



Sex and gender in inflammatory bowel disease outcomes and research

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Extensive patient heterogeneity is a challenge in the management of inflammatory bowel disease (IBD). Sex and gender, as well as the interaction of sex and gender with other social identities, referred to as intersectionality, contribute to this heterogeneity and might affect IBD outcomes. An interdisciplinary team of clinicians, researchers, patients, and sex and gender experts reviewed current literature on the effect of sex and gender dimensions on IBD outcomes. The team also investigated the role that stakeholders have in advancing sex-based and gender-based IBD knowledge, as comprehensive studies are scarce. Acknowledging and integrating sex and gender into the organisation and content of research (eg, study design, participant recruitment, data analysis, data interpretation, data dissemination, and impact evaluation) could enhance the validity, relevance, and applicability of research. Such gendered innovation has potential for advancing personalised medicine and improving the quality of life for people with IBD.

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal system consisting of two main subtypes—Crohn's disease and ulcerative colitis.^{1,2} IBD is a common disease with an increasing global prevalence that is predicted to reach 1% by 2030 in many regions of the western world (defined as western Europe and North America).³ The majority of new IBD diagnoses are made in adolescence and early adulthood (aged 13–35 years) and so many people have to live most of their lives with the disease. IBD management is challenging due to vast patient heterogeneity and the scarcity of tools capable of adequately measuring and monitoring IBD.⁴ Heterogeneity in IBD is due to genetic predisposition, environmental influences, lifestyle, and microbial diversity.⁵ IBD outcomes are also influenced by factors such as sex and gender, age, ethnicity, geography, and socioeconomic status.^{6–14}

The existence of sex and gender disparities in health care has increasingly been recognised.^{14–16} This recognition has prompted the development of recommendations to incorporate sex and gender aspects into clinical research, such as the Sex and Gender Equity in Research (SAGER) guidelines.^{17,18} However, despite these guidelines, adherence has been low, with few publications referring to them. Nevertheless, interest in understanding the impact of sex and gender on health and disease, including IBD, is growing (figure).^{19–21} Integrating dimensions of sex and gender into research has the potential to enhance both the interpretation and the validity of research findings (panel 1).^{19,22} In recognition of this, stakeholders (eg, health organisations, funding agencies, patient associations, and researchers) are increasingly advocating for the consideration of sex and gender in research to improve patient outcomes. Furthermore, although direct evidence is sparse, addressing sex and gender inequity at an organisational level might also improve the validity and applicability

of research within IBD. Diversity in research teams, coupled with inclusivity and psychological safety, could allow diverse voices and perspectives to be raised, heard, and actioned.

This Review aims to investigate the effects of sex and gender in IBD and benefits from the various perspectives of an interdisciplinary Nordic team of clinicians, researchers, patients, and sex and gender experts from Denmark, Iceland, Norway, and Sweden. We acknowledge that we cannot provide perspectives from non-western countries or from people with diverse gender identities. We first review the concept of sex and gender and the relation to intersectionality, which is the way in which equality dimensions and identities, such as class, disability, race, and sex and gender, interact to create interdependent systems of discrimination and privilege. We then discuss sex and gender in the context of IBD phenotypes. Finally, we concentrate on the research process and the roles of research stakeholders in accounting for sex and gender in both the content of research and the organisations that do the research. We also report on specific actions after consideration of a multicentre Nordic clinical study, NORDTREAT. The NORDTREAT study is a collaborative research initiative involving Norway, Sweden, Iceland, and Denmark, and includes a clinical trial (NCT05180175) and a prospective study of patients with IBD (NCT05414578). This Review highlights the potential of applying a systematic approach to sex, gender, and intersecting categories in IBD research on a much wider scale than previously considered. It also shows how this integration might be done and the associated gaps, pitfalls, and key areas for attention.

