Medication Utilization and the Impact of Continued Corticosteroid Use on Patient-reported Outcomes in Older Patients with Inflammatory Bowel Disease

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Background: Older individuals with inflammatory bowel disease (IBD) require ongoing medications. We aimed to describe (1) medication use in older and younger IBD patients and (2) medication associations with patient reported outcomes (PROs) in older patients.

Methods: We conducted cross-sectional and longitudinal analyses within CCFA Partners internet-based cohort of patients with self-reported IBD. We assessed medication use by disease sub-type and age. We used bivariate analyses to (1) compare medication use in older and younger patients and (2) determine associations between continued steroid use and patient reported outcomes in older patients.

Results: We included 5382 participants with IBD; 1004 were older (≥age 60). Older patients with Crohn's disease (CD) had lower antitumor necrosis factor alpha (anti-TNF) use at baseline (29.1% versus 44.3%, $P < 0.001$), comparable steroid use (16.0% versus 16.5%, $P = 0.77$), and higher aminosalicylate use (40.3% versus 33.9%, $P = 0.003$) versus younger patients. Older ulcerative colitis (UC) patients had similar anti-TNF use (16.0% versus 19.2%, $P = 0.16$), lower steroid use (9.6% versus 15.4%, $P = 0.004$), and higher aminosalicylate use (73.8% versus 68.2%, $P = 0.04$) at baseline. In longitudinal analyses, older CD patients had higher continued steroid use (11.6% versus 7.8%, $P = 0.002$); which was associated with worsened anxiety ($P = 0.02$), sleep ($P = 0.01$), and fatigue ($P = 0.001$) versus nonuse. Older CD patients on steroids, versus anti-TNF or immunomodulators, had increased depression ($P = 0.04$) and anxiety ($P = 0.03$).

Conclusions: Medication utilization differs in older patients with IBD. Older CD patients have higher continued steroid use associated with worsened patient reported outcomes. As in younger IBD populations, continued steroid use should be limited in older patients.

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Key Words: older, inflammatory bowel disease, Crohn's disease, ulcerative colitis

The populations of developed countries, such as the United States (US), are aging because of low fertility and mortality rates.[1,2] The 65+ age group is the fastest growing in the United States with an estimated 31% increase over the past decade.[3] In addition to an aging US population, inflammatory bowel disease (IBD) has a bimodal incidence distribution with 15% of cases occurring in the second peak after 65 years of age.[4] Because of these factors, the number of older patients living with IBD is expected to rise—including older persons newly diagnosed with IBD. Older-onset IBD may be associated with a milder disease phenotype with decreased progression to more severe stages such as stricturing or penetrating disease.[5,6] Despite a milder phenotype, older IBD patients, regardless of age of onset, have higher resource utilization with increased rates of in-hospital morbidity and mortality compared with younger IBD patients.[4] Therefore, optimizing the management of IBD in the older is increasingly important.[7]

Prior investigations have shown that the medical treatment strategies used in older IBD patients may be different compared with younger IBD populations, with an increased reliance on corticosteroids and 5-aminosalicylates (5-ASA) as maintenance therapies.[8–10] Steroid-sparing strategies such as immunomodulators or biological agents are used less frequently in older IBD patients despite current guidelines that support their use in this population for moderate to severe disease activity.[9,11,12] Factors such as adverse effects from prolonged or repeated corticosteroid use and delay in the use of appropriate steroid-sparing therapies

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related to disease activity may contribute to the lower short-term therapeutic efficacy and increased rates of adverse events seen in older IBD patients.[4,13,14] The adverse effects of corticosteroid use among IBD patients have been well-established[15,16] including increased risks of serious infections, mortality, and accelerated bone loss, which are further potentiated when factoring in the independent risk factor of advanced age. However, it is unknown how ongoing continued steroid use affects patient reported outcomes (PROs) such as anxiety, depression, sleep, and fatigue in older IBD patients.

