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# The need for interdisciplinary quality of life studies for patients with Crohn's Disease – a systematic review

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**Abstract**

Crohn's disease is a chronic, lifelong condition with increasing rates of morbidity. It can have a significant impact on one's physical, emotional, economic and social functioning. Both medical as well as social fields of studies have adapted the construct of Quality of Life to assess the well being of patients. The purpose of this paper is to investigate the nature of scientist's research concerning Quality of Life in Crohn's disease patients from an interdisciplinary, medical and psychological perspective exceeding beyond a single definition or a paradigm. EBSCOhost Research Databases platform was used to conduct the preliminary search. Then, a further qualitative analysis of texts was conducted. The results showed a declining interest in Quality of Life of Crohn's disease patients in the studied 10-year scope on average by 11.49% from year to year. Also, an underrepresentation of studies of the nature of psychological variables in relation to studies of the medical description was found. An information gap in scientific cognition related to the interdisciplinary approach regarding the studied topic was recognized. There is a necessity to broaden the horizons of the conducted research to include further issues at several levels of inference. This approach would be needed not only in the dimension of scientific considerations, but also or above all in the practical dimension.

**quality of life; health related quality of life; Crohn's Disease; QoL measures**

## INTRODUCTION

Crohn's disease (CD) among Ulcerative Colitis (CU) is classified as a type of chronic Inflammatory Bowel Disease (IBD). Both CU and CD are lifelong, incurable conditions. The etiology of these disorders is yet uncertain but is believed to be multifactorial, whereby genetically susceptible subjects develop the disease that may be triggered by environmental factors and perpetuated by an abnormal host immune response [1]. Both CD and CU are chronic diseases, which characterize by alternating periods of remissions and relapses [1]. The most common symptoms are rectal bleeding, abdominal pain and diarrhea [1].

Over the past decades, there has been a significant increase in the incidence of Crohn's. In the United Kingdom for instance, morbidity has risen from 220 to 400 cases of illness per 100 thousand people just between the years 2000 and 2018 [2]. These results are in line with a recent Canadian study which findings estimate a 35% increase in CD incidence over the next decade [3]. Crohn's disease is geographically conditioned with highest morbidity rates in North America and Europe. Also, rapid increases are being noted in developing nations adopting a Westernized lifestyle whereas incidence of CD were seldom. In the literature on the sub-

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ject, the increasing incidence of CD is yet unexplained. There are no studies confirming the cause of rising morbidity. It seems rational to look for dependencies in the popularization of access to health care, the development of medical diagnostics, and the constant improvement of doctors' competences through education.

Few factors are recognised yet to have an impact on the course of IBD. Some of them are: cigarette smoking (increased severity of symptoms in Crohn disease, decreased in ulcerative colitis) [4], higher socioeconomic class [5], use of nonsteroidal anti-inflammatory drugs [6]. So far, however, these environmental factors are suggested to play only a mediating role, rather than being directly involved in the disease course and its etiology [1].

Living with an incurable, chronic disease is challenging and can have an influence on one's Quality of Life (QoL). In the context of health and disease, QoL is commonly referred to as health-related quality of life (HRQoL) to differentiate it from other aspects of quality of life. It has become apparent that HRQoL is an important outcome variable on its own independent of medical treatment results. Furthermore, HRQoL outcomes can guide decisions on alternative treatments or efficacy of interventions at a patient group level [7].

HRQoL is a comprehensive and complex concept for which no universally accepted definition is available [8]. However, two aspects of HRQoL are key in most interpretations. Firstly, it is a multidimensional concept that can be recognised as a latent construct which describes the physical and social role functioning, as well as psychological aspects of well-being [9], [10], [11]. Secondly, in contrast to QoL, which is by very nature subjective [12], HRQoL can include both objective and subjective perspectives in each of these domains [13]. The objective assessment focuses on what the individual can do, and it is important in determining the degree of health. While the subjective assessment includes the meaning to the individual; essentially it involves the translation or appraisal of the more objective measurement of health status into the experience of QoL. Differences in appraisal account for the fact that individuals with the same objective health status can report very different subjective QoL. [14, 15].

Another important topic concerning patients with CD is the psychological distress which can be a common and significant factor that influences one's QoL.

Symptoms of psychological distress such as heightened levels of anxiety or depression are well recognized to co-occur with chronic diseases. Empirical studies have shown that: anxiety or depression as well as anxiety and depression are reported jointly by up to 61.7% of CD patients [16], people with CD have an increased frequency of anxiety and depressive disorders in every period of their lives, compared to control groups [17, 18] and the level of mental health is further reduced by the activity of Crohn's disease symptoms [19, 20]. Increased levels of perceived distress, as well as physical complaints, reduce the quality of life of people with Crohn's disease. It has been proven that, apart from disease activity and the intensity of its somatic symptoms, psychological symptoms also have a negative impact on the quality of life of people with CD [21]. It therefore seems necessary to measure and consider the aforementioned variables in the context of estimating CD patients.

Crohn's disease can also impact one's social and economic context. Patients with severe chronic diseases such as CD are undoubtedly a significant challenge for the health systems of many countries, and the costs of treating these patients are not only the costs incurred by the payer, which is the National Health Fund, but also other components, affecting the total social and economic cost [22, 23].

On a personal level an average patient with CD spent about PLN 1,000 (225 USD) in 2018 per month on treatment. On a collective level according to data from the Polish National Health Fund Crohn's disease-related hospitalizations have tripled in recent years [24]. The consequences of the disease lead to a reduction in professional activity, which translates into the state of the economy and indirectly the state finances. Reducing the effectiveness of the patient's work due to his absence from work or reduced productivity translates into the GDP indicator.

These values unequivocally indicate that raising QoL of CD patients and preventing the progression of the disease could cause significant savings on the part of the patient, but even greater extent reduces the indirect costs affecting economy and society [25].

