

# **Considerations on Multimorbidity and Frailty in Inflammatory Bowel Diseases**

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## Abstract

There are growing numbers of older people with inflammatory bowel diseases [IBD]. These older patients are more likely to have other comorbidities and polypharmacy, which can make recognizing and treating IBD complex. Frailty is a newer concept in the IBD field, and we are beginning to recognize the importance of this as a marker of biological age and its association with risk of adverse IBD-related outcomes. In this review article we aim to provide practical insight into the specific challenges facing older patients and their clinicians at each stage of the patient journey. We also discuss the latest understanding of the impact of frailty for these patients with IBD and highlight areas for future research.

Key words: Ageing; frailty; IBD

# 1. Introduction

Inflammatory bowel diseases [IBD] encompassing ulcerative colitis [UC] and Crohn's disease [CD] were traditionally considered disorders affecting mainly young adults in Western populations. More recently, a rapid increase in incidence combined with rising compound prevalence due to lack of a cure and low mortality rates has resulted in a large proportion of older IBD patients, with current estimates suggesting that up to a third of the IBD population are aged over 60 years.<sup>1,2</sup> This cohort of older patients can be split into two groups: those who were diagnosed before age 60 and those with a diagnosis of IBD after age 60, defined by the European Crohn's and Colitis Organisation [ECCO] as older onset IBD, the latter of which constitutes ~15% of the IBD population.<sup>2,3</sup>

IBD in older individuals presents a unique set of challenges in diagnosis, medical and surgical therapies, and monitoring. The aim of this review article is to summarize the important issues to consider when caring for older patients with IBD and we aim to describe these at each stage throughout the patient journey.

# 2. Ageing and the frailty concept

A combination of improved survival and falling fertility rates means that the majority of countries internationally are anticipating an increase in the size of their older populations.<sup>4</sup> This is evidenced in the rise projected in the number of people globally aged over 65 years old from 0.7 billion in 2019 to 1.55 billion in 2050; regionally this rise is largest in North Africa and Western Asia [120%] and smallest in Europe and North America [48%].<sup>4</sup>

As people are living longer and living for an extended proportion of that time with greater disability and comorbidity, there is a wide variation in the health of older people. Ageing is a continuous and gradual process throughout adulthood, and chronological age alone is insufficient to capture the variation in this process among individuals.<sup>5</sup> A person's chronological age, defined as the number of years alive, is not necessarily equivalent to their biological age, defined as the cumulative biological changes associated with ageing. Over time, humans accumulate damage at a cellular and molecular level, including for example telomere attrition and mitochondrial dysfunction.6 The accumulation of this damage, and the degree to which damage is repaired, varies between individuals, and relates to factors across the life course such as smoking, physical activity, being under or over weight, and living alone or in poverty. In inflammatory conditions such as IBD there is cytokine-induced acceleration of biological ageing due to low-grade inflammation and senescence of cells.

Frailty represents a means of measuring biological age. Frailty can be defined as a loss of physiological reserve whereby relatively minor stressors, such as a minor infection, can precipitate sudden and dramatic changes in a person's health including delirium, becoming bedbound, and/or requiring care for basic daily needs.<sup>8</sup> There is no consensus on how best to measure frailty, but it may be best understood as an accumulation of the additive effects of health deficits across organ systems on the overall health of an individual.<sup>9</sup> Deficits may include diseases but also impairments that do not meet disease diagnostic criteria, including biochemical or physiological abnormalities. Frailty is common and prevalence estimates in older adults living in the community range from 4 to 59% with an overall weighted average of 10.7%.<sup>10</sup> Older people living with frailty are at higher risk of adverse

© The Author(s) 2024. Published by Oxford University Press on behalf of European Crohn's and Colitis Organisation. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/ licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com Table 1. Outline of frailty assessments that have been used to date in IBD research.

