Inflammatory bowel disease in older patients: from gut feeling towards evidence-based medicine

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Systematic review: components of a comprehensive geriatric assessment in inflammatory bowel disease – a potentially promising but often neglected risk stratification

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ABSTRACT

Background The population of older patients with inflammatory bowel disease (IBD) is increasing. Patient age does not fully account for poor outcomes and its clinical utility for risk stratification is limited. Comprehensive Geriatric Assessment (CGA), comprising a somatic, functional, mental and social assessment or frailty, could be a predictor tool.

Aims To systematically review literature on the kind of components of a CGA being used in adult IBD patients and the association of these components with adverse health outcomes.

Methods An electronic literature search was performed on 16th January 2018 using PubMed, Embase, Web of Science, the Cochrane Library, CENTRAL, Emcare and PsycINFO. Longitudinal studies relating somatic, functional, mental and social assessment or frailty to adverse health outcomes during follow-up in IBD patients were included. The Newcastle-Ottawa scale was used to assess individual study quality.

Results Of 4080 identified citations, 27 studies were included reporting 169 associations. Median sample size was 108 patients (IQR 60-704). No studies performed subgroup analyses on older patients and the highest mean age reported was 52.7 years. Somatic and functional assessments were used in three studies; mental in 24 and social in five. No study assessed cognitive status, functional performance or frailty. In 62 associations (36.7%) components of a CGA were significantly associated with adverse health outcome measurements.

Conclusions Components of a CGA were associated with adverse health outcomes in IBD patients, but older patients were underrepresented. More studies among older patients with IBD are warranted to further establish the clinical impact of a CGA.

INTRODUCTION

The number of older patients with inflammatory bowel disease (IBD) is increasing.[1] This increase can be explained by both a rising prevalence due to the aging of the population and a rising incidence of IBD in older patients,[1 2] but also by greater availability of treatment options.[3] A recent population-based epidemiologic study from the Netherlands reported a doubling of the IBD incidence in older patients, from 11.71 per 100,000 persons in 1991 to 23.66 per 100,000 persons in 2010.[1]

Older patients with IBD are at higher risk of IBD-related hospitalization and surgery than younger patients.[4] They are also at higher risk of developing serious adverse events during IBD treatment such as infections or lymphoproliferative disorders.[4] Older patients show a larger heterogeneity in their somatic, functional, mental and social abilities or frailty compared to younger patients.[5 6] A CGA aims to systematically explore these components of a patients' health.[7] In other medical fields such as oncology and nephrology, research performed in older patients shows a relationship between impairments found during a CGA and adverse health outcomes which could be helpful in clinical decision making.[8 9] In IBD, preliminary baseline results from our cohort study in 135 IBD patients aged ≥65 years, indicated a high prevalence of frailty, measured with the Geriatric 8 questionnaire and impaired physical capacity, measured using handgrip strength.[10] However, how impairments in these components of a CGA may be related to (adverse) health outcomes in IBD patients has not been systematically evaluated.

Therefore, the aim of this systematic review is to study the literature on the different components of a CGA used in adult IBD patients and the association of these components with adverse health outcomes, impaired quality of life (QoL) and functional or cognitive decline after follow-up.

MATERIALS AND METHODS

Search strategy

Our literature search aimed to identify original longitudinal studies in IBD patients in which the association between components of a CGA at baseline and IBD-related adverse health outcomes, non-IBD-related adverse health outcomes, (HR)QoL questionnaires and functional or cognitive decline after follow-up was examined. In our search strategy IBD was defined as Crohn's disease (CD) or ulcerative colitis (UC). If a study included patients with IBD-unclassified (IBD-U) or indeterminate colitis (IC), these results were taken into account as well.[11]

Components of a Comprehensive Geriatric Assessment

The purpose of a CGA is to systematically explore four different domains as a reflection of patients' health namely the somatic, functional, mental and social domains.[7] The somatic domain includes malnutrition by using malnutrition screening tools, taking a medical history, medication use and anthropometrics. This domain is usually included as part of routine care. The functional domain includes functional performance, and can be measured with questionnaires such as (instrumental) activities of daily living ((I)ADL)) as well as physical capacity, measured with tests such as handgrip strength, gait speed or balance, or measured with questionnaires. The mental domain includes both cognitive status (measured with tests such as the Six Item Cognitive Impairment Test (6CIT) or the Mini-Mental State Examination (MMSE)) and depression or anxiety (measured with questionnaires such as the Geriatric Depression Scale (GDS)). The social domain assesses social support and is measured by questionnaires assessing living situation or marital status. The above-mentioned domains are integrated into an assessment of the overall level of frailty. Frailty is a state of increased vulnerability to poor resolution of homeostasis following a stress. Its presence, which can be assessed using frailty indices such as the Groningen Frailty Indicator,[12] increases the risk of adverse outcomes.[8 13]

Outcome parameters

Outcome parameters were categorized in IBD-related adverse health outcomes, non-IBD-related adverse health outcomes, (HR)QoL questionnaires and functional or cognitive decline after follow-up.

The following outcomes were considered IBD-related: An exacerbation or flare-up of disease measured with IBD disease activity scores such as (simplified) Crohn's disease activity index ((S)CDAI), simple clinical colitis activity index (SCCAI), Harvey Bradshaw index (HBI), partial Mayo score (PMS) or modified Truelove and Witts activity index (MTWAI), or with biological parameters such as c-reactive protein, faecal calprotectin, haemoglobin, haematocrit, mean corpuscular volume, leucocytes, platelet count or erythrocyte sedimentation rate or established with endoscopic/radiologic examination. The need to step up medication, use of corticosteroids, the need for IBD-related surgery and the occurrence of IBD-related complications such as strictures, fistulas and extra intestinal manifestations were also considered to be relevant IBD-related outcomes. The (Short) Inflammatory Bowel Disease Questionnaire ((S)IBDQ) was considered to be an IBD-related outcome parameter because of the amount of questions considering IBD symptoms.

The following outcomes were considered to be non-IBD-related adverse health outcomes: Emergency department visits, outpatient department visits, all-cause hospitalization, any surgery or any abdominal surgery, length of any hospital stay and mortality.

Outcome parameters reporting on (HR)QoL, functional decline (using questionnaires such as (I)ADL) or cognitive decline (using measurements or questionnaires such as the six item cognitive impairment test (6CIT)) were also considered relevant outcome measures.

Literature search

On January 16th, 2018 seven online databases (PubMed, Embase, Web of Science, the Cochrane Library, CENTRAL, Emcare and PsycINFO) were searched using synonyms of IBD, combined with synonyms of different components of a CGA. As we surmised that the number of studies addressing components of a CGA in an older IBD population would be low, we included all studies that investigated components of a CGA known to influence adverse health outcomes in older patients in adult patients. After the initial search a second search was performed solely regarding anxiety terms. For full details of the search strategy for PubMed, see supplemental material A. The searches were restricted to articles in Dutch and English. Also, conference and meeting abstracts were excluded. There were no restrictions in publication date.

Study selection

The eligibility of all studies identified by the search was independently evaluated by at least two authors (VA, FLK or EK). For any article that seemed potentially relevant based on the title and abstract, the full text was retrieved and screened. Studies were included when containing original data reporting on an association between any component of a CGA at baseline and an outcome of interest after follow-up in IBD patients in a longitudinal study design. In case of disagreement on the eligibility of studies, consensus was reached after discussion with at least one additional author (FvD, SM or PM). Discussion with additional authors because of disagreement on eligibility took place in 24 out of 4080 studies, which represents a 99.4% agreement on the selection of studies during evaluation of eligibility. Cross-referencing was performed using the reference list of the included publications to ensure all relevant studies were identified.

Data extraction and quality assessment

The following items were extracted from each study: Publication data (author, year and journal), study design, setting, duration of follow-up, patient characteristics (sample size, mean age, disease type, inclusion criteria), type of geriatric assessment (somatic, functional, mental and social assessment or frailty), correction for confounding factors, the outcome and conclusion of the study. To assess the methodological quality and risk of bias of the studies included, we adapted the Newcastle-Ottawa scale to the purpose of this review (supplemental material B).[14] Two authors (VA and FLK) performed data extraction and quality assessment, in case of disagreement a third author was consulted (PM). The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist, which is a checklist for evidence-based minimum set of items for reporting in systematic reviews, is available upon request.[15]

Data presentation

Study characteristics are presented in tables per included study. Accumulated descriptive statistics of the included studies are presented by calculating the percentage of studies reporting on associations between components of a CGA with outcomes. The overall

sample size of included studies is expressed as median and interquartile range (IQR). In this review, an "association" implies an investigated, but not necessarily a statistically significant relationship between a component of a CGA and an outcome of interest. The main findings of the included studies regarding the associations of components of a CGA with outcomes of interest are presented in tables. When authors performed an adjustment for potential confounders, these confounders are tabulated per included study and when hazard ratio (HR), odds ratio (OR) or relative risk (RR) were adjusted for confounders, this is reported as an adjusted ratio (aHR, aOR or aRR). When possible, the fully adjusted model was reported.

Supplementary analysis

Because of the low median sample size in the included studies a supplementary analysis was performed. The six studies with the largest sample size were analysed and the association of components of a CGA with outcomes of interest was described.

RESULTS

Search results and study selection

The first database search identified 3296 unique citations (figure 1). After initial screening of title and abstract, 246 studies were potentially eligible and full text was screened. After full-text review, 226 were excluded and the remaining 20 studies were included. A second additional database search identified 784 citations and yielded 5 studies (for flowchart see supplementary figure 1). Cross-referencing yielded two additional relevant studies, which resulted in a total of 27 studies included in this review.

Study characteristics

Table 1 shows an overview of the included studies. The median sample size of all included studies was 108 patients (IQR 60-704). Out of the 27 included studies, 22 (81.5%) were performed in the United States or Europe.[16-37] The majority of the included studies had an observational prospective study design (77.8%).[18 20-24 26-31 33-42] The median follow-up time was 12 months (IQR 10-22.9) and follow-up data were extracted from medical records or insurance data in 38.6% of associations,[16 17 19 25 27 32 42] assessed during hospital visits in 33.1%[18 21 23 24 27 29-31 33 34 36-38] and self-reported in 28.6%.[20 22 25 26 28 35 39-41] Twelve (44.4%) studies included both CD and UC,[16 17 19 20 22 28 32-35 40 41] two of these included IBD-U or IC as well.[33 40] Ten studies included only CD patients,[18 23-27 31 36 38 42] five studies only UC.[21 29 30 37 39] None of the studies were specifically designed for older patients or performed subgroup analyses on older patients.