We used data from a large Internet-based study of IBD to describe current medical therapies in older IBD patients, rates of continued steroid use, and associations between continued steroid use and PROs. Better information on the treatment experience of older IBD patients might aid in optimizing treatment strategies for this growing population.

METHODS

CCFA Partners is an Internet-based prospective cohort study of over 14,000 adults living with self-reported IBD, including both CD and ulcerative colitis (UC). The cohort initially began recruitment in 2011. The details of cohort development have been previously described.[17] Briefly, individuals with IBD are recruited to join CCFA Partners through social media, emails, advertising from the Crohn's and Colitis Foundation of America (CCFA), CCFA events, and through physicians' offices. Participants complete surveys every 6 months providing data on disease type, activity, course, medications, and selected PROs. Diagnoses in a randomly selected sample of the cohort have been validated, with over 96% of this sample having IBD confirmed by their physician.[18] The surveys include a number of indices previously validated for self-report, including the short Crohn's disease activity index (sCDAI),[19] simple clinical colitis activity index (SCCAI),[20,21] and short IBD questionnaire (SIBDQ).[22]

For the current analysis, we included all individuals who had completed at least 2 surveys over the course of a 12-month period (baseline and at least 1 follow-up) and whose disease type (CD or UC) had not changed over the course of the study time period. Those with indeterminate colitis (IC) were analyzed in the UC group. We used data from the baseline surveys to conduct a cross-sectional analysis of medication use, disease activity, and other characteristics comparing older individuals (age ≥60 yr) to younger individuals (age 18–59 yr). We then conducted 2 separate longitudinal analyses[1]: Comparisons of rates of long-term continued steroid use (defined as steroid use on 2 consecutive surveys at least 6 mo apart) in older versus younger individuals and[2] associations of continued versus noncontinued steroid use with various health and quality-related patient reported outcomes (PROs) among only older participants. Sensitivity analyses included an analysis of PROs in older IBD patients on continued steroid monotherapy as compared to biological and/or anti-TNF therapy. To eliminate confounding by disease activity, a second sensitivity analysis evaluated the effects of continued steroid use on PROs restricted to those individuals who met criteria for remission at follow-up. Remission was defined using a score of <150 on the sCDAI[22] for patients with CD or a score of ≤2 on the SCCAI for patients with UC.[20,21] PROs were measured using 5 domains (anxiety, sleep disturbance, pain interference, fatigue, and depression) from the patient reported outcomes measurement information system (PROMIS) as previously described for this cohort.[23] Briefly, all PROMIS measures have undergone rigorous development and validation in both general and chronically ill populations. Items are calibrated using a T-score metric with the mean of the US population equal to 50 and standard deviation (SD) of 10. Higher scores indicate "more" of the domain being measured, that is, worse anxiety, sleep disturbance, pain interference, fatigue, and depression. Emerging data suggest that minimally important differences (MIDs) in PROMIS measures are in the range of 2 to 6[24] as suggested by our prior work in this cohort.[23]

Statistical Analysis

All analyses were performed using STATA 12.0 (College Station, TX). The population was characterized using descriptive statistics, including proportions, means, standard deviations, stratified by CD and UC. Outcomes were compared used bivariate statistics as appropriate. Confidence intervals were 95% and $P < 0.01$ was considered statistically significant. The Institutional Review Board at the University of North Carolina at Chapel Hill approved the study protocol.

RESULTS

Cross-sectional Analyses of Baseline Surveys

A total of 5382 individuals with self-reported IBD were included. Of these, 3392 had CD and 1873 had UC/IC. Figure 1 shows geographic variation in corticosteroid use and biological use for the entire cohort, with the highest overall use of biologics in patients with CD. There were 1004 older participants (≥60 yr of age), 636 individuals with CD, and 368 with UC. The median age for both the older CD and UC populations was 65 years. Characteristics of the CD and UC populations by age group are shown in Tables 1 and 2, respectively.