Assessment	Summary	Comments
Hospital Frailty Risk Score <sup>19</sup>	Calculated from weighted sum of 109 ICD-10 codes	Relies on accurate ICD coding. Can be imple- mented into hospital electronic systems but otherwise challenging to use in clinical practice. Less focus on ADLs
Fried phenotype <sup>20</sup>	Defined as having any 3 of the following: unintentional weight loss, self-reported exhaustion, weak grip strength, slow gait speed, and low physical activity	Relatively simple and inexpensive to perform with standardized questions and assessments, but weight loss, fatigue, and sarcopenia are common in IBD so may overestimate frailty in IBD
FRAIL scale <sup>21</sup>	Three of the following self-reported questions on: fa- tigue, ability to climb 1 flight of stairs, ability to walk 1 block, 5 or more illnesses and weight loss >5% in 6 months Simple and can be done remotely. Again, w loss and fatigue are common in IBD so f may be overestimated	
Claims-based frailty index <sup>22</sup>	Score calculated using ICD-9 codes, procedural codes, and supplies/services codes	Relies on accurate coding and includes codes not available in all countries. Impractical to use in clinical settings unless incorporated into elec- tronic systems
Clinical Frailty Scale <sup>23</sup>	Seven-point scale ranging from very fit to severely frail with descriptors	Easy to use but potential for inter-rater variability
Frailty trait counts <sup>24,25</sup> —modi- fied Frailty Index <sup>26</sup> and simplified Frailty Index <sup>27</sup>	Total present from 5 or 6 of diabetes, COPD, HTN, CHF, dependent functional status and >10% weight loss in 6 months	Simple and quick but very limited number of deficits so probably do not fully capture frailty
Modified Frailty Index <sup>28</sup>	Proportion of which 12 are present: non-independent functional status, diabetes, COPD or pneumonia, CHF, previous MI, history of PCI, cardiac surgery or angina, HTN, PVD, impaired sensorium, TIA, and CVA	Simple and quick but limited deficits with over- emphasis on cardiovascular comorbidity
Geriatric assessment <sup>29</sup>	Explores somatic, ADL, physical, mental, and social domains by using questionnaires and assessments, e.g. grip strength and gait speed	Comprehensive assessment covering multiple relevant domains but takes 15–45 min to complete
G8 questionnaire <sup>30</sup>	Includes age and 7 questions about food intake, weight loss, mobility, neuropsychological issues, BMI, polypharmacy, and health status	Short and simple but developed as a screening tool for identifying which oncology patients required more in-depth geriatric assessment, not intended to diagnose frailty
Johns Hopkins Adjusted Clinical Groups frailty defining diag- noses <sup>15</sup>	Presence of any one condition associated with frailty: dementia, decubitus ulcers, malnutrition, faecal incon- tinence, etc.	Simple but very limited number of deficits with potential for overlap with IBD symptoms

ADL, activities of daily living; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; HTN, hypertension; ICD, International Classification of Disease; IBD, inflammatory bowel disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischaemic attack.

outcomes, including falls, longer and more frequent hospitalizations, more peri-operative complications, long-term disability, and mortality.<sup>11</sup>

Research looking at the impact of frailty in IBD has been expanding recently. The prevalence of frailty in patients with IBD has been shown to be around 18%.<sup>12</sup> A link between active disease and frailty has been suggested but more evidence is required to understand this.<sup>13,14</sup> Frailty has been shown to be associated with poor IBD-related outcomes including hospitalization and mortality and therefore it is vital we understand how to assess and manage these patients.<sup>15-17</sup>

Evidence in general populations suggests that health outcomes may be improved for people with frailty through multi-component interventions.<sup>18</sup> We need to understand whether and to what degree these multi-component interventions are effective in patients with IBD and to what degree frailty in IBD may be reversible with disease therapy. To do this we require frailty assessments that can accurately predict risk of adverse events designed specifically for patients with IBD. There have been several frailty assessments used to date to investigate frailty in IBD patients [Table 1]. However, a major challenge with IBD frailty assessments to date is that many include deficits which overlap with symptoms of IBD disease activity including extraintestinal manifestations and disorders directly related to IBD.