When treating patients, the effectiveness of the therapy is important, but also awareness of the potential side effects should be considered. Modern clinical observations lead to the conclusion that the average drug works adequately on patients in 40-60%, and the next 15% experience side effects. Therefore, an important part of medical therapy is considering the individual patient's characteristics, including environment and genetic makeup [26, 27]. The process of optimizing, individualizing therapy and adapting the drug to the needs of a particular patient is defined as personalized medicine. In Crohn's disease this customized approach could prove extremely useful due to the variety of symptoms experienced in this type of illness (intestinal, skin, eye, joint, mental disorders) and diverse medical specialty drugs involved in their treatment. This strategy could be deemed functional however applying a focus on multidimensional characteristics of QoL in CD and future research is necessary.

In summary, it could be highly beneficial to further investigate and understand the determinants of QoL of CD patients from an interdisciplinary, biopsychosocial perspective exceeding beyond a single definition or a paradigm.

## The literature and research

The analysis of Polish and foreign literature about Qol of CD patients is usually discussed by scientists representing medical fields, mainly in the specialization of gastrology and surgery. These studies, however, focus mainly on medical variables such as: type of treatment [28-34] surgical interventions [35-36] intestinal resections [37-39] or nutrition [40].

In the medical approach questionnaires and tools such as: IBDQ (Inflammatory Bowel Disease Questionnaire), SIBDQ (Short Inflammatory Bowel Disease Questionnaire), EQoL-5D (Euro QoL 5 Dimension Health Questionnaire), SF-36 (The Short Form Health Survey) CDAI (Cronhn's Disease Activity Index) or HBI (Harvey-Bradshaw Index) are often used to determine HRQoL (alone or combined). All of the above mentioned, however focus mainly on measuring severity of clinical symptoms and have a limited ability to assess the social and emotional function as well as the appraisal of health in context of subjective QoL of CD patients.

This means that QoL and its relation to health is understood and operationalized in a different way than in psychology, whereas the subject of interest is the functioning of a sick person, their attitudes towards the disease and ways of coping with it.

In psychological terms and behaviors patients can vary in extremely different ways of addressing a health problem, experiencing opinions about their own functioning or subjective health, despite a similar intensity of disease symptoms. For instance, there's evidence that illness perception [41], psychological factors [42], personality traits [43], stress, anxiety and depression [44] as well as coping strategies [45] have a significant impact on HRQoL scores of CD patients. This may mean that there are differences between high-functioning and low-functioning people with CD that cannot be grasped by the traditional clinical paradigm. While HRQoL is a well-recognised outcome measure of CD activity in the medical domain, its influence on other outcome measures, including exacerbation of CD is yet poorly understood. Furthermore, the association between QoL and subsequent inflammation suggests that QoL measures might be useful in detecting upcoming flares before they become clinically apparent [46]. This means that a reduced value of this variable may co-occur or predict early manifestation of exacerbation and be beneficial information in the course of early treatment.

The analysis of this diverse reasoning leads to the search for complex determinants of the QoL of people with CD disease.

However, the paradigm of humanistic medicine emphasizes the importance of interdisciplinary approach in the field of medical practice, literature on the subject reveals a cognitive gap in understanding QoL in CD patients. There is no comprehensive research on this topic in the psychological context, and relatively few works give ambiguous results. Therefore, an analysis has been conducted to determine the nature of investigated variables, QoL measures, quantity and types of publications devoted to the subject of Quality of Life of CD patients.

## METHOD

The Prisma technique was adapted in this systematic review. In order to collect data the EBSCOhost Research Databases platform was used with „Crohn’s Disease” and „quality of life” imputed as keywords phrases. (The concept of quality of life concerns so many aspects of human functioning in society that in order to conduct in-depth analysis in this area, it was deemed necessary to clarify the scope, limiting it to issues related to CD disease. On the other hand, the author’s intention is to examine the specific determinants of the functioning of individuals with CD, ignoring the issues not directly related to their quality of life, but focusing on aspects such as financing of biological therapies, pharmacology, fibrogenesis or statistical analysis).

The following sub databases were included in the search protocol: OpenDissertations, APA PsycTests, APA PsycInfo, Health Source – Consumer Edition and MEDLINE.

The search criterias included: Both keyword phrases had to occur in the title, the paper had to be a scientifically peer-reviewed text, written in English language and published in the last ten ten years, that is between 01.01.2012 and 31.12.2021.

Because of the author’s interest in the adult human population suffering from CD an additional age criterion was added. Accordingly, the 18 years and older age group box was checked as a necessary condition for the data collecting model.

Extensions with the use of equivalent themes and the boolean phrase search model was applied.

In the next step all identified texts were collected into a database. Studies which met the search protocol criteria were included in further analysis. All abstracts and subsequently 72 enclosed articles were screened.

Before the research, the following hypotheses were formulated, which together constitute a logical sequence of assumptions:

- H1: Due to the increased incidence of CD in scientific journals, the number of articles devoted to this subject is increasing.
- H2: Due to the spreading of the humanistic medicine paradigm, including personalized treatment, the interest of medical scientists in issues related to the quality of life of patients is increasing, and therefore, more and more often, in medical articles, explanatory variables are sought based on psychological sciences.
- H3: In the scientific journals, there is an underrepresentation of research in psychological variables in relation to the research of the medical description of CD.

## RESULTS

As a result of the preliminary query, 149 hit results were obtained meeting the basic search criteria, i.e. they contained in the title both keyword phrases: Quality of Life and Crohn’s Disease. After extracting the database and reading the articles, 72 units of analysis that did not meet the criteria were identified (due to the lack of a keyword in the title), as well as repetitions of articles or their discussions (comments, statements or meta-analysis). Subsequently, 5 articles that did not meet the age criteria of the study population (under 18 years of age) were identified. Finally, 72 subjects were included in the further analysis.