Crohn's Disease

Older individuals with CD reported a higher rate of remission (64.2% versus 59.7%, $P = 0.05$) determined by short Crohn's Disease Activity Index (sCDAI) score <150. Older CD individuals also reported a better health-related quality of life: Short Inflammatory Bowel Disease Questionnaire (SIBDQ) scores were 5.3 (IQR 4.5–6.0) versus 4.9 (IQR 3.9–5.7), $P < 0.001$ at baseline. For CD patients, older participants had markedly higher rates of prior surgery (65.2% versus 48.1%, $P < 0.001$) compared with the younger participants. Within the CD population, there was no significant difference in use of corticosteroids between the older and younger populations (16.0% versus 16.5%, $P = 0.77$). However, significantly fewer older CD individuals reported biological anti-

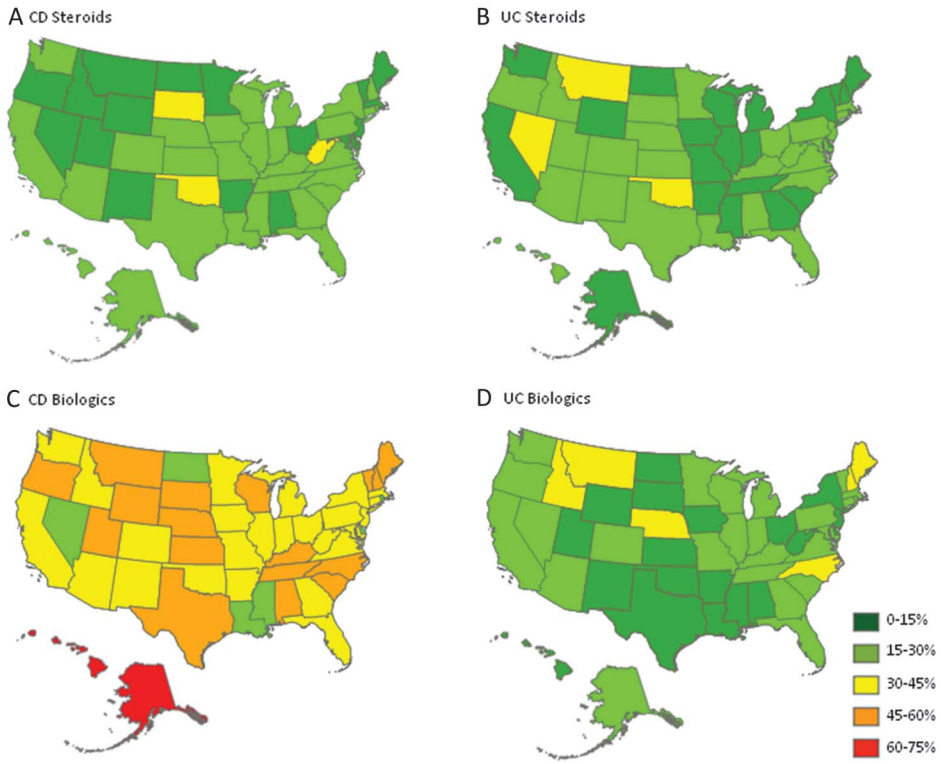

FIGURE 1. Baseline rates of corticosteroid (A and B) and biologic (C and D) use in patients with CD and UC in CCFA Partners.

tumor necrosis factor alpha (anti-TNF) use compared with younger CD patients (29.1% versus 44.3%, $P < 0.001$). Aminosalicylate (5-ASA) use was higher among older CD patients as compared to younger (40.3% versus 33.9%, $P < 0.001$).