### 3. Considerations for IBD diagnosis in older adults

In general, lower gastrointestinal symptoms are common in older people. One study demonstrates these may occur in up to 57% of older patients with only 24% seeking medical attention.<sup>31</sup> Constipation is particularly common and is likely to be related to a combination of factors including decreased mobility, presence of comorbid conditions such as Parkinson's disease, polypharmacy [e.g. anticholinergic or diabetic medications] and dietary changes.<sup>32</sup> Additionally, cardiovascular comorbidities are more common in older patients and the use of antiplatelet and anticoagulant medication can add a level of complexity to assessment of rectal bleeding. Whilst typical IBD symptoms such as bloody diarrhoea, abdominal pain, and weight loss are common at presentation regardless of age, the frequency at which particular symptoms occur does differ slightly. In a French cohort, older-onset patients with CD had less diarrhoea, abdominal pain, and systemic symptoms [i.e. fever and weight loss] than younger patients at presentation, but more rectal bleeding, whilst older-onset UC patients experienced less rectal bleeding and abdominal pain.<sup>33</sup>

Furthermore, the range of potential differential diagnoses for older patients is more extensive than for younger patients. These include diverticular disease, ischaemic colitis, microscopic colitis, radiotherapy-induced colitis, and colorectal cancer which are more prevalent in older patients.<sup>34</sup> Older patients are also more likely to be hospitalized for infectious colitis, and are at higher risk of developing *Clostridium difficile*-associated colitis.<sup>35</sup> Evidence suggests that patients diagnosed with UC after 65 years were more likely to receive an alternative diagnosis first, such as diverticulitis, than those diagnosed at a younger age.<sup>36</sup> This also highlights the importance of taking mapping biopsies as rectal involvement is less likely in diverticular disease. These reasons may in part explain why older patients tend to experience a greater diagnostic delay than younger patients.<sup>37,38</sup>

It is also important to mention that some older patients will have cognitive impairment. One population-based cohort study followed patients up for up to 16 years and demonstrated an association between IBD and subsequent development of dementia with a further study showing impairment in neurocognitive function of IBD patients when compared to age- and sex-matched 'healthy' controls.<sup>39,40</sup> Cognitive impairment may affect the patients' ability to report and describe symptoms and therefore involvement from a care giver can be helpful in achieving an early diagnosis.

## 4. Considerations for IBD Investigation in Older Adults

The main considerations for older patients should be whether the diagnostic gain outweighs the risk associated with the chosen investigation and whether the patient is able to tolerate the suggested test. Ileocolonoscopy and biopsy is advised by ECCO for the diagnosis of both UC and CD.<sup>41</sup> Evidence suggests that the risk of adverse events following colonoscopy is higher for older patients with a meta-analysis demonstrating a cumulative adverse event rate [perforation, bleeding, and cardio-pulmonary complications] for those aged over 65 of 26/1000 with this rising to 34.9/1000 in those aged over 80 years.<sup>42</sup> It is also important to highlight that the consequences of a complication such as a perforation are likely to be more severe in an older patient or someone with frailty compared to a younger, fitter patient. A further study has also demonstrated that colonoscopy completion rate is lower in patients aged over 90 when compared with those aged over 70 years, with inadequate bowel preparation being the main cause.43

Bowel preparation can be difficult to tolerate.<sup>44</sup> There are also practical considerations for older patients as it can be associated with risks including hypovolaemia and electrolyte disturbance.<sup>45</sup> Furthermore, it is important to think about the risk of falls associated with bowel preparation in patients with impaired mobility, visual impairment, or postural hypotension. Individual types of preparation may be contraindicated for certain comorbidities, for example avoiding sodium phosphate preparations in patients with renal disease, heart failure, or those on specific medications.<sup>45</sup> Inpatient admission is sometimes considered, with or without administration of intravenous fluid, to ameliorate some of these risks, but this is associated with poor preparation and therefore the appropriateness of colonoscopy for these patients should be reviewed with consideration given to alternative investigations.<sup>46</sup> In those deemed appropriate, we should try to optimize the safety of endoscopy in older patients and this includes choosing appropriate bowel preparation, ensuring this is split dose and low volume if needed, ensuring society guidelines are followed regarding antiplatelet and anticoagulant medications, using lower starting doses of sedation with careful titration, and close monitoring.47 Clearly the risk associated with the procedure and preparation should be considered prior to requesting these investigations, and consideration should be given to a limited flexible sigmoidoscopy in older patients with frailty where appropriate to facilitate and guide safe treatment. For patients with suspected CD, making a diagnosis based on small bowel imaging may be appropriate in some patients.