To verify the first of the hypotheses, the distribution of articles in the time series was analyzed. The histogram on *chart 1.* presented below

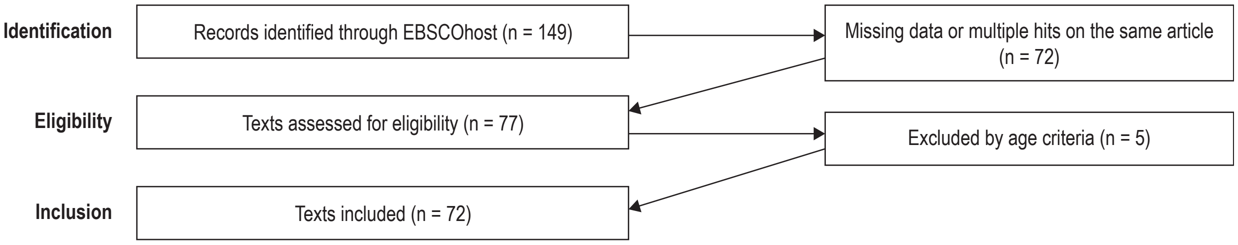

**Figure 1.** Identification, eligibility and inclusion of search results

clearly shows that, contrary to assumptions, the trend is declining.

Moreover, it should be noted that in the initial scope of the research period, 12 units of analysis were registered – the most in the studied temporal range, and in the last one, only 4 – which are the lowest indicator in the 2012-2021 scope.

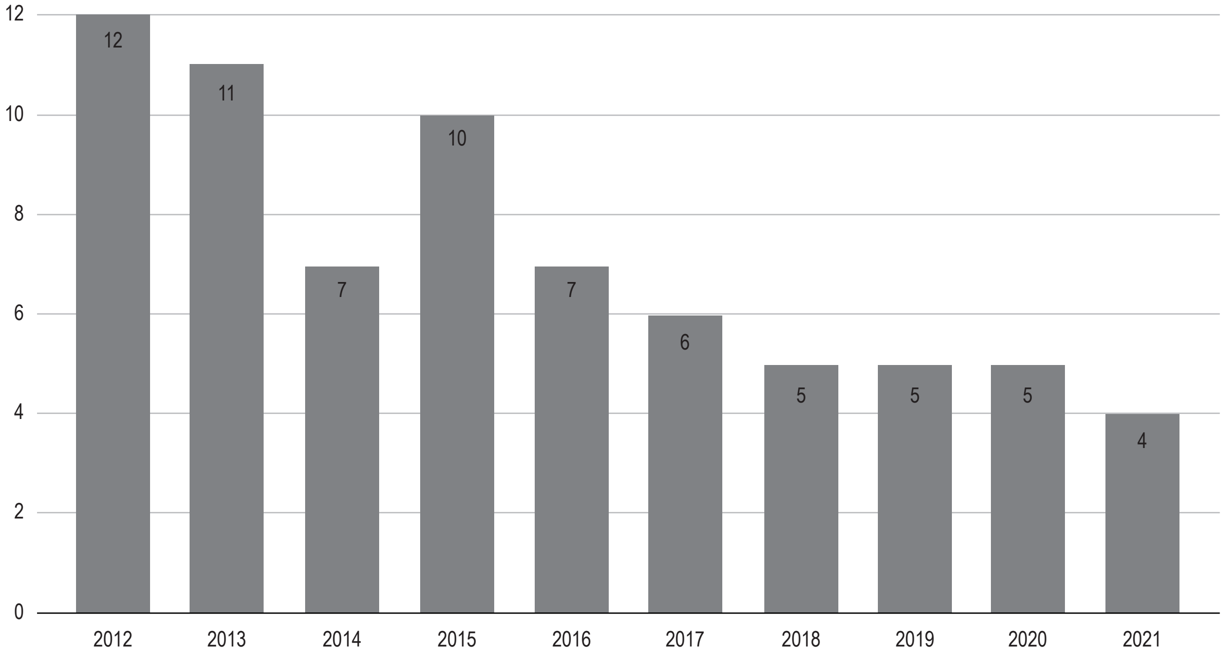

**Chart 1.** Distribution of publications in years 2012-2021.

Analyzing the average pace of changes in publications on the topic of interest to us, it should be noted that in the 10-year period of 2012 – 2021, the number of articles decreased on average by 11.49% from year to year.

In the 2012 – 2021-year scope, the average number of articles was 7,2 and the distribution in time is clearly asymmetric to the right, which means that there was more interest in publishing on CD topic in the initial 5-year study period than in the second half of it.

The author's deliberation also concerned the publishers taking up the analyzed subject matter. The review presented in this text clearly shows that the dominant title is the Journal of Crohn's & Colitis, which published as many as 18 texts on the quality of life of people with CD. The remaining articles are published within other titles which, although admitting articles on the analyzed subject, do not constitute the main area of a given journal. Digestive Diseases and Sciences and Inflammatory Bowel Diseases deserve special attention. The rest of the articles have been scattered over 36 titles. This distribution indicates the limited concentration of scientists around the Journal of Crohn's & Colitis and deconsolidation in other titles, as well as the dominant importance of medical publications among all subjects related to the QoL of patients with CD.

It should also be noted that articles by psychologists or those undertaking research using the methodology characteristic of psychology are published in Value in Health with two publications and one in each of the following: Psychiatria Danubina, Journal of Crohn's & Colitis, The Scientific World Journal, Journal of the American College of Surgeons, Digestive diseases and sciences, PLoS ONE, Arquivos de gastroenterology.

To conduct a qualitative analysis, it was decided to divide the publications into 4 main groups, differing in the type of measured variables. When measurements of mainly clinical variables such as treatment response, clinical symptoms severity, c-reactive protein levels etc. were used, the article was included in the medical group

