Older Age and Steroid Use Are Associated with Increasing Polypharmacy and Potential Medication Interactions Among Patients with Inflammatory Bowel Disease

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Background: Comorbidity and polypharmacy, more prevalent among older persons, may impact the treatment of patients with inflammatory bowel disease (IBD). The aims of this study were to assess the frequency of polypharmacy and medication interactions within a cohort of older patients with IBD and describe IBD treatment patterns.

Methods: Cohort study of 190 patients with IBD 65 years or older followed at a tertiary IBD referral center from 2006 to 2012. Data collected included demographics, IBD-specific characteristics including disease activity, and comorbidity. Medication histories were extracted from medical records, and data were used to classify polypharmacy, frequency, and severity of potential medication interactions and inappropriate medication use.

Results: Older patients with IBD were prescribed an average of 9 routine medications. Severe polypharmacy (≥10 routine medications) was present in 43.2% of studied patients and associated with increasing age, greater comorbidity, and steroid use. Overall, 73.7% of patients had at least 1 potential medication interaction, including 40% of patients with potential IBD medication-associated interactions. Chronic steroids were prescribed to 40% of the older patients including 24% who were in remission or with mild disease activity. Only 39.5% of patients were on immunomodulators and 21.1% on biologics. Approximately, 35% of patients were given at least 1 Beers inappropriate medication and almost 10% were receiving chronic narcotics.

Conclusions: Older patients with IBD are at increased risk for severe polypharmacy and potential major medication interactions especially with increasing comorbidity and chronic steroid use. Steroid-maintenance therapies are prevalent among the older patients with IBD with lower utilization of steroid-sparing regimens.

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Key Words: inflammatory bowel disease, elderly, polypharmacy, medication interactions

Older Americans, aged 65 years and above, represent the fastest growing age group with an estimated 31% increase in the number of older persons during this decade.1 This elderly subgroup, partly due to the implementation of Medicare Part D, also represents the largest consumers of prescription medications with an increased risk of medication-related adverse effects.2,3 Older age is associated with greater comorbidity and polypharmacy, which can add to the risk for medication interactions and adverse effects due to iatrogenesis.4 The National Social Life, Health, and Aging Project reported over 80% of the older patients use at least 1 prescription medication on a daily basis with over 50% taking more than 5 medications or supplements daily.5 With the aging of the population, the number of older patients with inflammatory bowel disease (IBD) is also expected to increase. Little is known about the prevalence of polypharmacy and medication interactions among the older patients with IBD. These factors, potentially overlooked by practicing gastroenterologists, may impact IBD medication adherence, efficacy, and safety and lead to increased morbidity.

The older patients with IBD are already a higher-risk group as increased age is associated with an increased risk of serious infections, venous thromboembolic events, hospitalizations, postoperative complications, and mortality.6–9 Elderly patients with IBD also have greater outpatient resource utilization compared with other age groups including physician visits, ambulatory care visits, and pharmacy claims.10–11 There are few studies of the presently available IBD medications that comment on the therapeutic efficacy among the older patients with IBD. The anti-tumor necrosis alpha agents (anti-TNFs), currently among the most effective treatments for moderate to severe disease activity, may be associated with increased serious infection and mortality when administered to the older patients with IBD with higher rates of medication discontinuation due to lack of response or adverse effects.12–14
Corticosteroids are often prescribed to the older patients with IBD, with over 30% geriatric patients with IBD maintained on steroids for greater than 6 months of therapy.\textsuperscript{15} However, steroids are associated with numerous adverse effects, particularly within the elderly patients with IBD, including infection, hypertension, worsened glycemic control, and bone loss.\textsuperscript{16} Therefore the optimum treatment strategy, balancing safety and efficacy, for the older patients with IBD has yet to be determined as there are additional factors to consider in addition to disease activity. Studies looking at prescribing patterns among older patients with IBD consistently show aminosalicylates and corticosteroids are often the mainstays of therapy with lower rates of immunomodulator or biological use.\textsuperscript{15,17,18} These trends may reflect prescribers’ concerns about the safety and efficacy of immunosuppression among this higher risk age group; however, the older patients’ ability to handle increased disease activity may be less than younger patients.

The primary aims of this study were to assess the prevalence and severity of polypharmacy and potential medication interactions within a cohort of older patients with IBD. The secondary aims were to describe the prescribing patterns in the treatment of IBD, particularly relating to disease severity and age at diagnosis.

