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Correlation between Oral Mucosal Changes and Intestinal Histopathology in Inflammatory Bowel Disease Patients: Impact of Clinical Activity and Psychosocial Stress

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Abstract: IBD (inflammatory bowel disease), which is a combination of ulcerative colitis and Crohn's disease, is a chronic inflammatory disease that has substantial effects outside the intestines. Since changes in the oral mucosa correspond to the clinical manifestation of intestinal inflammation, changes in the oral mucosa of patients with IBD are common. The aim of the study was to establish how the clinical and psychosocial level of stress interacts with the clinical disease level of activity, as well as the variation in the intestinal and oral mucosal histological severity of the IBD patients. 177 participants with IBD were recruited (63 with Crohn disease, and 44 with ulcerative colitis). All patient data were collected between June 2024 and June 2025 at different hospitals in Iraq. Clinical disease activity was measured using the Harvey-Bradshaw Index (in Crohn victims) and the Mayo Score (in ulcerative colitis victims). The mucosal changes were identified and categorized with the help of oral examination and were classified in terms of the specific lesion. Lintel histology was assessed under three variables, namely mild, moderate, and severe inflammation. The psychosocial levels of stress were measured with the help of the Perceived Stress Scale (PSS). There was also a considerable difference between the presence of oral lesions and the current clinical disease ($p<0.001$) as well as moderate to severe intestinal inflammation ($p=0.003$). The oral lesions acquired by the patient were dose-dependent, and more oral lesions would be acquired when the patient was under a lot of stress (73.1%). A satisfactory clinical outcome to assess the condition of the disease can be the lesions in the IBD mucosa of the mouth that can be a powerful indicator of the severity of the intestinal histology and clinical activity. Psychosocial stress, which is a complication of the oral symptoms, also indicates the degree of whole-person care which influences the psychological well-being.

Keywords: Inflammatory Bowel Disease, Variations Of Oral Mucosal, Clinical Activity Pss Outcomes, And Risk Factors.

Introduction

Inflammatory bowel disease (IBD) refers to a chronic, relapsing-remitting disorder, mostly including Crohn's disease (CD) and ulcerative colitis (UC), and is recognized by inflammation of the gastrointestinal tract (1, 2). It has a complex interaction between genetic, immunological, microbial, and environmental factors leading to chronic mucosal intestinal damage (3). Though the main pathological process takes place in the bowels, there are also extraintestinal manifestations (EIMs), which often accompany IBD and play a major role in terms of morbidity and poor quality of life (4). Oral mucosal changes are one of these and are an indication of systemic involvement outside of the gut, and one of the first signs which appear (5).

Moreover, IBD patients have a range of oral lesions, which include aphthous ulcers, stomatitis angulare, mucosal erythema, and cheilitis (6). These alterations not only deteriorate the functions of the mouth, but they can also be evidence of underlying disease activity and inflammation in the body as a whole (7). The most common ones are crypt architectural distortion, mucosal ulceration, and inflammatory cell infiltration, which correlate with clinical activity indices (8).

Moreover, psychosocial stress is also noted to be a more and more modifiable factor that affects the onset of IBD as well as its exacerbations (9). Immune response changes, gut permeability changes, and changes in the hypothalamic-pituitary-adrenal (HPA) axis, which could increase mucosal inflammation, are some of the mechanisms related to stress (10, 11). Additionally, oral health may be affected by psychosocial stress that affects the mucosal immunity and promotes lesions (12). According to a cross – sectional study, we assessed the association between oral mucosal changes and intestinal histopathology in patients who were diagnosed with inflammatory bowel disease.

Materials and Methods

The Department of Gastroenterology, as well as Oral Medicine, conducted a cross-sectional research at several hospitals in Iraq between June 2024 and June 2025. The study's primary goal was to investigate the association between intestinal histological severity and oral mucosal change in people who have inflammatory bowel disease (IBD) and assess how clinical disease activity, along with psychosocial stress, affected this relationship.

According to the European Crohn's and Colitis Organization (ECCO) criteria, 107 adult patients (age 20 and older) with a confirmed diagnosis in both Crohn's Disease (CD) and Ulcerative Colitis (UC) were progressively enrolled in the outpatient Gastroenterology Clinic.

