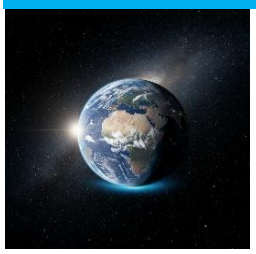
NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ



Quality in Sport. eISSN 2450-3118.

Journal Home Page
https://apcz.umk.pl/QS/index

GRABOWSKI, Krzysztof, MIODUSZEWSKA, Joanna, ROT, Paweł, PONIEWOZIK, Piotr, DZIUBA, Natalia, SIM, Aleksandra, PERNAL, Maja, ROGUSKA, Zofia, ZUZAK, Andrzej Paweł and PONIEWOZIK, Paweł. The Impact of Smoking on Inflammatory Bowel Disease: A Literature Review. Quality in Sport. 2026;54:70360. eISSN 2450-3118. https://doi.org/10.12775/QS.2026.54.70360

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 l.p. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 29.03.2026. Revised: 30.03.2026. Accepted: 30.03.2026. Published: 10.04.2026.

The Impact of Smoking on Inflammatory Bowel Disease: A Literature Review

Krzysztof Grabowski

Dr. Tytus Chałubiński Radom Specialist Hospital, Adolfa Tochtermana 1 Street, 26-610 Radom, Poland

krzysztofgrabowski444@gmail.com

https://orcid.org/0009-0004-1482-7188

Joanna Mioduszewska

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

Asia.mioduszewska01@gmail.com

https://orcid.org/0009-0001-1024-1217

Paweł Rot

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

pawel_rot@outlook.com

https://orcid.org/0009-0004-4140-4463

Piotr Poniewozik

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

piotr.poniewozik01@gmail.com

https://orcid.org/0009-0001-6350-4981

Natalia Dziuba

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

nat.dziuba@gmail.com

https://orcid.org/0009-0002-4719-9208

Aleksandra Sim

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

misardnaskela@gmail.com

https://orcid.org/0009-0001-6475-4595

Maja Pernal

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

pernalmaja@gmail.com

https://orcid.org/0009-0003-9616-2361

Zofia Roguska

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

zosia.roguska@gmail.com

https://orcid.org/0009-0007-8588-2784

Andrzej Pawel Zuzak

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

andrzejzuzak1@gmail.com

https://orcid.org/0009-0008-6578-1457

Paweł Poniewozik

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

poniewozikpawel01@gmail.com

https://orcid.org/0009-0006-2057-2219

Abstract

Background. Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated condition with a rapidly rising global prevalence. While genetic factors are significant, environmental modifiers—specifically tobacco use—play a critical role in disease onset and progression.

Background. Smoking cigarettes is a highly prevalent habit worldwide that has a massive impact on the human immune system, significantly influencing the onset and progression of various inflammatory conditions, including inflammatory bowel disease.

Background. Cigarette smoking is one of the most common environmental exposures globally, significantly affecting the gut immune system and serving as a major modifying factor in chronic conditions such as inflammatory bowel disease.

Aim. This literature review aims to synthesize current evidence regarding the impact of smoking on the development and clinical trajectory of CD and UC.

Methodology. A comprehensive review was conducted using the PubMed and Google Scholar databases, focusing on peer-reviewed literature and consensus guidelines published between 2021 and 2026.

Results. The literature confirms that smoking significantly increases the risk and severity of CD. In contrast, observational data traditionally suggest a protective effect of current smoking on UC onset, a phenomenon termed the "smoking paradox". However, recent genetic investigations using Mendelian randomization challenge the causality of this protection, suggesting it may stem from residual confounding.

Conclusions. Despite the observational paradox in UC, the systemic harms and treatment interference associated with tobacco use necessitate universal cessation strategies. This review provides a clinical roadmap for managing smoking status in the modern era of IBD care.

Keywords. IBD; Crohn's disease; ulcerative colitis; smoking; nicotine; environmental factors.