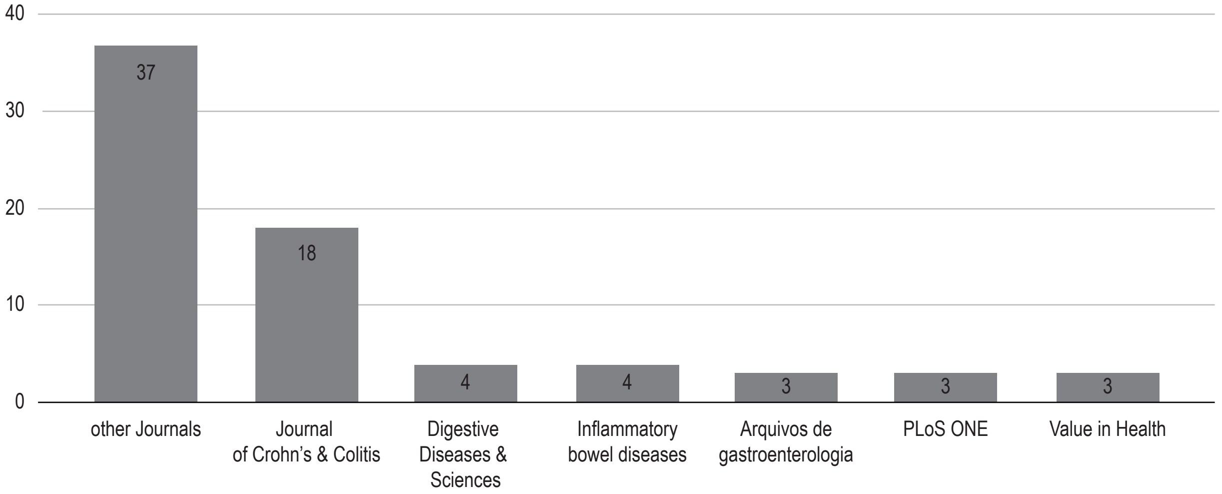

**Chart 2.** Distribution of publications in particular journals

When psychological variables played a high impact role in the article, the text was qualified to the psychological group Variables classified as psychological were for instance: illness perception, ways of coping, self-perceived health, neuroticism, satisfaction with life and so on. An aspect worth mentioning is the measurement of depression and anxiety, because these variables appeared both in the medical and psychological groups. It was assumed that if the anxiety and depression were used for screening diagnostics, as a small subscale of typically used questionnaires or as a background rather than a figurative role or personality trait in the study, then the article was included in the group of medical texts. An intermediate category, i.e. one whose authors used both clinical and psychological variables, were articles from the medical/psychological grou The last category were texts in which topics that were difficult to classify, i.e. those concerning nursing care or osteopathy, were classified as other group.

The tables below present all the analytical units that were left in the database which was the basis for the analysis.

**Table 1.** HRQoL questionnaires and other variables measured in articles classified as Medical.

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 1 | 2012 | A cross-sectional observational study of clinical and demographical factors affecting work disability and health related quality of life in Crohn's disease patients. [47] | Aceituno et al. | IBDQ (Inflammatory Bowel Disease Questionnaire) | Adherence to treatment, work impairment productivity. |
| 2 | 2012 | Adalimumab produces high responder and remission rates and has an independent effect on quality of life in Crohn's disease patients. [48] | Mudter et. al | CDAI (Crohn's Disease Activity Index), HBI (Harvey-Bradshaw Index). | Impact of adalimumab biological treatment. |
| 3 | 2012 | Changing Crohn's disease management: Need for new goals and indices to prevent disability and improve quality of life. [49] | Hommes, et al. | Novel disability index for Crohn's disease, IMPACT survey. | The Lémann score (extent and severity of bowel damage). |

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 4 | 2012 | Effect of standard treatment (ST) versus episodic (ET) or maintenance (MT) infliximab on healthcare cost (HC) and quality-adjusted life years (QALYs) in a community-based incidence cohort of adult Crohn's disease patients with 10 years follow-u [50] | Odes, et al. | QALYs (Quality-adjusted life years). | Infliximab biological treatment response, other types of treatment, healthcare costs. |
| 5 | 2012 | Factors associated with the improvement of quality of life among Crohn's disease patients treated with adalimumab. [51] | Mudter, et al. | SIBDQ (The Short Inflammatory Bowel Disease Questionnaire). | Adalimumab biological treatment response, disease duration, BMI (Body Mass Index). |
| 6 | 2012 | Health related quality of life results through week 22 from the CERTIFI study, a multicenter, randomized, double-blind, placebo-controlled Phase2b study of ustekinumab in patients with moderately to severely active Crohn's disease. [52] | Feagan, et al. | IBDQ. | Ustekinumab biological treatment response. |
| 7 | 2012 | Health-related quality of life in Spanish Crohn disease patients. [53] | Muñoz, et al. | IBDQ. | Work Productivity and Activity Impairment, Overall Work Productivity Loss, Daily Activities Impairment. |
| 8 | 2012 | Is quality of life worse in operated Crohn's disease patients? [54] | Barreiro-de Acosta, et al. | IBDQ, SF-36 (36 Item Short Form Survey), HBI. | Impact of colonic surgery, impact of bowel resection. |
| 9 | 2012 | Quality of life: a potentially useful measure to indicate subclinical flares in Crohn disease. [36] | Cámara, et al. | IBDQ, SF-36, CDAI. | Type of medication intake, subsequent flare ups. |
| 10 | 2012 | Factors influencing quality of life after abdominal surgery for Crohn's disease. [55] | Hotokezaka, et al. | SF-36v2 (36 Item Short Form Health Survey version 2). | Duration of disease, type of surgery procedure, nutritional therapy, presence of penetrating variation of disease. |
| 11 | 2013 | Clinical response, quality of life and work activity in patients with Crohn's disease treated with adalimumab in routine clinical practice. [56] | Saro, et al. | SIBDQ, Euro-QoL 5D (standardized measure of health-related quality of life in 5 dimensions). | Response to Adalimumab, CDAI, PDAI (Perianal Disease Activity Index), Work Productivity and Activity Impairment. |