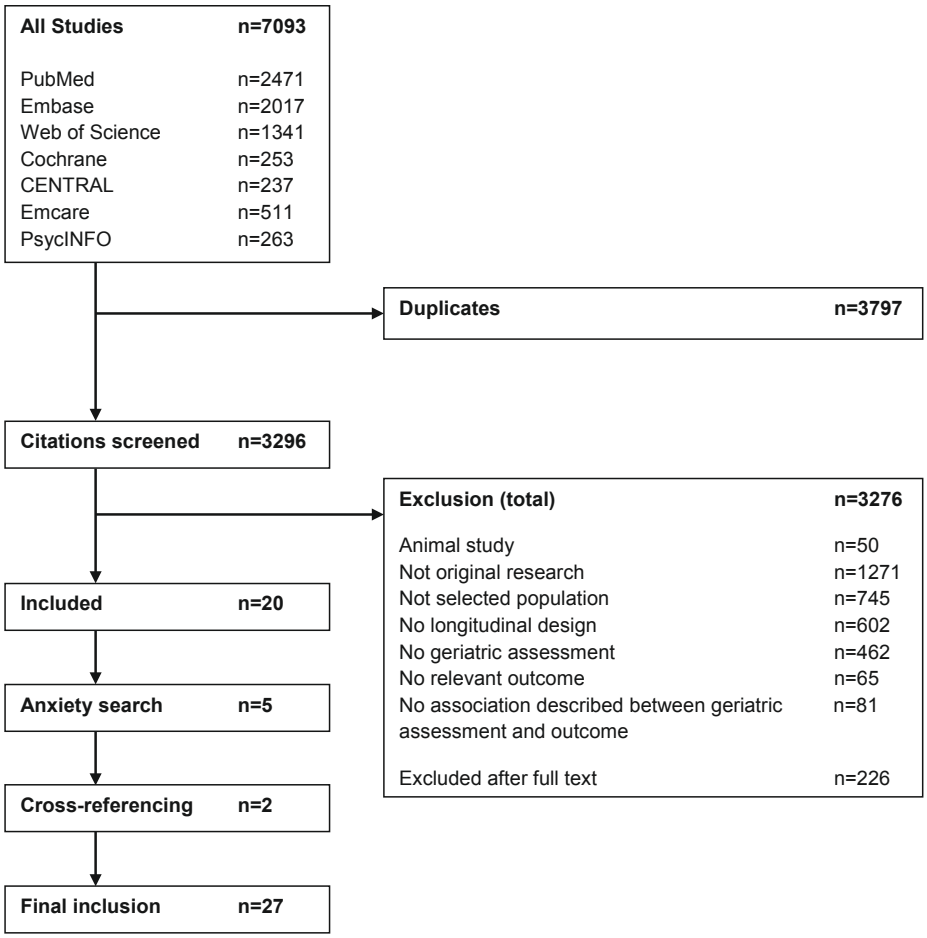

Figure 1. Flowchart

Reported components of a Comprehensive Geriatric Assessment

The included studies reported on a total of 169 associations in which the relationship between a component of a CGA and outcome measurement was investigated. An "association" therefore implies an investigated, but not necessarily a statistically significant relationship. Somatic and functional assessment were measured in 39 associations (23.1%),[27 32 42] mental in 117 associations (69.2%)[16-22 24-26 28-41] and social in 13 associations (7.7%).[16 20 22 23 36] None of the studies used a measurement of functional performance, cognitive status, or frailty (figure 2).

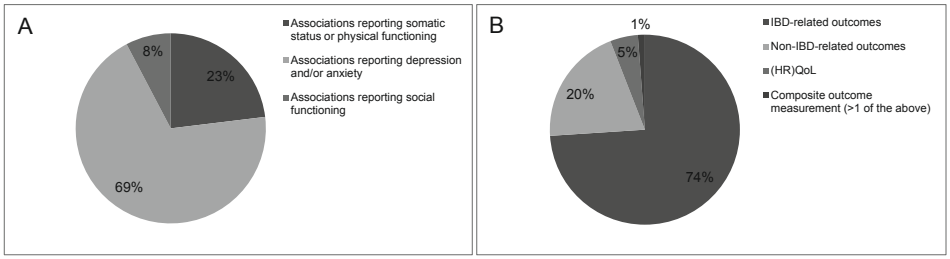

Figure 2. Visual representation of associations described in the included studies. A: percentage of associations described per component of a comprehensive geriatric assessment. No association reported on cognitive impairment, functional decline, or frailty. B: percentage of associations described per adverse health outcome measurement. No association described functional or cognitive decline as an outcome measurement. [HR]QoL, health-related quality of life.

Reported outcomes

IBD-related adverse health outcomes were the main outcome of interest, reported as an outcome measurement in 125 associations (74.0% of all associations)).[17 18 20 21 23-31 33-42] (HR)QoL was used as an outcome measurement in eight associations (4.7%).[18 25] One of the included studies (1.2% of the associations) used a composite outcome measurement comprising (HR)QoL, disease progression and any readmissions or hospitalizations.[25] None of the studies used functional or cognitive decline as an outcome measurement (figure 2).

Association of geriatric impairments and outcomes

Table 2 shows an overview of the investigated associations of components of a CGA with adverse health outcomes. A significant association between a component of a CGA and outcome of interest in which more geriatric impairment leads to worse outcome was presented as '+'. A significant association between a component of a CGA and outcome of interest in which more geriatric impairment leads to better outcome was presented as '-'. A non-significant association was presented as 'ns'. In supplementary table 1 the available association measures are presented. In 62 associations (36.7%) there was a statistically significant association between an impairment in somatic, functional, mental or social assessment and a higher risk of adverse health outcomes (figure 3).[16-19 22-28 31-34 36 42] When the authors performed an adjustment for potential confounders, these confounders are tabulated in supplementary table 2. The detected effect of geriatric impairments on the outcomes of interest is summarized in figure 4.

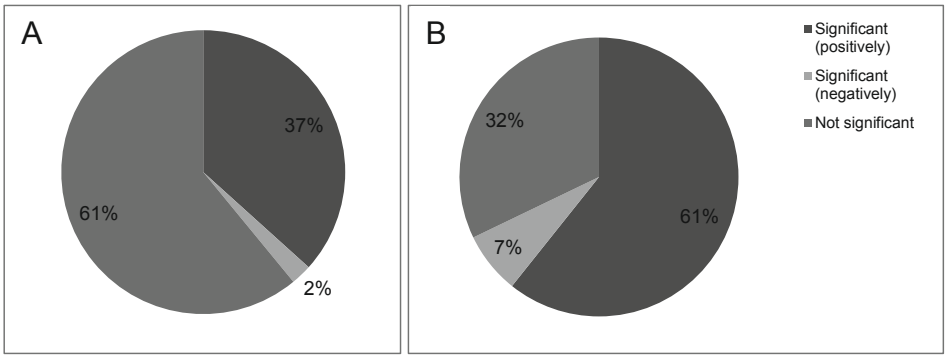

Figure 3. Visual representation of significant associations. Positive significant associations are associations in which more geriatric impairment led to more adverse outcomes, negative significant associations in which more geriatric impairment led to less adverse outcomes. A: percentage of significant associations in associations of all included studies. B: percentage of significant associations in associations of the six largest studies.

Somatic and functional assessment

Somatic and functional assessment was performed in three studies, resulting in 39 associations (23.1% of all associations). Of these, 32 associations reported on malnutrition and seven reported on physical capacity (all handgrip strength). None of the studies reported on functional performance using questionnaires such as ADL or IADL.

The different studies used a variety of screening tools to measure malnutrition. These were the malnutrition universal screening tool,[42] malnutrition inflammation risk tool,[27] subjective global assessment,[27 42] nutrition risk screening 2002,[42] Onodera's prognostic nutritional index,[42] controlling nutritional status,[42] bioelectrical impedance analysis measuring phase angle[27] and malnutrition diagnosis code.[32]

Malnutrition or high risk of malnutrition was highly prevalent in the included studies, with a range between 10.6% and 72.5%. Takaoka et al, using the Onodera's prognostic nutritional index, reported that up to 72.5% of included hospitalized patients were at high risk of malnutrition.[42] Micic et al. analyzed hospital discharges in 55.942 patients and found that, when using ICD-9 malnutrition code, 10.6% of patients were diagnosed with malnutrition.[32] In their study, malnutrition was an independent predictor of 30-day readmission (aOR 1.37, 95% CI 1.22-1.54).[32]

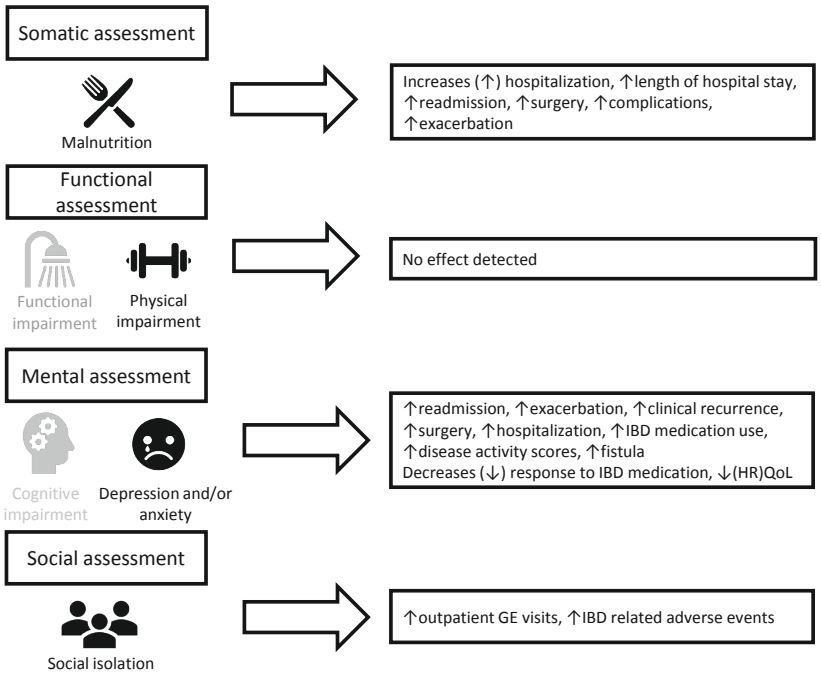

Figure 4. The detected effect of geriatric impairments on adverse health outcomes in inflammatory bowel disease patients. No studies on functional or cognitive impairment were found.

Jansen et al. reported on physical capacity using handgrip strength, resulting in seven associations. A mean handgrip strength at baseline of 38.2 kg (SD 9.9) was reported but no data on the prevalence of impaired handgrip strength were presented.

Handgrip strength did not predict different measures of disease activity, disease-related complications or a composite endpoint in this study.[27] 97.4% of the associations on somatic or physical capacity included only CD patients. Malnutrition or impaired physical capacity was a significant predictor of adverse health outcomes in 10 out of 39 associations (25.6%) (figure 5).

Mental assessment

Mental assessment was evaluated in 24 studies, resulting in 117 associations (69.2% of all associations). Of these, all associations reported on depression and/or anxiety. None of the studies reported on cognitive status.