Options for diagnosing small bowel disease in CD include computed tomography [CT], magnetic resonance imaging [MRI], intestinal ultrasound [IUS], or capsule endoscopy with ECCO guidelines suggesting which of these is first line to be guided by local availability and expertise.<sup>41</sup> ECCO guidelines specifically suggest that CT should ideally be avoided other than in the emergency setting or in older patients where radiation exposure is less of a concern.<sup>41</sup> These tests tend to be relatively well tolerated, but it is important to consider whether a patient is able to take the required oral preparation or, in the case of MRI, tolerate the time needed to be still on a hard surface and ability to breath-hold.<sup>48,49</sup>

A relatively common clinical scenario which is important to mention is the older person found to have colonic inflammation following a radiological test done for another reason. The appropriateness of further testing to confirm diagnosis should rely upon an accurate history including use of medication such as non-steroidal anti-inflammatories and symptom burden. In a patient who is relatively asymptomatic and at high risk of complications based on a diagnostic test, consideration should be given to watchful waiting, re-imaging and symptomatic treatment if required. Alternatively, if only leftsided colonic inflammation is seen, a flexible sigmoidoscopy for tissue diagnosis may be an acceptable alternative to a full colonoscopy.

It is also important to remember the use of biomarkers for monitoring and assessing disease activity. C-reactive protein [CRP] has demonstrated utility in recognizing disease activity and aid decision-making in IBD.<sup>50</sup> However, higher levels of CRP are also associated with frailty and so this should always be interpreted in the context of the individual patient and their comorbidities.<sup>51,52</sup> Faecal calprotectin has also demonstrated a clear role for identification of disease activity and has been shown to correlate with endoscopic inflammation.<sup>50</sup> However, it is important to remember that calprotectin is a marker of bowel inflammation which is not specific to IBD and can be seen in other conditions more common in older patients such as diverticulitis and use of nonsteroidal anti-inflammatory drugs [NSAIDs].

# 5. IBD Treatment Considerations in Older Adults

There is a paucity of evidence regarding the efficacy and safety of IBD treatments in older individuals. The older cohort of IBD patients is poorly represented in clinical trials of advanced medicines owing to strict inclusion and exclusion criteria and clinician reluctance to enter patients with complex health issues into placebo-controlled clinical trials. A recent review confirmed that older patients were excluded from IBD clinical trials because of their age in 129 [58%] of the 222 phase 3 trials.<sup>53</sup> Even when trials allowed for inclusion of older patients only 5.4% of participants were older than 65 years.<sup>53</sup> Additionally exclusion criteria listed common comorbidities seen in older patients such as renal, hepatic, and cardiovascular diseases in 76% of trials,<sup>53</sup> so that even if older people were not explicitly excluded by age, they were implicitly excluded by their comorbidities.

This limited evidence may explain the often-observed discrepant approaches to treating older IBD patients.<sup>54,55</sup> Older IBD patients are more often maintained on basic medications and less likely to be escalated to more effective therapies than younger patients.<sup>56–59</sup> Worryingly, despite society guidance against the use of aminosalicylates [5-ASA] for CD, 36–77% of those older patients with CD are taking 5-ASAs based on population-based studies.<sup>56,60,61</sup> This may relate to clinicians appreciating the benign safety profile of 5-ASAs but paying little attention to the lack of clinical efficacy in CD. Older patients are more likely to receive steroids despite the known risks associated with this therapy compared to younger patients and are less likely to receive immunomodulators or biologics.<sup>56,62</sup> Furthermore, older patients with IBD are more likely to be offered surgery instead of medical therapies.<sup>57,63</sup>

The main aims of IBD treatment are to induce and maintain steroid-free remission but also to prevent long-term disease complications.<sup>64</sup> These aims are still relevant for a significant proportion of older patients; however, targets may change for those older patients with frailty or those with a reduced life expectancy. Prevention of long-term complications should be reappraised according to a person's overall life expectancy. For example, in a newly diagnosed 85-yearold with UC, steroid-free clinical remission and avoidance of colectomy may be the most relevant targets and aiming for deep healing to avoid dysplasia risk is a less clinically relevant target. Clinicians will therefore apply a risk-benefit calculation that is adapted to the individual patients' circumstances. Ability to self-care and maintain independence may also be key goals for older patients. This may include giving consideration to how medications are delivered, which should be guided by individual issues such as arthritis making some injection pens harder to use or preferring tablets to granules that can become stuck in dentures.

