Quality of Life and IBD

Subjects: Health Care Sciences & Services

Contributor: Manuel Barreiro-de Acosta

Inflammatory bowel diseases (IBDs) are chronic disabling conditions, characterized by an unpredictable course with flare-ups and periods of remission, that frequently affect young people and require lifelong medical follow-up and treatment. For years, the main endpoints of IBD treatment had been clinical remission and response, followed by biomarker normalization and mucosal healing. In the last decades, different therapies have been proved to be effective to treat IBD and the use of patient reported outcome (PRO) have become more relevant. Therefore, health-related quality of life (HRQoL) that has been defined as the value assigned to the duration of life influenced by physical and mental health, has been suggested as an important endpoint for IBD management since multiple studies have shown that IBD impairs it, both physically and psychologically.

quality of life | Crohn's disease | ulcerative colitis

1. Introduction

Traditional medicine was focused on the physical side of the illness and death rates and life expectancy were the main measures used to evaluate people's health. This excludes the fact that, in most diseases, the state of health is deeply influenced by mood, coping mechanisms to different situations and social support. The higher prevalence of chronic conditions, as a consequence of the decline of infectious diseases, as well as the development of new technologies that reduced pain, have made necessary newer and more sensitive outcomes beyond morbidity and biological functioning [1]. Quality of life (QoL) has been considered as a component of health since 1947 when the World Health Organization (WHO) began to define health not only as the absence of disease, but also as a state of physical, mental and social well-being [2]. Health-related quality of life (HRQoL) has been defined as the value assigned to the duration of life influenced by health, which is modified by impairments, functional state, perceptions and opportunities that are in turn influenced by diseases, injury and treatments [3]. HRQoL only includes components that are part of an individual's health and, therefore, excludes other aspects of QoL, as political or economic factors [4].

Inflammatory bowel diseases (IBD) are chronic, progressive and disabling conditions affecting young people that have a negative impact on their HRQoL [5]. For years, the main endpoints of IBD treatment had been clinical remission and response. Afterwards, new targets like biomarkers and mucosal healing have been introduced in new drug evaluations and, in the last decades, the use of patient-reported outcome (PRO) has also become especially important. In 2015 the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) program was initiated by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD). It examined potential treatment targets for IBD to be used for a "treat-to-target" clinical management strategy using an

evidence-based expert consensus process. In these first recommendations, improvement of HRQoL was only suggested as part of PRO [6]. In the recently published STRIDE II consensus, HRQoL has more weight and it is recommended as an important endpoint for IBD management [7].

2. How Can We Measure HRQoL in IBD?

There are two main types of HRQoL tools to evaluate patients with IBD: disease-specific and generic. Disease-specific tools evaluate symptoms and compare the effect of different treatments, while generic tools allow for comparisons between different population and illnesses.

It is important to take into account two psychometric considerations for choosing which instrument to measure HRQoL:

- − Reliability is the probability that a questionnaire will perform its intended function adequately. A reliable measure is one that provides consistent and accurate information.
- − Validity is how accurately a method measures what it is intended to measure. A tool is valid when it measures the characteristic that it claims to measure.

Plenty of IBD-specific HRQoL tools have been developed and validated for IBD patients [8]. Nevertheless, the majority of these instruments have had no patient involvement in their development [9]. In **Table 1**, we summarize the main characteristics of the most widely used tools and some other options designed for specific IBD cohorts.

Table 1. Characteristics of tools for measure HRQoL in IBD.

		Target	Recall Period	Number of Items	Response Options	Range of Scores (Worst-Best)	Reliability
Specific-disease tools	IBDQ-32	IBD	2 weeks	32	7-Level Likert (1–7)	32–224	+++
	SIBDQ	IBD	2 weeks	10	7-Level Likert (1–7)	10–70	++
	IBDQ-36	IBD	2 weeks	36	7-Level Likert (1–7)	36–252	NA