Sex versus gender

Sex and gender are crucial aspects of the health of individuals.¹⁹ They refer to different but inter-related concepts. Sex refers to the biological factors that

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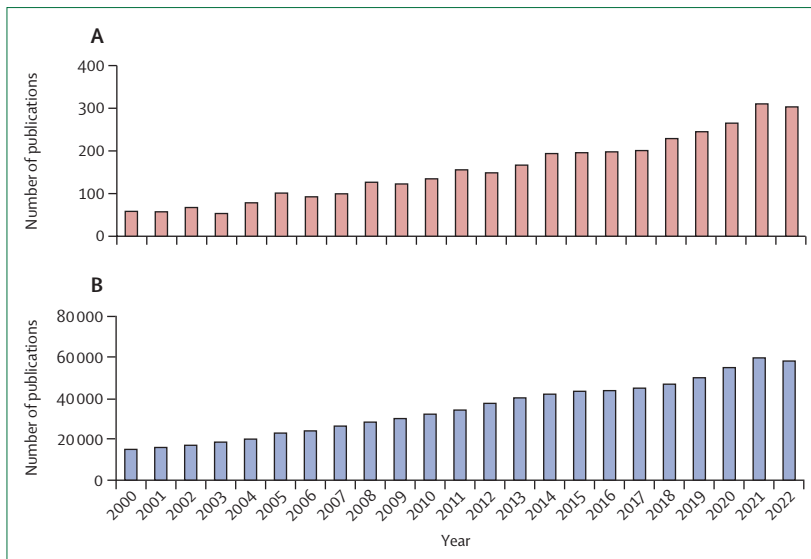


Figure: Recognising the role of sex and gender in research over time

Results from a PubMed search between Jan 1, 2020, and Jan 4, 2024, for all publications in all languages with the search terms "sex" and "gender" (A) and "inflammatory bowel disease" AND "sex" and "gender" (B).

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distinguish male, female, and intersex, and is assigned at birth. Gender refers to the sociocultural norms, identities, and relationships of women, men, and individuals with diverse gender identities that structure societies and organisations and shape behaviours, interactions, and how people perceive themselves.^{19,23} Gender is multi-dimensional, complex, and changes by time, place, and culture. Sex and gender interact in multiple ways and are influenced and shaped by other social characteristics. In this Review, individuals who do not identify as cisgender (having a gender identity corresponding to sex assigned at birth) are referred to as transgender, gender non-conforming, gender diverse, or minority gender (having a gender identity that differs from the sex assigned at birth).

Sex and gender definitions

Sex and gender inequalities in health refer to the differences in health outcomes and experiences between patients due to social, economic, and cultural factors related to sex and gender. These disparities can manifest in various ways. People might be differently affected by diseases due to biological factors of their assigned sex at birth, which might change the prevalence or severity of specific disease manifestations. Moreover, biological differences between all sexes can affect how medications are metabolised and how the body responds to treatments. Hormonal variations, genetic differences, body composition, and organ functions are among the factors that can lead to differences in drug effectiveness and side-effects.^{21,24}

Gender norms are the constructed societal expectations of all genders, often based on sex. They influence health behaviours such as diet, exercise, alcohol intake, and

Panel 1: How considering sex and gender in research can enhance personalised health care in inflammatory bowel disease

What is investigated: research content

- Integrating sex and gender analyses into research design has the potential to improve social equality by creating more reliable and reproducible results, which enhances applicability across the whole of society
- Integrating sex and gender into study design can identify biases related to sex and gender, offer new perspectives, and pose novel questions
- Awareness of sex-specific and gender-specific symptoms and disease phenotypes allows for tailored management; for example, by preventing or reducing complications (ie, unfavourable results of a disease)
- Insights into sex and gender differences in terms of treatment outcomes and adherence to therapy can improve disease management and foster an individualised approach to treatment
- Use of LGBTQIA+ inclusive practices in patient-clinician interactions and strategies designed to create a safe and welcoming clinical care setting will increase patient trust and improve the overall health-care experience for people with minoritised sexual and gender identities with inflammatory bowel disease
- Understanding the source of sex and gender inequality in health-care access gives options to mitigate sex and gender biases and implement solutions