Depressive and/or anxiety symptoms were mostly measured with the Hospital Anxiety and Depression Scale (HADS), in eight studies (33 associations).[18 24 29 33 36 37 40 41] The presence of a depression diagnosis code, anxiety diagnosis code or a combination of these was used in four studies, resulting in 30 associations.[16 17 19 32]

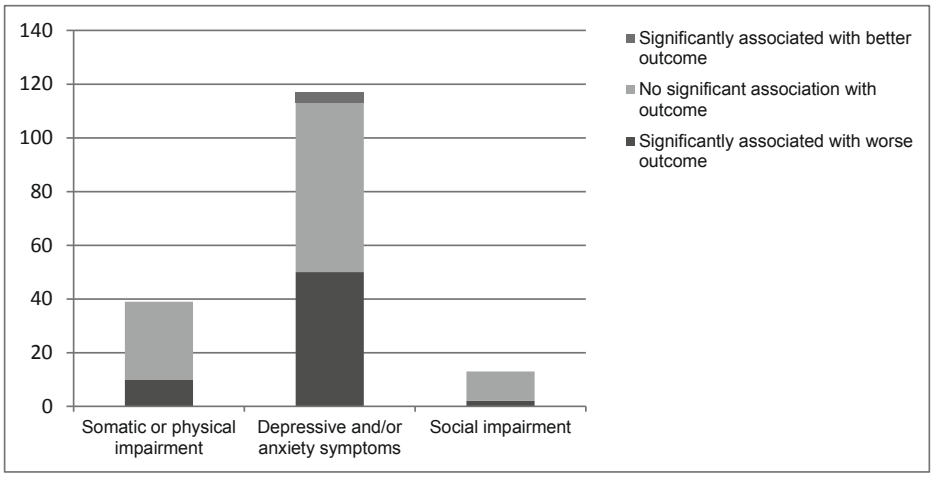

Figure 5. Graphic representation of associations of somatic or physical impairment, depressive and/or anxiety symptoms, and social impairment with adverse health outcomes in inflammatory bowel disease patients. No studies reported on cognitive impairment, functional impairment, or frailty.

Depressive symptoms or a diagnosis of depression were present in between 2.3% and 32.0% of patients.[16 19] Anxiety symptoms or diagnosis were present in between 9.4% and 39.0% of patients.[19 41]

Ananthakrishnan et al. combined a diagnosis of a depressive disorder and/or a generalized anxiety diagnosis into one 'psychiatric comorbidity' factor. In their cohort of 10.834 patients, this factor was associated with the occurrence of several adverse health outcomes. For instance, psychiatric comorbidity was associated with an increased risk of IBD-related surgery in CD (aOR 1.22 (95%CI 1.01-1.47)) and the use of steroids in CD patients (aOR 1.83 (95% CI 1.58-2.13)).[17]

A study by Mikocka-Walus et al. assessing depressive and anxiety symptoms with the HADS found that depression was associated with their composite outcome measure "clinical recurrence" in both CD and UC. Anxiety was associated with clinical recurrence in CD, but not in UC.[33]

Half of all associations on depressive and/or anxiety symptoms (49.5%) described CD patients, the other associations described UC patients (26.4%) or no distinction was made in IBD type (23.9%). Depressive and/or anxiety symptoms were predictive of adverse health outcomes in 50 out of 117 associations (42.7%) (figure 5).[16-19 24-26 28 31-34 36] Of the associations reporting on patients with CD, 57.9% was statistically significant and 42.9% of associations reporting on UC patients was statistically significant.

Social assessment

Social assessment was evaluated in five studies and this resulted in 13 associations (7.7% of all associations). Three associations reported on marital status or living situation (living together versus alone).[16 20 22] The other 10 associations assessed social support or social functioning using the Social Network Index, Social Support Inventories (medical outcomes study (MOS) and enhancing recovery in coronary heart disease (ENRICHD)) or Social Support List.[20 22 23 36]

Allegretti et al. reported the highest percentage of 57.9% patients being single, divorced or widowed.[16] A study by De Boer et al. reported 12% of patients as living alone.[22]

Bernstein et al. assessed the amount of high-contact roles using the Social Network Index.[20] This index calculates the number of different social roles in which the patient participates at least once every two weeks involving contact with a familiar person.[20] The study reported a presence of 19.9% of ≤4 high-contact roles in the 'flare' group compared to 17.4% in the 'non flare' group, this difference was not significant.[20] In a study by Camara et al. mean social support was 24.26, SD 5.50, measured with the ENRICHD Social Support Inventory on a scale from 6 (low social support) to 30 (high social support). Better social support was an independent predictor of less adverse events (aOR 0.666, 95%CI 0.516-0.859, p=0.002).[23]

Four associations (30.8%) described CD patients, in other associations on social functioning no difference was made regarding IBD type. There were no associations on social functioning in UC patients alone. In two out of the 13 associations (15.4%) a significant relationship between lower social functioning and adverse health outcomes was reported (figure 5).[22 23]

Supplementary analysis

The average sample size of the included studies was relatively low, which causes a low power to detect statistical significance. Hence, to enhance statistical power, we selected the six studies with the largest sample size.[17 19 26 28 32 33] These studies accounted for 56 associations (33.1% of total associations) with a minimum sample size of 2289 patients and a maximum of 52.498 patients. The associations described in these studies mostly (98.2%) assessed depressive and/or anxiety symptoms. 62.5% of these associations showed a statistically significant relationship between a component of a CGA and a higher risk for adverse health outcomes (figure 3).

Quality assessment

The overall study quality assessed by the modified Newcastle-Ottawa scale was moderate to low (table 3). There were concerns about the representativeness of the cohorts, the duration of follow-up and the adequacy of follow-up.

None of the studies focused on older patients or performed separate analyses on a subgroup of older patients. Six studies (partly) excluded older patients with the lowest

maximum age of exclusion of 55 years reported in the study by Deter et al.[21 25 27 29 34 38] Ten studies had a questionable duration of follow-up which was partly or not enough for investigated outcomes to occur[18 20-22 26 27 36-38 41] and six studies did not report on patients lost to follow-up.[17 18 25 28 32 42]

DISCUSSION

This systematic review aimed to identify longitudinal studies describing components of a CGA in IBD patients and their associations with adverse health outcomes. There were three main findings. First, components of a CGA were used in 27 studies and none of these studies specifically described older patients with IBD, nor performed subgroup analyses on older patients. Second, cognitive status, functional performance and frailty were not assessed and objectively measured physical capacity was assessed in only one study. Third, a statistically significant association was present between a component of a CGA and a higher risk of adverse health outcomes in more than one-third of the associations.

The purpose of a CGA is to systematically explore different geriatric domains as a reflection of patients' health. However, none of the studies described a complete geriatric assessment at baseline in relation to outcome measures. Therefore, the components of which a CGA is ought to be constructed and which are considered geriatric relevant components, were assessed in this review. In 27 out of all screened citations a component of a CGA was assessed. Besides this, the population of the included studies was young; the highest mean age reported in a study was 52.7 years.[17] Several studies employed an upper age limit for exclusion of patients and most studies had exclusion criteria concerning the presence of comorbidities or IBD-disease history such as bowel resection or stricturing disease as well. Although the increasing incidence and prevalence (between 10-30%) of IBD in older patients is well known,[1 43] our systematic review found that components of a CGA are scarcely used in IBD literature and have not been used in older IBD patients. Therefore, there is currently no evidence for a relationship between any of these components and adverse health outcomes in the older IBD patient population. Unfortunately this underrepresentation of older patients is not only present in the IBD literature. As a result of an upper age limit or exclusion criteria regarding comorbidities, clinical trial evidence on the treatment of older patients in general is still absent.[44] Due to this lack of evidence, guidelines concerning older patients with IBD are falling behind and decision making in this patient group is a challenge for clinicians.

Besides the underrepresentation of older patients with IBD in the included studies, several components of a CGA were also underrepresented, or not assessed at all. Promising geriatric measurements, such as cognitive status and frailty were not assessed in patients with IBD. Only one study reported objectively measured physical capacity using handgrip strength.[27]

Cognitive impairment is prevalent and associated with adverse health outcomes in older patients, as shown in research conducted in oncology and nephrology.[5 6 9 45] Even in community-dwelling older adults cognitive impairment is prevalent. A study by Thein et al. in community-dwelling Chinese older adults with and without diabetes aged ≥55 years found that 12.4% of the overall cohort (2696 patients) was cognitively impaired.[46] Frailty, defined as a state of increased vulnerability,[8 13] is strongly associated with adverse health outcomes in both community-dwelling older adults as in patients as well.[8 47 48] Physical capacity, which can be assessed with gait speed or handgrip strength, is understood as the ability to integrate physiological systems into coordinated, efficient movements to achieve optimum functioning.[49 50] The association between physical capacity and adverse health outcomes has been examined by several studies in other fields of medicine and in community-dwelling older adults.[51 52]

In this systematic review we did not find any study on cognitive status or frailty in IBD patients. This is reason for concern as geriatric problems are prevalent in the older IBD population. For instance, in our multicentre cohort study, over half of all patients had one or more aberrant test results in their geriatric assessment. A weak handgrip strength was present in 22.7% and frailty, measured with the Geriatric 8 questionnaire, was found in 43.7% of older patients with IBD.[10 53] We did find one study by Jansen et al. reporting an objective measurement of physical capacity (handgrip strength). Handgrip strength is often used to diagnose sarcopenia,[54] and there is a growing evidence for the association between sarcopenia and adverse health outcomes.[55] However, the study by Jansen et al. did not find a significant association between reduced handgrip strength and adverse health outcomes. This could be explained by the short follow-up duration (6 months), low mean age (40 years) and small sample size (55 patients).[27] Thus, in older patients with IBD, evidence regarding impairments in psychical capacity, cognitive status or frailty and its associations with adverse health outcomes is lacking.

Despite the relatively young population included and the lack of a CGA, we found impairments in the components of a CGA to be prevalent and, in more than one-third of the associations, significantly associated with adverse health outcomes. Older patients are more susceptible to geriatric impairments such as depression, low physical capacity and malnutrition compared to younger patients[56-58]. It is very likely that prevalence of geriatric impairment and its association with adverse health outcomes have been underestimated in this review when applied to older patients. Evidence on the underlying pathophysiological relationship between components of a CGA and adverse health outcomes is still scarce, especially in IBD. In figure 6 we present a summary of the potential pathophysiological interactions between these components and IBD disease outcomes. In IBD patients, depression contributes to lower pain thresholds, more reported symptoms and a poorer well-being.[59 60] This could contribute to the relationship between depressive symptoms and adverse health outcomes found in this systematic review. In the Health Aging and Body Composition (Health ABC) study on 3075 individuals aged 70-79 years a significant and independent association between physical capacity, measured with both low quadriceps

muscle strength and low handgrip strength, and serum levels of the inflammatory markers tumor necrosis factor (TNF) and interleukin (IL)-6 was found.[61 62] High levels of inflammatory markers are associated with increased morbidity and mortality in older persons.[63] In IBD patients, these proinflammatory markers correlate with disease activity and it has been shown that patients with IL-6 serum levels >20 picograms per millilitre have a 17-fold increased risk of relapse over a 1-year period compared with patients with a lower level.[64 65] The latter could also contribute to the relationship between low physical capacity and (IBD-related) adverse health outcomes. Malnutrition, besides being one of the principal mechanisms involved in the genesis of sarcopenia,[66] is also a well-known risk factor for poor prognosis in IBD, especially postoperative complications.[67]

The disease course of IBD could also influence several components of a CGA, in this way causing a bidirectional relationship between geriatric impairment and adverse health outcomes. For example, IBD patients experiencing an exacerbation of disease express a higher risk of malnutrition, due to the decrease of oral food intake or increased gastrointestinal nutrient loss.[66] While studying the predictive role of a CGA in IBD, relationships should therefore be interpreted with caution and associations should be corrected for disease activity to take into account this possible bi-directional relationship. The multimodal effects of IBD and its treatment may very well be an important cause of geriatric impairments or frailty.