1. Introduction

Inflammatory bowel disease (IBD), encompassing Crohn’s disease and ulcerative colitis, is an immune-mediated condition that has emerged as a critical global health issue at the turn of the 21st century [1]. The prevalence of IBD now exceeds 0.5% in early industrialized regions of North America, Europe, and Oceania, with projections suggesting a rise to 1% of the population in several countries by 2030 [1]. While genetic susceptibility is well-documented, heritability explains only a fraction of cases, highlighting the imperative role of environmental exposures in disease pathogenesis [1]. This environmental influence is further underscored by the rising incidence in newly industrialized regions across Asia and Latin America [2].

Tobacco smoking remains the most frequently identified environmental modifier in this context, characterized by a unique "smoking paradox" that distinguishes the two primary IBD phenotypes [3]. This clinical dogma posits that smoking exerts diametrically opposing effects: it nearly doubles the risk of developing Crohn’s disease and exacerbates its clinical course, whereas current smoking is observationally associated with a reduced risk of ulcerative colitis [3]. However, whether these associations reflect true causality or are merely the result of residual confounding and reverse causation remains a subject of intense debate in contemporary epidemiology [3]. Recent genetic analyses using Mendelian randomization have failed to find

evidence supporting a protective causal link for ulcerative colitis, necessitating a re-evaluation of established clinical perspectives [3].

As the global incidence of IBD continues to grow and patient management increasingly incorporates personalized lifestyle modifications, understanding the contemporary evidence regarding tobacco use is paramount for quality clinical care [2]. Identifying the mechanisms through which tobacco constituents interact with the gut microbiome and immune system is essential for developing preventative health strategies [1]. Therefore, the present literature review aims to evaluate the current literature regarding the impact of smoking on the development and clinical course of inflammatory bowel disease.

2. Methodology

A narrative review of the literature was conducted using the PubMed and Google Scholar databases to identify relevant articles published between 2021 and 2026. The search strategy utilized specific keywords including "smoking", "IBD", "ulcerative colitis", and "Crohn's disease". Articles were selected based on their relevance to the environmental and clinical impact of tobacco and nicotine products on gastrointestinal inflammation, as well as their focus on recent genetic and epidemiological advancements. To ensure a comprehensive synthesis, the reference lists of the selected studies and major recent consensus statements from international organizations were manually scanned to identify further significant data. This approach allowed for the inclusion of high-quality meta-analyses and prospective cohort studies that reflect the current state of IBD research.

3. Smoking and the Risk of Developing IBD

Beyond active tobacco use, passive smoking has emerged as a significant environmental risk factor for the incidence of inflammatory bowel disease (IBD). Approximately 37% of the global population is exposed to secondhand smoke, which contains many of the same toxic compounds—such as nicotine, nitrosamines, and heavy metals—found in mainstream smoke [4]. Systematic reviews indicate that passive smoking exposure during childhood is associated with a 1.19-fold increase in the odds of developing Crohn’s disease (CD), while exposure in utero via maternal smoking increases the risk to 1.27 [4]. These findings emphasize that children are particularly vulnerable to environmental tobacco smoke, as prolonged involuntary exposure can compromise intestinal epithelial barrier function and alter early microbiome composition [4].

The impact of early life exposure is further supported by meta-analyses focusing on pediatric populations, which show that passive smoking is a novel risk factor specifically associated with pediatric IBD (PIBD) development [5]. Maternal smoking during pregnancy has been identified as a significant driver of pediatric CD risk, with odds ratios reaching as high as 4.4 in some studies [5]. Furthermore, prospective Scandinavian birth cohorts have demonstrated that a higher intensity of maternal smoking (averaging ≥6 cigarettes per day) results in an adjusted hazard ratio of 1.60 for offspring IBD, while exposure during the first year of life remains a critical window for later disease manifestation [6]. These data suggest that the long-term consequences of early smoke exposure are more deleterious than previously recognized, potentially priming the immune system for chronic inflammation [6].

The relationship between smoking and disease onset is also modulated by genetic predisposition. Population-based cohort studies have revealed a significant interaction between smoking status and family history in the development of ulcerative colitis (UC) [7]. While familial risk alone remains a strong predictor for developing the condition, the protective association of current smoking appears more pronounced in individuals with a positive family history, whereas the harmful impact of former smoking is significantly amplified in this genetically predisposed group [7]. This suggests that smoking and genetic variants have an interactive relationship that dictates the overall clinical risk profile [7].