After goal setting the main consideration for older patients and those who are living with frailty is to weigh the risks and benefits of any proposed intervention. In terms of risks, the risk of severe infections, malignancy, and hospitalization for any cause rises with age and frailty.<sup>65-67</sup> Adverse events may also have more serious long-term consequences such as death and disability when, for example, a patient with frailty is hospitalized with pneumonia compared to a younger patient, in whom pneumonia is more quickly reversible with treatment.

The differential benefit and risk profile for current IBD treatment is shown in Table 2. Steroids are used early in treatment algorithms and frequently prescribed. They may erroneously be perceived as 'low-risk' despite their association with an increased risk of adverse effects and mortality in older patients.<sup>59,68,69</sup> Immunomodulators are associated with increased risk of infection and malignancy in older adults with IBD and infections in those with frailty.<sup>70-73</sup> Anti-tumour

necrosis factor alpha [anti-TNFs] may take longer to exert a treatment effect in older patients and older patients more frequently discontinue treatment.74,75 Anti-TNF treatments are also associated with an increased risk of infection, especially in patients with frailty,73,76,77 which may explain the reluctance of some clinicians to prescribe them in older people. Retrospective studies of vedolizumab have shown similar effectiveness outcomes between younger and older patients.<sup>78,79</sup> As a gut-specific biologic, it may have a better safety profile from a mechanistical point of view, but may be associated with an increasing risk of Clostridium difficile infection, although data are limited and conflicting in older patients.<sup>79-83</sup> Emerging data for ustekinumab suggest similar or slightly reduced response rates for older patients but similar infection risk to younger patients.<sup>84,85</sup> A higher rate of malignancy was noted in one study but numbers were small and probably reflected expected increased risk associated with age in the general population.<sup>84</sup> There are insufficient data on newer biologics [risankizumab and mirikizumab] and novel small molecules [tofacitinib, filgotinib, upadacitinib, ozanimod, and etrasimod] to make evidence-based recommendations. However, the European Medicines Agency has restricted the use of tofacitinib, filgotinib, and upadacitinib in patients over 65 years to those where no viable alternative options exist. This recommendation is based on the associated increased risk of venous thromboembolism [VTE], infection, major adverse cardiovascular events, and malignancy observed in the ORAL SURVEILLANCE study of tofacitinib in rheumatoid arthritis when compared to anti-TNF therapy.<sup>86</sup>

The impact of frailty on patients with IBD is a growing research area. Whilst the numbers of studies are currently small, it is likely that frailty rather than age is associated with the greatest risk of adverse events following treatment, particularly infection, although data are somewhat conflicting.73,92 This discrepancy may result from issues with how we currently assess frailty in patients with IBD. As discussed above, there is some overlap between symptoms or 'health deficits' associated with frailty and active IBD symptoms, such as weight loss and fatigue, and therefore it is possible the current methods of assessing frailty may lead to an 'overdiagnosis' of frailty in patients with IBD. However, whilst further research is needed, links between disease activity and frailty are starting to emerge.<sup>13,93</sup> Where frailty is caused by active IBD it may be that appropriate IBD treatment can lead to improvement in frailty scores and this has been demonstrated in two studies, although it is not clear whether this translated into a meaningful impact for patients.<sup>13,93</sup> Given this, for patients in whom frailty is driven by active disease it may be appropriate to initiate treatment with the aim to reverse this with close monitoring. It is important to highlight the limitations within the current evidence as to how to identify these individuals, whether reversal of frailty is truly possible, and if so, how this is best done safely and whether this has a positive impact on patients' functional capacity and quality of life.