Who does the research: research organisation

- Sex and gender diversity among researchers could improve the quality of clinical studies, as researchers from diverse backgrounds might be more likely to include diversity considerations in study design, address biases, and deliver research that reflects population diversity

health-care-seeking habits. For example, gender norms can influence what foods are considered socially acceptable for men and women to eat, which in turn affects dietary habits.²⁵

Gender bias relates to the prejudiced belief that one gender identity is better or worse than the others. These biases can affect the clinician-patient relationship, communication, treatment recommendations, and options provided to patients.²⁶ Subsequent gender-based health disparities can manifest in various ways, including differences in the utilisation of health-care services, access to preventive services, quality of care received, and health outcomes. Gender disparities in health-care access are further influenced by social, economic, cultural, and systemic factors.²⁰ Gender dynamics refer to the relationships and interactions between and among people based on gender.

Inequalities often interact, simultaneously enhancing and neutralising each other, which is referred to as intersectionality.^{20,23} Intersecting factors include sex and gender,

ethnicity, race, age, class, socioeconomic status, religion, language, geographical location, disability status, migration status, sexual orientation, and political situation.^{6–12} These factors have been studied in IBD. In an analysis of data from the 2019 Global Burden of Diseases, Injuries, and Risk Factors study, the burden of IBD was found to be higher in countries with higher sociodemographic indexes, with Norway having the highest burden in 2019.⁹ Evidence on geographical disparities in IBD is sparse, however, a 2023 paper discussed rural versus urban health care in IBD.⁷ The authors argued that inadequate access to gastroenterological specialists in rural areas affects the diagnostic process and care on all levels of patient management.⁷ Furthermore, race and ethnicity might affect various aspects of IBD, such as incidence and presentation.¹¹ Additionally, emerging studies, mostly from the USA, suggest disparities in care linked to race and ethnicity, with delayed diagnoses, differences in prescribing patterns, potentially worse disease outcomes, and poorer representation in clinical trials for minoritised racial groups.^{10–12}

Sex, gender, and IBD outcomes

A 2020 review provided an overview of the sex dimensions of IBD.¹³ This section complements this review by elaborating on the current knowledge concerning sex and gender in the context of IBD risk, diagnosis, disease course, treatment outcomes, and quality of life (table), although data are sparse.

Minoritised gender identities in IBD

The gender spectrum encompasses a wide range of identities.²⁷ Data on people with minoritised gender identities and IBD are sparse. A systematic review of epidemiology and patient-reported health outcomes related to IBD in sexual and gender minoritised people found that the prevalence of IBD among transgender individuals was similar to that of the general population, although numbers were small.²⁷ Moreover, the review highlighted concerns expressed by gender minoritised individuals, such as inadequate support and lack of discussions regarding worries about colonic surgery and sexual concerns, all of which remain unaddressed.^{27–29,42} Managing IBD for those who have undergone gender-affirming surgery can pose challenges. A review and case reports have raised concerns about medication interacting with hormone treatment (eg, leading to suboptimal hormone levels or increased side-effects), challenges from complex anatomy arising from gender-affirming surgeries, risk of inflammation and ulcerative colitis in the sigmoid-derived neovagina, and the increased risk of mental ill health compounded by the interaction of IBD status and gender diverse status, both of which are associated with increased risk of mental ill health.^{43–45} Hormones, particularly oestrogen, have a major influence on both the aetiopathogenesis and the clinical course of IBD in women.¹³ The gastrointestinal effects of hormone

therapy for transgender men and women has not been rigorously assessed. Schenker and colleagues²⁸ write that up to 33% of transgender and gender non-conforming adolescents and young adults who seek general health care report experiencing mistreatment. Awareness of the experiences of gender diverse individuals and creating an accepting and welcoming clinical environment should go hand in hand.^{29–30}

Sex and risk of IBD

Some reviews have focused on sex-based differences in IBD prevalence and incidence (table).^{13,31,32} One analysis of population-based studies from Europe, North America, Australia, and New Zealand reported that girls had a lower risk of Crohn's disease during childhood but a higher risk as women in adulthood compared with boys and men.³² By contrast, men had a higher risk of ulcerative colitis than women from age 45 years, but the risk did not differ between the sexes before this age.³² A similar analysis of population-based studies from the Asia–Pacific region found a male predominance of Crohn's disease and ulcerative colitis from adolescence to middle-to-older age.³¹ The differences in these study results might reflect the impact of intersecting factors, such as region, ethnicity, or environment.

