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Conflicts of interest
The authors disclose no conflicts.

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Reply. We thank van Dieren et al for their comments on our study. Individuals with Hereditary Diffuse Gastric Cancer (HDGC) syndrome face the difficult decision of when to proceed with a gastrectomy that could eliminate the risk for gastric cancer but at a significant cost in quality of life. This decision must be confronted as early as 20–30 years of age. Many patients will choose to defer surgery, but there have been limited data on their outcomes. In our experience with this unique group of patients, cancer-related outcomes in patients who pursued endoscopic surveillance were similar to in those who pursued immediate gastrectomy.

The question of targeted vs random biopsies in endoscopic surveillance is a good one. Our protocol included biopsies of any suspicious lesions as well as random samples. The overall rate of detection of foci of signet ring cell cancer (SRCC) was lower than the highest rate reported in the literature[1] but was not dissimilar to others.[2,3] These variations may reflect differences in patient populations, endoscopic and imaging devices, and subjective assessments of endoscopic abnormalities. It is noteworthy that scars from prior endoscopic biopsies are not easily distinguished from pale spots that may harbor SRCC. A broader question that remains unanswered is the clinical significance of recognizing microscopic foci of SRCC during endoscopy. Specifically, is the identification of such lesions associated with a higher subsequent risk of invasive gastric cancer, and will promptly proceeding to gastrectomy influence the natural history of the disease? It is well recognized that nearly all gastrectomy specimens from HDGC patients, even those in their early 20s, will harbor multiple microscopic foci of SRCC. However, the mean age of gastric cancer diagnosis is much older, at 47 years, and recent reports have revised the lifetime risk of invasive gastric cancer downward from 70% to 37%–42%.[4,5] Not every microscopic focus of SRCC will progress, and the development of a specific endoscopic or histologic marker that could inform the true risk of progression would be of great value.

Our results do not alter the existing recommendation that gastrectomy is the definitive approach for cancer risk reduction in HDGC. The current findings suggest that endoscopic surveillance may also have a role, but more precise risk stratification among *CDH1* mutation carriers will be necessary to select the best candidates for such an approach.

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The Challenges of Managing Inflammatory Bowel Diseases in Older Patients

Dear Editor:

With great interest we have read the review by Singh et al[1] discussing the challenges and solutions in the management of obese, older, and obstetric patients with inflammatory bowel disease (IBD). We would like to react on the second population described, namely the older patient. Indeed little evidence is available on (treatment of) older patients with IBD. Despite this lack of evidence, the authors propose a so-called evidence-derived algorithm on the treatment of older patients with IBD (Figure 2). We agree with the authors that characterizing the older patient not merely based on chronologic age, but based on patient characteristics reflecting a biologic age, such as frailty, could be an essential aspect of future therapy guidelines in older patients with IBD.

However, we do have some difficulty with the distinction made between fit and frail. The proposed algorithm suggests that frailty is an entity that is either absent or fully present. Frailty, however, is a complex term with little consensus on its definition.[2] When frailty is suspected, it is best measured by a comprehensive geriatric assessment, which assesses all geriatric domains. These domains comprise (1) somatic status (ie, the presence of multiple comorbidities, polypharmacy, and malnutrition), (2) mental status (ie, the presence of cognitive impairment or depression), (3) functional status (ie, dependency in [instrumental] activities of daily living and physical status), and (4) social status (ie, the presence of social support). The previously mentioned domains are then integrated into an assessment of the overall level of frailty. Such an algorithm as proposed by Singh et al[1] should not be focusing on frailty as a binary entity, but rather display a gradual scale from absence of geriatric impairments to a state of impairment in all geriatric domains. With an increase in the number of impaired domains, physicians could be advised to pay more attention to clinical rather than endoscopic remission and focus more on quality of life, such as preserving self-dependence or keeping the ability to maintain social contacts. Factors influencing quality of life differ greatly between patients and these factors could partly define therapy choices and treatment goals. However, very little evidence on geriatric impairments in older patients with IBD is available and more research is needed on the prevalence of geriatric impairments and the impact on adverse health outcomes or quality of life in this population.[3]

Furthermore, we note the authors' choices on preferred IBD medication in both the "non-frail" and "frail" patient groups. In the proposed treatment algorithm, immunomodulators have no place in treatment of both groups, even though methotrexate is safe in older patients with Crohn's disease because of its low risk on lymphoproliferative disorders or nonmelanoma skin cancer compared with other immunomodulators.[4] The use of methotrexate should therefore not be ruled out in older patients with IBD, especially in patients without impairments in their geriatric domains.

Furthermore, although the authors state in their manuscript that there are limited data on safety of non–tumor necrosis factor-α targeted biologic agents in older patients, they suggest starting vedolizumab or ustekinumab therapy in corticosteroid-dependent frail older patients. However, both therapies require a certain fitness of patients because these therapies have to be administered subcutaneously at home or require frequent hospital visits because of intravenous administration. Additionally, no data are presented about the effect of comorbid diseases on treatment outcomes in patients on vedolizumab and ustekinumab therapy. Thus, at least frequent monitoring of these patients with "multiple suboptimally controlled comorbidities" should be advised.

In conclusion, the IBD research field needs more evidence on older patients with IBD. We definitely support the use of a more biologic age–based treatment algorithm in the older patient with IBD; however, the term "frailty" is vague and should not be used as a binary entity. The proposed treatment options are, in our opinion, not evidence-derived and this treatment algorithm should be seen as a call for more research, rather than evidence-derived.

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Reply. We thank Dr. Asscher et al[1] for their interest in our work and for their comments. We welcome their recommendation for more evidence to help inform the management of older patients with inflammatory bowel disease in daily clinical practice. We completely agree that frailty is not a binary state, and exists as a spectrum, with impairment potentially impacting multiple domains to varying extent (somatic, mental, functional, and social status). Our intent was to highlight the distinction between chronological age and fitness, in determining optimal management strategies. We agree that a comprehensive and structured assessment of frailty be routinely considered in the management of older patients. With regard to our proposed pharmacologic management of older patients with inflammatory bowel disease, we acknowledge that this represents our opinion, based on our interpretation and extrapolation on the comparative efficacy and safety of pharmacotherapies.[2] Although studies have not directly compared the biologic monotherapy versus methotrexate monotherapy, indirect comparisons suggest that biologic therapy may be more effective than