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The impact social support and its different types have upon Crohn's disease: a double, case-control study on patients experiencing a flare-up or in remission, and healthy individuals

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Abstract

Background: The influence of social support upon several diseases has been studied and has been found to be beneficial, either by facilitating adjustment to the disease and improving its management, or by influencing the biological responses that lead to disorders.

Objective: The aim of this study was to investigate the role of received social support and its different types (informational, material and emotional) in people with varying stages of Crohn's disease (CD), compared to a sample of healthy individuals.

Design: An observational, double case-control study was conducted using validated scales to assess the impact of received social support and its different types upon CD.

Methods: The sample was divided into three groups: healthy individuals, CD patients experiencing a flare-up and CD patients in remission. Study variables were measured in the three groups, and a multivariate analysis of variance was performed to examine statistical significance. In addition, post hoc analyses were performed using either Tukey's test or the Games-Howell test (depending on the homogeneity of variances) to determine which groups differed.

Results: The principal results revealed statistically significant differences between the groups studied regarding received social support ($p = 0.001$), satisfaction with this support ($p = 0.018$), material support type ($p = 0.002$) and informational support type ($p = 0.016$). In the majority of cases, the most significant differences were observed between the group of healthy individuals and CD patients in remission, and between the latter group and CD patients experiencing a flare-up.

Conclusion: We propose directly engaging with CD patients in remission to thereby increase their perceived level of received social support, to consequently increase their satisfaction with such support. We also suggest specific interactions to increase the perception of material and informational support. This approach is also directly linked to the type of support provided by healthcare professionals.

Plain language summary

Providing actions to increase social support improves the well-being and quality of life of patients with Crohn's disease

Various studies have demonstrated the importance of psychosocial factors upon the development and progression of inflammatory bowel disease. Among these factors, social support has been identified as a key variable, not only because of its direct effect upon

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the subjective well-being of patients and their the ability to adapt to the disease, but also because of its indirect role as a stress modulator, acting like a cushion and contributing to stress reduction. This double, case-control study involved 320 participants who were divided into three groups: healthy individuals; patients with active Crohn's disease (flare-up); and patients with Crohn's disease in remission. Different types of social support were assessed using standardised and validated questionnaires, including received social support, the degree of satisfaction with it, and the types of support (emotional, material, and informational). The results revealed that individuals with Crohn's disease in remission place the least value on social support and its various forms. Based on these findings, there is a need to develop psychosocial actions aimed at this specific group, with the goal of promoting a greater use of both direct and indirect social support, and increasing the appreciation of its benefits to thereby improve how they cope with, manage and adjust to the disease, and enhance their well-being and quality of life. These are all potential benefits of social support and support styles.

Keywords: Crohn's disease, emotional support, informational support, material support, received social support

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Introduction

Crohn's disease (CD) is a chronic, inflammatory pathology of the gastrointestinal tract, classified as an inflammatory bowel disease. It can occur in any segment of the gastrointestinal tract from the oral cavity to the anus, and may affect all layers of the intestinal wall, presenting typical lesions such as granulomas.[1] The evolution of CD involves progressive gastrointestinal damage of disabling potential,[2] and its clinical course fluctuates between flare-ups and remission. Many flare-ups require hospitalization and have a significant impact on the patient's quality of life. Consequently, CD is a condition that generates a high degree of discomfort in those who suffer from it, making it essential to adopt a comprehensive approach to the same. Not only are organic actions called for, but psychosocial strategies are also required, aimed at improving the emotional, social and functional quality of life of the patient.

Research has highlighted the influence of psychosocial factors on inflammatory bowel disease.[3–8] Among these, social support has emerged as a key variable to bear in mind in a variety of diseases, both for its direct effect upon well-being, as well as for its indirect effect on stress, acting like a buffer. The direct effect refers to the beneficial impact of social support on individuals who feel loved, valued and appreciated as members of a social group.[9] Regarding the indirect or buffering effect of social support on stress, stress models acknowledge that both personal and situational variables can either mitigate or intensify the impact of stress on health.