Sex and disease diagnosis

Delayed diagnosis and hence delayed therapeutic intervention have been associated with increased rates of complications and surgeries in IBD (table).⁴⁶ Studies have shown a longer delay for the diagnosis of IBD in women compared with men.^{14,33} A Spanish multicentre cohort study of 190 patients with recently diagnosed IBD reported that the median diagnostic delay was twice as long for female than for male patients (7·8 months [IQR 3·3–18·9] vs 3·8 months [1·7–7·8]), despite there being no significant differences in the time from onset of symptoms to first consultation and broadly similar clinical presentations during the prediagnostic period.¹⁴ Women were also more likely to be misdiagnosed than men. Although data are sparse, these observations could suggest the presence of implicit bias, with women being more likely to be dismissed by doctors and more likely, for example, to have their IBD symptoms be attributed to functional rather than organic disorders or mistaken for gynaecological symptoms. A greater awareness of implicit biases among clinicians and perhaps implicit bias training could help to mitigate these diagnostic delays.

Sex and disease phenotypes and course

A 2023 study analysed sex-stratified data from more than 34 000 patients with IBD and identified sex-specific association patterns for Crohn's disease and ulcerative colitis.⁴⁷ Males were less likely to have a colonic-only disease location but more likely to have upper gastrointestinal disease and perianal disease complications in Crohn's disease than females. Males were also more likely to have extensive

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For more on sex and gender in research see <https://genderedinnovations.stanford.edu/index.html>

Type and design	Focus or endpoints	Major conclusion	
Sex and gender in IBD			
Goodman et al (2020) ¹³	Review	Sex-based differences and IBD	The authors conclude that IBD modestly yet consistently presents and manifests differently in men and women. Population-based studies from the past two decades indicate that Crohn's disease exhibits a slight female predominance in Western adult cohorts versus Asian adult cohorts. Largely, previous studies have shown a slight male predominance for ulcerative colitis in the adult population. Female patients with Crohn's disease and male patients with ulcerative colitis are more commonly affected by comorbidities, such as disease complications that manifest outside the gastrointestinal tract. Although male patients might be more likely to receive systemic therapies, they might be more non-compliant (intentionally or unintentionally). This could account for differences in clinical symptoms between men and women with IBD; greater access to biological agents could improve the clinical course in male patients, yet non-adherence could negatively affect disease.
Minoritised gender identities in IBD			
Newman et al (2023) ²⁷	Systematic review	Epidemiology of IBD and health outcomes in people with minoritised sexual and gender identities	No differences in IBD epidemiology have been identified in transgender individuals, but data are very scarce.
Schenker et al (2021) ²⁸	Short communications	Six cases of transgender and gender non-conforming individuals with IBD	Recommendations for the provision of high-quality care to the transgender and gender non-conforming IBD population were given, which were divided into three categories of medications, anatomy, and mental health.
Dibley and Duffy (2023) ²⁹	Comment	Access to health care for people of minoritised sexual or gender identities with IBD	Providing safe, sensitive, and effective IBD care for transgender and gender diverse individuals relies on building trusting relationships with health-care practitioners and delivering culturally competent care.
Boyd and Friedman (2023) ³⁰	Comment	Advancing research and improving care for sexual and gender minoritised people with IBD	Particular minoritised gender groups with IBD are disproportionately impacted by issues associated with sexual health, such as an increased prevalence of sexually transmitted infections and gynaecological and anorectal cancers. These issues might be further complicated by factors known to influence patients' disclosure of symptoms, including sexual stigma and fear of discrimination. Effective patient-clinician communication is essential in determining appropriate screening, disease prevention interventions, and timely management recommendations for sexual health issues. Further research efforts that investigate the impact of IBD on the sexual health of gender diverse patients might serve as an important step toward inclusive and culturally sensitive care for this diverse patient population.
Incidence			
Shah et al (2019) ³¹	Pooled analysis of population-based cohorts in the Asia-Pacific region	Sex-based differences in incidence	Starting in early adolescence until age 50 years, there was a 36–64% higher incidence of Crohn's disease in boys and men versus girls and women ($p < 0.001$); the incidence of ulcerative colitis was 20–42% higher in men versus women between the ages of 15 years and 65 years ($p < 0.05$).
Shah et al (2018) ³²	Pooled analysis of population-based cohorts in Europe, North America, Australia, and New Zealand	Sex-based differences in incidence	Girls generally had a lower incidence of Crohn's disease during childhood but a higher risk as women in adulthood compared with boys and men; incidence rates of ulcerative colitis were generally similar by sex until age 45 years, after which the incidence was higher in men than in women.
Diagnosis			
Sempere et al (2023) ¹⁴	Multicentre cohort study from Spain	Diagnostic delay	In 190 patients with recent IBD diagnoses (<7 months), the median time from symptom onset to diagnosis was twice as long in women than in men, and women were more likely to be misdiagnosed.
Vavricka et al (2012) ³³	Swiss IBD cohort study	Diagnostic delay	Women with ulcerative colitis had a longer diagnostic delay.
Disease course			
Dong et al (2023) ³⁴	Registry study from Germany	Disease course among children and adolescents with new-onset Crohn's disease	Sex was not associated with the progression of Crohn's disease in 338 children and adolescents.
Khrom et al (2023) ³⁵	Original work	Sex-based differences in disease course of Crohn's disease and ulcerative colitis	Males were less likely to have a colonic-only disease location but more likely to have upper gastrointestinal disease and perianal disease complications in Crohn's disease. Males were more likely to have extensive ulcerative colitis than females.
Guillo et al (2023) ³⁶	Cross-sectional study in 30 French referral centres	Risk of extraintestinal manifestations	Male gender was associated with a lower risk of extraintestinal manifestations.