METHODS

Study Population

Established patients with IBD aged 65 years and older routinely followed at the Johns Hopkins Inflammatory Bowel Disease clinics (i.e., more than 1 office visit within a 12-month period) from January 1, 2006 to December 31, 2012, were identified using the electronic medical record and the clinical IBD patient database at Johns Hopkins. Patients were excluded if they did not have a confirmed IBD diagnosis, were not routinely followed in the IBD clinical practice, had incomplete medical records (missing medication list or medical history), or had ulcerative colitis (UC) with total proctocolectomy at the time of last follow-up. Comorbid illnesses were recorded and categorized: infection, hypertension, worsened glycemic control, and bone loss.\textsuperscript{16,18}

During the 7-year study period, 190 elderly patients with IBD aged 65 years and older with routine IBD clinic follow-up were identified. 95 patients with CD and 95 patients with UC. The older IBD cohort was taking an average of 9 (95% confidence interval [CI], 8.7–10.0) routine medications including an average of 6 (95% CI, 6.0–6.9) prescription medications, 3 (95% CI, 2.5–3.2) OTC medications, and 2 (95% CI, 1.7–2.0) IBD medications. Approximately 9.0% (n = 17) of study patients were not taking any IBD medications reported by the patients was classified according to degree of polypharmacy: mild (2–4), moderate (5–9), or severe (≥10).

In the current IBD treatment regimens were assessed. Disease activity was classified as inactive, mild, moderate, or severe based on direct chart review including endoscopy, pathology, and radiology from available inpatient and outpatient medical records. The Institutional Review Board at the Johns Hopkins School of Medicine approved this study, July 2011.

Data Collection and Classification

Basic demographic information including gender, smoking history, and age at last follow-up were collected. Disease-specific information including age at diagnosis, disease duration, and current IBD treatment regimens were assessed. Disease activity was classified as inactive, mild, moderate, or severe based on direct chart review of endoscopic and radiologic activity, clinical symptoms, and physician’s global assessment as documented at the time of last follow-up. Comorbid illnesses were recorded and scored using the age-adjusted Charlson comorbidity index, and degree of comorbidity for analytic purposes was categorized as mild (0–2), moderate (3–4), and severe (>4).\textsuperscript{19}

Data on medication use, including over-the-counter (OTC), supplements, and prescription medications that patients reported taking on a regular basis were collected from the most recent gastroenterology clinic visit. The total number of routine medications reported by the patients was classified according to degree of polypharmacy: mild (2–4), moderate (5–9), or severe (≥10). OTC or prescription topical agents such as creams, emollients, or shampoos were excluded from the medication and polypharmacy count. IBD-specific medications were identified and categorized: antibiotics (specifically documented for the treatment of IBD or IBD-associated complications such as abscess), oral steroids (if specified for the treatment of IBD including budesonide), oral 5-aminosalicylates (5-ASAs), immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate), and biologics (infliximab, adalimumab, certolizumab pegol, and natalizumab). Additional information included any narcotic prescriptions, not specifically for IBD related symptoms, and medications classified as inappropriate for the elderly based on the Beers criteria (Table, Supplemental Digital Content 1, http://links.lww.com/IBD/A832).\textsuperscript{20}

Micromedex 2.0 was used to identify and classify potential drug interactions.\textsuperscript{21} The total number of potential interactions per patient was recorded, and any interaction with an IBD medication was further classified as contraindicated (contraindicated for concurrent use), major (may be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects), moderate (may result in exacerbation of the patients’ condition and/or require an alteration in therapy), or minor (limited clinical side effects).

Statistical Analysis

Descriptive statistics were reported as percentages, mean values, and standard errors of the mean. All continuous variable comparisons were unpaired and tests of significance were two-tailed. Fisher’s exact test was used to compare categorical variables. Logistic regression was performed to determine independent predictors of polypharmacy using the statistically significant variables from the univariate analysis. A P value of <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 20 (SPSS Inc., Chicago, IL).

