Using electronic health records in analysing medication adherence in southern New Zealand patients with inflammatory bowel diseases

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ABSTRACT

AIMS: Electronic health records (EHRs) are widely used in medication adherence (MA) assessment. Poor adherence in patients with inflammatory bowel diseases (IBD) can lead to worse disease outcomes and increased health costs. This study explores the suitability of southern New Zealand EHRs for estimating adherence, and the relationship between adherence and corticosteroid dispensings (indicating negative disease outcomes).

METHODS: Medication dispensing EHR data of former Southern District Health Board IBD patients were analysed to estimate 3-year adherence, using daily polypharmacy possession ratio. The correlation with the number of corticosteroid dispensings was investigated.

RESULTS: Of 248/1,290 (19%) consenting patients, only 108/248 (44%) had sufficient data available (46%/54% Crohn's disease/ulcerative colitis; 57% female; 89.8%/0.9% NZ European/Māori; mean 5.1 corticosteroid dispensings).

Mean adherence was 83.2% (95% confidence interval [CI] 80.0–86.4; standard deviation [SD]:16.7), with 69% of patients having MA ≥80% (good adherence). Median adherence was 13% higher for males versus females (96% vs 83%; p=0.0001). There was no correlation between adherence and the number of corticosteroid dispensings (Pearson's r=0.11; p>0.05). These findings should be considered with caution as the data were not obtained from all pharmacies and the quantum/nature of missing data is unknown.

CONCLUSIONS: The patients' adherence seems high, with no correlation with corticosteroid dispensings demonstrated. Useful EHR data are available but need optimisation for adherence assessments.

Inflammatory bowel diseases (IBD) are chronic diseases consisting of Crohn's disease (CD), ulcerative colitis (UC) and IBD-unclassified (IBD-U) and are typified by intestinal inflammation, and often by extra-intestinal manifestations.[1–4] A life-long medication regimen is central to IBD therapy alongside dietary/surgical/other interventions, besides ongoing monitoring for disease progression and complications.[1–4] Medication adherence (MA) is defined as "*the process by which patients take their medication as prescribed*" and comprises initiation, implementation and persistence/discontinuation (starting, continuing and ending a regimen as recommended).[5] Poor adherence is associated with negative disease outcomes in IBD including higher morbidity and mortality, and disability and health costs, alongside flare-ups and complications requiring therapy escalation (involving surgery and/or recurring corticosteroid use).[6] Adherence levels of patients with IBD have previously been reported as 31.1%[7] and 22.9%–77%[6,8,9] in southern Aotearoa New Zealand and abroad.

With an estimated yearly growth rate of 5.6%, IBD burden in Aotearoa New Zealand is poised to double by 2028 (to over 40,000) from 20,792 patients in 2016, with combined direct and indirect annual costs of NZ$245 million.[2] In Aotearoa New Zealand, access to advanced IBD therapy is restricted as several medications (e.g., biologics/Janus kinase inhibitors) available in other countries are not publicly funded.[10] Consequently, ensuring sufficient adherence is important for helping Aotearoa New Zealand IBD patients derive maximum benefits from available medications. Also, monitoring adherence can identify patients with low adherence levels for targeted interventions. A literature search identified only one study that has assessed adherence in Aotearoa New Zealand (Southern District Health Board [SDHB]) patients with IBD;[7] using self-reported survey tools, this study found that a third of patients had poor adherence.

Electronic health records (EHRs) including claims databases, commonly collected primary/secondary health databases, disease registries and others[11] often contain readily available, detailed,

cross-linked and population-wide data and are widely employed in assessing adherence[12,13] as they could provide more objective evaluations of adherence than self-reported measures. There are several publicly/privately owned EHRs used in different parts of the Aotearoa New Zealand health system, with some holding directly input data and others collating data from other EHRs. Individual patients' data are linked via a unique National Health Index (NHI) code across the databases, which include prescription, dispensing, hospitalisation and clinical information, among others. An NHI number is allocated to an individual at birth (or at first time accessing healthcare). This number is used at every healthcare event that allows comprehensive healthcare utilisation to be possible.