4. The "Smoking Paradox": Ulcerative Colitis vs. Crohn's Disease

The epidemiological relationship between smoking and ulcerative colitis is defined by a historical paradox wherein tobacco use is observationally associated with a reduced risk of disease onset. Meta-analyses of case-control studies suggest that active smokers have nearly half the likelihood of developing UC than non-smokers [8]. This phenomenon is often attributed to the anti-inflammatory properties of nicotine, which may modulate cytokine production and enhance the colonic mucus layer [8]. However, this "protective" effect is not uniform across all populations; recent evidence from Japan suggests that a history of ever smoking may actually be associated with an increased risk of UC in Asian cohorts, highlighting how ethnicity and geography may modify the impact of tobacco exposure [9].

A critical and highly consistent finding across the literature is the specific risk associated with smoking cessation. The phenomenon of "former smokers" developing UC after quitting is a cornerstone of the smoking paradox. Individuals who have ceased smoking face a significantly

higher risk of UC onset compared to both current smokers and those who have never smoked [8]. In Japanese populations, former smokers demonstrated a 2.4-fold increase in UC risk, with a positive dose-response relationship observed between cumulative pack-years and disease incidence [9]. Furthermore, passive smoking at home has been significantly associated with an increased risk of UC in non-smokers, suggesting that even lower-dose toxic exposure may be pathogenic in some contexts [9].

The timing of tobacco exposure is also a decisive factor in determining subsequent UC risk. Recent research indicates that the risk of UC in ex-smokers is heavily dependent on the age at which they initiated smoking [10]. Individuals who began smoking before the age of 20 and later ceased the habit face the highest risk of developing UC, even after adjusting for the total amount smoked [10]. While a modest protective effect of current smoking was observed in those who started later in life, the overall rate of UC diagnosis remains higher for both current and former smokers than for non-smokers [10]. This underscores the danger of adolescent smoking experimentation, as the resulting immune dysregulation following cessation can lead to a significant long-term risk of inflammatory bowel disease [10].

5. Biological Mechanisms: Immune System and Microbiome

The biological impact of nicotine on inflammatory bowel disease is characterized by a complex dualism, where its effects are dictated by the disease phenotype and the specific nicotinic acetylcholine receptor (nAChR) signaling pathways involved. Nicotine acts as an anti-inflammatory monomer in ulcerative colitis (UC) by stimulating α7nAChR, which activates the cholinergic anti-inflammatory pathway to inhibit the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 in macrophages [11]. Furthermore, in UC models, nicotine administration via transdermal or oral routes has been shown to induce protective autophagy, maintain intestinal barrier integrity by regulating occludin and ZO-1 expression, and suppress the recruitment of leukocytes to the inflamed colonic microvessels [11]. Conversely, in Crohn's disease (CD) models such as TNBS-induced colitis, high doses of nicotine can exacerbate mucosal necrosis, crypt damage, and lymphocytic infiltration [11]. This detrimental effect is often associated with the modulation of TLR2/MyD88 signaling and the worsening of inflammation in the presence of intracellular pathogens [11].

A central mechanistic bridge between nicotine exposure and reduced colonic inflammation in UC is the inhibition of the NLRP3 inflammasome. The assembly of this multiprotein

complex—comprising NLRP3, ASC, and pro-caspase-1—is a critical step in the innate immune response, leading to the proteolytic activation of caspase-1 and the subsequent secretion of mature IL-1β [12]. In vitro and in vivo investigations demonstrate that nicotine primarily impedes the assembly of the NLRP3 inflammasome, thereby suppressing the "cytokine storm" within the intestinal mucosa [12]. By downregulating NLRP3 expression and inhibiting the formation of the ASC-speck, nicotine effectively mitigates the immune-mediated tissue damage and hematochezia typically observed in acute colitis [12].