Exclusion criteria consisted of 1) having other systemic autoimmune or dermatological diseases known to cause oral lesion (Behccet disease, lupus erythematosus); 2) actively infected in the mouth (fungi, viruses, bacteria); 3) having oral surgery or trauma (within in 4 weeks); 4) being on medication that causes oral lesions (NSAIDs, chemotherapeutic agent); and 5) pregnant or lactating. The demographic and clinical information, nature of IBD, years of disease duration, and smoking were obtained with the help of a structured questionnaire and medical records review.

Validated indices were used in measuring disease activity, i.e., the Harvey-Bradshaw Index (HBI) of CD and the Mayo Score of UC. The oral examination was conducted in detail by an oral medicine specialist who is trained, but not aware of the histopathology of the intestinal sectors of the patient and their clinical activity scores. Oral lesions were also recorded descriptively, according to type (e.g., aphthous ulcers, angular stomatitis, erythematous mucosa, and cheilitis) and the presence/absence.

Also, psychosocial stress has been assessed with the Perceived Stress Scale (PSS-10), a 10-item self-report instrument that is considered to measure the levels to which a situation in a life is perceived to be a source of stress in the previous month. The total scores were classified into low (13 or less), moderate (14-26), and high (27 or more).

In addition, the intestinal biopsy specimen was assessed histopathologically on the biopsy collected during colonoscopy as a component of the routine clinical care within the three months following the oral examination. The severity of inflammation in the most prolific biopsy was determined on a semi-quantitative scale as mild, moderate, or severe, which included previously established criteria of architectural distortion, density of inflammatory infiltrate, crypt abscesses, and ulceration.

The SPSS software was used to carry out data analysis; that is, version 24.0. The descriptive statistics have been offered in the form of means with standard deviation of the continuous variables and in the form of frequencies (percentages) of the categorical variables. The results were in odds ratios (OR) and 95% confidence intervals (CI). The use of a two-tailed p-value below 0.05 was considered to be significant.

Results

The most prevalent specific observation was that of aphthous ulcers (29.9%), which have been previously shown to be related to IBD. There was a very important positive correlation between the existence of oral lesions and the severity of the intestinal histopathology (p=0.003). The proportion of oral lesions proportion of patients grew progressively with the increase of the mild histopathology group by 25.6% and severe group by 56.0%. The oral manifestations could be a clinical measure of the severity of the underlying mucosal immune dysregulation, a common pathogenic mechanism, or a systemic inflammatory load, which is reflected at gastrointestinal and oral mucosal surfaces.

Table 1. Identifying clinical characteristics of 107 patients who were diagnosed with inflammatory bowel disease.

Characteristic	**N (%) / Mean ± SD**
Gender	
- Male	62 (57.9%)
- Female	45 (42.1%)
Age (years)	35.4 ± 12.6
Inflammatory bowel disease type	
- Crohn's Disease (CD)	63 (58.9%)
- Ulcerative Colitis (UC)	44 (41.1%)
Duration of Disease (years)	6.2 ± 4.3
Smoking Status	
- Current Smoker	30 (28.0%)
- Non-smoker	77 (72.0%)

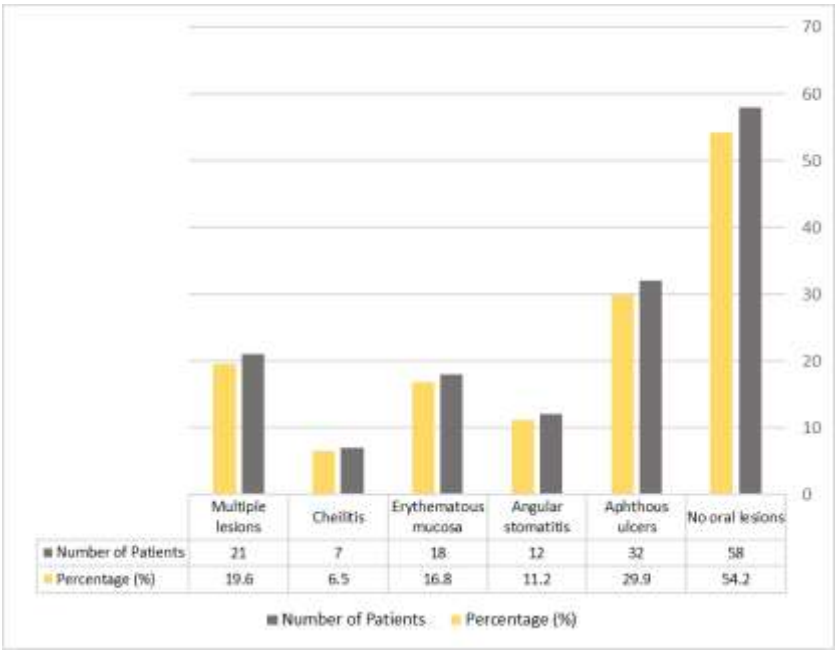

Figure 1. Categorizing the variations of the oral mucosa in patients who suffer from inflammatory bowel disease.