While nationwide databases exist, including hospitalisation data (both events and discharge information) and medication dispensing (claims) data,[14,15] the development of subscription-based EHRs that pool centrally held data with primary care subscribers (i.e., general practices and pharmacies) allow subscribers the ability to see a patient's journey more holistically and reduces some of the problems that occur with transition of care. The utilisation of shared EHRs could be useful in assessing patients' adherence. Therefore, the objective of this study was to determine whether the available subscription-based EHRs used by primary care practitioners in southern Aotearoa New Zealand provided suitable and sufficient information for adherence research by conducting the steps of calculating the adherence levels of local IBD patients and investigating the association between adherence and corticosteroid prescriptions (a proxy for negative health outcomes as corticosteroids are often used for managing IBD flare-ups[1,3]).

Methods

Study region

Until 30 June 2022, the SDHB was the regional health authority for the Otago and Southland Regions of Aotearoa New Zealand. Now superseded by the national Te Whatu Ora – Health New Zealand service, the SDHB patients still reside and/or receive healthcare within these regions, which are the settings for this study.

Study design

This was a retrospective longitudinal population-wide study, utilising dispensing data of IBD patients within the study region from 1 January 2015 to 31 December 2019, curated from a patient management database (PMD; detailed below) and used to calculate adherence levels. The adherence levels were calculated using a daily polypharmacy possession ratio[13] (DPPR; details provided below) for the first 3 years from the earliest dispensing (*DispDx*) of select chronic ongoing medications of interest for patients with at least 3 years of dispensings. The association between DPPR and the number of corticosteroid dispensings was also evaluated.

Ethics approval

Ethics approval was granted by the University of Otago Human Ethics Committee (Health) (H21/171).

Participant recruitment

The research population comprises patients (≥18yrs) with IBD residing in the area of the former SDHB. Patients hospitalised in the SDHB with an IBD International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)[16] code between 1 January 2015 and 31 December 2019 (see Appendix Table 1) were identified from SDHB coding records. The following three patient management databases used in the SDHB, EpiSoft (Episoft Australia),[17] Crohn's and Colitis Care (CCCare) (Crohn's Colitis Cure Australia)[18] and Health Connect South (HCS) (Orion Health New Zealand),[19] were used *solely* to *confirm* the IBD diagnoses and addresses of the identified patients. These three databases are used in the SDHB and contain patients' demographic data alongside disease information, clinic appointments, care plans, clinical reports/letters and more. Patients with a confirmed diagnosis of IBD were invited to participate (and provide informed consent) via post and email.

Data curation

The pharmacy dispensing data for specific medications of interest (chronic ongoing IBD medicines, namely: thiopurines—azathioprine and 6-mercaptopurine (6-MP); methotrexate; 5-aminosalicylic acid therapeutics—sulfasalazine and mesalazine, and adalimumab; alongside corticosteroids—budesonide, prednisone and hydrocortisone acetate) were curated from the PMD for consenting patients. The PMD is owned by a public-private partnership. The PMD contains health information, by NHI, for patients within the South Island of Aotearoa New Zealand, including on medications dispensed and

prescribed at community pharmacies and healthcare providers, e.g., general practices (GPs), who subscribe to the network.

The following data were extracted and curated manually per patient from the PMD: medications dispensed (name and formulation); administration instructions (wherefrom the dose, frequency and daily dose were derived); quantity dispensed and the date of dispensing. The days' supply (DS) is the number of days with the daily dose available to the patient; DS was calculated as the quantity dispensed/daily dose. These variables were used to calculate MA to chronic IBD medications, chosen because they are self-administered, are commonly used for IBD therapy in Aotearoa New Zealand and are intended for continuous long-term use. Similar data were curated on the number of concurrent corticosteroid dispensings as, although not meant for consistent use, they are often used for managing IBD flare-ups.[1,3]

The consolidated dataset compiled contained patients' dispensing data derived from the PMD and their demographic data from HCS.