Ulcerative Colitis

The older versus younger UC populations reported similar rates of remission (45.9% versus 43.9%, $P = 0.53$) as determined by a SCCAI score of 2 or lower. Even with similar reported disease activity, older UC patients scored higher on the SIBDQ (5.5 [IQR 4.6–6.0] versus 5.0 [IQR 4.0–5.8], $P < 0.001$). Furthermore, surgery rates in the older population were similar to the younger population for UC (13.6% versus 11.8%, $P = 0.35$). Additionally, the older population reported lower corticosteroid use at baseline than younger patients (9.6% versus 15.4%, $P = 0.004$). Differing from the CD population, the older UC patients had similar biological anti-TNF usage when compared with the younger UC patients (16.0% versus 19.2%, $P = 0.16$). There was a small significant difference between rates of 5-ASA use among the older and younger UC populations (73.8% versus 68.2%, $P = 0.04$).

Longitudinal Analyses

In the longitudinal analyses, using data from both baseline and follow-up visits 6 to 12 months apart, prevalence of continued steroid use (current use reported at both time points) was 48% higher along older versus younger CD patients (11.6% versus 7.8%, $P = 0.002$). In contrast, continued use of biological anti-TNF agents over this same time period was 60% lower in older CD participants, whereas prevalence of immunomodulator use was similar (Fig. 2A). For UC patients, continued steroids, biological anti-TNF agents, and immunomodulators were all used less frequently by the older (Fig. 2B).

Patient Reported Outcomes in Older Patients

We evaluated effects of continued medication use over 6 to 12 months on PROs measured at follow-up. Among older patients, those with continued steroid use had significantly worsened anxiety (mean 52.5), sleep (mean 52.4), and fatigue (mean 55.3) as compared to nonsteroid use. Pain (mean 53.9) and depression (mean 50.5) were also higher, albeit not statistically significantly when compared with nonsteroid users. Similar effects were observed within strata of CD and UC participants. Differences in PROs overall and by disease subtype are shown in Table 3. All comparisons that met statistical significant also met the threshold of ≥2, associated with a minimally important difference clinically. In a sensitivity analysis of only participants in remission at baseline, older patients with continued steroid use still had poorer health-related quality-of-life scores in all 5 PROMIS domains when compared with nonusers although these differences were only significant for the fatigue domain (mean 52.2 versus mean 48.2, $P = 0.02$). In a separate analysis comparing older IBD patients on continued steroid monotherapy to older IBD patients on immunomodulators or biological anti-TNF agents without steroids, those on continued steroids had significantly

TABLE 1. Characteristics of CCFA Partner's Crohn's Disease Patients by Age at Baseline

Characteristics	Older (Age ≥ 60), (n = 636), Median (IQR) or %	Younger (Age 18–59), (n = 2756), Median (IQR) or %
Age, yr	65 (62–70)	39 (29–50)
Gender (% female)	62.9	74.9
Education (% >high school)	90.9	91.7
Race, %		
Caucasian	97.8	94.5
African American	1.0	1.7
Other	1.2	3.8
Current smoking (% yes)	6.2	7.8
BMI	25.1 (22.2–28.6)	23.9 (21.2–27.9)
Disease duration, yr	31 (13–42)	10 (4–21)
Ever GI surgery (% yes)	65.2	48.1
Ever GI hospitalization (% yes)	81.3	71.4
Number hospitalizations	4 (2–6)	3 (2–6)
Current medications, %		
Biological anti-TNF	29.1	44.3
Immunomodulator[a]	27.6	32.9
Corticosteroids	16.5	16.0
5-ASA[b]	40.3	33.9
Remission (sCDAI[c] < 150) (% yes)	64.2	59.7
sCDAI	114 (72–184)	128 (72–198)
SIBDQ[d]	5.3 (4.5–6)	4.9 (3.9–5.7)

[a]Immunomodulator defined as 6-mercaptopurine, azathioprine, or methotrexate.
[b]5-aminosalicylate.
[c]Short Crohn's disease activity index.
[d]Short inflammatory bowel diseases questionnaire.