Social support has two dimensions: objective and subjective.[10] The first includes the more tangible aspects of social support, and the second, the more subjective aspects. The former includes the instrumental aspects of social support (help), and the latter refers to the expressive aspects (affection). Thus, social support is composed of different types (emotional, material and informational), and comes from different sources (family, friends and peer groups).

Satisfaction with received social support refers to the actual support an individual receives. It encompasses social ties and relationships with others, and the actions taken by others to assist them.

Received social support refers to an individual's perception of being reliably connected to and supported by others. It is defined as the set of emotional, informational, or material support a person receives from their social environment, whether through close relationships (family, partner and friends) or broader networks (colleagues, institutions and associations).

Emotional support refers to aspects such as intimacy, attachment, affection, comfort, care and concern received from other people that promote feelings of emotional well-being, of being loved, respected and wanted. This kind of support provides security and affection.

Material support provides an individual with instrumental help or assistance with the daily tasks that they must carry out. It involves somebody else carrying out activities to solve practical problems. This type of support reduces the burden on the affected person, allowing them to enjoy an improved state of well-being. In general, people are reluctant to ask for this type of support. It is also important to stress that this type of support is only effective if the recipient perceives the help as appropriate; otherwise, it could be a source of increased discomfort and create feelings of guilt.

Informational support includes advice, guidance, or information relevant to the situation in which people find themselves. It involves an exchange of opinions or specific actions for problem-solving, to help the affected person adapt to a situation. This type of support also helps them to understand a particular reality.[11]

Several studies have highlighted the importance of receiving social support and the influence it has upon the onset and subsequent management of the disease.[12–24]

The type and amount of social support a person receives may vary depending on the stage of the disease. During remission (the period during which the symptoms of the disease are minimal or absent), patients may feel they have greater control over their health, thereby influencing how they seek out and receive social support. During a flare-up (the active phase of the disease where symptoms are at their most intense and the risk of major complications is at its highest), the demand for social support may become greater and more diverse. An increased need for instrumental support related to helping with daily tasks, and emotional support related to existing complications of the disease, can be seen.[25]

Research regarding social support and its influence upon CD is scarce, particularly concerning the different types of support. Based on the benefits provided by this variable, and as demonstrated regarding other diseases, we believe that discovering the effect of social support upon CD is of special interest.

The following research question was posed: ‘*How do received social support, satisfaction with received social support, and support types (emotional, material, and informational), influence Crohn's disease patients during the different stages of the illness, compared to a sample of healthy individuals?*’

This study aimed to examine the role of received social support and its different types (informational, material and emotional), and to assess the level of satisfaction with that support among patients experiencing varying stages of CD, compared to a group of healthy individuals. This study is subsequent to our previous findings that demonstrated the influence of perceived social support upon flare-ups.[4] By gaining a deeper understanding of this variable, we can contribute to improving the care and management of individuals living with CD.

Materials and methods

Design and participants

An observational, double, case-control study was conducted using validated scales to assess the impact of received social support and its different types upon CD patients.

The sample included a total of 320 participants, divided into three groups: 160 healthy people, 80 CD patients experiencing a flare-up and 80 CD patients in remission. The sample size was estimated based on the number of patients in the care area of the Gregorio Marañón Hospital (630). The formula for estimating n in finite populations was used for the sample.

Figure 1 shows the STROBE flow chart for this study.

CD patients aged between 17 and 40 years were included. Participants needed to have a confirmed diagnosis of CD, either in the terminal ileum (L1), colon (L2), or ileocolic (L3) areas,