Data analysis

DPPR is used to calculate adherence for multiple-medicine regimens, alongside single-medicine regimens, and has been used in calculating adherence via secondary databases e.g., EHRs.[12,13,20] This equation shows the calculation:

$$DPPR = \frac{\sum(medication\ availability\ score\ per\ interval \times days\ per\ interval)}{observation\ window}$$

The numerator for the DPPR equation is the cumulative medication availability score per interval multiplied by the days per interval, and the denominator is the days in the observation window (OW). When a patient had an overlapping DS of the same medication, which occurs when refills are collected before current DS is exhausted, the second DS is considered to have started at the end of the first DS. A gap between two consecutive DS for a medication greater than 180 days was taken to indicate the discontinuation of that medicine. The "CMA_polypharmacy" function in the AdhereR package version 0.8.1[21] in R was used in computing the DPPR. The Appendix (Appendix Figure 1 and associated text) shows an illustration of the DPPR calculation and more details of the data analysis. Appendix Table 1 shows more detail of the ICD-10 codes and medications used as part of the analysis.

Participants are described by counts and proportions expressed as percentages. The association between DPPR scores and sex, IBD type and age group used a Wilcoxon test. The association between DPPR scores and corticosteroid dispensing was summarised by a product moment correlation coefficient. Appendix Table 2 shows more detail of the analyses conducted.

Results

Study sample

The flow of participants through the study is shown in Figure 1.

There were 108 participants who were included in the final analysis of the DPPR. This is 8% of the 1,290 IBD patients who were invited to participate in the study, although 31.2% (402/1,290) patients initially responded to the invitations, and 19% (248/1,290) consented to the study (Figure 1).

The demographics (Table 1) show that 46% (n=50) of the study population had CD and 54% (n=58) had UC, 43% (n=46) were male, 89.8% (n=97) were NZ European, 4.6% (n=5) were Other European and 0.9% (n=1) were Māori, while the median (interquartile range [IQR]) age at first dispensing was 52 years (39–62yrs; Table 1).

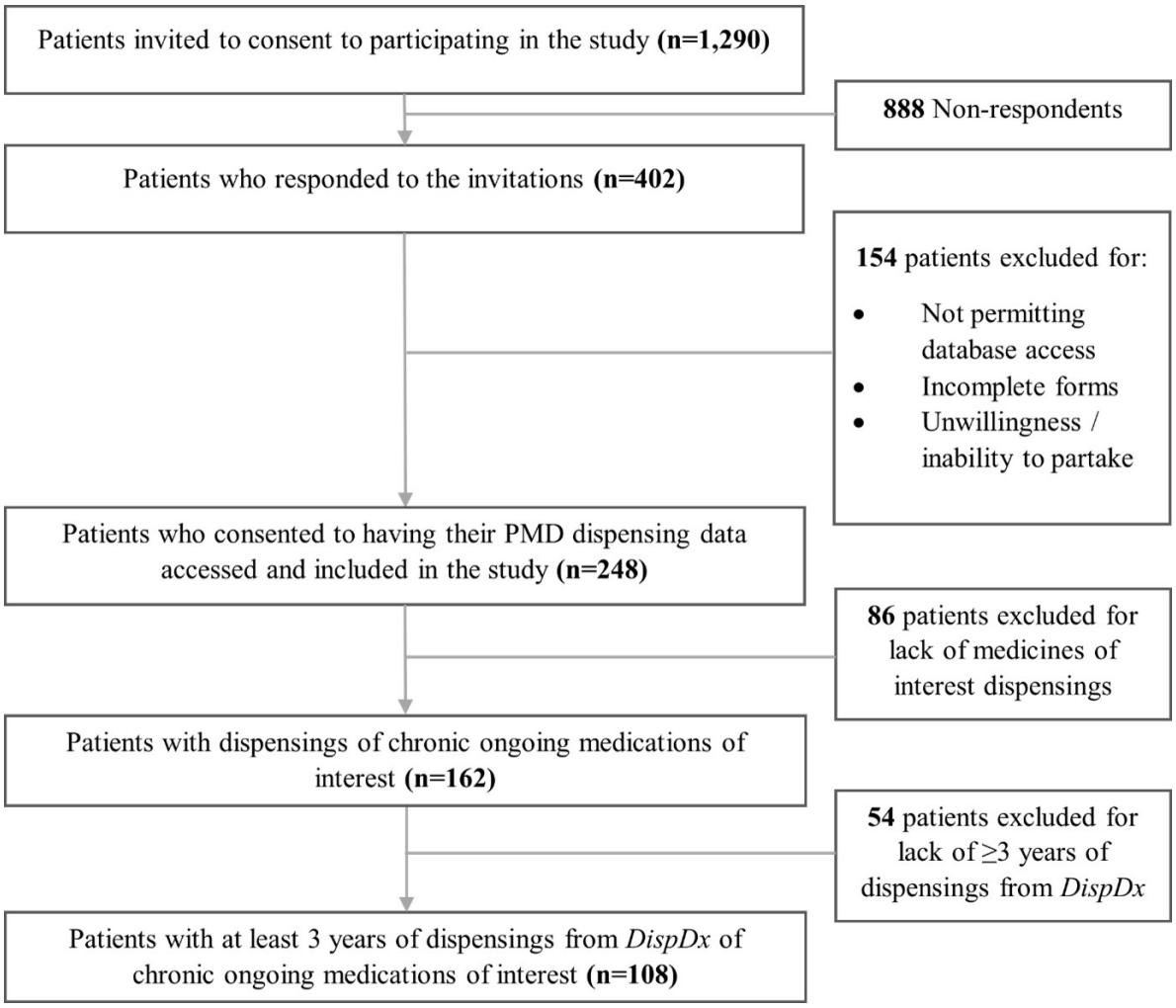
Each patient had mean (standard deviation [SD]) 35.5 (28.3) chronic medicine dispensings. Forty-six percent (n=50) of patients had corticosteroid dispensings; of these, each had mean 5.1 (7.1) corticosteroid dispensings. Regarding chronic medication type, 18.5% (n=20) of patients used three to four, 36.1% (n=39) of patients used two and 45.4% (n=49) of patients used one during the period. Mesalazine, mercaptopurine, methotrexate, sulfasalazine, adalimumab and azathioprine were used by 70% (n=76), 11% (n=12), 7% (n=8), 5% (n=5), 16% (n=17) and 37% (n=40) of patients, respectively (Table 1).

