006)
Average Rx. Volume	9.00	20.76 (34.31)	[1.00, 294.00]	(3.00, 23.00)
First Line Therapies (Proportions)				
Adalimumab	0.35	0.37 (0.215)	[0, 1]	(0.238, 0.480)
Infliximab	0.65	0.63 (0.21)	[0, 1]	(0.520, 0.762)
Second Line Therapies (Proportions)				
Vedolizumab	0.41	0.45 (0.215)	[0, 1]	(0.417, 0.583)
Ustekinumab	0.59	0.55 (0.21)	[0, 1]	(0.591, 0.722)

Table 3. CATEGORICAL VARIABLES FOR 175 PHYSICIANS

| Variable	Count (percent)
Published Twice Since 2019	
Yes	44 (25.00%)
No	132 (75.00%)
Coauthor, Supervisor, or Neither	
Coauthor	74 (42.05%)
Supervisor	24 (13.64%)
Neither	77 (43.75%)
Author on CD Treatment Guidelines	
Yes	8 (4.55%)
No	168 (95.45%)
Presented at Conference	
Yes	14 (7.95%)
No	162 (92.05%)
KOL	
Yes	8 (4.55%)
No	168 (95.45%)
Approximate Age	
30-40	6 (3.41%)
41-50	73 (41.48%)
51-60	45 (25.60%)
61-70	36 (20.45%)
71-80	15 (8.52%)
8 -90	1 (0.57%)
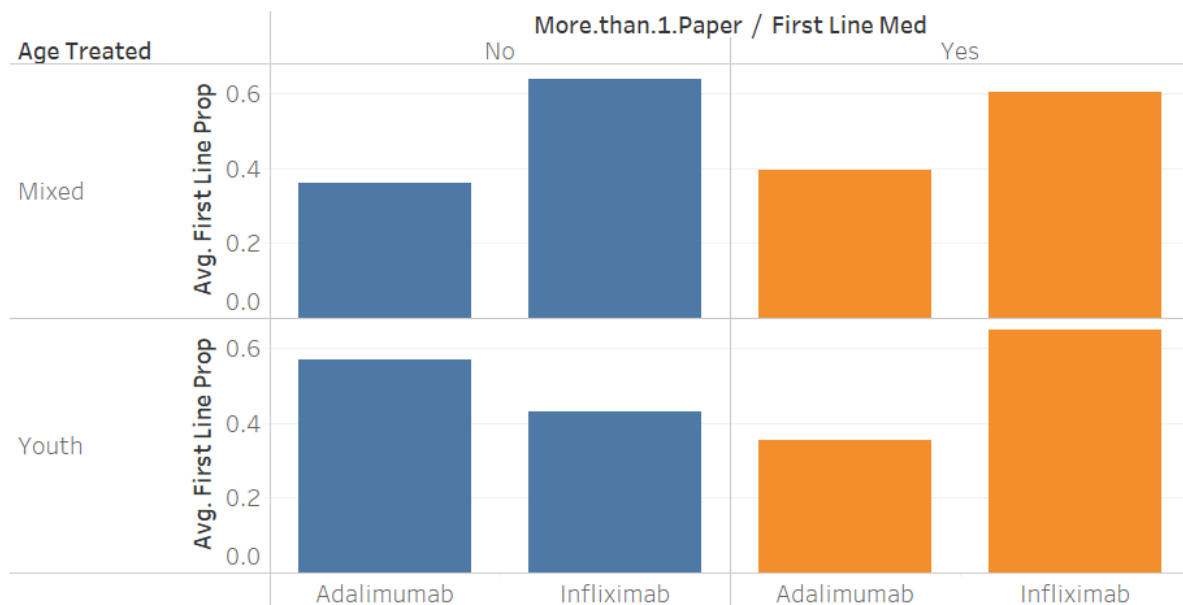
Figure 1. Barplot describing the proportion of prescriptions of first line therapies (adalimumab and infliximab) for moderate-severe Crohn's disease when segmenting physicians by the age of the patients treated and by whether the physician has published twice or more since 2019.