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 12 | 2013 | Effect of exclusive enteral nutrition on health-related quality of life for adults with active Crohn's disease. [57] | Guo, et al. | IBDQ, CDAI. | Exclusive enteral nutrition impact on disease activity. |
| 13 | 2013 | Quality of life and nutritional aspects after ileo-cecal resection for Crohn's disease. [40] | Sica, et al. | IBDQ. | BMI, biochemical levels of albumin. |
| 14 | 2013 | Sustained restoration of health related quality of life in Crohn's disease patients with adalimumab maintenance therapy. [58] | Casellas, et al. | IBDQ. | Response to biological treatment adalimumab. |
| 15 | 2013 | Sexual function and quality of life after surgical treatment for anal fistulas in Crohn's disease. [59] | Riss, et al. | SF-12 (Short Form-12 Health Survey), IBDQ. | International Index of Erectile Function (IIEF), Female Sexual Function Index (FSFI). |
| 16 | 2014 | A high-fiber diet may improve bowel function and health-related quality of life in patients with Crohn disease. [60] | Brotherton, et al. | IBDQ, HBI. | Inclusive diet influence. |
| 17 | 2014 | Opioid Use is Associated with Decreased Quality of Life in Patients with Crohn's Disease. [61] | Sanford, et al. | IBDQ. | Disease activity, opioid use. |
| 18 | 2014 | Health-Related Quality of Life in Italian Patients With Moderate and Severe Crohn's Disease: Interim Results from the Sole Study. [62] | Lazzaro, et al. | EQ-5D-3L EuroQoL 5-dimension 3-level, HBI, VAS (visual analogue scale). | Disease severity |
| 19 | 2014 | Racial Differences in Disease Activity and Quality of Life in Patients with Crohn's Disease. [63] | Ghazi, et al. | SIBDQ. | HBI, disease duration, disease phenotype, extraintestinal manifestations of disease, medication exposure, hospitalizations, surgeries. |
| 20 | 2014 | Switching from insulin to liraglutide improved glycemic control and the quality of life scores in a case of type 2 diabetes and active Crohn's disease. [64] | Kuwata, et al. | DTR-QOL (Diabetes Therapy-Related QoL Questionnaire). | Type of diabetes therapy. |
| 21 | 2015 | Delayed diagnosis is influenced by the clinical pattern of Crohn's disease and affects treatment outcomes and quality of life in the long term: a cross-sectional study of 361 patients in Southern Italy. [65] | Pellino, et al. | IBDQ. | Patterns and symptoms of CD. |

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 22 | 2015 | Development of a Short Questionnaire to Assess the Quality of Life in Crohn's Disease and Ulcerative Colitis. [66] | Alrubaiy, et al. | CUCQ (Crohn's and ulcerative colitis questionnaire), HBI. | - |
| 23 | 2015 | Effect of Intestinal Resection on Quality of Life in Crohn's Disease. [39] | Wright, et al. | SF-36, IBDQ. | Impact of a long-term ostomy, various demographics, disease factors, fecal calprotectin, CDAI. |
| 24 | 2015 | Implications of Infliximab Treatment Failure and Influence of Personalized Treatment on Patient-reported Health-related Quality of Life and Productivity Outcomes in Crohn's Disease. [34] | Steenholdt, et al. | IBDQ. | Work productivity and activity impairment, infliximab treatment results. |
| 25 | 2015 | Quality of life in Crohn's Disease Patients. [67] | Gavrilescu, et al. | IBDQ. | CDAI, smoking cigarettes. |
| 26 | 2015 | Assessing quality of life in Crohn's disease: Development and validation of the Crohn's Life Impact Questionnaire (CLIQ). [68] | Wilburn, et al. | Novel tool: CLIQ (Crohn's Life Impact Questionnaire). | Nottingham Health Profile and Unidimensional Fatigue Impact Scale. |
| 27 | 2015 | Predictive value of early restoration of quality of life in Crohn's disease patients receiving anti tumor necrosis factor agents. [28] | Herrera-deGuise, et al. | IBDQ. | CDAI, Anti tnf agents impact. |
| 28 | 2016 | Treatment of Anemia and Improvement of Quality of Life Among Patients with Crohn's Disease: experience using ferric carboxymaltose. [69] | Sobrado, et al. | IBDQ. | CDAI, CRP, Anemia. |
| 29 | 2016 | The Impact of Ostomy on Quality of Life and Functional Status of Crohn's Disease Patients. [70] | Abdalla, et al. | SIBDQ. | Presence of ostomy, various demographics. |
| 30 | 2016 | Clinical Activity and Quality of Life Indices Are Valid Across Ulcerative Colitis But Not Crohn's Disease Phenotypes. [71] | Taleban, et al. | SIBDQ. | Disease activity HBI, endoscopic scores for CD, Clinical Colitis Activity. |
| 31 | 2016 | Effect of the Medicinal Agaricus blazei MurillBased Mushroom Extract, AndoSanTM, on Symptoms, Fatigue and Quality of Life in Patients with Crohn's Disease in a Randomized Single-Blinded Placebo Controlled Study. [72] | Therkelsen, et al. | SF-36 Norwegian version 1.2. | CDAI, HBI, treatment effect. |

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 32 | 2016 | Quality of life after bowel resection for Crohn’s disease – first results. [38]] | Kunovsky, et al. | EORTC QLQ – CR29 (Core Quality of Life questionnaire). | Impact of surgery. |
| 33 | 2017 | Analysis of factors affecting the quality of life of those suffering from Crohn’s disease. [73] | Chrobak-Bień, et al.. | SF-36v2. | Age, stage of disease. |
| 34 | 2017 | Clinical status, quality of life, and work productivity in Crohn’s disease patients after one year of treatment with adalimumab. [32] | Saro, et al. | EuroQoL-5D, IBDQ. | Clinical status, work productivity Perianal Disease Activity Index (PDAI), or Irvine PDAI (26). |
| 35 | 2017 | Low toxicity and favorable clinical and quality of life impact after non-myeloablative autologous hematopoietic stem cell transplant in Crohn’s disease. [74] | Ruiz, et al. | SF-36v2 | Cyclophosphamide treatment, stem cell transplant. |
| 36 | 2018 | Medical factors determining the quality of life of patients with Crohn’s disease. [75] | Rachubińska, et al. | SF-36v2 | Disease duration, type of treatment, number of hospitalisations. |
| 37 | 2018 | The Effects of Ustekinumab on Health-related Quality of Life in Patients With Moderate to Severe Crohn’s Disease. [76] | Sands, et al. | IBDQ, SF-36. | Type of treatment. |
| 38 | 2018 | Ileocecal Anastomosis Type Significantly Influences Long-Term Functional Status, Quality of Life, and Healthcare Utilization in Postoperative Crohn’s Disease Patients Independent of Inflammation Recurrence. [77] | Gajendran, et al. | SIBDQ. | Disease type, type of biological treatment. |
| 39 | 2019 | Cytokine Genetic Variants and Health-Related Quality of Life in Crohn’s Disease: An Exploratory Study. [78] | Knisely, et al. | SIBDQ. | Genetic data, cytokine candidate genes. |
| 40 | 2019 | Visceral Adipose Tissue Is Associated With Stricturing Crohn’s Disease Behavior, Fecal Calprotectin, and Quality of Life. [79] | Bryant, et al. | SIBDQ. | Visceral adipose tissue. |
| 41 | 2019 | Improved Quality of Life With Anti-TNF Therapy Compared With Continued Corticosteroid Utilization in Crohn’s Disease. [33] | Scott, et al. | RTE (Remission time equivalent). | Type of treatment. |
| 42 | 2019 | Physical Activity in Daily Life, Exercise Capacity and Quality of Life in Patients with Crohn’s Disease on Infliximab-Induced Remission: A Preliminary Study. [80] | Cabalzar, et al. | SF-36, IBDQ. | Exercise capacity, peripheral muscle strength. |