RESULTS

During the 7-year study period, 190 elderly patients with IBD aged 65 years and older with routine IBD clinic follow-up were identified. 95 patients with CD and 95 patients with UC. The older IBD cohort was taking an average of 9 (95% confidence interval [CI], 8.7–10.0) routine medications including an average of 6 (95% CI, 6.0–6.9) prescription medications, 3 (95% CI, 2.5–3.2) OTC medications, and 2 (95% CI, 1.7–2.0) IBD medications. Approximately 9.0% (n = 17) of study patients were not taking any IBD medications at the time of clinical review. The patients with UC in our study population tended to be diagnosed at a later age (56.8 ± 14.4 yr) than the patients with CD (44.3 ± 18.6 yr). Otherwise, there were no differences between older patients with CD and UC in terms of smoking history, comorbidity, and polypharmacy (Table 1).
When stratified based on age at diagnosis, older-onset IBD patients, diagnosed at 60 years or older, were more likely to be diagnosed with UC, have greater disease activity, and were more likely to be currently on steroids compared with early-onset IBD patients, diagnosed less than 60 years of age (Table 2). There were no differences, however, in terms of comorbidity scores, degree of polypharmacy, and potential medication interactions between age groups at diagnosis.

### Disease Activity and Medication Utilization

Most of the older patients were in clinical remission or had only mild disease activity at the time of review (n = 119, 62.6%), whereas 33.2% of patients (n = 63) had moderate to severe disease activity. Medication prescribing patterns according to disease type and severity are presented in Figure 1. Of note, 5-ASAs were the most frequently prescribed IBD medications with 76.8% of older patients actively taking 5-ASAs (69.5% patients with CD and 84.2% patients with UC). Approximately 40% (n = 75) of patients were prescribed steroids, including 24% of patients with mild disease activity or in clinical remission maintained on chronic steroids. Among the steroid-exposed patients, only 21% (n = 16) were prescribed biologics, and 37% (n = 28) were taking thiopurines. Only 10% (n = 8) of these patients had previous exposure to biologics, and 5% (n = 4) had previous exposure to thiopurines. Overall, steroid-sparing therapies such as the immunomodulators were given to 39.5% of patients and anti-TNF therapies were administered to 21.1% of patients. Almost 10% of older patients with IBD were taking chronic narcotics (n = 18).

Medication utilization among the older-onset IBD patients with moderate to severe disease activity (n = 37, 48.7%) was anti-TNF agents (n = 9, 24.3%), immunomodulators (n = 13, 35.1%),
5-ASAs (n = 30, 81.1%), and steroids (n = 29, 78.4%). Comparatively, the early-onset elderly IBD patients with moderate disease activity (n = 26) were prescribed: anti-TNF (n = 8, 33.3%), immunomodulators (n = 10, 41.7%), 5-ASAs (n = 18, 75.0%), and steroids (n = 16, 66.7%). Approximately 30% of the older-onset patients with remission to mild disease activity (n = 40) were maintained on chronic steroids (n = 12), compared with 22.7% of the early-onset patients with remission to mild disease activity (n = 79).

Polypharmacy
Severe polypharmacy, defined as the routine use of 10 or more medications, was documented among 82 of the older patients with IBD (43.2%). Mild polypharmacy (2–4 routine medications) was present among 14.7% of the older patients with IBD (n = 28), and 42.1% had moderate polypharmacy (n = 80) (5–9 routine medications). Increasing age was associated with severe polypharmacy as the average age of patients with major polypharmacy was 71.4 years compared with an average age of 68.8 years for patients with minor polypharmacy (P = 0.02). Other factors associated with increasing polypharmacy included comorbidity index scores, Beers inappropriate medication use, and corticosteroid use (Table 3). Disease type, immunomodulator, and biological use among the elderly patients with IBD were not associated with increasing polypharmacy. Moderate to severe disease activity was numerically associated with greater polypharmacy; however, this did not reach statistical significance (P = 0.09). Logistic regression, performed to determine independent risk factors of severe polypharmacy, demonstrated a statistically significant association with Beers inappropriate medications (odds ratio [OR] = 2.28; 95% CI, 1.22–4.27) and Charleston Comorbidity Score (OR = 2.26; 95% CI, 1.19–4.27). Steroid use was no longer significant (OR = 2.71; 95% CI, 0.24–2.72).