For those patients in whom risk of treatment is considered to outweigh the benefit it is important to develop anticipatory care plans with step-up plans in case of flare aiming to prevent hospital admissions, as these are associated with significant morbidity for older patients including hospitalacquired infections and loss of functional independence on discharge.<sup>94,95</sup> Anticipatory care plans should include guidance on recognition and management of flares but also offer

	Recommended use	Evidence of benefits in older patients	Potential risks in older patients
Aminosalicylates	Induction and maintenance of mild to moderate UC	No age-related effectiveness data Frequently used in real-world practice	Well tolerated but can have mild side effects Small risk of nephrotoxicity
Corticosteroids	Induction of remission in UC and CD	No age-related effectiveness data Frequently used in real-world practice	Increased risk of: • Infection • Mortality • Osteoporosis
			<ul><li>Fractures</li><li>VTE</li><li>Diabetes</li><li>Psychological disturbance</li></ul>
Azathioprine/ Mercaptopurine	Maintenance therapy in moderate to severe UC and CD	Reduced colectomy rates in UC patients <sup>88</sup>	Increased risk of: • Infections • Malignancy • Myelotoxicity <sup>89</sup> • Hepatotoxicity <sup>89</sup>
			Significant interactions with warfarin, furosemide, and allopurinol
TNF $\alpha$ antagonists	Induction and maintenance therapy in moderate to severe UC and CD	Decreased rates of clinical remission with increasing age	Increased risk of:
			<ul> <li>Infections</li> <li>Unclear risk of malignancy<sup>90</sup></li> </ul>
Vedolizumab	Induction and maintenance therapy in moderate to severe UC and CD	Response rates similar to younger patients in real- world data	Despite 'gut-selective mechanism of action', in- creased risk of:
			• Infections
Ustekinumab	Induction and maintenance therapy in moderate to severe UC and CD	Limited data currently but probable similar response rates to younger patients	Limited data to estimate age-related risk but real- world data currently show similar infection risk to younger patients
Risankizumab	Induction and maintenance therapy in moderate to severe CD	Lack of RCT or real-world data in older patients	Further data needed to estimate age-related risk profile
Mirikizukumab	Induction and maintenance therapy in moderate to severe UC	Lack of RCT or real-world data in older patients	Further data needed to estimate age-related risk profile
Tofacitinib*	Induction and maintenance therapy in moderate to severe UC [†and Crohn's] European Medicines Agency advises use when no alternative in those >65 years	Lack of RCT or real-world data in older patients	Increased risk of:
Filgotinib Upadacitinib†			<ul> <li>VTE and MACE* in RA patients</li> <li>Infection* [especially herpes zoster]<sup>91</sup></li> <li>Malignancy* <sup>91</sup></li> </ul>
Ozanimod Etrasimod	Induction and maintenance therapy in moderate to severe UC	Lack of RCT or real-world data in older patients	Further data needed to estimate age-related risk Extra safety screening applies for patients with cardiac problems and those with diabetes

Table 2. Current medical treatment options for IBD and relevant age-related benefits and risks. Updated from Hong and Katz, 2021.87

CD, Crohn's disease; MACE, major adverse cardiovascular events; RA, rheumatoid arthritis; RCT, randomized controlled trial; UC, ulcerative colitis; VTE, venous thromboembolism.

advice on symptom control regarding pain, urgency, and stool frequency that may require analgesia, and bowel control with loperamide and or bile acid sequestrants, although the impact of polypharmacy and drug interaction is essential to consider.

Finally, in terms of treatments we should consider surgery. Several factors may influence the choice of surgical therapy in older IBD patients including comorbidity, and patient and physician preferences. Delays in surgery and high emergency surgery rates are reported in older IBD patients.<sup>96</sup> Older patients with IBD undergoing bowel surgery are reported to have a higher risk of postoperative morbidity and complications and the EPIMAD registry study demonstrated particular risk following emergency surgery with an odds ratio of 4.46 (95% confidence interval [CI] 1.75–11.3).<sup>97,98</sup> Furthermore,

the overall mortality rate from subtotal colectomy for UC in a UK study increased from 4.7% to 23% in patients aged 70 years or older.<sup>29</sup> Frailty alone, irrespective of chronological age, was associated with increased odds of postoperative complications in CD.<sup>27</sup> Similarly, UC patients with frailty had higher septic and cardiovascular complications following colectomy and frailty was an independent predictor for higher postoperative morbidity.<sup>28</sup> Clearly, comorbid conditions play a role in the overall increased postoperative complications with older patients with frailty and IBD. A multidisciplinary team working with physicians and surgeons is essential to optimize preoperative status and planning to also avoid emergency surgery where possible, and this is particularly the case in older patients with IBD and frailty.