Indicative DPPR value and relationship with clinical outcomes

The mean DPPR (%) estimate for the study population was 83.2% (95% confidence interval [CI] 80.0–86.4; SD 16.7), with 69% of patients having a DPPR at or above the ≥80% threshold of good adherence.[6] The median DPPR (%) scores were 13% higher for males versus females (96% vs 83%; p=0.0001), 1% higher for UC versus CD (88% vs 87%; p=0.2307) and 6% higher for ≥65 year olds versus those <65 years (92% vs 86%; p=0.3736).

There was no statistically significant

Figure 1: Patient flow diagram.



Abbreviations: DispDx = date of earliest dispensing of a chronic medication of interest; PMD = patient management database.

Table 1: Characteristics of patients and dispensing events in the study population dataset.

Patient characteristics	**n/108 (%)**		
Total patients	108		
Patients with steroid dispensings	50 (46)		
Patients per IBD type			
CD	50 (46)		
UC	58 (54)		
Sex			
Female	62 (57)		
Male	46 (43)		
Prioritised ethnicity			
NZ European	97 (89.8)		
Other European	5 (4.6)		
NZ Māori	1 (0.9)		
Others	5 (4.6)		
Number of chronic medications			
3–4	20 (18.5)		
2	39 (36.1)		
1	49 (45.4)		
Medication			
Mesalazine	76 (70)		
Azathioprine	40 (37)		
Adalimumab	17 (16)		
Mercaptopurine	12 (11)		
Methotrexate	8 (7)		
Sulfasalazine	5 (5)		
	Mean (SD)	**Median (IQR)**	**Min–Max**
Age at first dispensing	50.3 (16.2)	52 (38.5–62)	14–81
Chronic medicine dispensings per patient	35.5 (28.3)	34 (19–39)	7–218
Corticosteroid dispensings per patient*	5.1 (7.1)	2 (1.25–5.75)	1–42

CD = Crohn's disease; UC = ulcerative colitis; n = number of patients.
* For the 50 patients with corticosteroid dispensings.

(Pearson's r= 0.11; p>0.05) correlation or association between DPPR and the number of corticosteroid dispensings per patient in the concurrent period (see Appendix Table 2).