| Medical articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 43 | 2020 | Association between Health-Related Quality of Life and Nutritional Status in Adult Patients with Crohn's Disease. [81] | Cioffi, et al. | SF-36. | Anthropometry, nutritional variables, bioimpedance analysis, handgrip strength measures. |
| 44 | 2020 | Opioid Analgesics Do Not Improve Abdominal Pain or Quality of Life in Crohn's Disease. [82] | Coates, et al. | SIBDQ. | Negative outcomes (death, need for surgery), pain experience, inflammatory activity (using endoscopic/ histologic findings), laboratory studies, coexistent psychiatric disorders, medical therapy, opioid analgesic, tobacco use. |
| 45 | 2020 | Preliminary study of short – and long-term outcome and quality of life after minimally invasive surgery for Crohn's disease: Comparison between single incision, robotic-assisted and conventional laparoscopy. [36] | Zambonin, et al. | SF-36, GIQLI (Gastrointestinal Quality Of Life Index). | Surgery impact, body image, hospital experience. |
| 46 | 2021 | Is the Quality of Life of Patients with Fistulizing Perianal Crohn' s Disease Impaired by the Presence of Chronic Loose, Non-cutting Seton? [83] | Gklavas, et al. | The non-validated Greek translations of Cleveland Global QoL (CGQoL), validated Greek IBDQ, SF36. | Female Sexual Function Index (FSFI). Erectile Function, presence and severity of anal incontinence. |
| 47 | 2021 | Predictors of health-related quality of life in patients with Crohn's disease receiving biological therapy. [29] | Lundquist, et al. | SHS (Short Health Scale). | Disease activity, rectal fistula, arthralgia. |
| 48 | 2021 | Quality of Life and Work Productivity Improvements with Upadacitinib: Phase 2b Evidence from Patients with Moderate to Severe Crohn's Disease. [31] | Peyrin-Biroulet, et al. | IBDQ, EuroQoL-5D. | Disease phenotype, work impairment productivity, type of treatment. |

**Table 2.** HRQoL questionnaires and other variables measured in articles classified as Medical / psychological

| Medical / psychological articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 1 | 2012 | How do psychological variables influence health-related quality of life in Crohn's disease patients? [44] | Iglesias, et al. | IBDQ-36 SF-36. | Perceived stress, coping strategies: problem-focused coping, emotion-focused coping and avoidant coping, anxiety and depression symptoms. |

| Medical / psychological articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 2 | 2013 | Psychological well-being and quality of life in Crohn's disease patients with an ostomy: a preliminary investigation. [84] | Knowles, et al. | SQOL (The Stoma Quality of Life Scale). | Illness perceptions, anxiety, depression, elective versus emergency surgery, type of ostomy (permanent vs temporary), coping style. |
| 3 | 2013 | Quality of life of Crohn's disease patients under immunosuppressive therapy in Germany – preliminary results of the DaLi study. [85] | Reinshagen, et al. | EuroQoL-5D. | Anxiety, depression, anti-TNF therapy. |
| 4 | 2013 | The importance of illness perceptions, quality of life and psychological status in patients with ulcerative colitis and Crohn's disease. [86] | Rochelle, T. L., Fidler, H. | UK IBDQ (The UK Inflammatory Bowel Disease Questionnaire). | Anxiety, depression, coping, illness perception. |
| 5 | 2015 | Impact of Crohn's Disease on Marital Quality of Life: A Preliminary Cross-Sectional Study. [87] | Li, et al. | SF-12, SIBDQ, modified Harvey Bradshaw Index. | Marital relationship quality, gender. |
| 6 | 2016 | Quality of Life Is Related to Fecal Calprotectin Concentrations in Colonic Crohn Disease and Ulcerative Colitis, but not in Ileal Crohn Disease. [88] | Gauss, et al. | SIBDQ, HBI. | Calprotectin, depression symptomes, BMI, CR |
| 7 | 2016 | Illness perceptions and stress: mediators between disease severity and psychological well-being and quality of life among patients with Crohn's disease. [89] | Zhang, et al. | IBDQ. | Stress, psychological well-being, disease severity (CDAI), illness perceptions, coping strategies, anxiety, depression. |
| 8 | 2017 | Fluoxetine for Maintenance of Remission and to Improve Quality of Life in Patients with Crohn's Disease: a Pilot Randomized Placebo-Controlled Trial. [30] | Mikocka-Walus, et al. | WHOQoL (World Health Organization Quality-of-Life Scale). | Disease activity (CDAI), DSM disorders, fecal calprotectin, anxiety, depression, cytokine, chemokine levels. |
| 9 | 2017 | Quality of life and uncertainty in Crohn's disease. [90] | Niv, et al. | SIBDQ. | self-epistemic authority in CD (knowledge vs uncertainty), disease duration and disease status. |
| 10 | 2020 | Impact of surgery on quality of life in Crohn's disease: short – and mid-term follow-u [35] | D'Ugo, et al. | CGQL (Cleveland Global Quality of Life). | Overall Quality of Happiness (OQH), type of surgery (laparoscopic vs open) steroid use, age, gender. |

| Medical / psychological articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 11 | 2020 | The Impact of Spirituality and Religiosity on Mental Health and Quality of Life of Patients with Active Crohn's Disease. [91] | de Campos, et al. | IBDQ, HBI. | religious/spiritual coping, religious and spiritual beliefs and behaviors. |
| 12 | 2021 | Influence of Religiousness and Spirituality on Remission Rate, Mental Health, and Quality of Life of Patients With Active Crohn's Disease: A Longitudinal 2-Year Follow-up Study. [92] | de Campos, et al. | IBDQ, HBI | depression and anxiety, religious/spiritual coping, religious and spiritual beliefs and behaviors. |