The divergent clinical outcomes between CD and UC are further explained by the regulation of G protein-coupled receptor 15 (GPR15), a critical mucosal homing receptor that directs T cells to the large intestine. Cigarette smoke exposure selectively upregulates GPR15 expression on T cells, but the resulting immune response is context-dependent: in CD models, smoke-induced GPR15 facilitates the homing of pathogenic Th17 cells, which exacerbates inflammation via STAT3-dependent pathways; in UC models, however, it promotes the homing of regulatory T (Treg) cells, which secrete immunosuppressive cytokines like IL-10 and TGF-β to aid mucosal healing [13]. This environmental signaling is integrated through epigenetic modifications, specifically the smoking-induced hypomethylation of the GPR15 locus and other critical genes [13]. Genome-wide methylation analyses have identified that DNA methylation alterations within DNMT3A, AHRR, and LTA/TNF loci mediate the pathogenic effects of smoking [14]. Smoking-related transcriptional changes in CD are specifically associated with Paneth cell dysfunction, as evidenced by the hypomethylation of IER3 and the upregulation of DEFA5 and DEFA6 in smokers, which impairs antimicrobial defense [15].

Cigarette smoking also exerts profound effects on the composition and diversity of the gut microbiota, which in turn modulates the intestinal immune milieu. In UC models, nicotine administration has been shown to restore microbial diversity and enhance the abundance of beneficial taxa such as *Akkermansia muciniphila* and *Lactobacillus*, which are typically depleted during active disease [12]. Simultaneously, nicotine reduces the prevalence of potentially pathogenic bacteria, such as *Sphingobacteriaceae*, thereby aiding the reinstatement of intestinal homeostasis [12]. The interaction between tobacco constituents and the gut microbiome triggers metabolic shifts that influence the balance between Th17-driven inflammation and Treg-mediated tolerance [13].

Recent evidence comparing combustible cigarettes (CCs) to Electronic Nicotine Delivery Systems (ENDS) highlights distinct molecular and cellular mechanisms of immune modulation.

ENDS-sourced aerosols, which deliver nicotine without the high concentrations of tar and carbon monoxide found in CCs, are associated with the expansion of immunosuppressive cells, including tolerogenic CD11c+ dendritic cells, M2 macrophages, and FoxP3-expressing Tregs [16]. In contrast, CCs reduce the number of inflammatory Th1 and Th17 cells, but they also introduce toxic constituents—such as polycyclic aromatic hydrocarbons, benzene, and heavy metals like cadmium—which impair DNA synthesis, disrupt calcium homeostasis, and induce oxidative stress-mediated apoptosis in immune cells [16]. Consequently, while both delivery systems may paradoxically attenuate ongoing UC inflammation, ENDS appear to promote a more specific anti-inflammatory microenvironment through IL-10 and TGF-β production, whereas CCs primarily act through broad chemical immunosuppression and cellular toxicity [16].

6. Clinical Outcomes, Complications, and Surgery

The clinical impact of smoking on inflammatory bowel disease (IBD) is characterized by a stark divergence in hospital outcomes and disease-specific morbidity. Large-scale cohort studies in Asian populations confirm that smoking prevalence is significantly lower in patients with ulcerative colitis (UC) compared to controls, supporting a protective observational effect on disease development [17]. However, once the disease is established, the "protective" nature of tobacco is highly selective; while UC smokers may experience fewer total hospital admissions, they face significantly higher rates of new cancer development and overall mortality compared to non-smokers [17]. In contrast, smoking in Crohn’s disease (CD) is linked to more aggressive phenotypes, including higher rates of stricturing and penetrating disease, which ultimately leads to an increased risk of surgery [17]. Modern nationwide readmission data further highlight this phenotypic split: nicotine dependence is independently predictive of a 1.27-fold increase in 90-day readmissions for CD patients, whereas it appears protective against readmission in the UC population [18].

The relationship between tobacco use and advanced colorectal neoplasia (aCRN) remains a point of significant clinical debate, particularly regarding the dose-response effect. A comprehensive meta-analysis of 164 studies identified smoking as a protective factor against aCRN in univariable analysis for UC patients, with a pooled odds ratio of 0.66; however, this association failed to reach significance in multivariable models [19]. This suggests that simple "ever vs. never" smoking status may be an insufficient metric for risk stratification. Recent evidence indicates that the lifetime tobacco burden, measured in pack-years, is a more reliable

predictor of oncogenic risk [20]. Prospective data show that while smoking status alone may not influence recurrent neoplasia, an increase in cumulative pack-years is significantly associated with a higher risk of colorectal neoplasia across the IBD spectrum, even after adjusting for endoscopic inflammation [20]. Consequently, clinicians are increasingly urged to advise smoking cessation for all IBD patients to mitigate the long-term risk of malignancy [20].