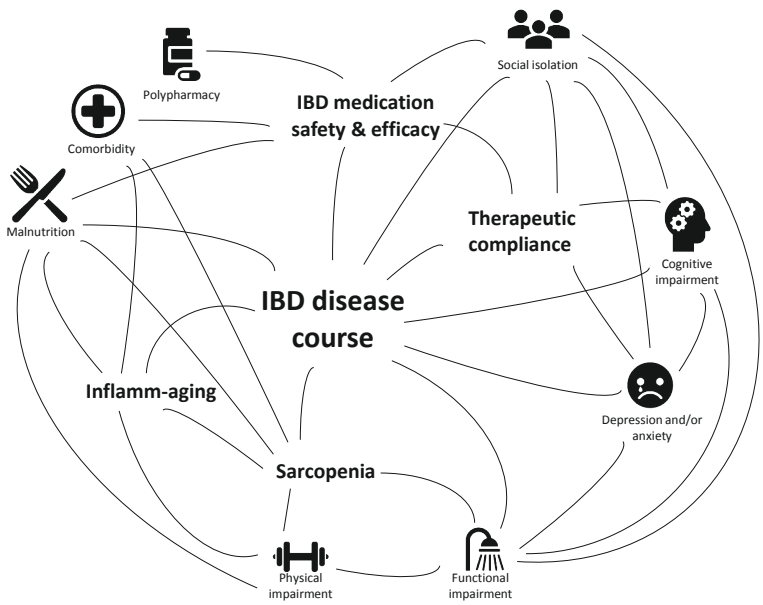

Figure 6. Potential pathophysiological interactions between components of a comprehensive geriatric assessment and inflammatory bowel disease [IBD] -related disease outcomes.

To enhance statistical power, as sample sizes in the included studies were small, a sensitivity analysis was performed by selecting six studies with the largest patient population. The percentage of statistically significant associations increased from 36.7% to 62.5%. This suggests that most included studies lacked statistical power to detect significant differences. However, 98.2% of the associations described by the six largest studies reported on depression and/or anxiety and therefore are not representative of a full CGA. We were unable to perform sensitivity analyses separately for each component of a CGA due to the few studies included per factor: three quarters of the associations included in our systematic review described depressive and/or anxiety symptoms. Alexakis et al. performed a systematic review and meta-analysis on the relationship between depressive state and disease course in adults with IBD but due to a lack of randomised controlled studies, small study populations and a large variety in depression symptom scores it was inconclusive.[68] Therefore, even though the majority of associations found in our systematic review concerned depression and/or anxiety, no firm conclusion can be drawn regarding the influence of depression and/or anxiety on adverse health outcomes.

A limitation of this review is the fact that, because of the heterogeneity of the components of a CGA, outcome measures and reported measures of association, we could not perform a formal meta-analysis. Furthermore, interpretation of the results regarding the number of significant associations has to be interpreted with caution due to a possibility of publication bias, as negative or non-significant associations may not have been reported in included studies. Besides this, the amount of older patients in the included studies is low, therefore it is not guaranteed that results of these studies can be extrapolated to the population of older patients with IBD.

The strengths of our review include the extended systematic search performed in seven online databases without a restriction on publication date. In this way all potential relevant studies concerning associations on components of a CGA and adverse health outcomes in IBD patients were assessed. In addition, a quality assessment using the adapted Newcastle Ottowa Scale was performed. One of the greatest strengths of this review is the important addition to existing literature regarding IBD in the older patient, because little research has been performed on this subject so far.

The findings of this study imply that more research regarding geriatric assessment in older IBD patients is needed. With more evidence available on the association between components of a CGA and adverse health outcomes, a risk stratification could be made regarding geriatric impairment. In this way, older patients at high risk for adverse health outcomes could be selected on time and monitored closely or even opt for an alternative treatment regimen according to their risk profile.

Table 1. Characteristics of the included studies

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Allegretti [16]	2015	USA	324	41.7	CD/UC	≥18 years, hospital admission for non-elective IBD-related reason	90 days
Ananthakrishnan [17]	2013	USA	10834	CD: 49.5 & 44.7; UC: 52.7 & 47.9†	CD/UC	Exclusion of patients with anxiety or depression date of diagnosis code prior to surgery	CD 11.5 years & 7.7 years; UC 12.5 years & 9.1 years†
Banovic [18]	2010	France	57	41.2	CD	Outpatients complaining of fatigue, no steroid dependence, no rheumatoid or peripheral arthritis	1 year
Barnes [19]	2017	USA	52498	CD: 20.2% ≥60 UC: 31.2% ≥60‡	CD/UC	≥18 years, excluding patients with discharge codes for both CD and UC	90 days
Bernstein [20]	2010	USA	704	52.1	CD/UC	>18 years	1 year
Bitton [21]	2003	USA	60	39	UC	>18 years and ≤80 years, clinical remission for ≥1 month, endoscopic remission at baseline, p.o. or rectal mesalamine dose stable for 1 month or 6-mercaptopurine and azathioprine dose stable for 3 months, no use of p.o. or rectal corticosteroids within the past 30 days	1 year
Bitton [38]	2008	Canada	101	33.6	CD	18-65 years, clinical remission for ≥1 month, p.o. or rectal mesalamine dose stable for 1 month or 6-mercaptopurine and azathioprine dose stable for 3 months, no use of p.o. or rectal corticosteroids within the past 30 days, no current complications, no previous extensive small bowel resection, no presence of ileostomy or colostomy, no antibiotic use at baseline	1 year

Table 1. Continued.

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Boer, de [22]	1998	The Netherlands	271	42	CD/UC	Attending IBD outpatient clinic in year prior to study, completion of follow-up	1 year
Cámara [23]	2011	Switzerland	467	41.6	CD	Complete/returned questionnaires at follow-up	1.5 year
Cámara [24]	2011	Switzerland	476	41.8	CD	Adult patients with recurrence of CD symptoms, no missing or invalid information on important control variables, returning baseline questionnaires within 6 months of inclusion	1.5 year
Deter [25]	2008	Germany	108	52.9% <30, 47.1% >30	CD	18-55 years, at least one active disease episode (defined as requiring drug treatment) in last 2 years, no psychotherapy, no resection for CD within last 2 years and no further relapse thereafter, no ongoing immunosuppressive therapy or resection in the near future, no colostomy or ileostomy	2 years
Gaines [26]	2016	USA	5707	43§	CD	≥18 years, internet access	1 year

Table 1. Continued.

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Jansen [27]	2016	Germany	55	40	CD	18–75 years, CDAI <200, occurrence of relapse/flare-ups, intestinal complication or hospitalization within the last 2 years, known disease location and behaviour within the last 2 years, absence of cancer or other severe disease, no pregnancy or lactation, no high-dose systemic corticosteroid treatment within 3 months before study entry, absence of stoma or short bowel syndrome and no BMI <17.5 or severe weight loss	6 months
Kochar [28]	2018	USA	2798	41	CD/UC	≥18 years, excluding patients without follow-up	Mean 22 months
Langhorst [29]	2013	Germany	80	45.1 & 48.7¶	UC	18-75 years, self-reported clinical remission for ≥1 week and <12 months, an interval of 4 weeks in remission for 4 weeks at the beginning of the 12-months interval, absence of clinically active disease, no infectious or chronic active colitis, no current use of antibiotics or corticosteroids, no treatment within the last 3 months with immunosuppressive drugs, no complete colectomy, no relevant somatic comorbidities, no pregnancy	1 year

Table 1. Continued.

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Levenstein [30]	2000	Italy	63	38.8	UC	Clinical remission, for at least 2 months off systemic or local steroids, using oral and rectal 5-aminosalicylate or oral azulfidine in maintenance doses as sole therapy, completion of follow-up	68 months
Mardini [31]	2004	USA	18	31§	CD	No history of psychosis and/or clinical depression that required hospitalization, no stricturing disease and/or history of ileostomy, total colectomy or short gut syndrome	2 years
Maunder [39]	2005	Canada	146	42.7	UC	≥18 years, no colectomy or indications of cardiovascular illness	7-37 months (median 686 days)
McCombie [40]	2015	New Zealand	54	33.5§	CD/UC/IBD-U	≥18 years, return of questionnaires <1 month of administration	6 months
Micic [32]	2017	USA	43680	47.8	CD/UC	≥18 years, primary discharge diagnosis of CD or UC, or primary diagnosis of an IBD-related complication and a secondary diagnosis of CD or UC, no death during index admission, exclusion of elective admissions	30 days
Mikocka-Walus [41]	2008	Australia	139	50∞	IBD/IBS/HCV	Sufficient knowledge of English	1 year

Table 1. Continued.

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Mikocka-Walus [33]	2016	Switzerland	2289	40.5§	CD/UC/IC	Diagnosis established ≥4 months before inclusion or at least 1 recurrence of symptoms, completion of baseline and follow-up visit, no pregnancy, no missing data on depression and anxiety scores	8 years
Mittermaier [34]	2004	Austria	60	31§	CD/UC	18-65 years, in remission 8 to 12 weeks after a flare defined as CDAI/CAI and in remission at baseline for at least 4 weeks (CDAI<150 or CAI <5), sufficient knowledge of German, no known or evident psychiatric diseases, no psychopharmacotherapy use, absence of stoma	1.5 year
North [35]	1991	USA	33Δ	39.8	CD/UC	At least one gastrointestinal exacerbation during study period, occurring no earlier than 4 months after date of enrolment	2 years
Persoons [36]	2005	Belgium	100	34	CD	≥18 years, refractory, active (CDAI>150) luminal disease treated with infliximab (5 or 10 mg/kg), no short bowel syndrome, absence of stoma, no participation in clinical trial	10 months

Table 1. Continued.

Publication characteristics			**Study population**				**Study characteristics**
Author	*Year*	*Country*	*Number of patients at baseline*	*Age, year (mean)*	*Disease type*	*Inclusion criteria*	*Follow-up duration*
Riley [37]	1990	UK	100	Range 20-78	UC	≥18 years, maintenance sulphasalazine (2-4 g daily) or delayed release mesalazine (800-1600 mg daily). Clinical remission (absence of blood in stool and macroscopic appearance of normal mucosa or erythema only on sigmoidoscopy), absence of oral or rectal steroids within one month of study entry	48 weeks
Takaoka [42]	2017	Japan	40	32.4§	CD	Hospitalized at gastroenterology unit during inclusion	A median of 25.5 days (IQR 13.5-45.0)

Abbreviations: USA, United States of America; CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; p.o., per os; CDAI, Crohn's disease activity index; BMI, body mass index; IBD-U, inflammatory bowel disease-unclassified; IBS, inflammatory bowel syndrome; HCV, hepatitis c virus; IC, indeterminate colitis; CAI, clinical activity index; mg, milligram; kg, kilogram; UK, United Kingdom; g, gram; IQR, interquartile range.

†Age and follow-up duration only mentioned separately for patients with CD or UC and with or without psychiatric comorbidity ‡Age only mentioned separately for CD and UC §Median, ¶Mean age only mentioned separately for relapse group and continued remission group, ∞Number of patients stated in table is number of IBD patients and only associations regarding IBD patients from this study are included, Δ33 patients out of 85 patients developed the endpoint (a flare) in the 2 year study period and were included in analyses.