According to the study, there are significant variations according to the IBD phenotype. The oral cavity is one potential beginning or co-existing site since the phenomenon of CD is characterized through a transmural, along with discontinuous inflammation, which can happen in any part of the gastrointestinal system.

Table 2. Assessment scores of clinical disease activity using the Harvey-Bradshaw index for Crohn's disease patients and the Mayo Score for ulcerative colitis patients.

Disease Activity Level	***Number of Patients***	***Percentage (%)***
Remission (HBI ≤4 / Mayo ≤2)	50	46.7
Mild activity	33	30.8
Moderate activity	17	15.9
Severe activity	7	6.5

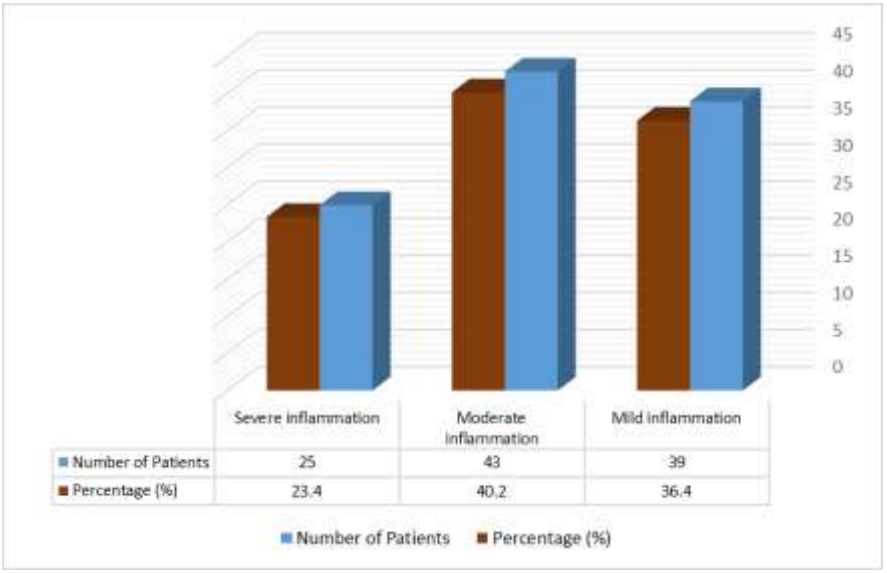

Figure 2. Distribution of the inflammation severity in intestinal histopathological findings.

Table 3. Distribution of the oral lesion presence in histopathological severity.

Oral Lesion Presence	Mild	Moderate	Severe	Total	p-value
Present	10 (25.6%)	19 (44.2%)	14 (56.0%)	43	0.003*
Absent	29 (74.4%)	24 (55.8%)	11 (44.0%)	64	

Table 4. Determining the outcomes of oral lesions which categorizing through inflammatory bowel disease type.

Oral Lesion	**CD (N=63)**	**UC (N=44)**	**p-value**
Present	38 (60.3%)	15 (34.1%)	0.009
Absent	25 (39.7%)	29 (65.9%)	

Moreover, psychosocial stress was found as a potent independent variable that was related to oral mucosal changes. The rate of oral lesions increased drastically with the PSS scores: 23.3, 47.1, and 73.1 in the low-stress group, moderate group, and high-stress group, respectively (p=0.001). Oral involvement was highly predicted by the clinical disease activity. Oral lesions were present in 68.3% of the active disease patients (mild to severe) and only 24.0% in those in remission (p<0.001).

Table 5. Assessment of psychosocial stress levels throughout the Perceived Stress Scale (PSS).