# 6. IBD surveillance and follow-up considerations in older adults

For patients with a history of colonic IBD, a surveillance colonoscopy is advised to enable early detection of pre-malignant lesions or cancers.<sup>100</sup> As discussed previously, colonoscopies are not without risk and therefore it is important that consideration is given as to when surveillance is discontinued. Whilst the British Society of Gastroenterologists post-polypectomy surveillance guidelines suggest stopping surveillance once patients are aged over 75 years or have a life expectancy of less than 10 years, this is following a 'full-clearance' colonoscopy, where all polyps are removed.<sup>101</sup> This is not possible to reliably achieve in IBD due to 'invisible' dysplasia,<sup>102</sup> and therefore an age-specific cut off for IBD is inappropriate. Instead, the appropriateness of ongoing surveillance must be discussed with older patients on an individual basis taking into consideration patient preference, the risks of the test, and whether the patient is fit for treatment if an abnormality is detected. There are limited data regarding detection of abnormalities and complications in older patients with IBD undergoing surveillance. A study of UC patients aged over 75 years undergoing surveillance demonstrated visible dysplasia in 19.4.%, random dysplasia in 3.6%, and colorectal cancer in 0.8%.<sup>103</sup> Importantly, abnormalities were significantly more likely in those with a prior history of dysplasia or colorectal cancer, suggesting it may be possible to adopt a more targeted approach to surveillance in those over 75, but further research would be valuable to guide this.<sup>103</sup>

Finally, patients with IBD have traditionally been followed up in secondary care lifelong. This results in regular appointments for older patients which alongside other healthcare follow-up for comorbidities may over-burden older adults.<sup>104,105</sup> Attending the hospital for appointments can be increasingly challenging due to transport and mobility limitations with age. During the Covid-19 pandemic, the use of virtual appointments via telephone or video increased dramatically. Satisfaction is generally high for virtual appointments from both older patients and clinicians, but there are limitations including technical difficulties, hearing impairment, and difficulty assessing a patient's fitness for tests or treatment without a face-to-face examination.<sup>106</sup> Clearly, it is important that patient preference is taken into consideration at the time of the clinic booking and caregivers are encouraged to attend appointments where appropriate. Patient-initiated-follow-up [PIFU] schemes are another possible way to reduce clinic burden for older patients who are stable on no medication or 5-ASA treatment. These allow patients to request an appointment at a time when they have issues and have been shown to reduce hospital admission and outpatient appointments.<sup>107,108</sup> It is also key that we stress the importance to patients and primary care of compliance with vaccination programmes and monitoring and treating anaemia and osteoporosis as older patients are at higher risk of adverse outcomes related to these.

### 7. Conclusion

Management of older patients is complex due to individual patient factors but also lack of research evidence to guide care. Initial presentation of IBD in older patients can be atypical and it is important to remember the impact of comorbidity and polypharmacy with consideration being given to the extensive range of differential diagnoses. Careful balancing of risk and benefit of investigations is also key throughout patient care. Whilst the risk of adverse events for some advanced IBD therapies rises with age and frailty, more data are needed to fully understand which advanced therapies have the most favourable safety profile in older patients and those with frailty. Finally, frailty is an important concept, and it is important that clinicians join the call for further research to allow us to understand how best to assess this in patients with IBD, how this is associated with disease activity, and to what extent frailty in IBD, when caused by disease activity, may be reversible with medical therapy and in which patients this is appropriate.

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### Author Contributions

All authors developed the idea for the manuscript. IC, OT, and CPS wrote the initial draft. All authors contributed to writing, reviewing, and editing the final manuscript.

### Data Availability

No new data were generated or analysed in support of this research.

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