		Target	Recall Period	Number of Items	Response Options	Range of Scores (Worst-Reliability Best)	
Generic tools	IBDQ-9	IBD	2 weeks	9	7-Level Likert (1–7)	0–100	++
	CUCQ-8	IBD	2 weeks	8	4-Level Likert (0–3) or ordinal format (0–14)	90–0	+++
	CLIQ	CD	Today	27	True/Not true (1–0)	27–0	+++
	IBDQ-D	UC-IPAA	2 weeks	32	7-Level Likert (1–7)	32–224	NA
	CAF-QoL	CD	6–8 weeks	28	4-Level Likert (0–4)	112–0	+++
	SF-36	Patients and general population	4 weeks	36	Linear transformation of raw scores	0–100	+++
	EQ-5D	Patients and general population	Today	6	• − 3-Likert (1–3) • − 5-Likert (1–5) • − visual analogue scale	243 health status, index 0–1 • − 0–100	+++

[10]

nnaire 36
ated to be

reliable and valid. It includes four aspects of the patients' life and the main domains are intestinal symptoms (10 items), systemic symptoms (five items), social (12 items) and emotional domains (five items). Häuser et al. conducted a validation study of the German version of the IBDQ (IBDQ-D) for patients with ileal pouch anal anastomosis (IPAA) for UC, and they observed that it was a reliable tool in this setting although it had some limitations in terms of validity [11]. The short version of IBDQ-32 is the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). SIBDQ also contains symptom, social and emotional sections. IBDQ-36 is a 36-item questionnaire that has also been proven to be valid and reliable. It comprises the following points: intestinal symptoms (eight items), systemic symptoms (seven items), social (6 items) and emotional domains (eight items),

and functional impairment (seven items). The short version of IBDQ-36 is IBDQ9. IBDQ9 only contains one domain (total score) and the comprehensiveness is lower than IBDQ-36 [9].

Another tool, Crohn's Life Impact Questionnaire (CLIQ), composed of 27 dichotomous items, is focused on how the impairments affect need fulfilment. It has demonstrated good validity and reproducibility, and it is easy to complete in a few minutes [12]. Recently, the Crohn's Anal Fistula Quality of Life (CAF-QoL) has been developed to evaluate the impact of anal fistula. It is a new PRO measure for Crohn's perianal fistula that has been validated. CAF-QoL is a 28-item questionnaire that has demonstrated to be internally consistent, reliable, stable and valid [13]. Among them, the best questionnaires related to relevance, comprehensiveness and comprehensibility are IBDQ-32 and CLIQ. In **Table 1**, we summarize the main characteristics of the most widely questionnaires used.

Other examples of disease-specific instruments are the Crohn's and Ulcerative Colitis Questionnaire (CUCQ), Inflammatory Bowel Disease Questionnaire 30 (IBDQ-30), Norwegian Inflammatory Bowel Disease Questionnaire (IBDQ-N), Cleveland Global Quality of Life (CGQL), Short Health Scale (SHS), Edinburgh Inflammatory Bowel Disease Questionnaire (EIBDQ), short Inflammatory Bowel Disease Questionnaire 10 (sIBDQ-10) and Inflammatory Bowel Disease Disability Index (IBD-DI). In paediatric IBD patients, the IMPACT series tools (IMPACT, IMPCT-II and IMPACT III) were used to evaluate the HRQoL. IMPACT was proven to be valid and contains 4 domains: symptoms, physical, emotional and social domains [8][14].

The generic questionnaires most commonly used are the Generic 36-item Short Form Survey (SF-36) and The EuroQoL–dimension (EQ-5D). SF-36 was developed in the USA for use in the Medical Outcomes Study (MOS). It is a generic scale that provides quantitative information related to HRQoL and has good validity and reliability. It is frequently reported as two separate figures, a physical component score (PCS) and a mental component score (MCS), which included a total of 36 items allocated in eight domains: physical functioning (10 items), role physical (four items), social functioning (two items), bodily pain (two items), mental health (five items), role emotional (three items), general health perceptions (five items) and one item about general health [15]. EQ-5D is a generic, reliable and valid instrument developed by the EuroQoL group. It can be used to assess HRQoL but also the cost-utility analysis of health care interventions [16]. Other similar instruments can be World Health Organization Quality of Life (WHOQOL)-BREF, Short Form SF-12, Satisfaction with Life Scale (SWLS), EORTC Quality of Life Questionnaire C-30, Quality of Well Being Scale or Health Utilities Index [17][18]. In paediatrics, the generic tools more widely used are PedsQ1, Child Health Questionnaire (CHQ), KINDL, KINSCREEN 27, DISABKIDS HRQOL [19].