Discussion

This study investigated the availability of EHRs for computing long-term MA of IBD patients residing in the area of the former SDHB in Aotearoa New Zealand. We excluded 35% (n=86/248) of patients' data as they had no dispensings of our chronic medications of interest recorded (Figure 1); data collation challenges would have contributed to this. The PMD used is a patient management system with data collected recording patients' health histories to aid clinical decision making, but these were not intended for adherence assessments. Hence, we suggest ways by which it might be improved for evaluating adherence.

Accurate adherence assessment requires EHRs that record all relevant details (including time/quantity/medicine type etc.) of patients' medications for all dispensings and prescriptions.[22] Currently, the dispensing and prescription data is automatically pooled from community pharmacy and healthcare provider/prescriber (e.g., GPs) systems respectively, for (nearly) all such vendors in the South Island of Aotearoa New Zealand, including the former SDHB region. This automatically excludes dispensings from other Aotearoa New Zealand regions, highlighting the need for a nation-wide database. All vendors need to be connected to the database network with newly opened vendors onboarded timeously. Dispensing and prescription data from public hospitals or hospital pharmacies are not collected, with limited contributions from private sector healthcare providers. Furthermore, the paucity of prescription data precluded the matching of prescriptions with dispensings (to highlight missing dispensings) and the assessment of *initiation* in adherence (primary non-adherence, i.e., a patient's failure to begin a medication regimen).[5] Linking prescriptions with the dispensing(s) in the EHRs—perhaps via a unique code—would allow better study and tracking of adherence by researchers and clinicians. As it is unclear what proportion of patients the foregoing affected, the quantum and nature of missing data are unknown; hence, the findings stated above should be treated with caution as they are for the patient sample with data available. Consequently, this valuable resource, containing the bulk of the needed data, needs optimisation for more reliable adherence assessments. Seemingly recognising this, the database disclaims assurance of the accuracy/completeness/reliability of the data notwithstanding best efforts in data collation.

Calculating adherence also requires EHR data presentation in an accessible format. The DS—essential for computing adherence—for each dispensing should ideally be contained in a consistent (numeric) format to limit room for misinterpretation and human error. Presently, DS is not provided and must be manually calculated by dividing the stated medication quantity dispensed by the daily dose, which itself is derived from the statement-formatted administration instructions available. These instructions/statements are sometimes non-specific or describe tapering/incremental doses requiring complex calculations to deduce the DS. Besides, the database should ideally allow for searches of data by specific dates and the time point of prescriber-advised medication discontinuations should be highlighted.

Although patients can purposely have their data excluded from the database, there was no indication of this for this study's participants and the overall number of patients opting off is thought to be infinitesimal. Moreover, there appears to have been a material increase in dispensing and prescription recordings on the database since 2020 (after our study period), driven by the adoption of digital health services since the start of the COVID-19 pandemic; the impact of this on adherence evaluation requires serious assessment.

For the 108 consenting patients with available data, their 3-year mean DPPR,[13] a new adherence measure, was high at 83.2%. Moreover, 69% of patients had a DPPR ≥80%, the general threshold of good adherence.[6] We consider these results to be indicative only and they should be considered with caution due to data quality factors discussed above. To our knowledge, no other studies have evaluated adherence in patients with IBD taking multiple concurrent medications (polypharmacy) by calculating DPPR. Other studies (cited below) have calculated adherence to single-medicine regimens using other adherence measures, e.g., medication possession ratio (MPR) and/or proportion of days covered (PDC) etc. Studies investigating IBD patients' polypharmacy adherence[23] commonly use self-reported surveys, which yield more subjective adherence estimates than those using EHRs. Moreover, the medicines for which adherence is calculated differ between studies.

These heterogeneities limit comparison of adherence results.

Using measures including MPR/PDC, 38–77%[6,24] of patients with IBD have been reported as adherent (MA ≥80%) to biologic/anti-tumor necrosis factor (anti-TNF) medicines. Likewise, 22.9%[9] and 60%[25] of IBD patients have been classed as non-adherent to non-biologic medicines e.g., thiopurines, 5-aminosalicylic acid (5-ASA) drugs etc. Other studies from southern Aotearoa New Zealand,[7] the Netherlands,[24] Australia and the United Kingdom,[8] using self-reported surveys, report that 31.1% of IBD patients had "below medium" adherence, 76% had medium and low adherence and 28.7% were non-adherent. Findings of other publications report associations between female gender and lower IBD adherence;[26] these align with our results showing that male patients had a statistically significantly higher DPPR than female patients.