In the context of Crohn's disease, active smoking is a primary driver of poor surgical outcomes and rapid disease recurrence. Patients who smoke at the time of abdominal surgery face markedly higher rates of 90-day postoperative complications, with a 2.17-fold increased risk for overall complications and a 3.20-fold risk for severe complications, such as anastomotic leaks and intra-abdominal collections [21]. Furthermore, smoking is associated with prolonged hospital stays and a trend toward increased intensive care requirements [21]. Beyond the immediate perioperative period, tobacco use remains the most consistent modifiable risk factor for endoscopic recurrence after ileocolic resection [22]. Postoperative smoking is independently associated with an odds ratio of 2.78 for early recurrence (Rutgeerts score ≥i2), underscoring the necessity of integrating cessation programs into surgical management plans [22].

For patients with ulcerative colitis, the surgical landscape is dominated by restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA). Although smoking is observationally protective against UC onset, it acts as a significant deterrent to successful surgical recovery. In state-level registry analyses, approximately 37% of UC patients experience complications within 30 days of the final stage of IPAA surgery, with ileus, abscesses, and leaks being the most common adverse events [23]. Current or former smokers have a nearly three-fold increased risk of experiencing these 30-day complications compared to never-smokers [23]. This detrimental effect is consistent across various stages of pouch surgery, suggesting that the systemic harms of tobacco exposure—such as impaired wound healing and microvascular dysfunction—outweigh any localized anti-inflammatory effects in the perioperative setting [23]. Therefore, uniform smoking cessation counseling is essential for all UC patients undergoing restorative surgery to improve clinical function and long-term pouch survival [23].

7. Impact on Medical Therapy

Insufficient efficacy of classical therapies has driven the rapid development of targeted and biological treatments for IBD, including novel Janus kinase inhibitors [24]. However, active

smoking significantly complicates this medical management by interfering with both the efficacy and safety of these advanced therapies. Prospective cohort data indicate that smokers initiating biologic treatment experience notably lower clinical response rates compared to their non-smoking counterparts, with successful responses occurring in only 43% of smokers versus 61% of the non-smoking population after a 14-to-16-week induction period [25]. This reduction in efficacy is accompanied by a worsening of the physical component of health-related quality of life, which appears to deteriorate more significantly in active smokers during the initial months of therapy compared to non-smokers [25].

Beyond impaired clinical response, tobacco use is a potent predictor for the development of treatment-related complications. Active smokers receiving biologic agents demonstrate a significantly higher prevalence of adverse events, particularly dermatological manifestations such as skin rashes across both IBD subtypes [26]. Furthermore, arthralgias appear specifically associated with active smoking in the Crohn's disease population, while ex-smokers and non-smokers report these side effects less frequently [26]. These findings suggest that the toxic constituents of tobacco smoke may enhance immune-mediated side effects, potentially leading to drug discontinuation or poor compliance [26]. Integrating smoking cessation counseling before initiating biological therapy is therefore essential to optimize the therapeutic index of these critical medications.

8. Smoking Cessation and Patient Behaviors

Despite the severe clinical risks associated with tobacco use, a substantial proportion of patients fail to alter their smoking behavior following an IBD diagnosis. Longitudinal cohort studies demonstrate that 70% of patients with Crohn’s disease and 44% of those with ulcerative colitis who are active smokers at the time of diagnosis continue to smoke post-diagnosis [27]. This persistence is particularly concerning given that smoking cessation around the time of diagnosis is associated with a dramatic reduction in all-cause mortality, with quitters experiencing a 59% to 72% lower hazard of death compared to those who continue smoking [27].

Maintaining long-term abstinence remains a significant challenge, especially for the Crohn’s disease population. Relapse rates are approximately 46% in CD patients, nearly double the 24% relapse rate observed in patients with ulcerative colitis [28]. Physiological nicotine dependence is the primary independent factor associated with relapse, highlighting the need for robust behavioral support [28]. While approximately 90% of patients attempt to quit smoking on their

own accord, evidence suggests that structured motivational interventions can improve success rates. Strategies such as telephone-based counseling using the "5 R's" model—focusing on relevance, risks, rewards, roadblocks, and repetition—have demonstrated a higher trend toward successful cessation in CD patients compared to standard care [29]. Given that patients with active disease and those living with other smokers are at higher risk of relapse, clinicians must adopt a proactive, multidisciplinary approach to behavioral modification [28,29].