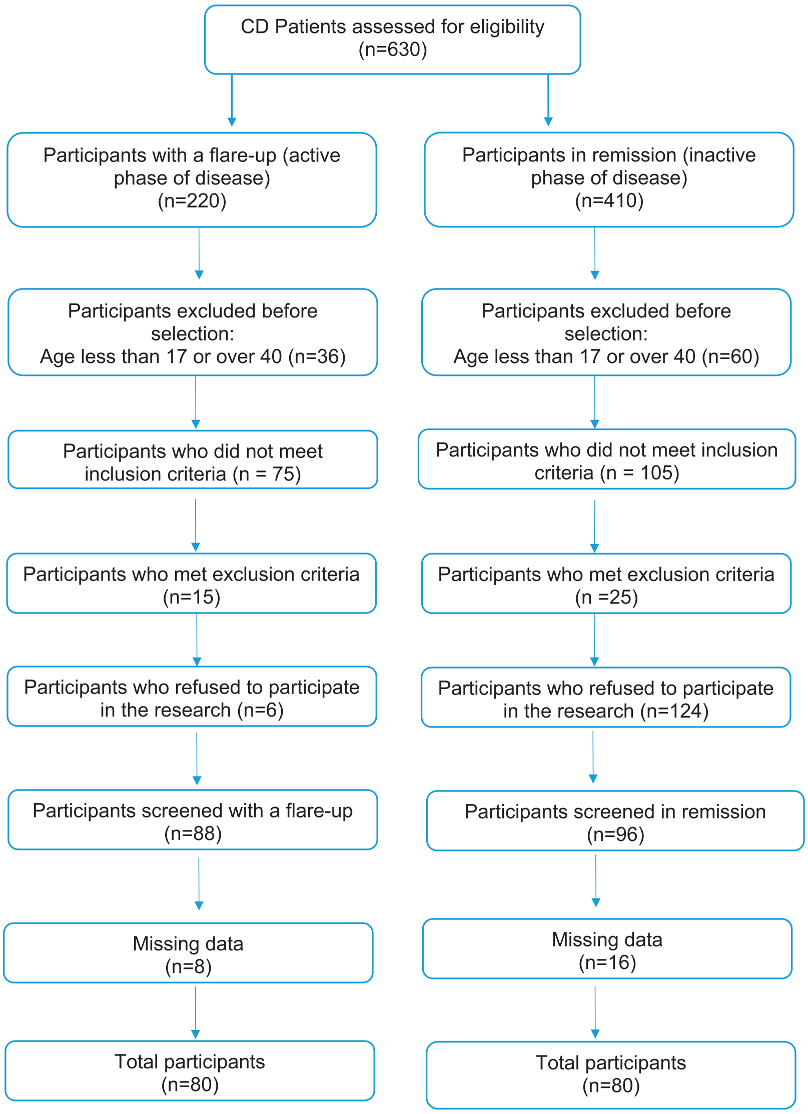

Figure 1. STROBE flowchart of the study.

which, according to the Montreal Classification, presented as non-stenosing, non-fistulizing or inflammatory (B1), or stenosing (B2). Participants with the disease located in the L4 area, or in a combined disease location that included the L4 area and/or B3 disease behaviour, were excluded.

Participating individuals experiencing a flare-up (active phase of the disease) had to score moderate or severe disease on the Harvey-Bradshaw index (>7), whilst those in remission had to score less than 5 on this index.

Participants with CD in remission (inactive phase) were members of the Madrid Association for Crohn's Disease and Ulcerative Colitis, and all were asymptomatic during the study. None were being treated with Prednisone.

Exclusion criteria were the presence of a chronic organic disease other than CD, and those being treated with medication for a psychiatric illness diagnosed by a specialist or primary care physician. Pregnant women and individuals who had undergone surgery within the last 18 months were also excluded.

Healthy individuals should not be suffering from any chronic, physical, or psychological disorder.

Procedure

CD patients diagnosed as experiencing a CD flare-up were recruited upon their admission to the Digestive Unit of the Gregorio Marañón University Hospital.

CD patients in remission were recruited through the Madrid Association for Crohn's Disease and Ulcerative Colitis.

Healthy people were recruited from various settings: students, teaching and administrative staff, or people undergoing preventive check-ups at the hospital who were found to have no chronic diseases.

All were recruited by the principal investigator of this study.

The study was presented to the participants in person, and the criteria for participation were explained. After checking that they had understood everything correctly, questionnaires were handed to those who were interested in participating. In all cases, participation was voluntary and disinterested. All subjects signed the informed consent form. A STROBE case-control checklist was used to guide research reporting (Supplemental Material).