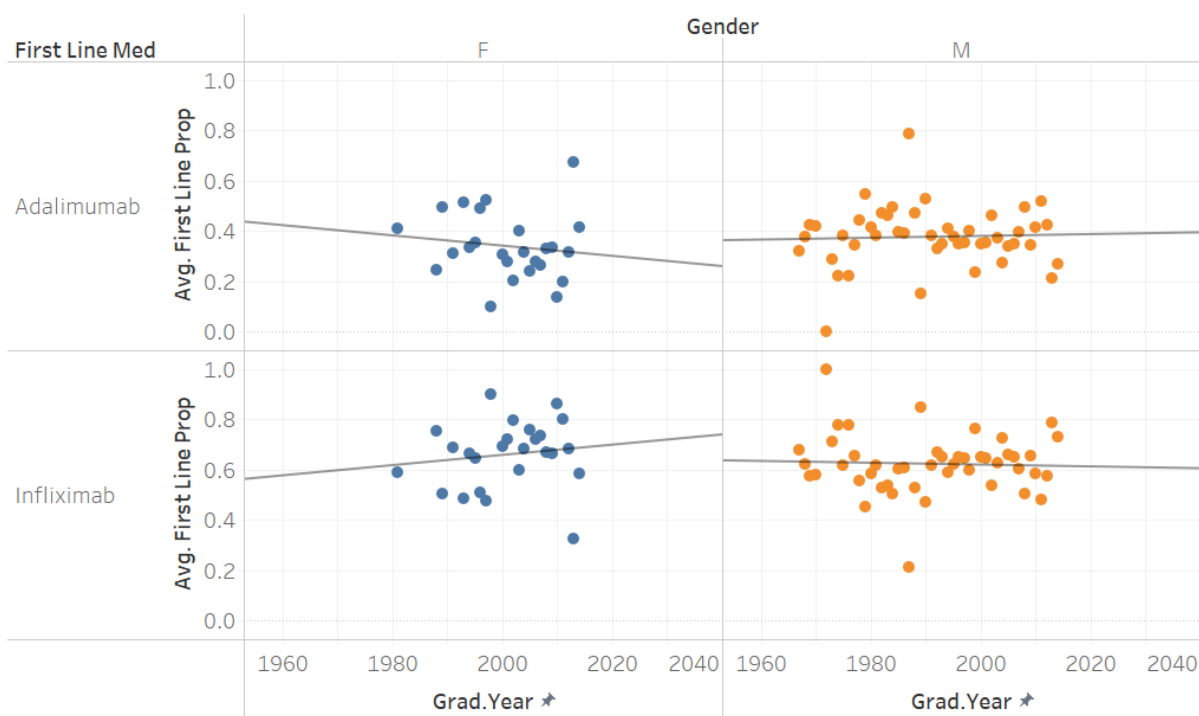
Figure 2. Trend describing the proportion of prescriptions of first line therapies (adalimumab and infliximab) for moderate-severe Crohn's disease when segmenting physicians by physician gender and by graduation year.
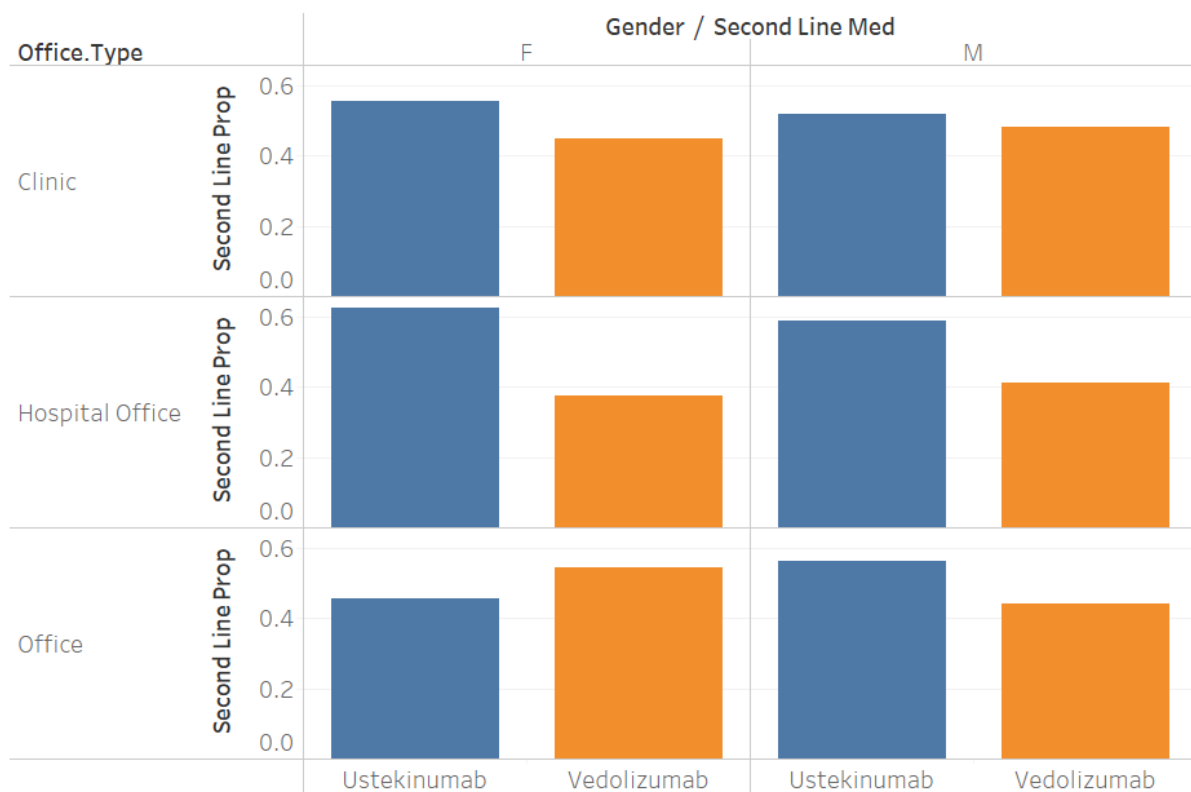
Figure 3. Barplot describing the proportion of prescriptions of second line therapies (vedolizumab and ustekinumab) for moderate-severe Crohn's disease when segmenting physicians by gender and by office type.
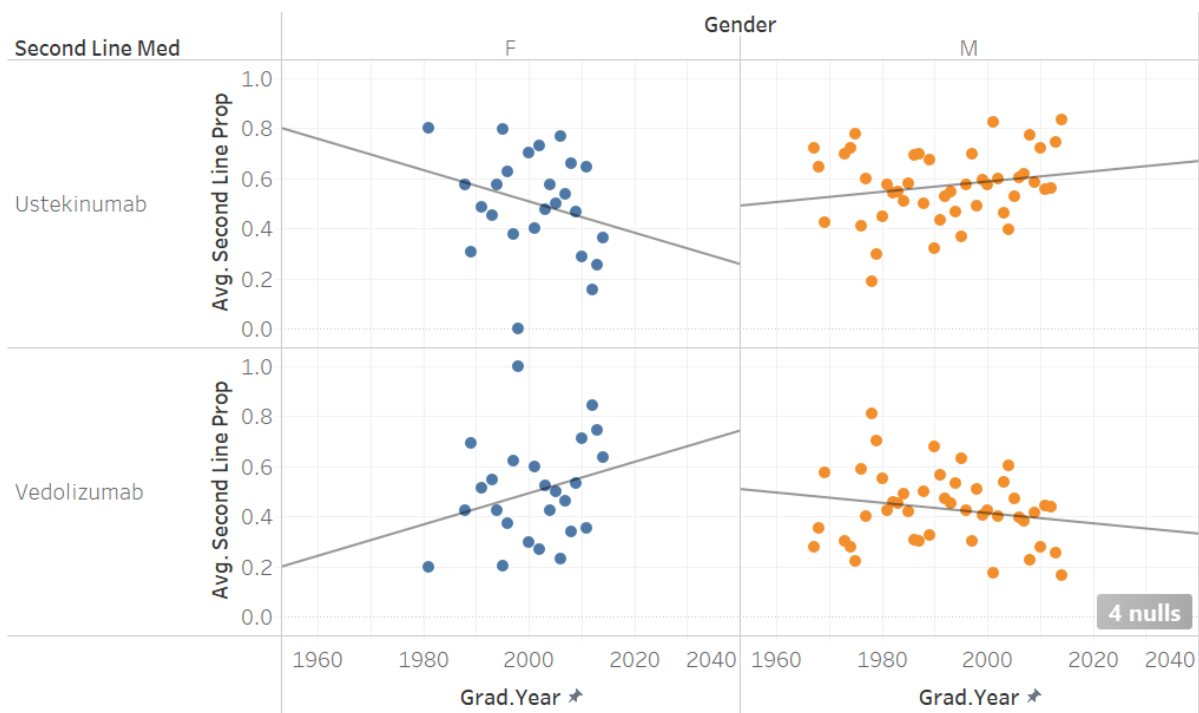
Figure 4. Trend describing the proportion of prescriptions of second line therapies (Vedolizumab and Ustekinumab) for moderate-severe Crohn's disease when segmenting physicians by physician gender and by graduation year.