(Table continues on next page)

ulcerative colitis than females. In a German registry study, gender was not associated with the progression of Crohn's disease among 338 children and adolescents.³⁴ By contrast, the male sex might be associated with a lower risk of extraintestinal manifestations in general, but men could be more likely to develop the comorbidities of primary sclerosing cholangitis, urolithiasis, and primary ankylosing spondylitis.^{13,35} The joints (except ankylosing spondylitis),

skin, and eyes seem to be more frequently involved for women with IBD.¹³

Sex and treatment outcome

Sex and gender differences in treatment response include differences in treatment access, patient acceptance, adherence, adverse effects, and therapeutic outcomes.^{36,37} A 2023 meta-analysis of 1149 people with

Type and design	Focus or endpoints	Major conclusion	
(Continued from previous page)			
Treatment outcomes and adverse effects			
Solitano et al (2023) ³⁷	Systematic review and meta-analysis of head-to-head studies	Risk of serious infection with biologics and oral small molecules	Data was not specifically available by sex, but the authors reported that sex did not affect the results.
Moens et al (2022) ³⁸	Retrospective cohort study in a Belgian tertiary referral centre	Serious infections and malignancies with exposure to several biological therapies	Serious infections after biological therapy exposure were associated with female gender.
Agrawal et al (2023) ³⁹	Meta-analysis of clinical trials	Gender-specific differences in treatment response in patients with ulcerative colitis	Men were less likely to achieve clinical remission, mucosal healing, and clinical response than women during induction treatment with TNFA inhibitor therapy, but there were no differences by gender during maintenance treatment.
Quality of life			
Janssen et al (2023) ⁴⁰	Prospective multicentre study	Association of clinical, lifestyle, and psychosocial factors with abdominal pain in patients with IBD in remission	198 (46%) of 429 patients had chronic abdominal pain, which was more common in female patients; sex was associated with abdominal pain over time in a multivariable analysis.
Shreiner et al (2021) ⁴¹	Swiss IBD cohort study	Prevalence of fatigue compared with the general population, address risk factors, and evaluate the impact of fatigue on daily life	Significantly higher levels of fatigue were found in female patients than in male patients.
IBD=inflammatory bowel disease.			
Table: IBD publications that discuss or analyse sex or gender			

ulcerative colitis in clinical trials studied gender differences in response to TNF inhibitors.³⁸ Men were less likely to achieve clinical remission, mucosal healing, and clinical response than women during induction treatment. There were no differences by gender during maintenance therapy.³⁸