Potential Medication Interactions
Overall, 140 of the 190 older patients with IBD (73.7%) had at least 1 potential interaction within their medication regimens with an average of 4.5 (95% CI, 3.9–5.2) potential interactions per patient (Fig. 2A). Approximately 40% (n = 81) of patients experienced at least 1 potential IBD medication-associated drug–drug interaction: 30.9% (n = 25) had potential major interactions, 84.0% (n = 68) had potential moderate interactions, and 11.1% (n = 9) had potential minor interactions. The majority of potential drug–drug interactions were associated with 5-ASAs (n = 70, 86.4%); however, 61.7% of interactions (n = 50) were due to immunomodulators, 51.9% linked to steroids (n = 42), and 22.2% related to the biologics (n = 18) (Fig. 2B). Disease activity, however, was not associated with increased frequency of medication interactions: 40.3% of patients in remission or mild activity and 50.8% of patients with moderate to severe disease activity had at least 1 potential IBD medication-associated drug interaction.

**DISCUSSION**
Increasing polypharmacy has been associated with a greater risk for adverse drug events including medication interactions. Our elderly patients with IBD had a high rate of polypharmacy with over 40% of patients taking more than 10 routine medications. Risk factors for major polypharmacy among these older patients with IBD included increasing age, increased comorbidity, corticosteroid use, and inappropriate medication use on univariate analysis. Multivariate analysis demonstrated increased comorbidity and inappropriate medication use were independently associated with severe polypharmacy. Approximately 35% of the patients with IBD were taking at least 1 potentially inappropriate medication (PIM) as determined by the Beers Criteria, most commonly benzodiazepines. The Beers criteria were developed in 1991, to limit the use of PIMs in the elderly patients, which are linked to a high risk for adverse events and lack of efficacy.20 These PIMs are associated with an increased incidence of hospitalizations, mortality, and health care expenditures.22,23 In our elderly patients with IBD, PIM use was
greater among patients with IBD with moderate and severe polypharmacy. Approximately 10% of the older patients with IBD were also on chronic narcotics, which are metabolized more slowly and associated with increased adverse drug events among the elderly and the patients with IBD.

Comorbidities are more likely to be present among older persons and contribute to risk of polypharmacy and subsequent medication interactions. This was corroborated by our findings, as increasing Charlson index scores were associated with greater polypharmacy and potential medication interactions. The majority of study patients had at least 1 potential medication interaction including 93% of patients with severe polypharmacy. Potential interactions with IBD medications occurred in almost half of the older patients, most frequently with 5-ASAs although immunomodulators and steroids were responsible for a sizeable fraction of interactions as well.

The combination use of thiopurines and 5-ASA was common among older patients with IBD. Notably, this combination of medications may lead to an increased risk of blood dyscrasias, including myelosuppression. Although this interaction has not commonly resulted in adverse outcomes among patients with IBD, awareness of the potential adverse outcomes of this combination therapy is important for the older patients who have altered drug metabolism relative to younger persons and for whom sustained higher levels of thioguanine may result in greater risk. Closer therapeutic monitoring may be advised for this age group. Additional 5-ASA interactions were with the proton pump inhibitors as the increased gastric pH could result in lower therapeutic efficacy. Again, although the impact of this medication combination is not clearly known, as the older patients are already susceptible to atrophic gastritis with its associated increased gastric pH, this may further affect drug absorption particularly with the pH dependent 5-ASA formulations. The 5-ASAs may also increase the effects of sulfonylureas, commonly used for patients with type 2-diabetes, leading to possibly greater risks for hypoglycemic events. Other potential medication interactions with IBD therapies