Table 2. Associations of components of a comprehensive geriatric assessment with adverse health outcome measurements

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Allegretti [16]	324	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis Social assessment by marital status	90-days readmission	Depression: readmission + Anxiety: readmission ns Marital status: readmission ns
Ananthakrishnan [17]	10834	Mental assessment by psychiatric comorbidity (depressive disorder diagnosis and/or generalized anxiety diagnosis)	IBD-related surgery, IBD-related hospitalization, all-cause hospitalization, anti-TNF use, immunomodulator use, steroid use, outpatient visits, GE visits, abdominal CT/MRI scan, lower GI endoscopies	IBD-related surgery: CD+ (anxiety+, depression ns) UC ns, IBD-related hospitalization: CD ns UC –, all-cause hospitalizations: CD + UC +, anti-TNF use: CD ns UC ns, immunomodulator use: CD + UC ns, steroid use: CD + UC +, outpatient visits: CD + UC ns, GE visits: CD ns UC ns, abdominal CT/MRI scan: CD ns UC -, GI endoscopies: CD- UC **-**
Banovic [18]	52	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	QoL (SF36 Vitality, mental health and general health), CDAI score	Depression: vitality +, mental health +, general health +, CDAI ns. Anxiety: vitality ns, mental health +, general health +, CDAI ns
Barnes [19]	52498	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis	90-days readmission	Depression: readmission CD + UC + Anxiety: readmission CD + UC +
Bernstein [20]	704	Mental assessment by Positive and Negative Affect Schedule Social assessment by Social Network Index Social assessment by married/not married	Exacerbation	Low positive mood: ns High negative mood: ns Social functioning: ns Marital status: ns
Bitton [21]	60	Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (SCL-90-R)	Exacerbation	Depression: ns Anxiety: ns
Bitton [38]	101	Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (SCL-90-R)	Exacerbation	Depression: ns Anxiety: ns

Table 2. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Boer, de [22]	222	Mental assessment by depression (CES-D) Mental assessment by emotional functioning (IBDQ) Social assessment by IBDQ Social assessment by living alone yes/no Social assessment by MOS Social Support Survey	GE and GP visits	Depression: GE ns GP ns Emotional functioning: GE ns GP ns Social functioning (IBDQ): GE + GP ns Social functioning (living alone): GE ns GP ns Social functioning (social support): GE ns GP ns
Cámara [23]	458	Social assessment by ENRICHD Social Support Inventory	IBD-related adverse event	Social functioning: +
Cámara [24]	461	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Exacerbation	Depression: +, anxiety: +
Deter [25]	87	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI)	Combined measurement of health care utilization, HRQoL, and the somatic course of disease	Depression: combined outcome ns, health care utilization ns, HRQoL ns, somatic course ns Anxiety: combined outcome ns, health care utilization ns, HRQoL +; somatic course ns
Gaines [26]	2144	Mental assessment by PROMIS depression questionnaire	SCDAI >150, any abdominal surgeries, any hospitalizations, use of anti-TNF therapy	Depression: SCDAI +, any abdominal surgeries ns, any hospitalizations +, use of anti-TNF ns
Jansen [27]	55	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MIRT) Somatic assessment by malnutrition (BIA Phase angle) Functional assessment by handgrip strength	CDAI, HBI, CD-related hospitalizations, flares, complications, CD-related surgeries, composite assessment of CD-related doctor visits, complications, CD-associated hospitalization, exacerbation, CD-related surgery and changes in CD medication	Malnutrition (SGA): all seven outcome parameters ns Malnutrition (MIRT): hospitalizations +, surgeries +, complications +, exacerbation +, composite assessment +, CDAI: ns, HBI ns Malnutrition (BIA phase angle) and handgrip strength: for both all seven outcome parameters ns

Table 2. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Kochar [28]	2798	Mental assessment by depression (PHQ-8)	Exacerbation, new biologic prescription, new steroid prescription, any hospitalization, IBD-related surgery	Depression: exacerbation CD + UC ns, new biologic prescription CD + UC +, new steroid prescription CD + UC ns, hospitalization CD + UC +, IBD-related surgery CD + UC +
Langhorst [29]	75	Mental assessment by depression (HADS-D)	Exacerbation	Depression: exacerbation ns
Levenstein [30]	62	Mental assessment by depression (CES-D)	Exacerbation	Depression: exacerbation ns; short term (<8 months) exacerbation ns
Mardini [31]	18	Mental assessment by depression (BDI) Mental assessment by anxiety (BAI)	CDAI score	Depression: CDAI +, anxiety CDAI +
Maunder [39]	99	Mental assessment by depression (CES-D)	Disease activity	Depression: disease activity ns
McCombie [40]	54	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	SIBDQ score	Depression: SIBDQ ns, anxiety: SIBDQ ns
Micic [32]	43680	Somatic assessment by Malnutrition diagnosis Mental assessment by Depression diagnosis Mental assessment by Anxiety diagnosis	All-cause hospital readmission within 30 days	Malnutrition: readmission +, depression: readmission ns, anxiety: readmission +
Mikocka-Walus [41]	59†	Mental assessment by depression (HADS-D) Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (HADS-A) Mental assessment by anxiety (SCL-90-R)	Exacerbation	Depression (HADS-D): exacerbation ns, depression (SCL90): exacerbation ns, anxiety (HADS-A): exacerbation ns, anxiety (SCL90): exacerbation ns

Table 2. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Mikocka-Walus [33]	2007	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Clinical recurrence, fistulas, exacerbation, IBD surgery, biologic use, steroid use	Depression: clinical recurrence CD + UC +, fistula CD +, exacerbation UC +, IBD surgery CD+, biologic use CD +, steroid use CD + Anxiety: clinical recurrence CD + UC -, exacerbation CD – UC +, biologic use UC +, steroid use UC +
Mittermaier [34]	60	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI1)	Exacerbation	Depression: exacerbation at 12 months +, exacerbation at 18 months +. Anxiety: exacerbation at 12 months ns, exacerbation at 18 months +
North [35]	32	Mental assessment by depression (BDI) Mental assessment by visual analog depression scale	Change in disease activity and exacerbation	Depression (BDI): gastrointestinal scale score 1-month lag ns, gastrointestinal scale score 2-month lag ns, 1 month before exacerbation ns, 2 months before exacerbation ns. Depression (visual analog depression scale): gastrointestinal scale score 1-month lag ns, gastrointestinal scale score 2-month lag ns, 1 month before exacerbation ns, 2 months before exacerbation ns.
Persoons [36]	100	Mental assessment by MDD presence (PHQ-9) Mental assessment by anxiety (HADS-A) Social assessment by SSL-I	Response to infliximab, achievement of remission, time to retreatment	Depression: response to infliximab ns, failure to achieve remission +, time to retreatment + Anxiety: response to infliximab ns, failure to achieve remission ns, time to retreatment ns. Social support: response to infliximab ns, failure to achieve remission ns, time to retreatment ns

Table 2. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Riley [37]	92	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Exacerbation	Depression: exacerbation ns Anxiety: exacerbation ns
Takaoka [42]	40	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MUST) Somatic assessment by malnutrition (NRS 2002) Somatic assessment by malnutrition (O-PNI) Somatic assessment by malnutrition (CONUT)	Intestinal resection, LOS	Malnutrition (SGA): intestinal resection ns, LOS + Malnutrition (MUST score): intestinal resection ns, LOS ns Nutritional risk (NRS 2002): intestinal resection ns, LOS + Malnutrition (O-PNI): intestinal resection ns, LOS + Malnutrition (CONUT): intestinal resection ns, LOS +

NB: +: a significant association between a component of a geriatric assessment and outcome of interest in which more geriatric impairment leads to worse outcome; -: a significant association between a component of a geriatric assessment and outcome of interest in which more geriatric impairment leads to better outcome. When both univariate and multivariate analyses were performed, only results from multivariate analyses (most corrected model) are tabulated. For an extended version of table 2 including association measures see supplementary table 1. For corrected confounders see supplementary table 2

Abbreviations: ns, non-significant; HR(QoL), (health related) quality of life; IBD, inflammatory bowel disease; anti-TNF, anti-tumor necrosis factor; GE, gastroenterologist; CT, computerized tomography; MRI, magnetic resonance imaging; GI, gastrointestinal; CD, Crohn's disease; UC, ulcerative colitis; HADS-D, hospital anxiety and depression scale-depression component; HADS-A, hospital anxiety and depression scale-anxiety component; SF36, short form 36; (S)CDAI, (short) Crohn's disease activity index; SCL-90-R, symptom checklist 90 revised; CES-D, center for epidemiologic studies depression scale; IBDQ, inflammatory bowel disease questionnaire; MOS, medical outcomes study; GP, general practitioner; ENRICHD, enhancing recovery in coronary heart disease; BDI, Beck depression inventory; STAI, stait trait anxiety index; PROMIS, patient reported outcomes measurement information system; SGA, subjective global assessment; MIRT, malnutrition inflammation risk tool; BIA, bioelectrical impedance analysis; HBI, Harvey Bradshaw index; PHQ, patient health questionnaire; BAI, Beck anxiety inventory; MDD, major depressive disorder; SSL-I, social support list-interactions; MUST, malnutrition universal screening tool; NRS, nutrition risk screening; O-PNI, Onodera's prognostic nutritional index; CONUT, controlling nutritional status; LOS, length of hospital stay. †Total of 124 patients, 59 IBD patients.

Table 3. Quality assessment of the included studies

Publication characteristics		**Selection**		**Outcome**		
Author	*Year*	*Representativeness of the exposed cohort*	*Ascertainment of exposure (geriatric measure)*	*Assessment of outcome*	*Sufficient duration of follow-up*	*Adequacy of follow-up*
Allegretti [11]	2015	+/-	+	+	+	+
Ananthakrishnan [12]	2013	+	+	+	+	?
Banovic [13]	2010	-	+	+	+/-	?
Barnes [14]	2017	+	+	+	+	+
Bernstein [15]	2010	+	+	+	+/-	+/-
Bitton [16]	2003	-	+	+	+/-	+
Bitton [35]	2008	--	+	+	+/-	-
Boer, de [17]	1998	+	+	+	+/-	+/-
Cámara [18]	2011	+/-	+	+	+	+
Cámara [19]	2011	+/-	+	+	+	+
Deter [20]	2008	--	+	+/-	+	?
Gaines [21]	2016	+	+	+	+/-	+/-
Jansen [22]	2016	-	+	+	-	+
Kochar [23]	2018	+/-	+	+	+	?
Langhorst [24]	2013	-	+	+	+	-
Levenstein [25]	2000	+/-	+	+	+	+
Mardini [26]	2004	-	+	+	+	+
Maunder [37]	2005	-	+	+	+	+/-
McCombie [33]	2015	+/-	+	+	+	+/-
Micic [27]	2017	+	+	+	+	?
Mikocka-Walus [34]	2008	+	+	+	+/-	+
Mikocka-Walus [28]	2016	+	+	+	+	-
Mittermaier [29]	2004	-	+	+	+	+
North [30]	1991	+/-	+	+	+	+
Persoons [31]	2005	-	+	+	+/-	+
Riley [32]	1990	+	+	+	+/-	+
Takaoka [36]	2017	-	+	+	+	?