The study was approved by the Ethics Committee of the Faculty of Psychology at the Complutense University of Madrid (Ref. 2018/19-022). The sample was collected between September 2021 and December 2022.

Instruments

The measurement tools used in this research included a socio-demographic questionnaire and two validated Social Support Questionnaires. The first was the Received Social Support Questionnaire, and the second was the Satisfaction with Received Social Support Questionnaire, both validated by Díaz Vega.[26] These questionnaires consider the sources and the types of social support, and direct scores can be obtained for each.

The first social support scale uses Likert scales from 1 (none) to 7 (maximum) to measure the emotional, material and informational types of social support received from family, friends, others and healthcare staff. The satisfaction with social support received scale assesses how satisfied the subject is with these different types of social support received using Likert scales from 1 (not satisfied) to 7 (very satisfied).

It is also possible to obtain scores for emotional, informational and material support on both scales.

The total social support score of each participant was calculated by adding together their self-reported scores for each social support dimension. A score of less than 30 is considered a low level of social support, between 30 and 48, a moderate level, between 48 and 66, a high level and above 66, a very high level.

The total score on the satisfaction with received social support scale is calculated similarly by adding the values assigned to each dimension measured. The lowest score would be 4 points, and the highest, 28. A score of less than 10 corresponds to a low level of received social support, between 10 and 16, a moderate level, between 16 and 22, a high level and above 22, a very high level.

With respect to the types of support scale, the minimum score on each scale is 4 points, and the maximum is 28. A score of less than 10 represents a low level of emotional support, material support or informational support, between 10 and 16, a moderate level, between 16 and 22, a high level and above 22, a very high level.

Statistical analysis

Qualitative variables were analysed using frequency analysis, while quantitative variables were examined using measures of central tendency (mean) and dispersion (standard deviation), in the three groups studied. The chi-square test was applied to identify any statistically significant differences between the qualitative variables of the groups.

A multivariate analysis of variance (MANOVA) was conducted to assess significant differences between the groups. The analysis examined age, received social support, satisfaction with received social support and types of support (emotional, informational and material), among healthy individuals and CD patients in remission or with a flare-up.

Levene's test was used to verify the homogeneity of the variances. Depending on the homogeneity of these, post hoc tests (either Tukey or Games-Howell) were performed to conduct pairwise comparisons between groups and specifically identify those with significant differences.

The Statistical Package for Social Sciences (SPSS) Version 23 (Chicago, IL, USA) was used for descriptive statistics, hypothesis testing and analyses of internal consistency, reliability and validity of the research instruments. All tests were conducted with a 95% confidence level, considering a p-value below 0.05 as significant.

Results

Socio-demographic characteristics

In terms of socio-demographic data, the total sample consisted of 320 individuals, of whom 43% were men and 57% were women. The average age was 30.1 years (SD = 7.6) for men and 29.8 years (SD = 7.2) for women. Regarding marital status, 60% of the sample were single, 32.5% were married and 7.5% were separated/divorced. In terms of education, 16% of participants had completed basic education, 39.7% secondary education, 21.2% intermediate university education and 23.1% higher university education. Regarding employment, 57.2% of participants worked full time, 20% worked part time and 22.8% were unemployed. In terms of household circumstances, 10% of participants lived alone, 25% lived with one other person, 25.3% with two others and 39.4% with three or more people. Table 1 presents the data for each group in the sample.

As regards the age variable, statistically significant differences were identified between the groups analysed ($p = 0.000$). Levene's test confirmed compliance with the assumption of homogeneity of variances ($p = 0.212$). The Tukey posthoc test revealed differences between healthy individuals and those with CD, regardless of the stage of the disease ($p = 0.000$). Additionally, differences were also found among individuals with CD at different stages of the condition ($p = 0.023$).

Concerning gender, the chi-square test did not reveal any statistically significant differences between the groups ($p = 0.054$). However, this same test did identify statistically significant differences between the three groups studied with regard to marital status ($p = 0.000$), household composition ($p = 0.003$), level of education ($p = 0.018$) and employment status ($p = 0.000$).