Stress Levels	Number of Patients	Percentage (%)
Low (PSS ≤13)	30	28.0
Moderate (PSS 14-26)	51	47.7
High (PSS ≥27)	26	24.3

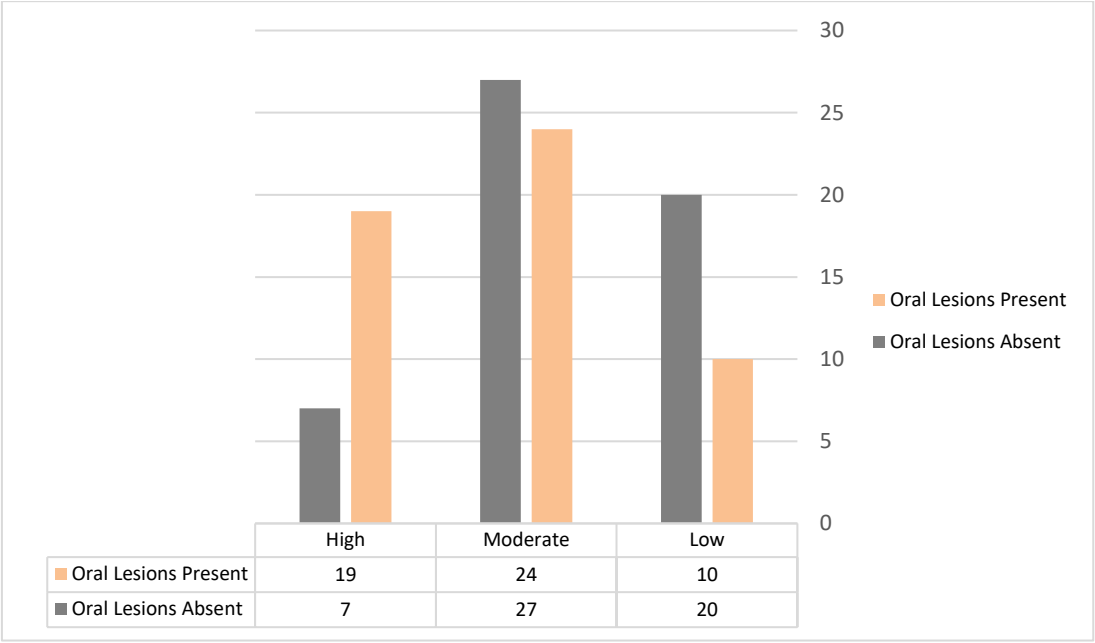

Figure 3. Evaluation of the psychological aspect by psychosocial stress grades in correlation with oral mucosal changes.

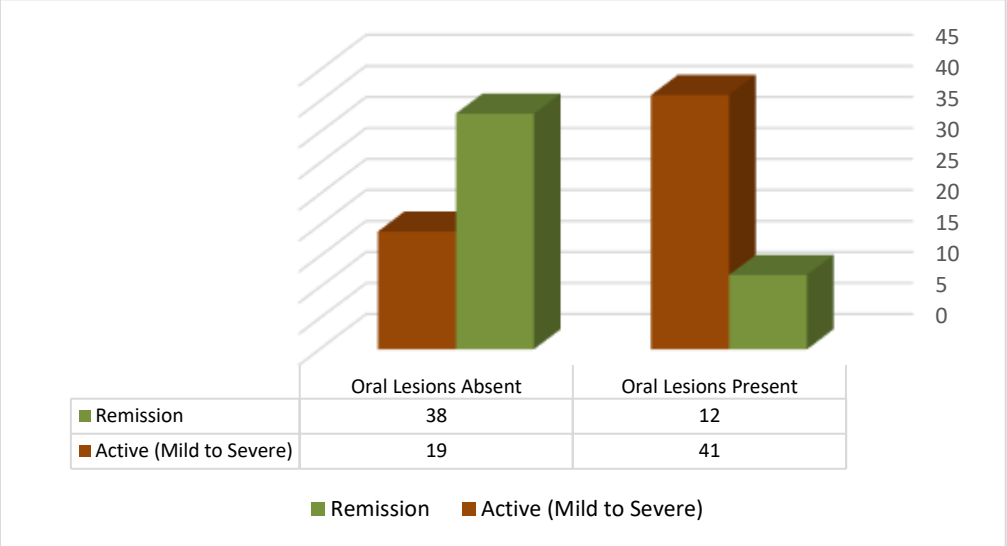

Figure 4. Classification the changes of the oral mucosa according to clinical disease activity.