| TABLE 3. Factors Associated with Increasing Polypharmacy Among Older Patients with IBD |
|-------------------------------|-----------------|-----------------|-----------------|-----------|
|                               | Mild            | Moderate        | Severe          | P         |
| Age, yr                       | 68.8 ± 3.0      | 69.5 ± 4.7      | 71.4 ± 5.7a     | 0.02a     |
| Gender, n (%)                 |                 |                 |                 | 0.60      |
| Male                          | 13 (46.4)       | 37 (46.3)       | 44 (53.7)       |           |
| Female                        | 15 (53.6)       | 43 (53.7)       | 38 (46.3)       |           |
| Disease type, n (%)           |                 |                 |                 | 0.43      |
| CD                            | 14 (50.0)       | 36 (45.0)       | 45 (54.9)       |           |
| UC                            | 14 (50.0)       | 44 (55.0)       | 37 (45.1)       |           |
| Smoking status, n (%)         |                 |                 |                 | 0.21      |
| Never smoked                  | 17 (60.7)       | 33 (41.3)       | 35 (42.7)       |           |
| Ever smoked                   | 11 (35.7)       | 45 (56.3)       | 46 (51.2)       |           |
| Comorbidity index (age-adjusted), n (%) |         |                 |                 | 0.005     |
| CCI, 0–2                      | 9 (32.1)        | 29 (36.3)       | 11 (13.4)       |           |
| CCI, 3–4                      | 13 (46.4)       | 28 (34.2)       | 33 (40.2)       |           |
| CCI, ≥5                       | 6 (21.5)        | 23 (28.8)       | 38 (46.4)       |           |
| Disease activity, n (%)       |                 |                 |                 | 0.09      |
| Remission/mild                | 21 (75.0)       | 47 (57.4)       | 49 (59.8)       |           |
| Moderate/severe               | 4 (25.0)        | 30 (36.6)       | 28 (34.2)       |           |
| IBD medications, n (%)        |                 |                 |                 |           |
| 5-ASA                         | 18 (64.3)       | 65 (81.3)       | 63 (76.8)       | 0.15      |
| Steroids                      | 2 (7.1)         | 35 (43.8)a      | 38 (46.4)a      | 0.0002    |
| Antibiotics                   | 2 (7.1)         | 10 (12.2)       | 18 (22.0)       | 0.10      |
| Immunomodulators              | 6 (21.5)        | 26 (31.7)       | 36 (43.9)       | 0.06      |
| Biologics                     | 4 (25.0)        | 13 (15.9)       | 23 (28.0)       | 0.12      |
| Narcotics                     | 1 (3.6)         | 6 (7.3)         | 11 (13.4)       | 0.27      |
| Beers inappropriate medication use, n (%) | 0 (0.0) | 30 (37.5) | 37 (45.1)a | <0.0001 |

*aCompared with patients with mild polypharmacy.
CCI, Charlson’s comorbidity index.
P values < 0.05 were considered statistically significant and are bolded.
are summarized in Table, Supplemental Digital Content 2, http://links.lww.com/IBD/A833.

Over 75% of patients with potential IBD medication-associated interactions had a comorbidity index score of 3 or higher, and 40% had a comorbidity index score ≥5. Additionally, 33% of the potential IBD medication-associated interactions were with PIMs, which already should be avoided among this patient group. Medication interactions and adverse effects are common reasons for emergency room visits and hospital admissions especially in the aging population.考虑老年患者与IBD的资源利用，仔细的药物治疗重整和简化可能是一个可优化的预防措施和减少疾病负担的手段。

The prescribing patterns seen in our study are consistent with previously published studies.考虑5-ASAs的药代动力学，5-ASAs是用于老年人IBD的初始维持治疗，无论疾病活动程度。尽管对于CD，70%的老年人CD患者在维持美沙拉秦治疗，包括71%的CD患者有中到重度疾病。虽然5-ASAs是一个相对安全的治疗药物，有少的副作用，这些药物并不是典型的用于类固醇依赖或中到重度疾病。多数组织的研究也已证明了类固醇在IBD中使用，包括继发性感染，机会性感染，骨质疏松，疾病，和死亡。因此，老年人是IBD中类固醇相关并发症风险最高的患者；然而，维持类固醇治疗外，"图2. A, Frequency and severity of potential medication interactions among older patients with IBD. B, Frequency of potential medication interactions stratified by IBD medication class."

![Image](image-url)

Overall, the use of chronic steroids was high among the older patients with IBD, including 24% of persons in remission or with mild disease on maintenance steroids; which were significantly associated with increasing polypharmacy in univariate analysis. In multivariate analysis, this was no longer significant, although the study was likely underpowered to detect a significant difference. Almost half of the steroid-dependent patients had no documented steroid-sparing therapy aside from 5-ASAs. When stratified based on moderate to severe disease activity, only 25% of the older patients received biologics, and just 35% were prescribed immunomodulators, the conventional steroid-sparing agents, compared with 71% with chronic steroid use. The older patient is already susceptible to steroid-associated complications including glaucoma, diabetes, hypertension, bone loss, and mortality.考虑类固醇使用在IBD中，包括继发性感染，机会性感染，骨质疏松，疾病，和死亡。因此，老年人是IBD中类固醇相关并发症风险最高的患者；然而，维持类固醇治疗
seems to be more commonly prescribed over the steroid-sparing immunomodulators and biologics.