Received social support, satisfaction with received social support, emotional support, material support and informational support

Descriptive analysis showed that both healthy individuals and CD patients experiencing a flare-up reported high levels of social support (M = 53.15 and M = 53.16, respectively), whereas CD patients in remission reported moderate levels (M = 46.10). Satisfaction with received social support was highest among patients experiencing a CD flare-up (M = 20.5), followed by healthy individuals (M = 19.6), and lastly, patients in remission (M = 18.5). However, the level of satisfaction was classified as high in all groups.

Higher levels of emotional support were identified among patients experiencing a CD flare-up (M = 20.2), followed by healthy individuals (M = 19.0), and lastly, those in remission (M = 18.5). In all three groups, the level of emotional support was considered high.

Regarding material support, healthy individuals reported the highest levels (M = 15.8), followed by patients experiencing a CD flare-up (M = 15.4), and finally, those in remission (M = 13.2). In all cases, this type of support was rated as moderate.

Finally, with respect to informational support, healthy individuals reported the highest levels (M = 18.4), followed by patients experiencing a CD flare-up (M = 17.8), and finally, patients in remission (M = 16.3). The level was considered high in all cases. The results of the descriptive analysis are detailed in Table 2.

Comparison of received social support, satisfaction with received social support, emotional, material and informational support between healthy individuals, individuals with CD in remission and individuals experiencing a CD flare-up

A MANOVA revealed statistically significant differences between the groups studied regarding received social support, satisfaction with received social support, informational support and material support variables (Table 3).

Table 1. Socio-demographic characteristics of the three groups included in the sample.

Sociodemographic variables	**Healthy individuals**		**CD patients in remission**		**CD patients with a flare-up**	
	M (SD)	**(%)**	**M (SD)**	***N* (%)**	**M (SD)**	***N* (%)**
Sex						
Men		40.0%		38.8%		55%
Women		60.0%		61.2%		45.0%
Age	27.2 (6.9)		34.1 (6.4)		31.2 (7.1)	
Marital status						
Single		77.5%		30.0%		55.0%
Married		20.6%		56.3%		32.5%
Divorced/Separated		1.9%		13.7%		12.5%
Education						
Secondary school		9.4%		23.8%		21.3%
Bachelor's degree		45.0%		27.5%		41.3%
Middle University		23.8%		21.3%		16.3%
Higher University		21.9%		27.5%		21.3%
Work						
Full time		42.5%		86.3%		57.5%
Part-time		22.5%		10.0%		25.0%
Unemployed		35.0%		3.7%		17.5%
Living situation						
Alone		8.8%		15.0%		7.5%
With one person		25.0%		28.7%		21.3%
With two people		21.3%		36.3%		22.5%
With three or more people		45.0%		20.0%		48.8%

CD, Crohn's disease.

The Levene test revealed that the variances of the four variables in the three groups were not equal. Since the homoscedasticity principle was not met, the Games-Howell post hoc test was used to determine the differences between groups (Table 4).

Subsequently, posthoc tests were performed to identify the specific groups in which statistically significant differences were found. Significant differences were observed in received social support between healthy individuals and those in remission ($p < 0.001$), and between CD patients experiencing a flare-up and those in remission ($p = 0.009$).

Regarding satisfaction with received social support, statistically significant differences were found between patients in remission and those experiencing a CD flare-up ($p = 0.022$).

Table 2. Average and standard deviation of received social support, satisfaction with received social support, emotional support, material support and informational support.

Components of social support	Healthy individuals		CD patients in remission		CD patients with a flare-up	
	M	SD	M	SD	M	SD
Received social support	53.15	11.9	46.1	13.5	53.16	14.9
Satisfaction with received social support	19.6	4.1	18.5	4.6	20.5	4.9
Emotional support	19.0	4.2	18.5	4.9	20.2	5.3
Material support	15.8	4.9	13.2	5.8	15.4	6.3
Informational support	18.4	4.5	16.3	5.6	17.8	5.3

CD, Crohn's disease.