9. Conclusions

In conclusion, the impact of smoking on inflammatory bowel disease is characterized by a complex biological divergence between Crohn's disease and ulcerative colitis. However, when examining the totality of clinical evidence, the observational "protective" paradox noted in ulcerative colitis onset is vastly outweighed by the systemic harms of tobacco exposure. Smoking is unequivocally linked to more aggressive disease phenotypes, an increased requirement for surgical intervention, and higher rates of postoperative complications. Moreover, active tobacco use significantly impairs the clinical efficacy of biological therapies, elevates the risk of treatment-related adverse events, and is associated with increased all-cause mortality. These findings emphasize that smoking cessation is not merely a lifestyle recommendation but a clinical priority that should be integrated into the standard care of all IBD patients. Addressing nicotine dependence through multidisciplinary support and motivational interventions is essential to improve long-term therapeutic outcomes and reduce the global burden of the disease.

Disclosure:

Author Contribution Statement

Conceptualization: Krzysztof Grabowski, Joanna Mioduszewska, Paweł Rot, Piotr Poniewozik;

Methodology: Krzysztof Grabowski, Natalia Dziuba, Joanna Mioduszewska

Formalanalysis: Aleksandra Sim, Piotr Poniewozik

Investigation: Natalia Dziuba, Joanna Mioduszewska, Paweł Rot, Piotr Poniewozik, Aleksandra Sim, Maja Pernal, Zofia Roguska, Krzysztof Grabowski, Andrzej Paweł Zuzak, Paweł Poniewozik

Resources: Krzysztof Grabowski

Data curation: Krzysztof Grabowski, Natalia Dziuba, Paweł Poniewozik, Paweł Rot

Writing – rough preparation: Krzysztof Grabowski, Natalia Dziuba, Joanna Mioduszewska, Paweł Rot, Piotr Poniewozik, Aleksandra Sim, Maja Pernal, Zofia Roguska, Andrzej Paweł Zuzak, Paweł Poniewozik

Writing – review and editing: Krzysztof Grabowski, Paweł Rot, Piotr Poniewoznik

Visualization: Natalia Dziuba, Joanna Mioduszewska
Supervision: Krzysztof Grabowski, Paweł Rot, Piotr Poniewoznik

Project administration: Krzysztof Grabowski

All authors have read and agreed with the published version of the manuscript.

Funding Statement

The authors did not receive special funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of Interest Statement

The authors declare no conflict of interest.

References:

1. Chhibba T, Gros B, King JA, Windsor JW, Gorospe J, Leibovitzh H, et al. Environmental risk factors of inflammatory bowel disease: toward a strategy of preventative health. J Crohns Colitis. 2025;19:jjaf042. https://doi.org/10.1093/ecco-jcc/jjaf042

2. Ananthakrishnan AN, Kaplan GG, Bernstein CN, Burke KE, Lochhead PJ, Sasson AN, et al. Lifestyle, behaviour, and environmental modification for the management of patients with inflammatory bowel diseases: an International Organization for Study of Inflammatory Bowel Diseases consensus. Lancet Gastroenterol Hepatol. 2022;7:666–78. https://doi.org/10.1016/S2468-1253(22)00021-8

3. Pedersen KM, Çolak Y, Vedel-Krogh S, Kobylecki CJ, Bojesen SE, Nordestgaard BG. Risk of ulcerative colitis and Crohn's disease in smokers lacks causal evidence. Eur J Epidemiol. 2022;37:735–45. https://doi.org/10.1007/s10654-021-00763-3

4. Mahajan A, Gupta B, Peterson A, Iyngkaran G, Valaydon Z. Passive smoking exposure and incidence and disease outcomes of inflammatory bowel disease: a systematic review and meta-analysis. Front Public Health. 2025;13:1670320. https://doi.org/10.3389/fpubh.2025.1670320