3. Quality of Life Studies in UC

To date, multiple studies have reported that UC impairs QoL, which can also be affected by demographic, psychological and socioeconomic factors [20][21]. Clinical activity was pointed out as the factor with the most negative impact in HRQoL [22], although it has been shown that it's still compromised during quiescent disease as compared to the general population [23]. Rasmussen et al. observed that bowel frequency, urgency and rectal bleeding are the symptoms that most significantly affect these patients' HRQoL [24]. Apart from the physical symptoms, IBD patients complain about an important emotional burden which is barely addressed during follow-up

appointments [25][26]. Different therapies have been proved to be effective to treat UC and improve the HRQoL of those who suffer from it (**Table 2**) although its administration schedules and side effects can also negatively affect HRQoL.

Table 2. IBD treatments that have been shown to improve HRQoL.

Treatment	Study	Measurement Tool(s)	No. Patients	HRQoL: Primary Outcome	Results
5-ASA	Robinson et al. [27]	5 disease-specific and 7 general items	374 UC	Yes	Mesalamine 2 g and 4 g daily was significantly superior to placebo in improving each of the 12 HRQoL parameters.
	Probert et al. [28]	EQ-5D-3L	115 UC	No	The combined (oral + rectal) therapy group reported a significant improvement in the 'mobility', 'usual activity' and 'anxiety/depression' domains at week 4.
Thiopurines	Alruthia et al. [29]	EQ-5D-3L EQ-5D-VAS	160 IBD (56% CD, 44% UC)	Yes	Patients on AZA presented higher HRQoL at six-month follow-up compared with patients on other treatments (β = 9.35; 95% CI: 0.486–18.22; p = 0.003).
	Bastida et al. [30]	SF-36 IBDQ	92 IBD (68 CD, 24 UC)	Yes	Compared with baseline, 68 and 64% patients' scores improved at 6 and 12 months, respectively (ΔIBDQ was 0.86 and 1.05, respectively). SF-36 showed a similar improvement.
	Calvet et al. [31]	SF-36	33 RCD [a], 14 ACD [b], 66 HC [c]	Yes	SF-36 were 85 in RCD, 85 in HC (p = 1), and 58.6 in ACD (p < 0.001 for comparison with RCD and HC).

Treatment	Study	Measurement Tool(s)	No. Patients	HRQoL: Primary Outcome	Results
	Feagan et al. [32]	IBDQ SF-36	728 UC	No	IBDQ score improvement was significantly greater in the IFX 5 and 10 mg/kg groups (40 and 36, respectively $p < 0.001$) vs. placebo (28).
Infliximab	Silva et al. [33]	IBDQ	31 UC	Yes	In IFX group ($n = 21$), the IBDQ scores ranges from 116.2 at baseline to 170.75 and 176.62 at week 30 and 54, respectively ($p \leq 0.02$)
	Feagan et al. [34]	IBDQ SF-36	335 CD	No	The mean change in the IBDQ at week 54 compared to baseline was 22.1 in the 5 mg/kg and 30.2 in 10 mg/kg IFX maintenance group while it was 8.9 in the placebo group ($p \leq 0.05$). SF-36 changed in the same line.
Adalimumab	Travis et al. [35]	SIBDQ EQ-5D-5L EQ-5D-VAS	463 UC	Yes	Significant improvements from baseline to week 26 were detected on SIBDQ (mean change 17.4) and EQ5D (index: 0.1 ± 0.2; VAS: 19.5).
	Louis et al. [36]	SIBDQ	945 CD	No	60% of IFX-naïve patients and 47% of IFX primary non-responders reported clinically significant improvements (≥9 points) on SIBDQ.
	Saro et al. [37]	IBDQ EQ-5D	126 CD	Yes	It has been shown a significant improvement on the EQ5D from 0.735 to 0.797, the EQ5D VAS from 50.0 to