TABLE 2. Characteristics of CCFA Partner's Ulcerative Colitis Patients by Age at Baseline

Characteristics	Older (Age ≥ 60), (n = 368), Median (IQR) or %	Younger (Age 18–59), (n = 1622), Median (IQR) or %
Age, yr	65 (63–70)	38 (29–48)
Gender (% female)	59.0	73.2
Education (% >high school)	90.9	93.9
Race		
Caucasian	97.3	91.9
African American	1.2	1.2
Other	1.5	6.8
Current smoking (% yes)	2.2	3.3
BMI	26.0 (23.3–29.4)	23.7 (21.3–27.4)
Disease duration, yr	16 (6–31)	7 (3–14)
Ever GI surgery (% yes)	13.6	11.8
Ever hospitalization (% yes)	39.7	47.4
Number hospitalizations	2 (1–3)	2 (1–3)
Current medications		
Biologic anti-TNF	16.0	19.2
Immunomodulator[a]	18.5	24.0
Corticosteroids	9.6	15.4
5-ASA[b]	73.8	68.2
Remission (SCCAI[c] ≤ 2) (% yes)	45.9	43.9
SCCAI	3 (1–4)	3 (1–5)
SIBDQ[d]	5.5 (4.6–6)	5 (4–5.8)

[a]Immunomodulator defined as 6-mercaptopurine, azathioprine, or methotrexate.
[b]5-aminosalicylate.
[c]Simple clinical colitis activity index.
[d]Short inflammatory bowel diseases questionnaire.

worsened depression (mean 50.8 versus mean 48.2, $P = 0.03$) and anxiety (mean 52.6 versus mean 49.8, $P = 0.04$) at follow up.

DISCUSSION

In a cross-sectional analysis, we found geographic differences in baseline medication utilization and differences between the older and younger CD and UC populations. Steroid use at baseline was similar between age groups for both CD and UC; however, biological use was markedly lower for older patients with CD as compared to the younger population.

Lower rates of biological use and higher 5-ASA use in older CD patients may suggest milder disease activity. This is supported by the higher rates of remission and better SIBDQ scores seen in this older CD population. However, despite these indicators supporting a milder disease activity, the reported GI surgery rates for both the older CD and UC populations suggest that disease activity may not be milder in the older. It is possible that providers are reluctant to prescribe biological agents in this older population. Although biological agents are highly effective, costs to the patient must be taken into account, especially for older patient populations on a fixed income. Per-patient yearly expenditure is estimated around $8265 to $11,129 for CD, more costly than diabetes, stroke, coronary artery disease, chronic obstructive pulmonary disease, or multiple sclerosis.[25–27] The lower rates of biological use in the older may be partially influenced by patients' out-of-pocket expenses for these medications. It is also possible that concerns about safety of these agents in older patients may impact prescribing patterns.[14,28] Interestingly, older patients with CD had significantly higher rates of continued steroid use than younger populations in our longitudinal analysis—perhaps related to these same factors of cost and perceived safety. In fact, corticosteroids, especially when used for more than 3 months duration, are considered potentially inappropriate