These relationships were synthesized with the multivariate logistic regression model and three independent predictors of oral mucosal changes after controlling for the effects of confounders, which were moderate-to-severe intestinal histopathology (OR=3.5), high levels of psychosocial stress (OR=4.1), and active clinical disease (OR=3.8). These associations are quite strong with odds ratios of between 3.5 and 4.1. The insignificance of the factor of smoking (OR=1.2, p=0.676) in the model indicates that its influence is diluted when all these more powerful inflammatory and psychoneuroimmunological factors are considered.

Table 6. A multivariate logistic regression of predication risk factors in patients with inflammatory bowel disease.

Risk factors	Odds Ratio (OR)	95% Confidence Interval	p-value
Moderate to Severe Histopathology	3.5	1.6 – 7.6	0.002
High Psychosocial Stress	4.1	1.7 – 9.8	0.001
Active Clinical Disease	3.8	1.6 – 8.9	0.003
Smoking (current)	1.2	0.5 – 2.8	0.676

Discussion

The results of this research explain the importance of a significant association between oral mucosal changes and intestinal histopathological severity in patients with inflammatory bowel disease (IBD), which is supported by the impact of clinical disease activity and psychosocial stress. The oral mucosal lesions that were common in our cohort (45.8) are consistent with some of the literature in Japan (13) (10-50%), establishing the oral cavity as a common site of extra-intestinal involvement. The most frequently occurring lesion was the aphthous ulcer (29.9%), as the same study conducted in China (14) found them to be one of the hallmark oral manifestations of IBD. The important connection between oral lesions and more serious intestinal histopathology (p=0.003) is an important discovery. It confirms the hypothesis of the presence of a common immunopathological pathogenesis, in which the systemic inflammatory mediators or a common mucosal immune system maladjustment might both affect the intestinal and oral epithelium (15, 16). In addition, the more frequent occurrence of oral lesions in patients with Crohn's disease (CD) (60.3) relative to Ulcerative Colitis (UC) patients (34.1, p=0.009).

We found that there was a strong relationship, which is graded, between changes in the oral mucosa and clinical disease activity. The finding of the strong independent relation between high psychosocial

stress and the condition of oral lesion (p=0.001) is new and interesting. High psychosocial stress was found to be a strong predictor (OR=4.1) by the multivariate analysis, second only to histopathological severity. Psychological stress has deregulated the hypothalamic-pituitary-adrenal axis and the autonomic nervous system, which could have increased systemic inflammation and altered mucosal immunity and barrier function (17, 18, 19, 20).

These interrelationships are cemented by the multivariate logistic regression model, which determined moderate-severe intestinal histopathology, active clinical disease, and high psychosocial stress as important independent predictors of oral mucosal changes (21, 22). Our model is not significant compared to a French study (23), which showed smoking to be related to oral aphthae.

Conclusion

To sum up, the findings strongly prove that in IBD patients, changes in the oral mucosa are strongly correlated with the reduction of intestinal histopathology severity. This association is much stronger in CD, and both clinical disease activity and perceived psychosocial stress, in particular, substantially alter it. These results recommend a comprehensive management strategy in IBD, which involves regular oral check-ups and stress evaluation since oral manifestations can be of significant benefit in measuring the burden of the intestinal disease, in addition to the general psychobiological condition of the patient.