Treatment	Study	Measurement Tool(s)	No. Patients	HRQoL: Primary Outcome	Results
		EQ-5D-VAS			80.0, and the IBDQ from 56.7 to 67.5 ($p < 0.05$ for all comparisons).
Golimumab	Feagan et al. [38]	IBDQ SF-36	1064 UC	No	It was determined a significantly greater improvement from baseline to week 6 in GLM vs. placebo groups in IBDQ (27.2 vs. 14.6), SF-36 PCS (4.14 vs. 2.46) and MCS (4.89 vs. 1.60, $p < 0.01$ for all comparisons).
Vedolizumab	Feagan et al. [39]	IBDQ SF-36 EQ-5D-3L ED-5D-VAS	373 UC	No	Patients on VDZ reported significantly greater improvements in IBDQ and EQ5D-VAS scores. For EQ-5D utility score, only the VDZ every 4 weeks group showed a significant difference from placebo. At week 52, more patients on VDZ met the minimal clinically meaningful difference thresholds for IBDQ, SF-36 physical component and EQ5D-VAS scores.
	Loftus et al. [40]	IBDQ	769 UC (383 VDZ, 386 ADA)	No	At week 52, clinically important IBDQ improvement was detected in a greater proportion of VDZ treated patients compared with ADA treated ones (52.0% vs. 42.2%). Likewise, 50.1% (VDZ) vs. 40.4% (ADA) of patients achieved IBDQ remission.
	Vermiere et al. [41]	IBDQ EQ5D-VAS	1349 CD	No	At week 80, the mean changes from baseline HRQL scores were >51 for IBDQ, >23 for EQ-5D VAS, >9 for SF-36 PCS and >10 for SF-36 MCS.

Treatment	Study	Measurement Tool(s)	No. Patients	HRQoL: Primary Outcome	Results
		SF-36			
	Parkes et al. [42]	SIBDQ	61 IBD (21 CD, 40 UC)	No	SIBDQ score increased by 8.5 and 10.2 points in CD and UC patients, respectively, at week 14.
	Eriksson et al. [43]	SHS	169 CD	No	It has been seen a significant decreased of the SHS score at week 52 (n = 68; p < 0.001)
	Sandborn et al. [44]	IBDQ SF-36	284 UC	No	55.6% of patients who had been treated with USK were in IBDQ remission. Regarding the SF-36, 50.0% and 45.1% of patients had a clinically meaningful improvement in the PCS and the MCS, respectively.
Ustekinumab	Sands et al. [45]	IBDQ SF-36	1368 CD	No	A clinically meaningful improvement in IBDQ score at week 8 was achieved in 68.1% of anti-TNF naïve patients and 54.8% of patients with previous failure to antiTNF. Similarly, greater improvements in SF-36 in the USK group have been determined.
	Marquès et al. [46]	IBDQ	33 CD	Yes	18% achieved IBDQ normalization at week 52.
Tofacitinib	Panés et al. [47]	IBDQ SF-36	1161 UC (induction)	No	In OCTAVE induction 1 and 2, mean IBDQ changes from baseline to week 8 was 40.7 and 44.6 with TFC 10mg

1. Schwartzmann, L. Calidad de vida Relacionada con la Salud: Aspectos Conceptuales. Cienc. Enfermería 2003, 9, 9–21.

Treatment	Study	Measurement Tool(s)	No. Patients	HRQoL: Primary Outcome	Results
			593 UC (sustain)		twice daily versus 21 and 25 with placebo, respectively ($p < 0.001$). Mean SF-36 changes were comparable with the IBDQ changes and both were sustained at week 52
Surgery (intestinal resection)	Wright et al. [48]	IBDQ SF-36	174 CD	No	A significant improvement has been observed at 6 months postoperatively compared to preoperatively in PCS (68 vs. 40), MCS (68 vs. 44) and IBDQ (171 vs. 125; $p < 0.001$ for all comparisons).
	Ha et al. [49]	5 generic tools 3 disease-specific tools	1108 CD	Yes	Both generic and disease-specific tools showed an improvement in HRQoL from 2 weeks after intestinal resection for up to 5 years.

AZA: azathioprine, IFX: infliximab, GLM: golimumab, VDZ: vedolizumab, ADA: adalimumab, USK: ustekinumab. TFG: tofacitinib. [a] Remission Crohn's disease. [b] Active Crohn's disease. [c] Healthy controls.