Table 3. Multivariate analysis of variance in received social support, satisfaction with received social support, emotional support, material support and informational support.

Components of social support	R^2	*F*	Sig.
Received social support	2260.84	7.70	0.001
Satisfaction with received social support	165.03	4.09	0.018
Emotional support	117.74	2.64	0.073
Material support	384.25	6.24	0.002
Informational support	213.58	4.22	0.016

Significant differences in material support were identified between healthy individuals and those in remission ($p=0.002$).

Finally, significant differences in informational support were also observed between healthy individuals and patients in remission ($p=0.020$). The results are shown in Table 5.

Reliability

The reliability of the instruments used was measured using Cronbach's alpha. In our study, Cronbach's alpha for the Received Social Support Questionnaire was 0.821 for healthy people, 0.817 for CD patients in remission and 0.852 for CD patients experiencing a flare-up.

Cronbach's alpha for the Satisfaction with Received Social Support Questionnaire was 0.548 for healthy people, 0.526 for CD patients in remission and 0.606 for CD patients experiencing a flare-up.

Cronbach's alpha for the emotional support scale was 0.552 in healthy subjects, 0.523 in CD patients in remission and 0.670 in CD patients experiencing a flare-up.

Cronbach's alpha for the informational support scale was 0.567 in healthy people, 0.599 in CD patients in remission and 0.597 in CD patients experiencing a flare-up.

Cronbach's alpha for the material support scale was 0.614 in healthy people, 0.646 in CD patients in remission and 0.724 in CD patients experiencing a flare-up.

Discussion

The main goal of this research was to examine the role of received social support and its different types (informational, material and emotional), and to assess the level of satisfaction with that support among patients experiencing varying stages of CD, compared to a group of healthy individuals.

In terms of received social support, results suggest that healthy individuals and those experiencing a CD flare-up report similar levels. Both groups

Table 4. Levene test on received social support, satisfaction with received social support, emotional support, material support and informational support.

Components of social support	Levene	df1	df2	Sig.
Received social support	4.64	2	302	0.010
Satisfaction with received social support	4.11	2	317	0.017
Material support	5.46	2	317	0.005
Informational support	4.95	2	303	0.008

Table 5. Games-Howell test on received social support, satisfaction with received social support, material support and informational support.

Components of social support	I	J	Difference (I–J)	Sig.
Received social support	Healthy individuals	CD patients in remission CD patients with a flare-up	6.9 −0.1	**0.001** 1.00
	CD patients in remission	Healthy individuals CD patients with a flare-up	−6.9 −6.9	**0.001** 0.009
Satisfaction with received social support	Healthy individuals	CD patients in remission phase CD patients with a flare-up	1.1 −0.90	0.162 0.344
	CD patients in remission	Healthy individuals CD patients with a flare-up	−1.1 −2.0	0.162 **0.022**
Material support	Healthy individuals	CD patients in remission CD patients with a flare-up	2.6 0.44	**0.002** 0.848
	CD patients in remission	Healthy Individuals CD patients with a flare-up	−2.6 −2.2	**0.002** 0.062
Informational support	Healthy individuals	CD patients in remission CD patients with a flare-up	2.0 0.58	**0.020** 0.687
	CD patients in remission	Healthy Individuals CD patients with a flare-up	−2.0 −1.5	**0.020** 0.221

CD, Crohn's disease.

scored seven points above the level reported by people with CD in remission. Statistically significant differences were also identified.

Regarding satisfaction with received social support, the results show that CD patients experiencing a flare-up report the highest levels of satisfaction, followed by healthy individuals, and finally, those in remission. Statistically significant differences were also observed.

The differences observed between CD patients in remission and other groups could be explained by the stage of their disease. Individuals with a stable symptom profile may have a reduced perceived need for social support. This, in turn, leads to decreased sensitivity to, or appreciation of, the support received, and therefore, less satisfaction with it too. Since they are not experiencing acute symptoms or requiring constant assistance, these individuals may not recognize or value social support as much as those experiencing a flare-up do.