**Table 3.** HRQoL questionnaires and other variables measured in articles classified as Psychological.

| Psychological articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 1 | 2012 | Chronic illness and family: Impact of schizophrenia and Crohn's disease on the family quality of life. [93] | Loga, et al. | FQOL (Family Quality of Life) | Chronic disease (schizophrenia, Crohn's disease). |
| 2 | 2013 | Substantial impact of illness perceptions on quality of life in patients with Crohn's disease. [41] | van der Have, et al. | IBDQ, SF-36. | Illness perception, coping, self-perceived health, neuroticism, endoscopic index. |
| 3 | 2013 | An evil backstage manipulator: psychological factors correlated with health-related quality of life in Chinese patients with Crohn's disease. [42] | Liu, et al. | IBDQ | Neuroticism, anxiety. |
| 4 | 2013 | An evil backstage manipulator: how personality traits affect the quality of life and clinical outcome evaluation in patients with Crohn's disease. [43] | Liu, et al. | IBDQ | Neuroticism, anxiety, lie scale. |
| 5 | 2014 | Associations Between Crohn's Disease Severity And Specific Socio-Demographic, Quality-Of-Life And Coping Factors. [94] | Friger, et al. | SF-36. | Ways of coping, socio-demographic details, disease severity (HBI), pharmaceutical and surgical therapies, hospitalizations. |
| 6 | 2015 | Predictors of health-related quality of life and adherence in Crohn's disease and ulcerative colitis: implications for clinical management. [95] | Tabibian, et al. | IBDQ, MOS (The Medical Outcomes Study). | adherence to provider recommendations, stress, The Crohn's and Colitis Knowledge Score (CCKNOW). |

| Psychological articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 7 | 2017 | Coping strategies, satisfaction with life, and quality of life in Crohn's disease: A gender perspective using structural equation modeling analysis. [45] | Sarid, et al. | SIBDQ. | HBI, coping, satisfaction with life. |
| 8 | 2018 | Symptoms of Anxiety and Depression, and Quality of Life of Patients with Crohn's Disease. [96] | Tomazoni, E. I., Benvegnú, D.M. | IBDQ. | Anxiety and depression symptoms, BMI. |
| 9 | 2019 | Changes in Health Related Quality of Life in Crohn's Disease Patient Following Mindfulness-Based Cognitive Intervention: Preliminary Results of a Randomized Controlled Trial. [97] | Sergienko, et al. | EQ-5D-3L, SF-12, HBI. | Mindfulness-based cognitive intervention (MBCI) |

**Table 4.** HRQoL questionnaires and other variables measured in articles classified as Other.

| Other articles | | | | | |
|---|---|---|---|---|---|
| No. | Year | Title | Author | HRQol/Qol measure | Other measured variables |
| 1 | 2014 | The reflection of the quality of life of people with Crohn's disease in nursing. [98] | Dolák, et al. | WHOQOL-100 (World Health Organization Quality of Life Questionnaire). | - |
| 2 | 2016 | Health-Related Quality of Life Impairment and Indirect Cost of Crohn's Disease: A Self-Report Study in Poland. [99] | Holko, et al. | EQ-5D-3L. | information on disease severity, surgical treatment of CD in the past, current pharmacotherapy.. |
| 3 | 2018 | Effect of the soft-tissue techniques in the quality of life in patients with Crohn's disease: A randomized controlled trial. [100] | Espí-López, et al. | (IBDQ-32), | Anxiety, depression, pain levels, Assessed with the Visual Analogue Scale (VAS), intervention soft tissue treatment. |

### Medical articles

Articles classified as medical (n=48) mainly refer to topics related to QoL of patients suffering from CD and the clinical properties of Crohn's disease. In this group of publications, investigated variables related mostly to the type and effectiveness of CD treatment. Commonly studied was for instance: the impact of biological treatment (adalimumab, infliximab, ustekinumab) and patient's response to it, type of other medication intake (opioids, immunosuppression). A significant portion of studies concerned: impact of surgery (colonic surgery, bowel resection, long term-ostomy), disease activity (CRP, CDAI, count of subsequent flare ups, BMI, extraintestinal manifestations of disease, fecal calprotectin, endoscopic and histologic scores, number of hospitalisations, fistulas), impairments caused by disease activity (work impairment, daily activity impairment, impairment of sexual functions), impact of nutrition (inclusive, exclusive), genetic and phenotype disease features as well as: anemia treatment, healthcare costs, presence of penetrating variation of disease, biochemical levels of albumin, type of diabetics therapy, cyclophosphamide treatment, stem cell transplant, genetic data, cytokine candidate genes, visceral adipose tissue, exercise capacity, peripheral muscle strength, handgrip strength measures, anthropometry, arthralgia, bioimpedance analysis, pain experience, tobacco use and numerous sociodemographic variables. The authors of three studies proposed a novel tool: the Lémann score, CUCQ and CLIQ to assess QoL in CD.

## Medical/Psychological articles

In this group of articles (n=11) both medical and psychological variables influencing QoL of CD patients were within the scope of the authors scientific interests. Among features measured in QoL questionnaires, psychological and medical variables were used together, both to a significant extent. An emphasis has been placed on the role of perceived stress, anxiety and depression as well as several coping strategies in context of the ongoing disease in the patient's perspective. Authors also examine the associations between Qol in CD and illness perception, psychological well-being, and the influence of self-epistemic authority in CD (knowledge vs uncertainty). Some studies included variables such as marital relationship quality, religious beliefs and behaviors, spiritual coping and overall quality of happiness. Apart from psychological, medical variables were also included such as: impact of surgery (emergency vs elective, laparoscopic vs open), permanent and temporary ostomy, type of biological therapy, steroid therapy, cytokine and chemokine levels as well as disease activity (BMI, CRP, CDAI, fecal calprotectin).