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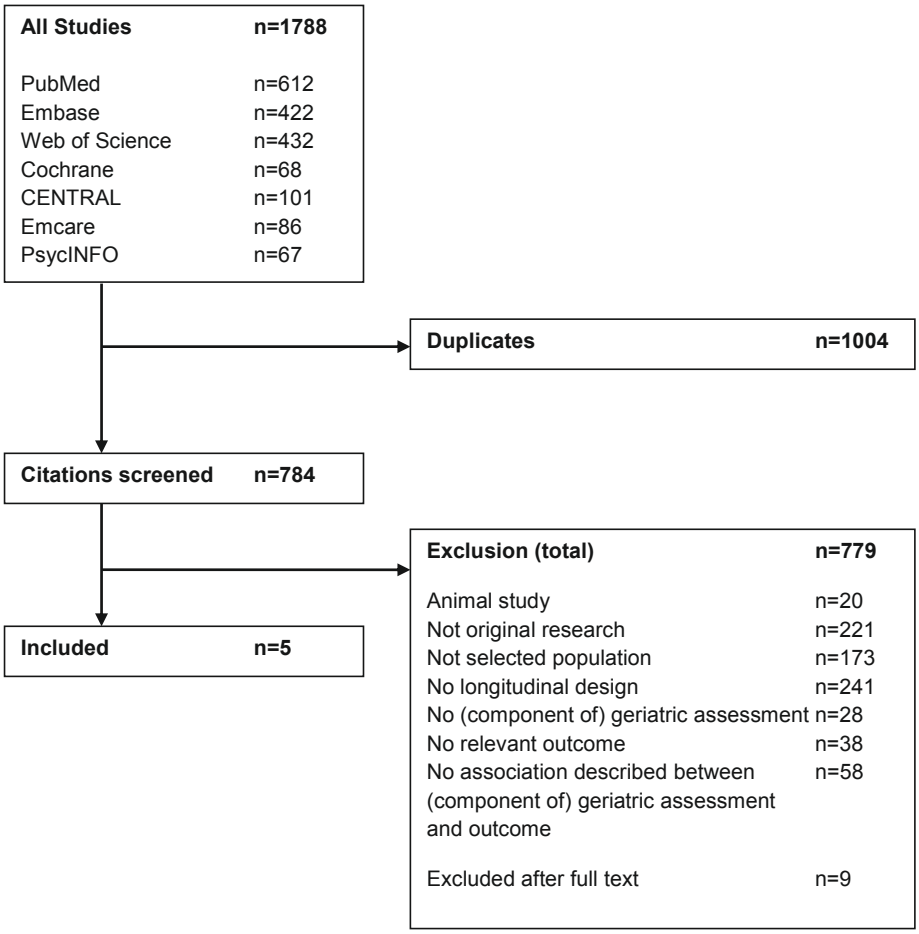

Supplementary figure 1. Additional flowchart

Supplementary table 1. Detailed table of associations of components of a comprehensive geriatric assessment with adverse health outcome measurements

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Allegretti [16]	324	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis Social assessment by marital status	90-days readmission	Depression: readmission + (aHR 1.99, 95% CI 1.33-3.00) Anxiety: ns¶ Marital status: ns¶
Ananthakrishnan [17]	10834	Mental assessment by psychiatric comorbidity (depressive disorder diagnosis and/or generalized anxiety diagnosis)	IBD-related surgery, IBD-related hospitalization, all-cause hospitalization, anti-TNF use, immunomodulator use, steroid use, outpatient visits, GE visits, abdominal CT/MRI scan, lower GI endoscopies	IBD-related surgery: CD+ (a[1]OR 1.22, 95% CI 1.01-1.47) (anxiety + (OR 1.36, 95% CI 1.05-1.75), depression ns (OR 1.20, 95% CI 0.95-1.53)) UC ns (aOR 1.01, 95% CI 0.80-1.28), IBD-related hospitalization: CD ns (aOR 1.05, 95% CI 0.88-1.26) UC – (aOR 0.77, 95%CI 0.63-0.93), all-cause hospitalizations: CD + (aOR 1.48, 95% CI 1.19-1.83) UC + (aOR 1.28, 95% CI 1.07-1.52), anti-TNF use: CD ns (aOR 1.17, 95% CI 0.96 – 1.43) UC ns (aOR 1.15, 95% CI 0.86 – 1.53), immunomodulator use: CD + (aOR 1.43, 95% CI 1.21 – 1.67) UC ns (aOR 1.16, 95% CI 0.97 – 1.39), steroid use: CD + (aOR 1.83, 95% CI 1.57 – 2.13) UC + (aOR 1.42, 95% CI 1.22-1.64), outpatient visits: CD + (aOR 2.80, 95% CI 1.54-4.06) UC ns (aOR 1.43, 95% CI 0.73-2.14), GE visits: CD ns (aOR 1.54, 95% CI 0.84-2.25) UC ns (aOR 0.72, 95% CI 0.24-1.20), abdominal CT/MRI scan: CD ns (aOR 1.06, 95% CI 0.77-1.34) UC - (aOR 0.69, 95% CI 0.40-0.90), GI endoscopies: CD- (aOR 0.56, 95% CI 0.33-0.79) UC - (aOR 0.50, 95% CI 0.24-0.75)
Banovic [18]	52	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	QoL (SF36 Vitality, mental health and general health), CDAI score	Depression: vitality + (r=-0.50, P<*0.005*), mental health + (r=-0.54, P<*0.005*), general health + (r=-0.38, P<*0.005*), CDAI ns (r=0.2). Anxiety: vitality ns (r=-0.37), mental health + (r=-0.66, P<*0.005*), general health + (r=-0.50, P<*0.005*), CDAI ns (r=0.03)
Barnes [19]	52498	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis	90-days readmission	Depression: CD + (aOR 1.18, 95% CI 1.11-1.26) UC + (aOR 1.28, 95% CI 1.14–1.45) Anxiety: CD + (aOR 1.27, 95% CI 1.07-1.50) UC + (aOR 1.35, 95% CI 1.07–1.70)

Supplementary table 1. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Bernstein [20]	704	Mental assessment by Positive and Negative Affect Schedule Social assessment by Social Network Index Social assessment by married/not married	Exacerbation defined as MIBDI	Low positive mood: ns (aOR 1.16, 95% CI 0.70-1.93) High negative mood: ns (aOR 1.04, 95% CI 0.58-1.88) Social functioning: ns (aOR 1.21, 95% CI 0.61-2.38) Marital status: ns (aOR 1.59, 95% CI 0.85-2.95)
Bitton [21]	60	Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (SCL-90-R)	Exacerbation defined as symptoms and endoscopy	Depression: ns (HR 1.011, 95% CI, 0.95-1.08) Anxiety: ns (HR 1.000, 95% CI 1.00-1.00)
Bitton [38]	101	Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (SCL-90-R)	Exacerbation defined as CDAI >150 with an increase of ≥70 points from baseline	Depression: ns (HR 1.6, 95% CI 0.9-2.7) Anxiety: ns (HR 1.4, 95% CI 0.77-2.6)
Boer, de [22]	222	Mental assessment by depression (CES-D) Mental assessment by emotional functioning (IBDQ) Social assessment by IBDQ Social assessment by living alone yes/no Social assessment by MOS Social Support Survey	GE and GP visits	Depression: GE ns¶ GP ns¶ Emotional functioning: GE ns¶ GP ns¶ Social functioning (IBDQ): GE +¶ GP ns¶ Social functioning (living alone): GE ns¶ GP ns¶ Social functioning (social support): GE ns¶ GP ns¶
Cámara [23]	458	Social assessment by ENRICHD Social Support Inventory	IBD-related adverse events comprising: progression of disease as measured by occurrence of flare, non response to medication, extraintestinal manifestations or complications	Social functioning: + (aOR 0.666, 95% CI 0.516-0.859)
Cámara [24]	461	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Exacerbation defined as ≥100 increase in CDAI, medication step-up, extraintestinal manifestations or complications	Depression: + (aOR 1.42, 95% CI 1.05-1.90) Anxiety: + (aOR 1.46, 95% CI 1.08-1.97)
Deter [25]	87	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI)	Combined measurement of health care utilization (defined as data on hospital days and sick leave days), the HRQoL (no definition given), and the somatic course of disease (CDAI)	Depression: combined outcome ns¶, health care utilization ns¶, HRQoL ns¶, somatic course ns¶ Anxiety: combined outcome ns¶, health care utilization ns¶, HRQoL + (aβ-0.45, P=*.0003*); somatic course ns¶

Supplementary table 1. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Gaines [26]	2144	Mental assessment by PROMIS depression questionnaire	SCDAI >150, any abdominal surgeries, any hospitalizations, use of anti-TNF therapy	Depression: SCDAI + (aOR 1.21, 95% CI 1.07-1.36), any abdominal surgeries ns (aOR 0.94, 95% CI 0.72-1.22), any hospitalizations + (aOR 1.26, 95% CI 1.06-1.49), use of anti-TNF ns (aOR 0.91, 95% CI 0.78-1.08)
Jansen [27]	55	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MIRT) Somatic assessment by malnutrition (BIA Phase angle) Functional assessment by handgrip strength	Disease activity (CDAI and HBI), CD-related hospitalizations, flares, complications (new stenosis, fistula or abscess), CD-related surgeries. The authors made a composite assessment of the parameters CD-related doctor visits, complications, CD-associated hospitalization, flare-up, CD-related surgery and changes in CD medication	Malnutrition (SGA): all seven outcome parameters ns¶ Malnutrition (MIRT): hospitalizations + (ρ 0.398, *P=.003*), surgeries + (ρ 0.371, *P=.006*), complications + (ρ 0.333, *P=.015*), flares + (ρ 0.299, *P=.030*), composite assessment + (ρ 0.528, *P<.001*), CDAI: ns (ρ 0.260, *P=.077*); HBI ns (ρ 0.188, *P=.195*) Malnutrition (BIA phase angle) and handgrip strength: for both all seven outcome parameters ns¶
Kochar [28]	2798	Mental assessment by depression (PHQ-8)	Exacerbation by disease activity index (modified HBI ≥5 or SCCAI >2), new biologic prescription, new steroid prescription, any hospitalization, IBD-related surgery	Depression: exacerbation CD + (aRR 2.3, 95% CI 1.9-2.8) UC ns (aRR 1.3, 95% CI 0.9-1.8), new biologic prescription CD + (aRR 1.8, 95% CI 1.4-2.3) UC + (aRR 1.6, 95% CI 1.1-2.3), new steroid prescription CD + (aRR 1.8, 95% CI 1.1-3.2) UC ns (aRR 1.8, 95% CI 0.9-3.8), hospitalization CD + (aRR 1.3, 95% CI 1.2-1.5) UC + (aRR 1.3, 95% CI 1.1-1.5); IBD-related surgery CD + (aRR 1.3, 95% CI 1.1-1.6) UC + (aRR 1.8, 95% CI 1.2-2.6)
Langhorst [29]	75	Mental assessment by depression (HADS-D)	Exacerbation defined as CAI>4 or an increase of CAI >3 from baseline, endoscopic activity index and histological evaluation	Depression: exacerbation ns (aHR 1.08, 95% CI 0.95–1.22)
Levenstein [30]	62	Mental assessment by depression (CES-D)	Exacerbation defined as symptoms rated ≥1 on a symptom scale of 0–8 that lasted ≥10 days and that were associated with at least one of two confirmation criteria: intensified therapy prescribed by a physician and/or rectal inflammation seen by study endoscopists.	Depression: exacerbation ns (middle/high tertile CES-D score vs low tertile: HR 0.83/HR 0.99, 95% CI 0.30-2.3/95% CI 0.36-2.7); short term (<8 months) exacerbation ns (middle/high tertile CES-D score vs low tertile: 22.2%/10.8% vs 20.5%, *P=.93*)