4. Quality of Life Studies in CD

There are several studies that have shown an association between CD and significant disability and impaired HRQoL. There is a systematic review and meta-analysis that compared HRQoL between CD and UC including physical (2370 participants) and mental scores (2564 participants). The HRQoL scores were shown to be lower in patients with CD compared with UC, but these differences were considered not significant [59].

In the systematic review of Van der Have et al. including 5735 patients with CD, the HRQoL was consistently impaired by the occupational disability, number of flares, disease activity, need for hospital admission and use of corticosteroids. Furthermore, the biological treatment had a beneficial impact in the HRQoL. The majority of the

9. Van Andel, E.M.; Koopmann, B.D.M.; Crouwel, F.; Noomen, C.G.; de Boer, N.K.H.; van Asseldonk, D.P.; Mokkink, L.B. Systematic review of development and content validity of patient-reported outcome measures in inflammatory bowel disease: Do we measure what we measure? J. Crohns Colitis 2020, 14, 1299–1315.
10. Yarlas, A.; Maher, S.; Bayliss, M.; Lovley, A.; Cappelleri, J.C.; Bushmakin, A.G.; DiBonaventura, M.D. The Inflammatory Bowel Disease Questionnaire in Randomized Controlled Trials of Treatment for Ulcerative Colitis: Systematic Review and Meta-Analysis. J. Patient Cent. Res. Rev. 2020, 7, 189–205.
11. Häuser, W.; Dietz, N.; Grandt, D.; Steder-Meukamm, U.; Janke, K.H.; Stein, U.; Stallmach, A. Validation of the Inflammatory Bowel Disease Questionnaire IBDQ-D, German Version, for Patients with Ileal Pouch Anal Anastomosis for Ulcerative Colitis. Z. Gastroenterol. 2004, 42, 131–139.
12. Wilburn, J.; McKenna, S.P.; Twiss, J.; Kemp, K.; Campbell, S. Assessing quality of life in Crohn's disease: Development and validation of the Crohn's Life Impact Questionnaire (CLIQ). Qual. Life

studies included, the review employed both generic and disease-specific HRQoL measures, the IBDQ and the SF-36 being the most commonly used [51].

Despite the thinking that HRQoL is mainly related with clinical activity in CD, in a study performed in 92 CD patients in remission, scores on the SF-36 were lower than in the general population of similar age and sex. Age, colonic location and previous surgery was related with worse HRQoL [52].

The effectiveness of different treatments improving HRQoL in patients with CD has been evaluated in clinical trials of new drugs, but also real-life studies (**Table 2**). Only a few studies have been conducted to assess the impact of thiopurines in HRQoL. A prospective study that included 92 IBD patients (68 CD) who started thiopurines showed a significant impairment HRQoL at week 0 with a basal median IBDQ score of 4.99 (range 2.37–6.84) as compared to patients in remission. In the first year after starting treatment, all dimensions of the IBDQ demonstrate a statistically significant improvement that was maintained throughout the study period [30]. A case–control study has shown a restoration of HRQoL in patients with CD in remission under thiopurines without differences with healthy controls [31].

Res. 2015, 24, 2279–2288.