Our findings also suggest a relative underutilization of biologics and immunomodulators among the older patients with IBD, particularly the older-onset IBD patients with active disease. Although steroids are typically used for induction of remission, they are not recommended for maintenance therapies due to the known steroid-associated adverse events and infections. For steroid-dependent patients with IBD, immunomodulators or biologics are often introduced to help maintain steroid-free remission. The anti-TNF agents are the most effective medications presently available for the induction and maintenance of remission in IBD. Early aggressive therapy, the “top-down” strategy with earlier introduction of biological agents rather than the “step-up” conventional management, may be associated with better long-term outcomes. Additionally, the SONIC trial demonstrated that the combination of immunomodulator and anti-TNF therapy is more effective than either treatment alone. As a result, biological utilization among patients with moderate to severe IBD has been increasing except perhaps within the older patients with IBD.

Little is known about the efficacy and safety of anti-TNF or immunomodulators, as monotherapy or combination, for the older patients with IBD. Elderly patients with IBD may frequently be maintained on steroids and less effective medications such as 5-ASAs due to fears of serious complications and infections from immunosuppressants. Additionally, concerns about malignancy risk, particularly with the thiopurines with the age and exposure-related increased risk of lymphoproliferative disorders and skin cancers, may limit their therapeutic role for the older patients.

There are no robust data on the safety of these medications in the elderly population and the available studies suggesting increased adverse effects and higher rates of discontinuation are confounded by concurrent steroid usage, underlying disease activity and comorbidity. These steroid-sparing strategies may also be initiated later during the disease course for the elderly patients when they may potentially be less efficacious or the tolls of disease burden such as anemia, malnutrition, or dehydration may be harder to maintain leading to more frequent hospitalizations, medication discontinuation, and/or infection.

The older patient with IBD is underrepresented in the major randomized controlled trials of the anti-TNF agents. However, using the patients with rheumatoid arthritis (RA) as a surrogate for presumed safety and efficacy, anti-TNFs were similarly efficacious among patients >65 years compared with those <65 years of age. There are conflicting data regarding safety of anti-TNF use in older patients with RA; however, a large British observational study showed that although older patients with RA may be at greater risk for serious infections, concurrent anti-TNF use was not associated with additive risk. Another study investigating serious infection risk among older patients with RA, reported a lower comparative risk of infection among anti-TNF users, (OR = 1.6) compared with steroid (OR = 4.0–7.6) and nonbiologic disease modifying antirheumatic drugs, including azathioprine (OR = 2.5) and methotrexate (OR = 2.4–3.0). Further investigation regarding therapeutic decision making for the older patients with IBD with continued disease activity is certainly needed to help guide practitioners, particularly as chronic steroid use may not be a medically responsible option, for this higher-risk age group.

The current mainstays of IBD treatment are the induction and maintenance of clinical and, ultimately, endoscopic remission. Clinical remission of IBD is associated with higher quality of life scores and allows patients to lead more active and independent lives. This is especially important for the older person at greater risk of declining functional status, hospitalization, and resource utilization if disease is poorly controlled. Additionally, other factors need to be considered in the management of the older patients with IBD such as medication costs given limited income for many older persons, complexity of medication regimens especially with increasing pill burden, and practicality of using injectables or infusions as maintenance regimens particularly for patients with limited caregiver support. Elderly patients are especially at risk for prescribing cascades that occur when an adverse effect of an existing medication is interpreted as a new symptom or illness and treated with increased dosages of other medications or the addition of new medications. Prescribing cascades increase polypharmacy as well as increase the risk of drug interactions or adverse drug events. An example of an IBD-associated prescribing cascade that may happen to the older patient is 5-ASAs hypersensitivity. The symptoms may be misinterpreted as a colitis flare, which may lead to the addition of steroids and antidiarrheals and exposure to additional adverse effects and greater pill burden. Medication prescribing for the older patients with IBD needs to be done with care and caution, making certain to avoid inappropriate medications, monitoring for adverse effects, updating medication lists (including OTC meds and supplements), and checking for interactions at each visit since older persons often see multiple physicians.