Supplementary table 1. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Mardini [31]	18	Mental assessment by depression (BDI) Mental assessment by anxiety (BAI)	CDAI score	Depression: CDAI + (aβ 5.92, *P=.0004*), anxiety CDAI + (aβ 2.42, *P=.02*)
Maunder [39]	99	Mental assessment by depression (CES-D)	Disease activity by St. Mark's index	Depression: disease activity ns (r=0.19, *P>.05*)
McCombie [40]	54	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	SIBDQ score	Depression: SIBDQ ns (*P=.61*)¶, anxiety: SIBDQ ns (*P=.20*)¶
Micic [32]	43680	Somatic assessment by Malnutrition diagnosis Mental assessment by Depression diagnosis Mental assessment by Anxiety diagnosis	All-cause hospital readmission within 30 days	Malnutrition: readmission + (aOR 1.37, 95% CI 1.22-1.54), depression: readmission ns¶, anxiety: readmission + (aOR 1.17, 95% CI 1.01-1.36)
Mikocka-Walus [41]	59†	Mental assessment by depression (HADS-D) Mental assessment by depression (SCL-90-R) Mental assessment by anxiety (HADS-A) Mental assessment by anxiety (SCL-90-R)	Exacerbation measured by CDAI or SCCAI	Depression (HADS-D): exacerbation ns (aOR 1.057, 95% CI 0.919-1.215), depression (SCL90): exacerbation ns (aOR 1.003, 95% CI 0.928-1.085), anxiety (HADS-A): exacerbation ns (aOR 0.967, 95% CI 0.841-1.111), anxiety (SCL90): exacerbation ns (aOR 1.040, 95% CI 0.989-1.092)
Mikocka-Walus [33]	2007	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Clinical recurrence (defined as CDAI/MTWAI, exacerbation or worsening of the disease as established by physicians, fistulas and stenosis, anal fissure, abscess, IBD surgery, biologic use, steroid use), fistulas, exacerbation, IBD surgery, biologic use, steroid use	Depression: clinical recurrence CD + (*P=.001*)¶ UC + (*P=.005*)¶, fistula CD + (*P=.009*)¶, exacerbation UC + (*P=.013*)¶, IBD surgery CD + (*P=.007*)¶, biologic use CD + (*P=.016*)¶, steroid use CD + (*P=.035*)¶ Anxiety: clinical recurrence CD + (*P=.031*)¶ UC - (*P=.066*)¶, exacerbation CD – (*P=.070*)¶ UC + (*P=.044*)¶, biologic use UC + (*P<.001*)¶, steroid use UC + (*P=.013*)¶
Mittermaier [34]	60	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI)	Exacerbation (defined as clinical criteria, CDAI≥150 or an increase of 70 points, or by a CAI of ≥6 for UC plus assessment of laboratory parameters)	Depression: exacerbation at 12 months + (*P<.01*)¶, exacerbation at 18 months + (*P<.01*)¶. Anxiety: exacerbation at 12 months ns (Kendall τ 0.1949), exacerbation at 18 months + (Kendall τ=0.1844 *P<.05*)

Supplementary table 1. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
North [35]	32	Mental assessment by depression (BDI) Mental assessment by visual analog depression scale	A change in disease activity using gastrointestinal scale score Exacerbation using gastrointestinal scale score	Depression (BDI): gastrointestinal scale score 1-month lag ns (regression slope 0.19 (95% CI -0.15-0.52)), gastrointestinal scale score 2-month lag ns (regression slope -0.16 (95% CI -0.65-0.34)), 1 month before exacerbation ns (regression slope -0.46 (95% CI -1.58-0.67)), 2 months before exacerbation ns (regression slope -0.02 (95% CI -1.36-1.32)). Depression (visual analog depression scale): gastrointestinal scale score 1-month lag ns (regression slope 0.03 (95% CI -0.09-0.15)), gastrointestinal scale score 2-month lag ns (regression slope 0.06 (95% CI -0.05-0.18)), 1 month before exacerbation ns (regression slope 0.25 (95% CI -0.23-0.72)), 2 months before exacerbation ns (regression slope -0.21 (95% CI -0.70-0.28)).
Persoons [36]	100	Mental assessment by MDD presence (PHQ-9) Mental assessment by anxiety (HADS-A) Social assessment by SSL-I	Response to infliximab, achievement of remission (CDAI<150), time to retreatment	Depression: response to infliximab ns¶, failure to achieve remission + (aOR=0.166, 95% CI=0.049-0.567, *P=.004*), time to retreatment + (aHR=2.271, 95% CI=1.36-3.79, *P=.002*) Anxiety: response to infliximab ns¶, failure to achieve remission ns¶, time to retreatment ns¶. Social support: response to infliximab ns¶, failure to achieve remission ns¶, time to retreatment ns¶
Riley [37]	92	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Exacerbation defined as symptomatic deterioration and sigmoidoscopy	Depression: exacerbation ns¶ Anxiety: exacerbation ns¶

Supplementary table 1. Continued.

Author	Number of patients	Component of comprehensive geriatric assessment and measured method	Outcome	Association
Takaoka [42]	40	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MUST) Somatic assessment by malnutrition (NRS 2002) Somatic assessment by malnutrition (O-PNI) Somatic assessment by malnutrition (CONUT)	Intestinal resection, LOS (defined as <28 days vs ≥28 days)	Malnutrition (SGA): intestinal resection ns (operation 53.8%, non-operation 29.6% *P=.071*), LOS + (LOS≥28: 52.6% vs LOS<28: 23.8%, *P=.008*) Malnutrition (MUST score): intestinal resection ns (operation 76.9%, non-operation 51.9%, *P=.314*), LOS ns (LOS≥28: 79.0% vs LOS<28: 42.9%, *P=.058*) Nutritional risk (NRS 2002): intestinal resection ns (operation 76.9%, non-operation 51.9%, *P=.109*), LOS + (LOS≥28: 84.2% vs LOS<28: 52.4%, *P=.032*) Malnutrition (O-PNI): intestinal resection ns (operation median 32.8, non-operation median 37.2, *P=.078*), LOS + (LOS≥28: 33.9 vs LOS<28: 38.2, *P=.006*) Malnutrition (CONUT): intestinal resection ns (operation median 8.0, non-operation median 5.0, *P=.078*), LOS + (LOS≥28: 7.0 vs LOS<28: 5.0, *P=.019*)

NB: +: a significant association between a component of a geriatric assessment and outcome of interest in which more geriatric impairment leads to worse outcome; -: a significant association between a component of a geriatric assessment and outcome of interest in which more geriatric impairment leads to better outcome. When both univariate and multivariate analyses were performed, only results from multivariate analyses (most corrected model) are tabulated. For corrected confounders see supplementary table 2. When a study used more than one model for confounder corrections this is presented as [1] and displayed in supplementary table 2.

Abbreviations: (a)HR, (adjusted) hazard ratio; ns, non-significant; CI, confidence interval; IBD, inflammatory bowel disease; anti-TNF, anti-tumor necrosis factor; CT, computerized tomography; MRI, magnetic resonance imaging; GI, gastrointestinal; GE, gastroenterologist; (a)OR, (adjusted) odds ratio; CD, Crohn's disease; UC, ulcerative colitis; HADS-D, hospital anxiety and depression scale-depression component; HADS-A, hospital anxiety and depression scale-anxiety component; SF36, short form 36; (S)CDAI, (short) Crohn's disease activity index; r, Pearson's correlation coefficient; MIBDI, Manitoba IBD index; SCL90R, symptom checklist 90 revised; CES-D, center for epidemiologic studies depression scale; IBDQ, inflammatory bowel disease questionnaire; MOS, medical outcomes study; GP, general practitioner; (a)β, (adjusted) standardized regression coefficient; ENRICHD, enhancing recovery in coronary heart disease; BDI, Beck depression inventory; STAI, stait trait anxiety index; PROMIS, patient reported outcomes measurement information system; SGA, subjective global assessment; MIRT, malnutrition inflammation risk tool; BIA, bioelectrical impedance analysis; HBI, Harvey Bradshaw index; ρ, Spearman's correlation coefficient; PHQ, patient health questionnaire; (a)RR, (adjusted) relative risk; CAI, colitis activity index; BAI, Beck anxiety inventory SCCAI, simple clinical colitis activity index; MTWAI, modified Truelove Witts activity index; MDD, major depressive disorder; SSL-I, social support list-interactions; MUST, malnutrition universal screening tool; NRS, nutrition risk screening; O-PNI, Onodera's prognostic nutritional index; CONUT, controlling nutritional status; LOS, length of hospital stay. †Total of 124 patients, 59 IBD patients.

Supplementary table 2. Adjustment for confounders per included study

Author	Component of comprehensive geriatric assessment	Corrected for confounders
Allegretti [16]	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis Social assessment by marital status	Age, LOS, sex, race, chronic pain, IBD type, previous abdominal operation, tobacco use, ethanol abuse, opiate use, steroids in the previous 6 months, infliximab use at index admission, pain clinic follow-up scheduled after discharge, gastrointestinal follow-up scheduled after discharge, and psychiatric follow-up scheduled after discharge. Employment, insurance, education.
Ananthakrishnan [17]	Mental assessment by psychiatric comorbidity (depressive disorder diagnosis and/or generalized anxiety diagnosis)	Age, age at first diagnosis, gender, modified Charlson co-morbidity score, duration of follow-up, and propensity score (to address confounding by disease activity). [1]: adjusted as well for use of anti-TNF or immunomodulator therapy prior to surgery.
Banovic [18]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Not mentioned
Barnes [19]	Mental assessment by depression diagnosis Mental assessment by anxiety diagnosis	Age, female sex, tobacco abuse, chronic pain, comorbidity score, location and teaching status of hospital, payer/insurance, CDI, need for IBD-related surgery, LOS for index hospitalization, fistula presence.
Bernstein [20]	Mental assessment by Positive and Negative Affect Schedule Social assessment by Social Network Index Social assessment by married/not married	Sex, IBD type, age at diagnosis ≤25 years, smoker, any use of NSAIDs, any infection, use of antibiotics, low childhood SES, fewer high-contact roles ≤4, any major life stress event, high perceived stress, low positive mood, high negative mood.
Bitton [21]	Mental assessment by depression (SCL-90R) Mental assessment by anxiety (SCL-90R)	ns in univariate analyses
Bitton [38]	Mental assessment by depression (SCL-90R) Mental assessment by anxiety (SCL-90R)	ns in univariate analyses
Boer, de [22]	Mental assessment by depression (CES-D) Mental assessment by emotional functioning (IBDQ) Social assessment by IBDQ Social assessment by living alone yes/no Social assessment by MOS Social Support Survey	Age, sex, insurance, education, living alone, co-morbidity, disease activity, disease duration, disease type, IBDQ subscores, experienced burden of disease, social support, depression score (CES-D).

Supplementary table 2. Continued.