13. Adegbola, S.O.; Dibley, L.; Sahnan, K.; Wade, T.; Verjee, A.; Sawyer, R.; Mannick, S.; McCluskey, D.; Bassett, P.; Yassin, N.; et al. Development and initial psychometric validation of a patient-reported outcome measure for Crohn's perianal fistula: The Crohn's Anal Fistula Quality of Life (CAF-QoL) Scale. Gut 2020, 1–8.
14. Otley, A.; Smith, C.; Nicholas, D.; Munk, M.; Avolio, J.; Sherman, P.; Griffiths, A.M. The IMPACT questionnaire: A valid measure of health-related quality of life in pediatric inflammatory bowel disease. J. Pediatr. Gastroenterol. Nutr. 2002, 35, 557–563.
15. Ware, J.; Sherbourne, C. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med. Care 1992, 30, 473–483.
16. EuroQol Group. EuroQol—A new facility for the measurement of health-related quality of life. Health Policy 1990, 16, 199–208.
17. Kaplan, R.M.; Anderson, J.P.; Wu, A.W.; Mathews, W.C.; Kozin, F.; Orenstein, D. The quality of well-being scale: Applications in AIDS, cystic fibrosis, and arthritis. Med. Care 1989, 27, S27–S43.
18. Feeny, D.; Furlong, W.; Boyle, M.; Torrance, G.W. Multi-Attribute Health Status Classification Systems: Health Utilities Index. Pharmacoeconomics 1995, 7, 490–502.
19. Haraldstad, K.; Wahl, A.; Andenæs, R.; Andersen, J.R.; Andersen, M.H.; Beisland, E.; Borge, C.R.; Engebretsen, E.; Eisemann, M.; Halvorsrud, L.; et al. A systematic review of quality of life research in medicine and health sciences. Qual. Life Res. 2019, 28, 2641–2650.
20. Hoivik, M.L.; Moum, B.; Solberg, I.C.; Cvancarova, M.; Hoie, O.; Vatn, M.H.; Bernklev, T. Health-Related Quality of Life in Patients with Ulcerative Colitis After a 10-year Disease Course: Results from the IBSEN Study. Inflamm. Bowel. Dis. 2012, 18, 1540–1549.
21. Bitton, A.; Sewitch, M.J.; Peppercorn, M.A.; Edwardes, M.D.D.B.; Shah, S.; Ransil, B.; Locke, S.E. Psychosocial Determinants of Relapse in Ulcerative Colitis: A Longitudinal Study. Am. J. Gastroenterol. 2003, 98, 2203–2208.
22. Han, S.W.; McColl, E.; Barton, J.R.; James, P.; Steen, I.N.; Welfare, M.R. Predictor's of quality of life in ulcerative colitis: The importance of symptoms and illness representations. Inflamm. Bowel. Dis. 2005, 11, 24–34.
23. Verma, S.; Giaffer, M.H. Does better disease-related education improve quality of life? A survey of IBD patients. Dig. Dis. Sci. 2001, 46, 865–869.
24. Rasmussen, B.; Haastrup, P.; Wehberg, S.; Kjeldsen, J.; Waldorff, F.B. Predictors of health-related quality of life in patients with moderate to severely active ulcerative colitis receiving biological therapy. Scand. J. Gastroenterol. 2020, 55, 656–663.

25. Iglesias-Rey, M.; Acosta, M.B.-D.; Caamano-Isorna, F.; Rodríguez, I.V.; Ferreiro, R.; Lindkvist, B.; González, A.L.; Dominguez-Munoz, J.E. Psychological factors are associated with changes in the health-related quality of life in inflammatory bowel disease. Inflamm. Bowel. Dis. 2014, 20, 92–102.

26. López-Sanromán, A.; Carpio, D.; Calvet, X.; Romero, C.; Cea-Calvo, L.; Juliá, B.; Argüelles-Arias, F. Perceived Emotional and Psychological Impact of Ulcerative Colitis on Outpatients in Spain: UC-LIFE Survey. Dig. Dis. Sci. 2017, 62, 207–216.

27. Robinson, M.; Hanauer, S.; Hoop, R.; Zbrozek, A.; Wilkinson, C. Mesalamine capsules enhance the quality of life for patients with ulcerative colitis. Aliment. Pharmacol. Ther. 1994, 8, 27–34.

28. Probert, C.S.; Dignass, A.U.; Lindgren, S.; Pool, M.O.; Marteau, P. Combined oral and rectal mesalazine for the treatment of mild-to-moderately active ulcerative colitis: Rapid symptom resolution and improvements in quality of life. J. Crohns Colitis 2014, 8, 200–207.

29. Alruthia, Y.; Alsharif, W.; Almuaythir, G.; Alrasheed, H.; Alharbi, O.; Azzam, N.; Almadi, M.; Saeed, M.; Hajkhder Mullaissa, B.; Aljebreen, A. P444 The impact of azathioprine on inflammatory bowel disease patients' overall health-related quality of life: A single-centre retrospective cohort study. J. Crohns Colitis 2020, 14 (Suppl. S1), S400–S401.

30. Bastida, G.; Nos, P.; Aguas, M.; Beltrán, B.; Iborra, M.; Ortiz, V.; Garrigues, V.; Estevan, R.; Ponce, J. The effects of thiopurine therapy on health-related quality of life in Inflammatory Bowel Disease patients. BMC Gastroenterol. 2010, 10.