There are several inherent limitations to our study findings. This was a retrospective study of older patients with IBD seen at a tertiary care IBD referral center. Therefore, the patient population may represent to have more complicated disease, comorbidities, or contraindications to standard therapies. Medication utilization was based on patient recall and chart documentation and may be subject to recall bias or errors relating to medical charting. Disease activity was not formally assessed using a standardized scoring system as this was not routinely done in practice but characterized based on the provider’s clinical assessment at the time of the most recent follow-up. Additionally, as this was a retrospective study, assessments for medication adherence were not performed and polypharmacy was defined based on documentation of prescribed medications. There is also no standardized definition of polypharmacy as within the published literature, polypharmacy is defined with vague terms such as “excessive,” “complicated,” or “inappropriate” prescription or based on the presence of medication interactions. Two studies defined polypharmacy as 5 or more routine medications, with one study defining “major polypharmacy” as the...
use of >5 medications and “mild polypharmacy” as the use of 2 to 4 medications.4,45 For the purposes of our study, we defined polypharmacy as mild, moderate, and severe based on the fact that the majority of our patients (85%) were taking 5 or more medications to allow for further analyses based on number of routine medications. However our findings still underscore the complexities associated with older IBD care, particularly with more refractory disease.

Our study highlights the risk for severe polypharmacy and potential major medication interactions among our elderly patients with IBD, particularly persons with increasing age, steroid dependence, greater comorbidity, and inappropriate medication use. There seems to be a reliance on corticosteroids and 5-ASAs as dependence, greater comorbidity, with IBD, particularly persons with older IBD care, particularly with more refractory disease.