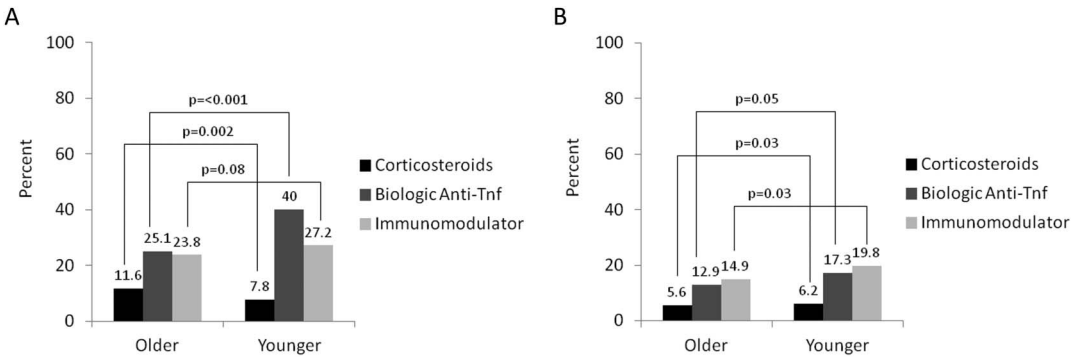

FIGURE 2. A, Continued medication use in Crohn's disease by age. B, Continued medication use in ulcerative colitis by age. Defined by use at baseline and follow-up at least 6 months apart.

medications (PIM) by the Beers Criteria. PIMs are associated with increased hospitalizations, costs of care, and mortality among older persons.[29] Furthermore, it is important to note that steroids, not biological anti-TNF agents or immunomodulators, have been associated with increased mortality in patients with IBD.[15]

Prior studies of medication utilization among the older IBD cohort indicate greater reliance on corticosteroids and 5-aminosalicylates as maintenance therapies.[8,9,30] Biological agents are used less frequently despite literature supporting efficacy in moderate-to-severe CD and UC. Delays in starting appropriate steroid-sparing therapies may contribute to the potentially lower therapeutic efficacy seen in the few studies available and the increased rates of adverse events.[14] Higher rates of discontinuation associated with these medications in older patients may be due to poorer response rates but also may be due to evolving disease activity and declines in physical reserve. Consequences of prolonged disease activity (anemia, malnutrition, dehydration, etc.) can be associated with increased infection risk and increased hospitalizations.[4] Biological agents have recently been associated with increased risks of adverse events in older patients with IBD, but this may be confounded by complications of disease activity.[14] In contrast to data from IBD, the rheumatology literature does not describe differing rates of biological anti-TNF use by age. Data from the anti-rheumatic drug intervention and utilization study (RADIUS), a real-world prospective observational program of rheumatoid arthritis patients aimed at assessing prescribing patterns, safety and effectiveness of disease modifying anti-rheumatic drugs (DMARDs) and biologics, showed similar rates of biological prescribing for the older (≥65 yr) and younger (<65 yr) patients.[31] Extrapolations from rheumatoid arthritis-based studies focusing on the older population indicate an increased risk of serious infection and hospitalization with immunosuppression, but the safety signals are greater with corticosteroids and nonbiological DMARDs compared with anti-TNF-based therapies.[32,33]

Importantly, our study assessed the association of continued steroid use on important PROs in the older population. Given the effects we found on depressive symptoms, anxiety, fatigue, and sleep, continued steroid use should not be considered a "milder" treatment when compared with other forms of immunosuppression. These therapies directly impact a patient's quality of life. These effects can have a greater impact even than well-known complications of corticosteroids including weight gain, bone health, metabolism, diabetes, and cataracts. These untoward effects can be particularly debilitating in an older population. Factors such as anxiety, fatigue, and depression negatively impact functional status. Declines in functional status in the older may result in increased disability, morbidity, and cognitive impairment.[34]

The strengths of this cohort study include the geographically diverse and large sample size of participants in CCFA Partners, with members in every US state. As older patients are

TABLE 3. Patient Reported Outcomes Measured by PROMIS in Older Patients with IBD

Patient Reported Outcome	Continued Steroid Use	No Continued Steroid Use	P[a]
IBD overall	n = 90	n = 871	
Anxiety	52.5	50.3	0.02
Sleep	52.4	50.1	0.01
Pain	53.9	50.9	0.07
Fatigue	55.3	51.6	0.001
Depression	50.5	48.8	0.07
Crohn's disease	n = 70	n = 535	
Anxiety	52.4	50.0	0.03
Sleep	52.3	50.6	0.11
Pain	53.1	50.9	0.25
Fatigue	55.7	52.6	0.02
Depression	50.8	48.7	0.05
Ulcerative colitis	n = 20	n = 336	
Anxiety	52.9	50.7	0.31
Sleep	52.9	49.5	0.08
Pain	56.3	50.9	0.11
Fatigue	54.2	50.2	0.08
Depression	49.6	49.0	0.79