This finding is consistent with previous research suggesting that the perception of, and satisfaction with, social support depends not only on its objective availability, but also on the emotional state, contextual demands and the subjective perception of need.[27,28]

Furthermore, these individuals do not require the information or tangible assistance that others provide, which may prevent them from fully appreciating the beneficial behavioural and emotional effects of social support.[29]

With regard to emotional support, data showed that levels were high in all three groups. Ideas, thoughts and emotions shared with others can help us adapt to complex situations. This is precisely one of the beneficial effects of social support. Thus, emotional support provides protection against a wide range of stressful events for the individual.[28]

Furthermore, these results confirm that emotional support is universally valued. Consequently, emotional support plays a key role in regulating emotions, regardless of the health context.

Regarding material support, the level was moderate in all cases. The results found could be explained by the fact that individuals in the remission phase feel they have a balanced state of health, and thus do not perceive this type of support as necessary, thereby resulting in lower levels.

With regard to informational support, the mean values indicated that the level of this type of support was high in all groups. Statistically significant differences in informational support were found between healthy individuals and CD patients in remission. One possible explanation is that CD patients in remission do not feel the need for counselling, guidance, or learning further about their condition, since they can continue with their usual activities without additional support.

Our results align with the specificity of support theory,[30] which posits that the most effective support is that which is tailored to the specific needs arising from a problem, and that these needs vary across the different stages of the illness.

The main strength of this study is the exploration and understanding of the effect that social support and its various types have on CD. Another strength is that it has statistically demonstrated how received social support and satisfaction with received social support influence the different stages of this disease. These findings pave the way to new approaches in the treatment and care of CD and enhance existing knowledge in the field. In addition, it has been confirmed that both dimensions of social support (objective and subjective) must be considered in new models of comprehensive care for these individuals.

The main limitations of this study are its sample size and nature. We believe that future research should not only involve larger samples, longitudinal studies and explore sources of support, but also include other variables that shape the role of social support in the treatment and care of CD patients.

Conclusion

In summary, given the high levels of social support observed in CD patients experiencing a flare-up, combined with the existing knowledge of its beneficial effects, we can conclude that social support plays a positive role in disease management. It contributes to improved emotional well-being, feelings of affection and security, while reducing the perceived threat felt by these patients during relapses.

It has also been demonstrated that patients have different support needs during the different stages of the disease, so engagement protocols should be adapted accordingly.

Furthermore, the results obtained indicate that CD patients in remission perceive a lower level of both received social support and satisfaction with such support.

Emotional support is also valued positively by all participants, who consistently highlight the importance of its fundamental components. On the other hand, material support has the lowest levels of appreciation in all cases, being perceived to a lesser extent by CD patients in remission, a situation also replicated in the case of informational support.

We can therefore conclude that CD patients in remission benefit the least from the direct and protective effects that social support can have on their coping and adjustment processes.

We propose directly engaging with CD patients in remission to thereby increase their perceived level of received social support, to consequently increase their satisfaction with such support. Specific interactions aimed at improving the perception of material and informational support are also proposed. These actions could be complemented with structured training programmes through support groups for the purpose of strengthening the positive perception of the dimensions of social support. This type of action would not only help to delay possible hospital admissions for people with CD, but would also aid better adaptation to the disease, enhancing both the direct and indirect effects of social support. In this way, patients could develop an improved ability to effectively manage their health condition.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Psychology at the Complutense University of Madrid (Ref. 2018/19-022). All subjects signed the informed consent form.

Consent for publication

Not applicable.

Author contributions

María José de Dios Duarte: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Andrés Arias: Conceptualization; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Writing – review & editing.

Juan Brea Iglesias: Conceptualization; Methodology; Supervision; Visualization; Writing – original draft.

Iria de la Osa Subtil: Conceptualization; Data curation; Formal analysis; Methodology; Software; Validation; Writing – original draft.

Ana Barrón: Conceptualization; Investigation; Methodology; Supervision; Validation; Visualization; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The dataset generated and analysed during the study is stored in a secure, localized database but is available from the corresponding author in an anonymous format upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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