References

1. Li, C. J., Wang, Y. K., Zhang, S. M., Ren, M. D., & He, S. X. (2023). Global burden of inflammatory bowel disease 1990-2019: A systematic examination of the disease burden and twenty-year forecast. World Journal of Gastroenterology, 29 (42), 5751.
2. Aniwan, S., Santiago, P., Loftus Jr, E. V., & Park, S. H. (2022). The epidemiology of inflammatory bowel disease in Asia and Asian immigrants to Western countries. United European gastroenterology journal, 10 (10), 1063-1076.
3. Torres J, Bonovas S, Doherty G, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. J. Crohn's Colitis. 2019;2020:4–22.
4. Dignass A, Lindsay JO, Sturm A, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part 2: Current management. J. Crohn's Colitis. 2012;6:991–1030.
5. Sandborn WJ, Feagan BG, Loftus E V., et al. Efficacy and Safety of Upadacitinib in a Randomized Trial of Patients With Crohn's Disease. Gastroenterology. 2020;158:2123–2138.
6. Lankarani, K. B., Sivandzadeh, G. R., & Hassanpour, S. (2013). Oral manifestation in inflammatory bowel disease: a review. World journal of gastroenterology: WJG, 19 (46), 8571.
7. Besharat, S., Amiriani, T., Roshandel, G., Besharat, M., Semnani, S., & Kamkar, M. (2012). Depressive mood and disease activity in inflammatory bowel disease. Arab Journal of Gastroenterology, 13 (3), 136-138.
8. Trindade, I. A., & Sirois, F. M. (2021). The prospective effects of self-compassion on depressive symptoms, anxiety, and stress: a study in inflammatory bowel disease. Journal of Psychosomatic Research, 146, 110429.
9. Fairbrass, K. M., Gracie, D. J., & Ford, A. C. (2022). Relative contribution of disease activity and psychological health to prognosis of inflammatory bowel disease during 6.5 years of longitudinal follow-up. Gastroenterology, 163 (1), 190-203.

10. Colombel JF, Reinisch W, Mantzaris GJ, et al. Randomised clinical trial: Deep remission in biologic and immunomodulator naïve patients with Crohn's disease - A SONIC post hoc analysis. Aliment. Pharmacol. Ther. 2015;41:734–746.

11. Narang, V., Kaur, R., Garg, B., Mahajan, R., Midha, V., Sood, N., & Sood, A. (2018). Association of endoscopic and histological remission with clinical course in patients of ulcerative colitis. Intestinal research, 16 (1), 55.

12. Geboes, K., Riddell, R., Öst, A., Jensfelt, B., Persson, T., & Löfberg, R. (2000). A reproducible grading scale for histological assessment of inflammation in ulcerative colitis. Gut, 47 (3), 404-409.

13. Saxena, A.; Fletcher, E.; Larsen, B.; Baliga, M.S.; Durstine, J.L.; Fayad, R. Effect of exercise on chemically-induced colitis in adiponectin-deficient mice. J. Inflamm. 2012, 9, 30.

14. Parragi L, Fournier N, Zeitz J, et al. Colectomy Rates in Ulcerative Colitis are Low and Decreasing: 10-Year Follow-up Data From the Swiss IBD Cohort Study. J. Crohn's Colitis. 2018;12:811–818.

15. Keegan, D., Byrne, K., Cullen, G., Doherty, G. A., Dooley, B., & Mulcahy, H. E. (2015). The stressometer: A simple, valid, and responsive measure of psychological stress in inflammatory bowel disease patients. Journal of Crohn's and Colitis, 9 (10), 881-885.

16. Marrie, R. A., Graff, L. A., Fisk, J. D., Patten, S. B., & Bernstein, C. N. (2021). The relationship between symptoms of depression and anxiety and disease activity in IBD over time. Inflammatory bowel diseases, 27 (8), 1285-1293.

17. Laranjeira, N., Fonseca, J., Meira, T., Freitas, J., Valido, S., & Leitão, J. (2015). Oral mucosa lesions and oral symptoms in inflammatory bowel disease patients. Arquivos de gastroenterologia, 52 (2), 105-110.

18. Alatab S, Sepanlou SG, Ikuta K, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol. Hepatol. 2020;5:17–30.

19. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet. 2017;390:2769–2778.

20. Knowles SR, Graff LA, Wilding H, et al. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses - Part I. Inflamm. Bowel Dis. 2018;24:742–751.

21. Aldini, R.; Micucci, M.; Cevenini, M.; Fato, R.; Bergamini, C.; Nanni, C.; Cont, M.; Camborata, C.; Spinozzi, S.; Montagnani, M.; et al. Anti-inflammatory effect of phytosterols in experimental murine colitis model: Prevention, induction, remission study. PLoS ONE 2014, 9, e108112.

22. Valk ME Van Der, Mangen MJJ, Leenders M, et al. Healthcare costs of inflammatory bowel disease have shifted from hospitalisation and surgery towards anti-TNFα therapy: Results from the COIN study. Gut. 2014;63:72–79.

23. Mirkov MU, Verstockt B, Cleynen I. Genetics of inflammatory bowel disease: beyond NOD2. Lancet Gastroenterol. Hepatol. 2017;2:224–234.