[a]By Student's t test.

not well-represented in randomized controlled trials and are not necessarily seen in large numbers at individual centers, this unique cohort allows for comparisons of important PROs in a large sample of older IBD patients. Additionally, within our cohort, we are able to capture outcome data using validated instruments for self-report. There are also several limitations to this study. First, the patient volunteers who make up the CCFA Partners cohort are not necessarily representative of the IBD population of the United States. Therefore, these findings may have limited external generalizability. As internet capability is required to participate, the CCFA Partners members may have higher education levels and socioeconomic status when compared with the IBD population in general. We also do not have access to pharmacy data or records of all prior medications and reasons for discontinuation. We did not collect data on steroid-specific physical manifestations such as striae, fluid retention, cataracts, or fractures. We chose to focus on PROs instead, such as mood effects, sleep and fatigue, as these manifestations have not been systematically evaluated in a population of older patients on continued corticosteroids. We also do not have validation of all IBD diagnoses from within our cohort. However, in a validation study of a sample within CCFA Partners, over 97% of individuals accurately reported their disease type when compared with records from their treating physician.[18] Longitudinal data from within this cohort do have internal validity and the study design allows for optimal collection of PRO data.

In conclusion, older patients with IBD have different medication utilization patterns when compared with those of younger patients. There were large differences in biological anti-TNF utilization in older versus younger CD patients. Continued steroid use was significantly higher in older CD patients and was negatively associated with important PROs. A better understanding of the complications of continued steroid use in this population will help drive age-specific guidelines for medication use. Ultimately, quality-of-life measures for older patients with IBD will be improved if continued steroid use can be minimized. With the aging of the IBD population, we need to understand the impact of our various therapies on both IBD activity and patient related outcomes.

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REFERENCES

1. Vincent GraysonK, Velkoff Victoria Averil; Bureau USC. *The Next Four Decades, the Older Population in the United States: 2010 to 2050*. Available at: https://www.census.gov/prod/2010pubs/p25-1138.pdf. Accessed December 1, 2015.
2. Benchimol EI, Manuel DG, Guttmann A, et al. Changing age demographics of inflammatory bowel disease in Ontario, Canada: a population-based cohort study of epidemiology trends. *Inflamm Bowel Dis.* 2014;20:1761–1769.
3. Administration on Aging (AoA) Profile of Older Americans. Available at: http://www.aoa.acl.gov/Aging_Statistics/Profile/index.aspx. Accessed December 1, 2015.
4. 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.
5. 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.
6. Ha CY, Newberry RD, Stone CD, et al. Patients with late-adult-onset ulcerative colitis have better outcomes than those with early onset disease. *Clin Gastroenterol Hepatol.* 2010;8:682–687.e1.
7. Ha CY, Katz S. Clinical outcomes and management of inflammatory bowel disease in the older patient. *Curr Gastroenterol Rep.* 2013;15:310.
8. 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.
9. Juneja M, Baidoo L, Schwartz MB, et al. Geriatric inflammatory bowel disease: phenotypic presentation, treatment patterns, nutritional status, outcomes, and comorbidity. *Dig Dis Sci.* 2012;57:2408–2415.
10. Johnson SL, Bartels CM, Palta M, et al. Biological and steroid use in relationship to quality measures in older patients with inflammatory bowel disease: a US Medicare cohort study. *BMJ Open.* 2015;5:e008597.
11. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American college of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol.* 2010;105:501–523; quiz 524.
12. Lichtenstein GR, Hanauer SB, Sandborn WJ. Management of Crohn's disease in adults. *Am J Gastroenterol.* 2009;104:465–483; quiz 464, 484.
13. Parian A, Ha CY. Older age and steroid use are associated with increasing polypharmacy and potential medication interactions among patients with inflammatory bowel disease. *Inflamm Bowel Dis.* 2015;21:1392–1400.
14. Lobaton T, Ferrante M, Rutgeerts P, et al. Efficacy and safety of anti-TNF therapy in elderly patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2015;42:441–451.
15. Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infections and mortality in association with therapies for Crohn's disease: TREAT registry. *Clin Gastroenterol Hepatol.* 2006;4:621–630.
16. Ezzat Y, Hamdy K. The frequency of low bone mineral density and its associated risk factors in patients with inflammatory bowel diseases. *Int J Rheum Dis.* 2010;13:259–265.
17. Long MD, Kappelman MD, Martin CF, et al. Development of an internet-based cohort of patients with inflammatory bowel diseases (CCFA Partners): methodology and initial results. *Inflamm Bowel Dis.* 2012;18:2099–2106.
18. Randell RL, Long MD, Cook SF, et al. Validation of an internet-based cohort of inflammatory bowel disease (CCFA partners). *Inflamm Bowel Dis.* 2014;20:541–544.
19. Thia K, Faubion WA Jr, Loftus EV Jr, et al. Short CDAI: development and validation of a shortened and simplified Crohn's disease activity index. *Inflamm Bowel Dis.* 2011;17:105–111.
20. Turner D, Seow CH, Greenberg GR, et al. A systematic prospective comparison of noninvasive disease activity indices in ulcerative colitis. *Clin Gastroenterol Hepatol.* 2009;7:1081–1088.
21. Jowett SL, Seal CJ, Phillips E, et al. Defining relapse of ulcerative colitis using a symptom-based activity index. *Scand J Gastroenterol.* 2003;38:164–171.
22. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. *Am J Gastroenterol.* 1996;91:1571–1578.