5. Thacker N, Duncanson K, Eslick GD, Dutt S, O'Loughlin EV, Hoedt EC, et al. Antibiotics, passive smoking, high socioeconomic status and sweetened foods contribute to the risk of paediatric inflammatory bowel disease: A systematic review with meta-analysis. J Pediatr Gastroenterol Nutr. 2024;79:610–21. https://doi.org/10.1002/jpn3.12303

6. Wetwittayakhlang P, Lakatos PL. Unravelling the Smoke Trail: Maternal Smoking, Childhood Exposure, and their Impact on Inflammatory Bowel Diseases. J Crohns Colitis. 2024;18:659–60. https://doi.org/10.1093/ecco-jcc/jjae032

7. Ahn HS, Swan H, Kazmi SZ, Kim YS, Hong G, Choi S, et al. The Impact of Smoking on Ulcerative Colitis and Interaction With Family History: A Population-Based Cohort Study. J Gastroenterol Hepatol. 2025;40:446–55. https://doi.org/10.1111/jgh.16834

8. Mi Y, Tan Y, Yu Y, An D, Mo R, Shi S, et al. Relationship between smoking status and ulcerative colitis: a meta-analysis based on a case-control study. Sci Rep. 2025;15:13329. https://doi.org/10.1038/s41598-025-97617-9

9. Nishikawa A, Tanaka K, Miyake Y, Nagata C, Furukawa S, Andoh A, et al. Active and passive smoking and risk of ulcerative colitis: A case-control study in Japan. J Gastroenterol Hepatol. 2022;37:653–9. https://doi.org/10.1111/jgh.15745

10. Jun YK, Kim B, Choi Y, Shin CM, Park YS, Kim N, et al. Smoking Experience before Adulthood Is Associated with an Increased Risk of Developing Ulcerative Colitis in Adult Ex-Smokers. Yonsei Med J. 2025;66:9–15. https://doi.org/10.3349/ymj.2023.0612

11. Zhang W, Lin H, Zou M, Yuan Q, Huang Z, Pan X, et al. Nicotine in Inflammatory Diseases: Anti-Inflammatory and Pro-Inflammatory Effects. Front Immunol. 2022;13:826889. https://doi.org/10.3389/fimmu.2022.826889

12. Zhang Y-X, Chi X-Q, Li M, Zhang W, Guan Y, Wu L-Q. Nicotine improves DSS-induced colitis by inhibiting NLRP3 and altering gut microbiota. J Asian Nat Prod Res. 2024;26:616–35. https://doi.org/10.1080/10286020.2024.2331773

13. Gao L, Zheng H, Zhao Q, Wang Y, He Y, Hou C, et al. GPR15 differentially regulates the effects of cigarette smoke exposure on Crohn's disease and ulcerative colitis. Signal Transduct Target Ther. 2025;10:306. https://doi.org/10.1038/s41392-025-02384-8

14. Zhang H, Kalla R, Chen J, Zhao J, Zhou X, Adams A, et al. Altered DNA methylation within DNMT3A, AHRR, LTA/TNF loci mediates the effect of smoking on inflammatory bowel disease. Nat Commun. 2024;15:595. https://doi.org/10.1038/s41467-024-44841-y

15. Yan Ang Q, Plichta D, Kim S, Hyun-A Kim I, Gregory S, Xia Y, et al. Differential Impact of Smoking on Methylome and Transcriptome in Crohn's Disease and Ulcerative Colitis. Inflamm Bowel Dis. 2024;30:981–91. https://doi.org/10.1093/ibd/izad268

16. Kastratovic N, Markovic V, Arsenijevic A, Volarevic A, Zdravkovic N, Zdravkovic M, et al. The Effects of Combustible Cigarettes and Electronic Nicotine Delivery Systems on Immune Cell-Driven Inflammation and Mucosal Healing in Ulcerative Colitis. Nicotine Tob Res. 2025;27:542–52. https://doi.org/10.1093/ntr/ntae193

17. Chen B-C, Weng M-T, Chang C-H, Huang L-Y, Wei S-C. Effect of smoking on the development and outcomes of inflammatory bowel disease in Taiwan: a hospital-based cohort study. Sci Rep. 2022;12:7665. https://doi.org/10.1038/s41598-022-11860-y