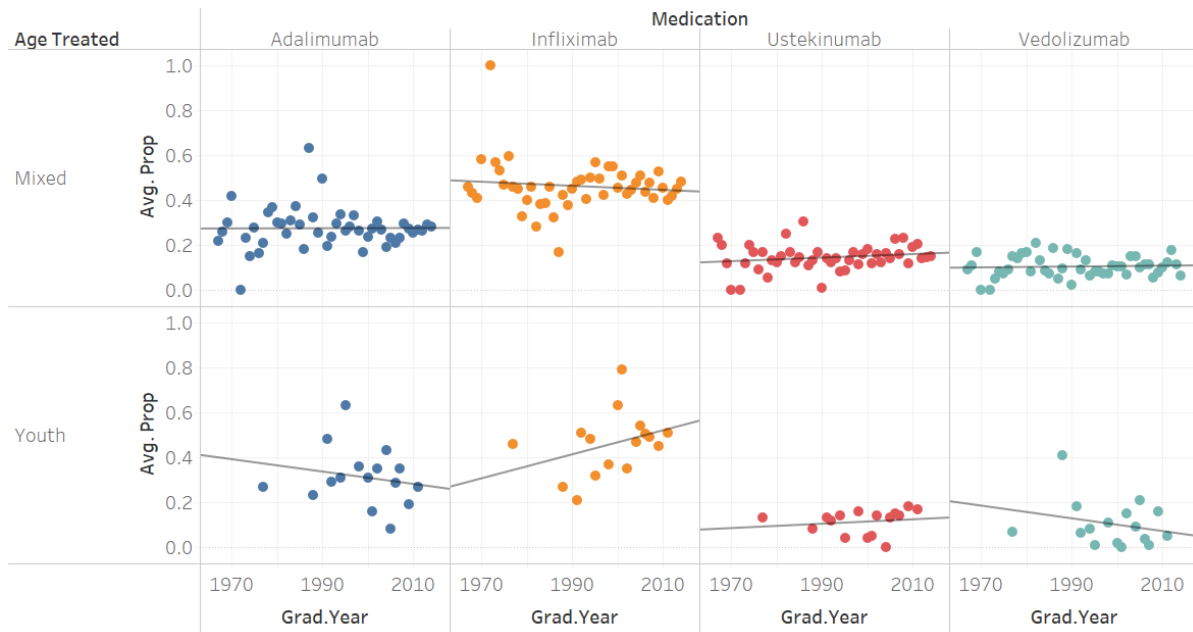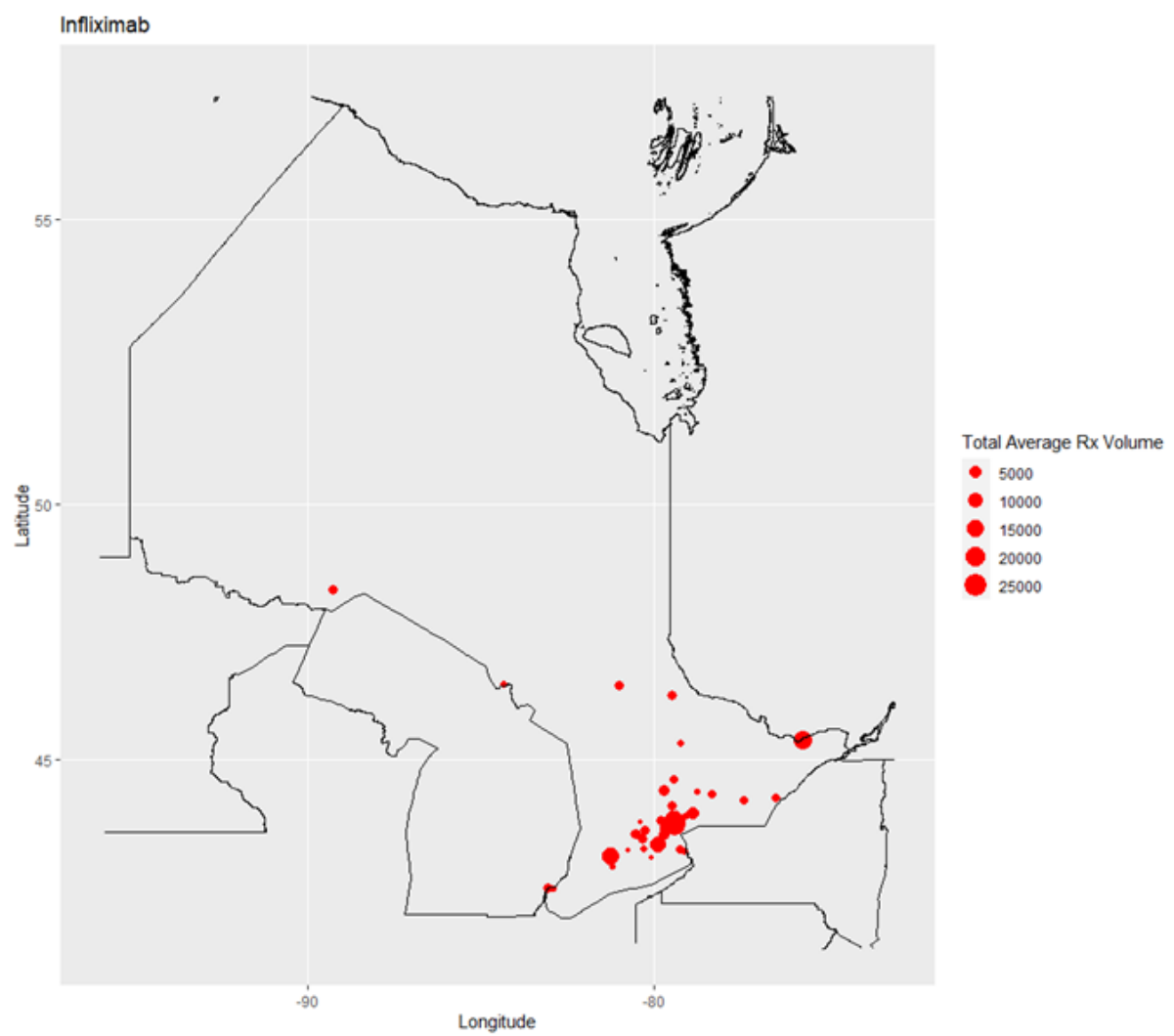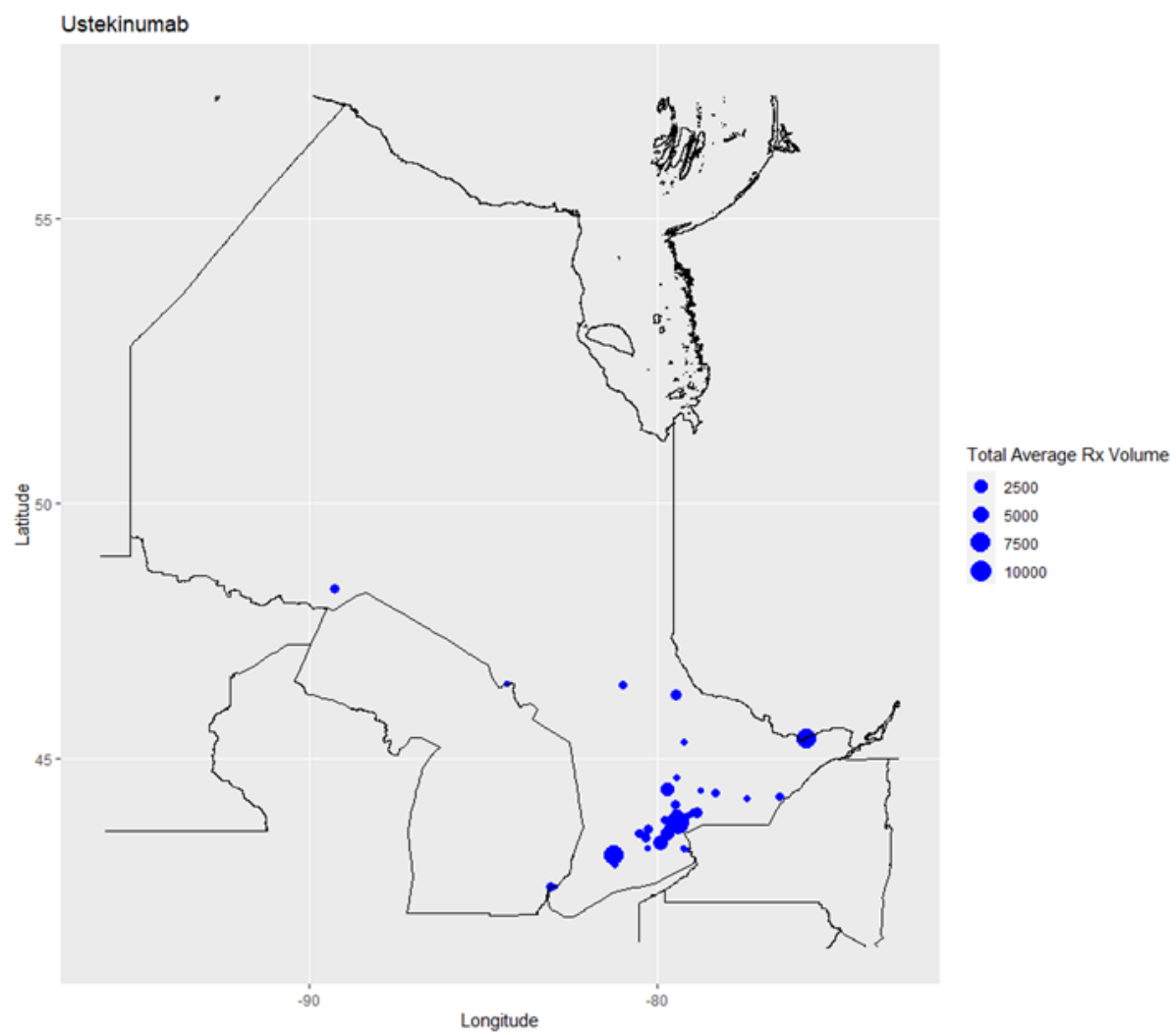

Figure 5. Barplot describing the proportion of prescriptions for all moderate-severe Crohn's disease therapies in the data set when segmenting physicians