## Psychological articles

Authors of publications in this category (n=9) also undertook the topic of QoL however the main emphasis was concentrated on the impact of psychological variables. Studies included questionnaires to assess personality traits (neuroticism, lie subscale), anxiety, depression, illness perception, self-perceived health, adherence to medical recommendations, coping strategies, satisfaction with life as well as the effectiveness of a mindfulness-based cognitive intervention. One of the studies examined and compared Family Quality of Life (FQoL) with a CD and Schizophrenic members. Some medical variables included in this category group were: endoscopic measures of disease activity, pharmaceutical and surgical therapies, number hospitalizations, BMI.

Other articles in this group (n=3) also concerned QoL but referred to further accompanying aspects of CD. Texts concerned topics such as nursing needs of CD patients, life impairment and indirect costs of Crohn's disease as well as the impact of soft tissue osteopathic techniques.

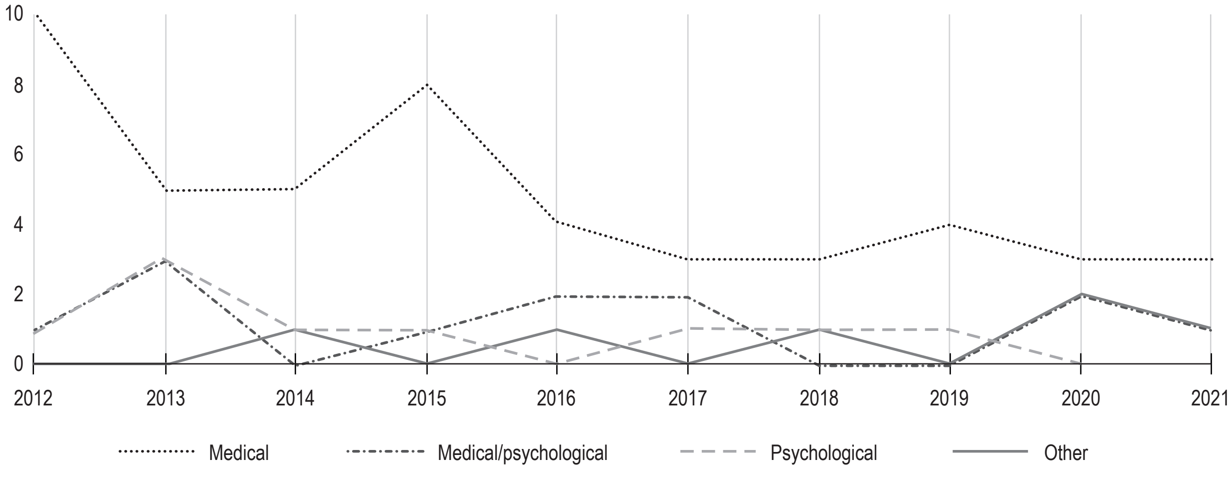

**Chart 3.** Frequency of publication types in the study time frame.

Results presented on chart 3 indicate that the frequency of texts in the studied time frame decreases. Regardless of the publication type, the number of publications regarding QoL in CD has a descending character.

## DISCUSSION

As a result of the conducted analysis, the outcomes were clearly opposed to the first hypothesis presented in the introduction. It seemed that due to the increased incidence of CD, the number of articles in scientific journals devoted to this subject would also increase. Meanwhile, an exactly opposite tendency is noticeable, indicating a declining interest in QoL of CD patients. It can therefore be presumed that from the clinical point of view, this situation is a consequence of the exhaustion of the topic and the lack of breakthrough medical research on this subject. Due to the spreading of the humanistic medicine paradigm, including personalized treatment, it could be expected that the focus of the research would be shifted from strictly medical issues to aspects of psychological measurements, or that the quality of life study of patients with CD would be expanded to include aspects typical to psychological cognition.

The conducted analysis allowed for accepting hypothesis three, according to which it was assumed that in the scientific journals there is an underrepresentation of studies of the nature of psychological variables in relation to studies of the medical description of CD.

Thus, the number of scientific publishers dealing with the subject of disease clearly shows the dominance of medical journals. Hence, the analysis made it possible to identify an information gap in scientific cognition related to the interdisciplinary approach to the quality of life of people struggling with CD.

Also, it should be emphasized that psychological or psychiatric care would be advised to all, but especially to recently diagnosed CD patients due to high risk of anxiety and depressive symptoms co-occurrence and their negative influence on one's well-being. As the above-mentioned research indicated, psychological distress can be present in any stage of CD and can have a significant and lifelong impact on QoL. Subsequent flair ups can cause physical, economic and social impairment as well as psychological distress. Psychotherapy could prove beneficial by helping in dealing with disease as well as its consequences. Recognizing and training in using proper coping strategies and techniques could also improve the well-being of CD patients.

It seems that there is a necessity to broaden the horizons of the conducted research to include psychological distress, concern of social security of patients and their families, as well as economic issues at several levels of inference.

This approach would be needed not only in the dimension of scientific considerations, but also or above all in the practical dimension. Justifications for such postulate can be found in many areas. First, CD implies, in the personal unit dimension, above average costs related to treatment, hygiene and quality of life. Secondly, it is worth focusing on the genetic, geographic and social determinants of the disease that affect the health policy of the state. As a rule, preventive programs and early diagnostics require the payer to commit funds lower than the costs of treating the patient.

## CONCLUSION

There is a declining interest in QoL of CD patients despite significantly increasing disease morbidity. Focus of the research applies mainly to medical issues and lacks psychological and studies that comprise combined medical and psychological variables.

From a research perspective, it would be a valuable direction to perform a multidisciplinary analysis undertaking psychological, psychiatric, medical as well as methods and techniques adequate to other domains of science to fully understand QoL of CD patients.

From a practical perspective more attention should be emphasized on psychological and mental health as data strongly indicates that an extensive number of CD patients may be experiencing some forms of psychiatric disorders which may affect their QoL significantly.

In summary, QoL of CD patients consists of many dimensions. Their well-being can vary due to their social, economic, physical and psychological resources and needs. Therefore, it seems that additional research is deemed vital.

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