Author	Component of comprehensive geriatric assessment	Corrected for confounders
Cámara [23]	Social assessment by ENRICHD Social Support Inventory	Baseline disease activity, female sex, age, disease duration, days in hospital, 5-Aminosalycilates, Sulfasalazine, Steroids, Immunosuppressors, anti-TNF agents, antibiotics, smoking, BMI, positive family history, adherence, time difference, social diversion, social inhibition.
Cámara [24]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Stress, baseline disease activity, days in hospital, type of therapy (5-Aminosalycilates, sulfasalazine, steroids, immunosuppressors, anti-TNF agents, antibiotics), BMI, smoking, gender, age, disease duration.
Deter [25]	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI)	CDAI at baseline, steroid intake, disease duration, sick leave at randomization, behaviour control.
Gaines [26]	Mental assessment by PROMIS depression questionnaire	Age, gender, race, baseline SCDAI, disease duration, baseline anti-TNF use, BMI, current smoking, level of educational attainment, and sleep, baseline history of hospitalization or surgery, use of steroids and adherence to oral medications.
Jansen [27]	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MIRT) Somatic assessment by malnutrition (BIA Phase angle) Functional assessment by handgrip strength	Not mentioned
Kochar [28]	Mental assessment by depression (PHQ-8)	Sex, remission status, disease activity.
Langhorst [29]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Sex, baseline mucosal healing, baseline histology healing, baseline long-term stress, short term stress at last visit before relapse.
Levenstein [30]	Mental assessment by depression (CES-D)	ns in univariate analyses
Mardini [31]	Mental assessment by depression (BDI) Mental assessment by anxiety (BAI)	Age, smoking history, alcohol consumption, employment status, current use of psychotropic medications.
Maunder [39]	Mental assessment by depression (CES-D)	Not mentioned

Supplementary table 2. Continued.

Author	Component of comprehensive geriatric assessment	Corrected for confounders
McCombie [40]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Baseline SIBDQ
Micic [32]	Somatic assessment by Malnutrition diagnosis Mental assessment by Depression diagnosis Mental assessment by Anxiety diagnosis	Disease type, age, sex, smoking, opioid dependence, cannabis dependence, primary payer, median income, teaching status of hospital, intraabdominal fistula or abscess, bowel obstruction, Clostridium difficile colitis, hypovolemia, electrolyte disturbance, anemia, blood transfusion during hospitalization, any surgery performed, elective surgery.
Mikocka-Walus [41]	Mental assessment by depression (HADS-D) Mental assessment by depression (Symptom Checklist-90R) Mental assessment by anxiety (HADS-A) Mental assessment by anxiety (Symptom Checklist-90R)	Disease activity at baseline, IBD subtype, sex, years since diagnosis and age.
Mikocka-Walus [33]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Sex (only adjusted in clinical recurrence (composite outcome measurement) analyses)
Mittermaier [34]	Mental assessment by depression (BDI) Mental assessment by anxiety (STAI1)	Depression analyses corrected for: number of flares within the previous year, medication and smoking at baseline, baseline CDAI scores. STAI1 analysis was not corrected.
North [35]	Mental assessment by depression (BDI) Mental assessment by visual analog depression scale	IBD type, BDI was adapted because of overlap with gastrointestinal scale (appetite, weight loss (two questions), general fatigue, and worries about health were removed).

Supplementary table 2. Continued.

Author	Component of comprehensive geriatric assessment	Corrected for confounders
Persoons [36]	Mental assessment by MDD presence (PHQ-9) Mental assessment by anxiety (HADS-A) Social assessment measured with SSL-I	Response to infliximab: all ns in univariate analyses Achievement of remission analysis: baseline CDAI, 'significant biological variables', previous surgery, female gender. Time to retreatment analysis: MDD, use of antidepressant, HADS-A, age, age of diagnosis, member of patient association, any treatment for flare within the previous year, colonic localization, number of days since previous treatment, CDAI, CDAI at re-evaluation, response at re-evaluation.
Riley [37]	Mental assessment by depression (HADS-D) Mental assessment by anxiety (HADS-A)	Not mentioned
Takaoka [42]	Somatic assessment by malnutrition (SGA) Somatic assessment by malnutrition (MUST) Somatic assessment by malnutrition (NRS 2002) Somatic assessment by malnutrition (O-PNI) Somatic assessment by malnutrition (CONUT)	Not mentioned

Abbreviations: LOS, length of hospital stay, IBD, inflammatory bowel disease; HADS-D, hospital anxiety and depression scale-depression component; HADS-A, hospital anxiety and depression scale-anxiety component; CDI, Clostridium difficile infection; NSAID, non-steroidal anti-inflammatory drug; SES, socioeconomic status; SCL90R, symptom checklist 90 revised; ns, non significant; CES-D, center for epidemiological studies depression scale;
IBDQ, inflammatory bowel disease questionnaire; MOS, medical outcomes study; ENRICHD, enhancing recovery in coronary heart disease; TNF, tumor necrosis factor; BMI, body mass index; BDI, Beck depression inventory; STAI, Stait trait anxiety index; (S)CDAI, (short) Crohn's disease activity index; PROMIS, patient reported outcomes measurement information system; SGA, subjective global assessment; MIRT, malnutrition inflammation risk tool; BIA, bioelectrical impedance analysis; PHQ, patient health questionnaire; BAI, Beck anxiety inventory; MDD, major depressive disorder; SSL-I=Social Support List-Interactions; MUST, malnutrition universal screening tool; NRS, nutrition risk screening; O-PNI, Onodera's prognostic nutritional index; CONUT, controlling nutritional status;

SUPPLEMENTAL MATERIAL A – PUBMED SEARCH DETAILS

("Inflammatory Bowel Diseases"[Mesh] OR "Inflammatory Bowel Diseases"[tw] OR "Inflammatory Bowel Disease"[tw] OR "IBD"[tw] OR "crohn"[tw] OR "crohns"[tw] OR "crohn's"[tw] OR "ulcerative colitis"[tw] OR "colitis ulcerosa"[tw] OR "Inflammatory Bowel"[tw])

AND

("Geriatric Assessment"[Mesh] OR "Geriatric Assessment"[tw] OR "Geriatric Assessments"[tw] OR "Frail Elderly"[mesh] OR "Frailty"[tw] OR "frail"[tw] OR "Groningen Frailty Indicator"[tw] OR "Geriatric 8"[tw] OR "tilburg frailty indicator"[tw] OR "frailty indicator"[tw] OR "Fried criteria"[tw] OR "frailty index"[tw] OR "frail scale"[tw] OR "Edmonton Frail Scale"[tw] OR "Vulnerable Elders Survey-13"[tw] OR "VES-13"[tw] OR "Groningen Activity Restriction Scale"[tw] OR "Montreal Cognitive Assessment"[tw] OR "Comprehensive Geriatric Assessment"[tw] OR "multidimensional geriatric assessment"[tw] OR "Geriatric Depression Scale"[tw] OR "functional status"[tw] OR "Cognition"[mesh:noexp] OR "cognition"[tiab] OR "cognitive"[tiab] OR "social"[ti] OR "Comorbidity"[Mesh] OR "comorbidity"[tw] OR "co morbidity"[tw] OR "co-morbidities"[tw] OR "comorbidities"[tw] OR "multi morbidity"[tw] OR "multimorbidity"[tw] OR "polypharmacy"[tw] OR "Polypharmacy"[Mesh] OR "Katz Index"[tw] OR "Lawton IADL"[tw] OR "Physical Performance Test"[tw] OR "health-related quality of life"[tw] OR "health related quality of life"[tw] OR "Mini-Nutritional Assessment"[tw] OR "Mini-Nutritional Assessment short form"[tw] OR "Mini-Mental State Examination"[tw] OR "Six Item Cognitive Impairment Test"[tw] OR "6CIT"[tw] OR "6 CIT"[tw] OR "clock drawing test"[tw] OR "Mini-cog"[tw] OR "frax tool"[tw] OR "short physical performance battery"[tw] OR "handgrip strenght"[tw] OR "Charlson Comorbidity Index"[tw] OR "Adult Comorbidity Evaluation-27"[tw] OR "Timed Up and Go"[tw] OR "Timed Up Go"[tw] OR "Timed Up & Go"[tw] OR "tugt"[tw] OR "Nutritional Risk Screening"[tw] OR "Malnutrition Screening Tool"[tw] OR "neuropsychological assessment"[tw] OR "Neuropsychological Tests"[Mesh] OR "Neuropsychological Tests"[tw] OR "Neuropsychological Test"[tw] OR "activities of daily living"[tw] OR "Activities of Daily Living"[Mesh] OR "gait speed"[tw] OR "loss of independence"[tw] OR "muscle strenght"[tw] OR "Mobility Limitation"[Mesh] OR "Risk Assessment"[Majr] OR "risk stratification"[tw] OR ("MNA"[tw] AND nutrition*[tw]) OR "SNAQ"[tw] OR "simplified nutritional appetite"[tw] OR "simplified nutritional assessment"[tw] OR "malnutrition universal screening"[tw] OR ("must"[tw] AND nutrition*[tw]) OR ("Health Reported"[tw] AND "Quality of Life"[tw]) OR "HRQOL"[tw] OR "HR QOL"[tw] OR "Depression"[Mesh] OR "Depressive disorder"[Mesh] OR "mental depression"[tw] OR "depressive disorder"[tw] OR "depressive disorders"[tw] OR "mood"[tw] OR "GDS"[tw] OR "geriatric depression scale"[tw] OR "CES-D"[tw] OR "HADS"[tw] OR "Beck Depression Inventory"[tw] OR "BDI"[tw])

Additional anxiety PubMed search:

("Inflammatory Bowel Diseases"[Mesh] OR "Inflammatory Bowel Diseases"[tw] OR "Inflammatory Bowel Disease"[tw] OR "IBD"[tw] OR "crohn"[tw] OR "crohns"[tw] OR "crohn's"[tw] OR "ulcerative colitis"[tw] OR "colitis ulcerosa"[tw] OR "Inflammatory Bowel"[tw])

AND

("Anxiety"[Mesh] OR "Anxiety"[tw] OR "Anxiety Disorders"[Mesh:NoExp] OR "Beck Anxiety Inventory"[tw] OR "Stait Trait Anxiety Inventory"[tw])

SUPPLEMENTAL MATERIAL B - QUALITY ASSESSMENT OF STUDIES, BASED ON THE NEWCASTLE-OTTAWA SCALE[9]

1. Selection

Representativeness of the exposed cohort

++ Study focusses on older patients (≥60 years) or makes a clear statement about the group of older patients included and population is representative of the average IBD patient and beholds a heterogeneous population

+ Some older patients (≥60 years old) included and representative of the average IBD patient

+/- almost no older patients included (≥60 years old), somewhat representative of the average IBD patient

- No older patients and somewhat representative of the average IBD patient

-- No older patients and not representative of the average IBD patient

? No clear description of abundance of older patients or IBD characteristics

Ascertainment of exposure (geriatric assessment)

+ Clearly described and validated geriatric assessment tool/questionnaire, or validated diagnosis /diagnosis code.

+/- Partly described or validated geriatric measurement, or a partly described code / diagnosis is used with vague statement on how diagnosis was obtained

- A Geriatric assessment tool/questionnaire is used but not validated nor described, or a code / diagnosis is used without statement on the obtainment of diagnosis.

2. Outcome

Assessment of outcome

+ Clear description of method measuring outcome (validated GA or validated diagnosis)

+/- Partly described outcome or only status description of a diagnosis

- Unclear description of method measuring outcome

? No description

Sufficient duration of follow-up

+ Yes, follow-up was long enough for outcomes to occur

+/- Partly enough

- No

? No description of follow up period

Adequacy of follow up of cohorts

+ Complete follow up (all subjects accounted for), or subjects lost to follow up unlikely to introduce bias (loss to follow up < 10%),

+/- loss to follow up more than 10% but clear description of those lost

- Follow up rate < 90% and no description of those lost

? No statement