by age of patient treated and graduation year
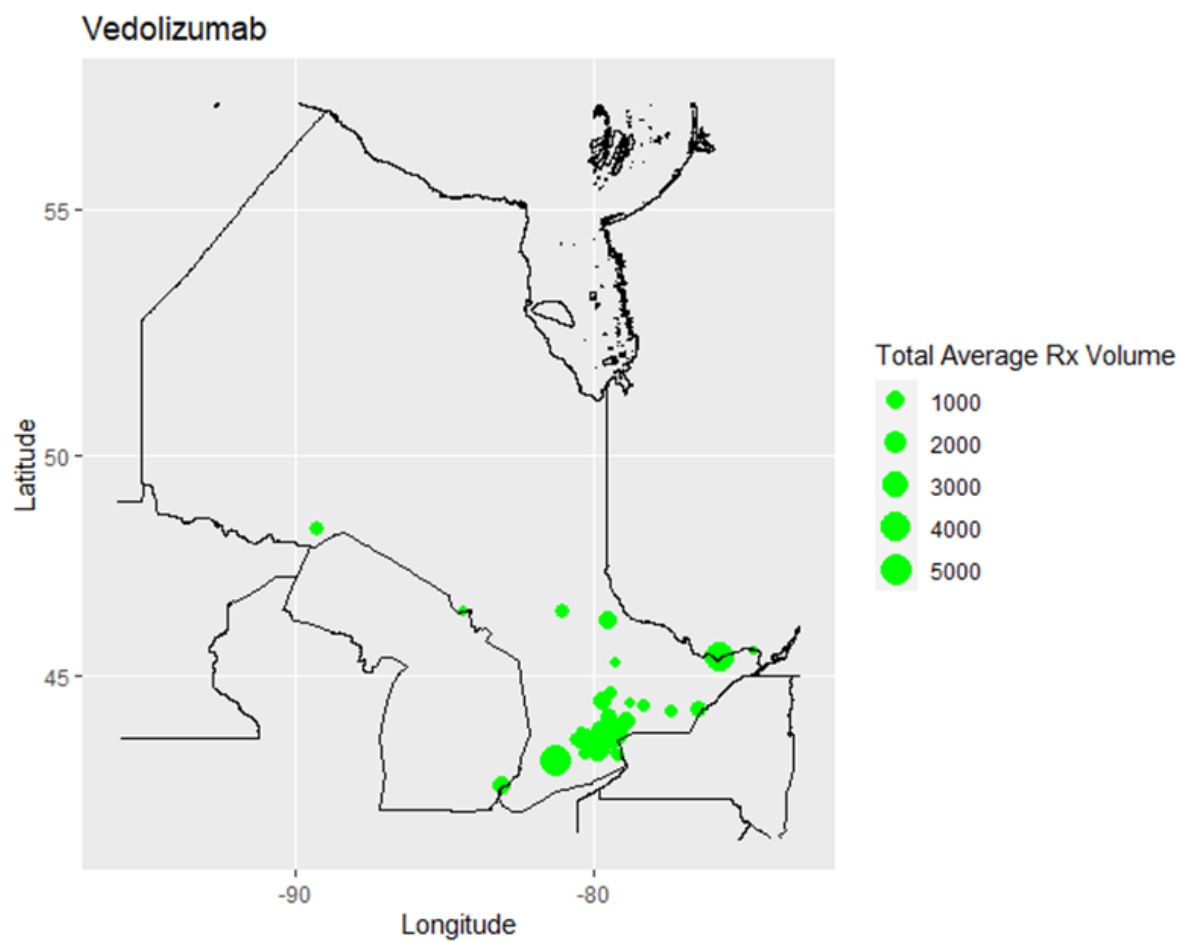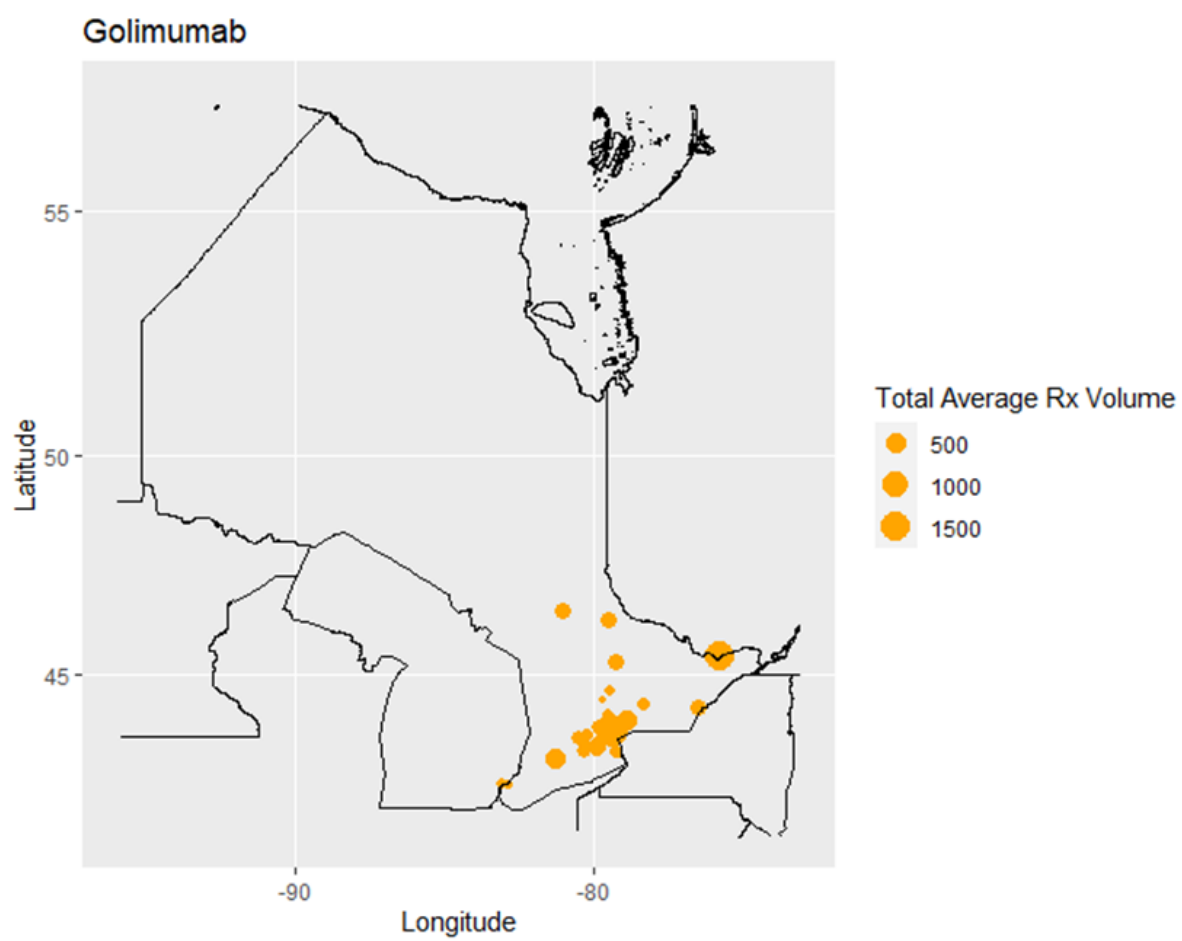
Supplementary Figures

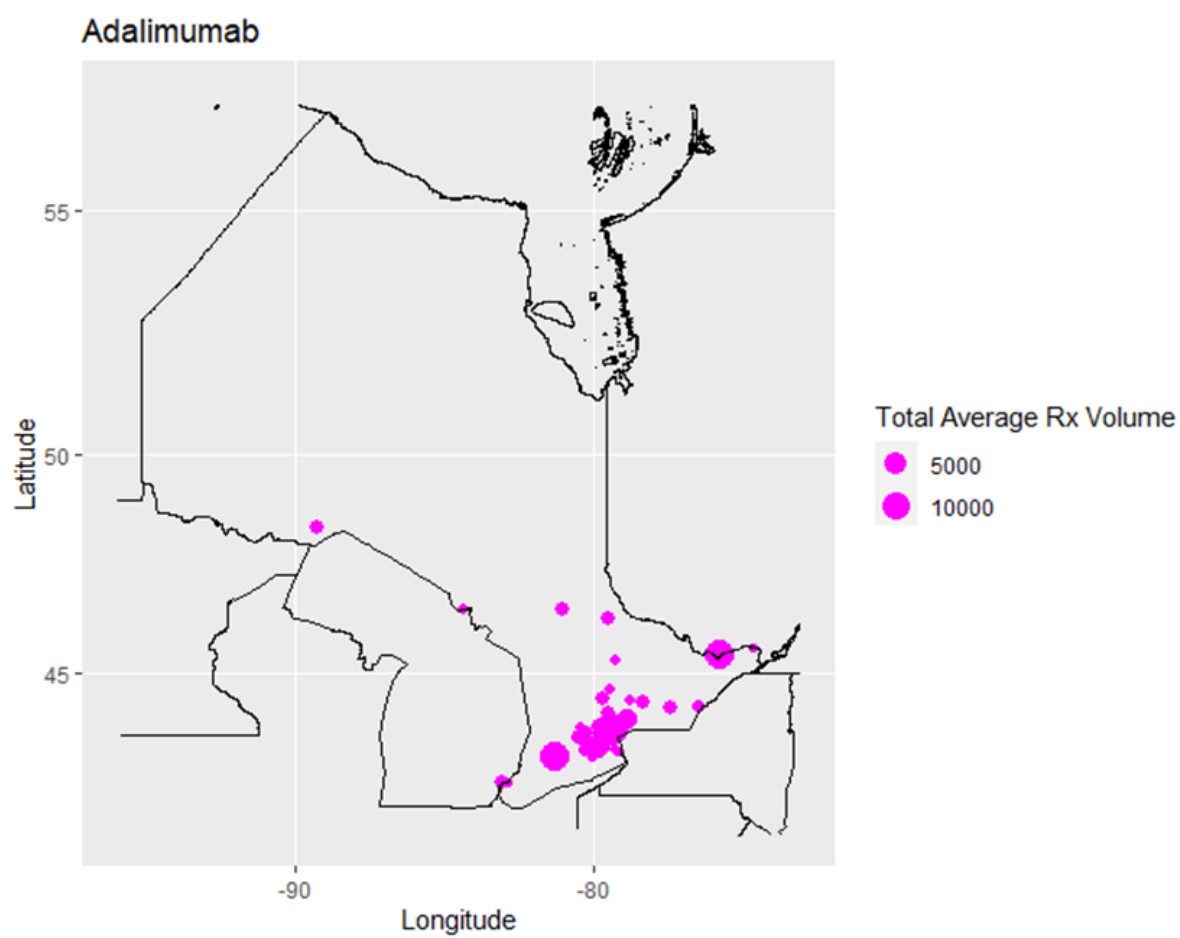**Supplementary Figure 1**. Regional distribution of Infliximab.

Supplementary Figure 2. Regional distribution of Ustekinumab.

Supplementary Figure 3. Regional distribution of Infliximab.

Supplementary Figure 4. Regional distribution of Golimumab.

Adalimumab

Total Average Rx Volume
- 5000
- 10000

Supplementary Figure 5. Regional distribution of Infliximab.

Table Outlining Work Done By Each Group Member

Andrew	Vivian	Kevin
Data cleaning and analysis	Literature research on drugs and Crohn's disease, treatment guidelines, physician prescribing habits and segmentation	Data cleaning and analysis
Figures 1-5	Intro section, summary of data, limitations section	Personas (last paragraph of each segment)
Methods section, segment/persona section	Editing and proofreading	Tables 1 and 2
Tables 2 and 3	Citations	Conclusion
Citations		Supplementary figures 1-5
Editing and proofreading		Summary of Data