Forty-six percent of patients had corticosteroid dispensings in the 3-year period, which compares to United States CD patients, 40% of whom used corticosteroids within a year from starting infliximab use.[27] In the present study, the correlation between DPPR and the number of concurrent corticosteroid dispensings (a clinical outcome indicator, as corticosteroids are used for managing IBD flare-ups[1,3]) was not statistically significant. Further research could consider if DPPR predicts future steroid dispensings, although literature posits that chronic disease DPPR does not predict future hospitalisations,[12,20] another indicator of clinical outcomes. There is, however, little consensus about the appropriate lag period parameters for determining when adherence might impact the outcomes.[12,20] We counted the corticosteroid dispensings within the same period as DPPR was calculated to maximise patient inclusion, as using a lag period would have meant excluding patients with shorter durations of total data contribution. Furthermore, as a heterogenous mix of medicines of interest (each therapeutic may have different effects on disease outcomes and adherence per medication may be different[28]) and study participants (of varying ages, disease statuses/severities etc.) were included, these could have also contributed to this outcome. Moreover, corticosteroids could have been prescribed for comorbidities, rather than for IBD. The lack of readily available data precluded analysis of these factors.

The insights gained from using the SDHB EHRs in this study align broadly with those addressed in literature.[11,29] Although adherence can be calculated from the SDHB PMD, the aforementioned issues limit the reliability of the results. Therefore, to be best optimised for adherence computation, the database should pool real-time dispensing and prescription data from all primary to tertiary healthcare providers/vendors across the public and private health sectors. Also, the data should be provided with the DS calculated and presented in a numeric format with the database being searchable by date.

Nonetheless, we recognise that EHRs of dispensing/prescription data, no matter how complete or accurate, are secondary databases and might not necessarily reflect patients' medication-taking behaviours. For instance, patients might increase or decrease their dosage depending on their IBD disease activity, as some prescribers recommend due to its linkage with better health outcomes in diverse chronic diseases.[30] Notwithstanding, EHRs like those available in the SDHB are a valuable resource for adherence assessment both for research and patient support purposes. Moreover, patients who did not consent to partaking in this study may have been aware of their non-adherence, which could have contributed to the high adherence we found among the consenting patients.

Dispensing/prescription datasets exist in the now-defunct SDHB region, the PMD especially, which indicate that adherence for IBD patients is high. Nonetheless, optimisation in data collation is needed to improve the data quality for more accurate adherence calculations.

COMPETING INTERESTS
The authors have no conflicts of interest to declare.
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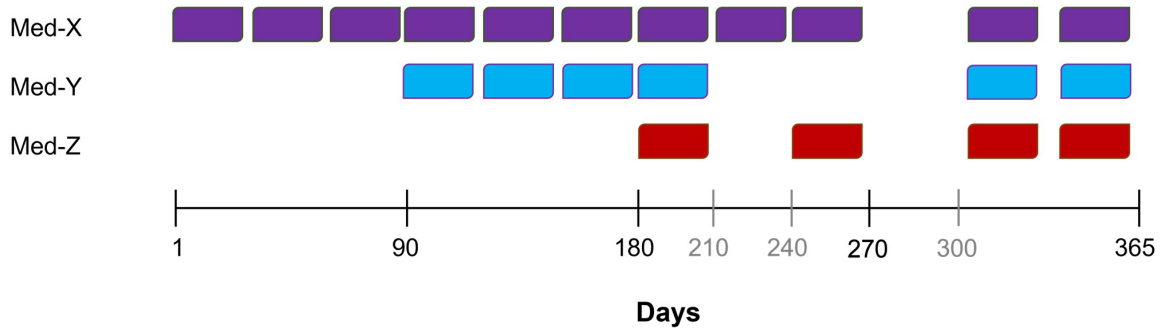
Appendix

Appendix Table 1: ICD-10 codes and medications of interest used for patient selection.