31. Calvet, X.; Gallardo, O.; Coronas, R.; Casellas, F.; Montserrat, A.; Torrejon, A.; Vergara, M.; Campo, R.; Brullet, E. Remission on thiopurinic immunomodulators normalizes quality of life and psychological status in patients with Crohn's disease. Inflamm. Bowel. Dis. 2006, 12, 692–696.

32. Feagan, B.G.; Reinisch, W.; Rutgeerts, P.; Sandborn, W.J.; Yan, S.; Eisenberg, D.; Bala, M.; Johanns, J.; Olson, A.; Hanauer, S.B. The effects of infliximab therapy on health-related quality of life in ulcerative colitis patients. Am. J. Gastroenterol. 2007, 102, 794–802.

33. Silva, R.; Baima, J.; Bissoli, G.; Farinelli, E.; Sibia, C.; Barros, J.; Biondi, R.; Renosto, F.; Hossne, R.; Sassaki, L. N816 Anti-TNF therapy improves the quality of life in patients with ulcerative colitis. J. Crohns Colitis 2017, 11 (Suppl. S1), S498–S499.

34. Feagan, B.G.; Yan, S.; Bala, M.; Bao, W.; Lichtenstein, G.R. The Effects of Infliximab Maintenance Therapy on Health-Related Quality of Life. Am. J. Gastroenterol. 2003, 98, 2232–2238.

35. Travis, S.; Feagan, B.G.; Peyrin-Biroulet, L.; Panaccione, R.; Danese, S.; Lazar, A.; Robinson, A.M.; Petersson, J.; Pappalardo, B.L.; Bereswill, M.; et al. Effect of adalimumab on clinical outcomes and health-related quality of life among patients with ulcerative colitis in a clinical practice setting: Results from InspirADA. J. Crohns Colitis 2017, 11, 1317–1325.

36. Louis, E.; Löfberg, R.; Reinisch, W.; Camez, A.; Yang, M.; Pollack, P.F.; Chen, N.; Chao, J.; Mulani, P.M. Adalimumab improves patient-reported outcomes and reduces indirect costs in patients with moderate to severe Crohn's disease: Results from the CARE trial. J. Crohns Colitis 2013, 7, 34–43.

37. Saro, C.; Ceballos, D.; Muñoz, F.; De La Coba, C.; Aguilar, M.D.; Lázaro, P.; García-Sánchez, V.; Hernandez, M.; Barrio, J.; De Francisco, R.; et al. Clinical status, quality of life, and work productivity in Crohn's disease patients after one year of treatment with adalimumab. Rev. Esp. Enferm. Dig. 2017, 109, 122–129.

38. Feagan, B.; Gibson, P.; Marano, C.; Strauss, R.; Han, C.; Johanns, J.; Zhang, H.; Guzzo, C.; Colombel, J.-F.; Reinisch, W.; et al. P225 Impact of subcutaneously administered golimumab on disease specific and generic health-related quality of life in patients with moderately to severely active ulcerative colitis: Results from PURSUIT-SC induction. J. Crohns Colitis 2013, 7 (Suppl. S1), S99–S100.

39. Feagan, B.G.; Patel, H.; Colombel, J.-F.; Rubin, D.T.; James, A.; Mody, R.; Lasch, K. Effects of vedolizumab on health-related quality of life in patients with ulcerative colitis: Results from the randomised GEMINI 1 trial. Aliment. Pharmacol. Ther. 2017, 45, 264–275.

40. Loftus, E.V.; Schreiber, S.W.; Danese, S.; Peyrin-Biroulet, L.; Colombel, J.F.; Sands, B.E.; Wang, S.; Chen, J.; Lirio, R.A. DOP24 Patient-reported health-related quality-of-life outcomes with vedolizumab vs. adalimumab treatment of ulcerative colitis: Results of the VARSITY trial. J. Crohns Colitis 2020, 14 (Suppl. S1), S063.

41. Vermeire, S.; Loftus, E.V.; Colombel, J.-F.; Feagan, B.G.; Sandborn, W.J.; Sands, B.E.; Danese, S.; D'Haens, G.R.; Kaser, A.; Panaccione, R.; et al. Long-term Efficacy of Vedolizumab for Crohns Disease. J. Crohns Colitis 2016, 11, jjw176.