23. Kappelman MD, Long MD, Martin C, et al. Evaluation of the patient-reported outcomes measurement information system in a large cohort of patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol.* 2014;12:1315–1323.e2.
24. Yost KJ, Eton DT, Garcia SF, et al. Minimally important differences were estimated for six Patient-Reported Outcomes Measurement Information System-Cancer scales in advanced-stage cancer patients. *J Clin Epidemiol.* 2011;64:507–516.
25. Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol.* 2007;5:1424–1429.
26. Kappelman MD, Rifas–Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US Children and adults. *Gastroenterology.* 2008;135:1907–1913.
27. Gunnarsson C, Chen J, Rizzo JA, et al. Direct health care insurer and out-of-pocket expenditures of inflammatory bowel disease: evidence from a US national survey. *Dig Dis Sci.* 2012;57:3080–3091.
28. Ha C, Katz S. Management of inflammatory bowel disease in the elderly: do biologicals offer a better alternative? *Drugs Aging.* 2013;30:871–876.
29. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2012;60:616–631.
30. Taleban S. Challenges in the diagnosis and management of inflammatory bowel disease in the elderly. *Curr Treat Options Gastroenterol.* 2015;13:275–286.
31. Gibofsky A, Palmer WR, Goldman JA, et al. Real-world utilization of DMARDs and biologics in rheumatoid arthritis: the RADIUS (Rheumatoid Arthritis Disease-Modifying Anti-Rheumatic Drug Intervention and Utilization Study) study. *Curr Med Res Opin.* 2006;22:169–183.
32. Atzeni F, Sarzi-Puttini P, Botsios C, et al. Long-term anti-TNF therapy and the risk of serious infections in a cohort of patients with rheumatoid arthritis: comparison of adalimumab, etanercept and infliximab in the GISEA registry. *Autoimmun Rev.* 2012;12:225–229.
33. 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.
34. Colon-Emeric CS, Whitson HE, Pavon J, et al. Functional decline in older adults. *Am Fam Physician.* 2013;88:388–394.