ICD-10 IBD Code		**Description**
K500		Crohn's disease of small intestine
K501		Crohn's disease of large intestine
K508		Other Crohn's disease
K509		Crohn's disease, unspecified
K510		Ulcerative (chronic) pancolitis
K512		Ulcerative (chronic) proctitis
K513		Ulcerative (chronic) rectosigmoiditis
K514		Inflammatory polyps
K515		Left-sided colitis
K518		Other ulcerative colitis
K519		Ulcerative colitis, unspecified
K523		Indeterminate colitis
Chronic medications used in IBD therapy[1,2]		
1.		Methotrexate
2.	Thiopurines	Azathioprine
3.		6-Mercaptopurine (6-MP)
4.		Adalimumab (Humira)
5.	5-Aminosalicylic acid (5-ASA) drugs	Sulfasalazine
6.		Mesalazine
Corticosteroid medicines		
7.		Budesonide
8.		Prednisone
9.		Hydrocortisone acetate

Appendix Figure 1: Illustrative pattern of dispensings for a patient with three medications dispensed (Med-X, Y, Z). Each box represents days' supply (DS) for that medication. Intervals are marked by the stated days. Medicines were assumed to be prescribed for continuous use from initiation until the end of the total period.



$$DPPR = \frac{([1/1 \times 90]_{\text{days 1-90}} + [2/2 \times 90]_{\text{days 91-180}} + [3/3 \times 30]_{\text{days 181-210}} + [1/3 \times 30]_{\text{days 211-240}} + [2/3 \times 30]_{\text{days 241-270}} + [0/3 \times 30]_{\text{days 271-300}} + [3/3 \times 65]_{\text{days 301-365}})}{365} = 0.84 \times 100 = 84\%$$

Calculating daily polypharmacy possession ratio (DPPR): an illustration

The illustrative patient, in Appendix Figure 1 above, was first dispensed Med-X, Med-Y and Med-Z on days 1, 91 and 181; therefore, the availability score for the 181–365 interval could be 3/3 (if all medications were available), 2/3 (if just two medicines were available), 1/3 (if one medication was available) or 0/3 (if no medicine was available). Likewise, between days 91 and 181, the possible daily values were 2/2, 1/2 or 0/2; and for days 1–91 the possible scores were 1/1 or 0/1.

Analysis methods and software

The "CMA_polypharmacy" function in the AdhereR package version 0.8.1[3] in R was used in computing the DPPR. Furthermore, the results of the correlation analysis between average DPPR and the number of corticosteroid dispensings in the concurrent period per patient was validated using negative binomial regression (used to account for over-dispersion in the count variable).[3] All data preparation and analyses were conducted using Python 3.9.14,[4] R (v4.2.2-win).[5]

Analysis results

The strength of the association between DPPR and the number of corticosteroid dispensings was estimated using a negative binomial model (Appendix Table 2). The Pseudo R^2 (0.004) represents a very low model fit, validating the lack of a correlation, and strongly indicates that more explanatory variables are needed to better understand the association. Data on such explanatory variables (e.g., comorbidities, disease severity, urban/rural residence among several others), some of which would be confounders, was not readily available to include in the model. Besides, the data quality considerations detailed in the discussion could also have impacted this outcome. Hence, confounding could have caused the relationship to be under- or over-estimated, or even completely reversed (Simpson's paradox). Future research should consider obtaining and including relevant covariates in multivariable models for better goodness of fit, perhaps after DPPR is re-computed with higher-quality data.

Appendix Table 2: Pearson's correlation and relationship between DPPR and number of corticosteroid dispensings using negative binomial regression analysis.

Daily polypharmacy possession ratio (DPPR %) values	
Mean (SD)	83.2% (16.7)
Minimum	28.0%
Q1	76.0%
Median	88.1%
Q3	96.7%
Maximum	100.0%
DPPR and number of steroid dispensings	
Pearson's r	0.11
Cor p-value	0.45
IRR (95% CI)	2.04 (0.48–8.04)
P-value	>0.05
Pseudo R^2	0.004

Abbreviations: SD = standard deviation; IRR = incidence rate ratio; 95% CI = 95% confidence interval; Cor = correlation

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