42. Parkes, G.; Akbar, A.; Beales, I.; Buckley, M.; Creed, T.; Din, S.; Fraser, A.; Plevris, N.; Meadowcroft, S.; Owen, G.; et al. P713 Effects of vedolizumab on health-related quality of life, work productivity and patient concerns in patients with ulcerative colitis and Crohn's disease in the UK and Ireland: OCTAVO cohort 2. J. Crohns Colitis 2020, 14 (Suppl. S1), S575–S576.

43. Eriksson, C.; Rundquist, S.; Lykiardopoulos, V.; Karlén, P.; Grip, O.; Söderman, C.; Almer, S.; Hertervig, E.; Gunnarsson, J.; Malmgren, C.; et al. P758 Clinical effectiveness of vedolizumab: Interim analysis of the Swedish observational study on vedolizumab assessing effectiveness and healthcare resource utilisation in patients with Crohn's disease (SVEAH CD). J. Crohns Colitis 2018, 12 (Suppl. S1), S494–S495.

44. Sandborn, W.J.; Rowbotham, D.S.; Leong, R.W.L.; Han, C.; Zhou, Y.; Zhang, H.; Johanns, J.; Marano, C.; Danese, S. DOP56 Ustekinumab maintained clinically meaningful improvement in health-related quality of life in patients with moderate to severe ulcerative colitis: Results from the UNIFI long-term extension. J. Crohns Colitis 2020, 14 (Suppl. S1), S094–S095.

45. E Sands, B.; Han, C.; Gasink, C.; Jacobstein, D.; Szapary, P.; Gao, L.-L.; Lang, Y.; Targan, S.; Sandborn, W.J.; Feagan, B.G. The Effects of Ustekinumab on Health-related Quality of Life in Patients With Moderate to Severe Crohn's Disease. J. Crohns Colitis 2018, 12, 883–895.
46. Marquès Camí, M.; Robles Alonso, V.; Borruel Sainzn, N.; Herrera de Guise, C.; Mayorga Ayala, L.; Casellas Jordá, F. Normalization of long-term quality of life in Crohn's disease patients receiving ustekinumab. Rev. Española Enferm. Dig. 2020.
47. Panés, J.; Vermeire, S.; Lindsay, J.O.; Sands, B.E.; Su, C.; Friedman, G.; Zhang, H.; Yarlas, A.; Bayliss, M.; Maher, S.; et al. Tofacitinib in Patients with Ulcerative Colitis: Health-Related Quality of Life in Phase 3 Randomised Controlled Induction and Maintenance Studies. J. Crohns Colitis 2018, 12, 145–156.
48. Wright, E.K.; Kamm, M.A.; De Cruz, P.; Hamilton, A.L.; Ritchie, K.J.; Krejany, E.O.; Gorelik, A.; Liew, D.; Prideaux, L.; Lawrance, I.C.; et al. Effect of Intestinal Resection on Quality of Life in Crohn's Disease. J. Crohns Colitis 2015, 9, 452–462.
49. Ha, F.J.; Thong, L.; Khalil, H. Quality of Life after Intestinal Resection in Patients with Crohn Disease: A Systematic Review. Dig. Surg. 2017, 34, 355–363.
50. Knowles, S.R.; Keefer, L.; Wilding, H.; Hewitt, C.; Graff, L.; Mikocka-Walus, A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part II. Inflamm. Bowel. Dis. 2018, 24, 966–976.
51. Van Der Have, M.; Van Der Aalst, K.S.; Kaptein, A.A.; Leenders, M.; Siersema, P.D.; Oldenburg, B.; Fidder, H.H. Determinants of health-related quality of life in Crohn's disease: A systematic review and meta-analysis. J. Crohns Colitis 2014, 8, 93–106.
52. Iglesias, M.; Vázquez, I.; De Acosta, M.B.; Figueiras, A.; Nieto, L.; Piñeiro, M.; Gómez, R.; Lorenzo, A.; Dominguez-Munoz, J.E. Health related quality of life in patients with Cohn's disease in remission. Rev. Esp. Enfermedades Dig. 2010, 102, 624–630.