REFERENCES
1. 2010 Census Data on Aging. Available at: http://www.aoa.gov/aoaroot/aging_statistics/Census_Population/census2010/Index.aspx. Accessed December 5, 2011.
2. Catlin A, Cowan C, Hartman M, et al. National health spending in 2006: a year of change for prescription drugs. Health Aff (Millwood). 2007;27:14–29.
3. Gurwitz JH, Field TS, Harrold LR, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA. 2003;289:1107–1116.
4. Field TS, Gurwitz JH, Avorn J, et al. Risk factors for adverse drug events among nursing home residents. Arch Intern Med. 2001;161:1629–1634.
5. Qato DM, Alexander GC, Conti RM, et al. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. JAMA. 2008;300:2867–2878.
6. Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infection and mortality in patients with Crohn’s disease: more than 5 years of follow-up in the TREAT registry. Am J Gastroenterol. 2012;107:1409–1422.
7. Nguyen GC, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. Am J Gastroenterol. 2008;103:2272–2280.
8. Ananthakrishnan AN, McGinley EL, Binion DG. Inflammatory bowel disease in the elderly is associated with worse outcomes: a national study of hospitalizations. Inflamm Bowel Dis. 2009;15:182–189.
9. Kaplan GG, McCarthy EP, Ayanian JZ, et al. Impact of hospital volume on postoperative morbidity and mortality following a colectomy for ulcerative colitis. Gastroenterology. 2008;134:680–687.
10. Beckston SJ, Waters HC, Dabbous O, et al. Administrative claims analysis of all-cause annual costs of care and resource utilization by age category for ulcerative colitis patients. J Manag Care Pharm. 2008;14:352–362.
11. Everhart JE, ed. The burden of digestive diseases in the United States. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Washington, DC: US Government Printing Office, 2008; NIH Publication No. 09-6443.
12. Cottenie M, Kolan A, Daperno M, et al. Advanced age is an independent risk factor for severe infections and mortality in patients given anti-tumor necrosis factor therapy for inflammatory bowel disease. Clin Gastroenterol Hepatol. 2011;9:30–35.
13. Desai A, ZatotZA, de Silva P, et al. Older age is associated with higher rate of discontinuation of anti-TNF therapy in patients with inflammatory bowel disease. Inflamm Bowel Dis. 2013;19:309–315.
14. Bhushan A, Pardi D, Loftus E, et al. Association of age with adverse events from biologic therapy in patients with inflammatory bowel disease. Gastroenterology. 2010;138:A413.
15. Juneja M, Baidoo L, Schwartz MB, et al. Geriatric inflammatory bowel disease: phenotypic presentation, treatment patterns, nutritional status, outcomes, and comorbidities. Dig Dis Sci. 2012;57:2408–2415.
16. Akerkar GA, Peppercorn MA, Hame MB, et al. Corticosteroid-associated complications in elderly Crohn’s disease patients. Am J Gastroenterol. 1997;92:461–464.
17. Benchimol EI, Cook SF, Erichsen R, et al. International variation in medication prescription rates among elderly patients with inflammatory bowel disease. J Crohns Colitis. 2013;7:878–889.
18. Charpentier C, Salleron J, Savoye G, et al. Natural history of elderly-onset inflammatory bowel disease: a population-based cohort study. Gut. 2014;63:423–432.
19. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic morbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–383.
20. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60:616–631.
21. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; c1974–2013. Available at: http://www.micromedexsolutions.com/micromedex2. Accessed May 5, 2014.
22. Lau DT, Kasper JD, Potter DE, et al. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Arch Intern Med. 2005;165:63–74.
23. Fu A, Jiang J, Reeves J, et al. Potentially inappropriate medication use and healthcare expenditures in the US community-dwelling elderly. Med Care. 2007;45:472–476.
24. Irving PM, Shanahan F, Rampton DS. Drug interactions in inflammatory bowel disease. Am J Gastroenterol. 2008;103:207–219.
25. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18,820 patients. BMJ. 2004;329:15–19.
26. Onder G, Pedone C, Landi F, et al. Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacopidemiology in the Elderly (GIFA). J Am Geriatr Soc. 2002;50:1962–1968.
27. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions to prescribed medications. JAMA. 1998;279:1200–1205.
28. Ford AC, Kane SV, Khan KJ, et al. Efficacy of 5-aminosalicylates in Crohn’s disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106:617–629.
29. Lim WC, Hanauer S. Aminosalicylates for induction of remission or response in Crohn’s disease. Cochrane Database Syst Rev. 2010; CD008870.
30. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105:501–523.
31. Lichtenstein GR, Hanauer SB, Sandborn WJ. Management of Crohn’s disease in adults. Am J Gastroenterol. 2009;104:465–483.
32. Thomas TP. The complications of systemic corticosteroid therapy in the elderly. A retrospective study. Gerontology. 1984;30:60–65.
33. Toruner M, Loftus EV Jr, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. Gastroenterology. 2008;134:929–936.
34. Azzopardi N, Ellul P. Risk factors for osteoporosis in Crohn’s disease: infliximab, corticosteroids, body mass index, and age of onset. Inflamm Bowel Dis. 2013;19:1173–1178.
35. D’Haens G, Baert F, van Assche G, et al. Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn’s disease: an open randomized trial. Lancet. 2008;371:660–667.
36. Colombel JF, Sandborn WJ, Reinisch W, et al. Infliximab, azathioprine, or combination therapy for Crohn’s disease. N Engl J Med. 2010;362:1383–1395.
37. Beaugerie L, Brousse N, Bouvier AM, et al. Lymphoproliferative disorders in patients receiving thiopurines for inflammatory bowel disease: a prospective observational cohort study. Lancet. 2009;374:1617–1625.
38. Peyrin-Biroulet L, Khosrotehrani K, Carrat F, et al. Increased risk for nonmelanoma skin cancers in patients who receive thiopurines for inflammatory bowel disease. Gastroenterology. 2011;141:1621–1628. e1–e5.
39. Bathon JM, Fleischmann RM, Van der Heijde D, et al. Safety and efficacy of etanercept treatment in elderly subjects with rheumatoid arthritis. J Rheumatol. 2006;33:234–243.
40. Galloway JB, Hyrich KL, Mercer LK, et al. Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 months of treatment: updated results from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. Rheumatology. 2011;50:124–131.
41. Widdifield J, Bernatsky S, Paterson JM, et al. Serious infections in a population-based cohort of 86,039 seniors with rheumatoid arthritis. Arthritis Care Res. 2013;65:353–361.
42. Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. BMJ. 1997;315:1096–1099.
43. Bushardt RL, Massey EB, Simpson TW, et al. Polypharmacy: misleading, but manageable. Clin Interv Aging. 2008;3:383–389.
44. Bergman-Evans B. Evidence-based guideline. Improving medication management for older adult clients. J Gerontol Nurs. 2006;32:6–14.
45. Preskorn SH. Multiple medication use in patients seen in the veterans affairs healthcare system: so what? J Psychiatr Pract. 2005;11:46–50.