18. Kunkle B, Singh H, Abraham D, Asamoah N, Barrow J, Mattar M. Independent predictors of 90-day readmission in patients with inflammatory bowel disease: a nationwide retrospective study. J Crohns Colitis. 2025;19:jjaf034. https://doi.org/10.1093/ecco-jcc/jjaf034

19. Wijnands AM, de Jong ME, Lutgens MWMD, Hoentjen F, Elias SG, Oldenburg B, et al. Prognostic Factors for Advanced Colorectal Neoplasia in Inflammatory Bowel Disease: Systematic Review and Meta-analysis. Gastroenterology. 2021;160:1584–98. https://doi.org/10.1053/j.gastro.2020.12.036

20. Marafini I, Monteleone G. Smoking and colorectal cancer in inflammatory bowel disease: Quantity matters? United European Gastroenterol J. 2023;11:589–90. https://doi.org/10.1002/ueg2.12433

21. Shaham D, Naveh S, Zemel M, Kariv Y, Leibovitzh H, Cohen NA, et al. Smokers with Crohn's face worse surgical outcomes: A 90-day perioperative analysis. Am J Surg. 2025;247:116458. https://doi.org/10.1016/j.amjsurg.2025.116458

22. Hernández-Rocha C, Walshe M, Birch S, Sabic K, Korie U, Chasteau C, et al. Clinical Predictors of Early and Late Endoscopic Recurrence Following Ileocolonic Resection in Crohn's Disease. J Crohns Colitis. 2024;18:615–27. https://doi.org/10.1093/ecco-jcc/jjad186

23. Barnes EL, Esckilsen S, Ashburn J, Barto A, Bloomfeld R, Cairns A, et al. Extensive Colitis and Smoking Are Associated With Postoperative Complications Within 30 Days of Ileal Pouch-Anal Anastomosis. Inflamm Bowel Dis. 2024;30:1326–33. https://doi.org/10.1093/ibd/izad177

24. Wiciun O, Skonieczna K, Ordon K, Badziąg M, Szulc P, Kurczoba L, et al. Janus Kinase Inhibitors in the Treatment of Crohn's Disease and Ulcerative Colitis: A Review. Qual Sport. 2025;41:60398. https://doi.org/10.12775/QS.2025.41.60398

25. Larsen MGR, Overgaard SH, Petersen SR, Møllegaard KM, Munk HL, Nexøe AB, et al. Effects of smoking on clinical treatment outcomes amongst patients with chronic inflammatory diseases initiating biologics: secondary analyses of the prospective BELIEVE cohort study. Scand J Immunol. 2024;100:e13395. https://doi.org/10.1111/sji.13395

26. Theodoraki E, Orfanoudaki E, Petroulaki E, Foteinogiannopoulou K, Koutroubakis IE. Active smoking is associated with the development of adverse events of biological therapy in patients with inflammatory bowel disease. Eur J Gastroenterol Hepatol. 2023;35:15–20. https://doi.org/10.1097/MEG.0000000000002445

27. Hua X, Lopes EW, Burke KE, Ananthakrishnan AN, Richter JM, Lo C-H, et al. Smoking Behaviour Changes After Diagnosis of Inflammatory Bowel Disease and Risk of All-cause Mortality. J Crohns Colitis. 2022;16:1030–8. https://doi.org/10.1093/ecco-jcc/jjac015

28. González-Muñoza C, Gely C, Gordillo J, Bertoletti F, Giordano A, López-Faba A, et al. Duration of smoking cessation in patients with inflammatory bowel disease. Gastroenterol Hepatol. 2024;47:591–7. https://doi.org/10.1016/j.gastrohep.2023.11.002

29. Navarro Correal E, Casellas Jorda F, Borruel Sainz N, Robles Alonso V, Herrera de Guise C, Ibarz Casas A, et al. Effectiveness of a Telephone-Based Motivational Intervention for Smoking Cessation in Patients With Crohn Disease: A Randomized, Open-Label, Controlled Clinical Trial. Gastroenterol Nurs. 2021;44:418–25. https://doi.org/10.1097/SGA.0000000000000572