People who live with IBD often experience reduced quality of life, with studies showing a bidirectional relationship between IBD and depression and anxiety.^{1,2,48,49} The relationship is multifaceted and affected by disease severity, the impact of the disease on daily life, and socio-cultural aspects. Women with Crohn's disease and men with ulcerative colitis might have more severe symptoms and a worse quality of life than the opposite gender.¹³ In particular, fatigue and abdominal pain are symptoms associated with low quality of life, and both have been observed more commonly in women than in men (table).^{39,40}

Sex and gender in the IBD research process

Incorporating sex and gender aspects into research could reveal fundamental biological, psychological, and social factors contributing to sex and gender differences and disparities and enhance the validity, relevance, and applicability of research outcomes and results. Such research is pivotal in advancing medical knowledge, informing evidence-based health-care practices, and improving patient outcomes (panel 1).

Many stakeholders are actively contributing to integrating sex and gender considerations within research practices, albeit with differing emphases. Historically and currently, the primary focus has been at the organisational level, centring on demographics, human resources,

and equal opportunity. There is much less emphasis on integrating sex and gender into the research content as standard and evaluating and actioning the impact. This lack of integration reflects a notable gap in knowledge and understanding as well as untapped potential for improving patient care.

Research organisation and gendered innovations

Research organisations have a crucial role in determining research outcomes. Structural gender equality efforts focus primarily on organisational aspects and on who does the work, such as efforts towards diversity and gender balance and inclusive working environments in research groups, consortia, and decision-making bodies (panel 1). Organisational innovations emphasise equitable treatment and opportunities in assessment and recruitment procedures, talent promotion, decision-making processes, career trajectories, and work-life balance. By contrast, gendered innovations in research focus on the content—ie, what is being investigated (panel 1). Gendered innovations encompass the incorporation of sex and gender into the core of research: data curation, methodological approaches, data analyses, and data interpretation. The aim is to use sex, gender, and intersectional analysis for innovation and discovery.

Gender mainstreaming

Gender mainstreaming is a policy-making approach that strives for gender equality by addressing disparities throughout all stages and levels of policies, programmes, and projects.⁶ It has five main principles: gender-sensitive language, gender-specific data collection and analysis, equal access to and use of services, women and men

being equally involved in decision making, and equal treatment being integrated into steering processes.⁶ In the context of health, the goal of gender mainstreaming is to minimise health risks among diverse groups by reforming attitudes, behaviours, and practices that might negatively affect their wellbeing. This approach acknowledges that sex and gender intersect with salient social categories, including age, race and ethnicity, sexual orientation, socioeconomic status, and disabilities, and that the situations of men, women, and gender diverse people—access to power, resources, and human rights—will vary according to these social categories.³⁰ However, this approach cannot counter inequality by itself. Equality needs to be practiced in everyday interactions, such as inclusive meetings and decision-making, where marginalised voices are taken into account. Furthermore, equality is promoted by integrating a nuanced and comprehensive understanding of sex, gender, and other intersecting social categories into the topics being studied—ie, gendered innovation.

International stakeholders in the research process

According to the UN, gender-sensitive approaches are essential to address inequalities and to build good health for all.^{31,52} Many stakeholders have sex and gender policies, often in the form of a gender mainstreaming manual or a gender equality strategy, including WHO, the EU, and the National Institutes of Health in the USA.^{6,52,53}

In the EU, representatives of national authorities and research funding organisations are working together to develop communities of practice.⁵⁴ An essential objective in the European Research Area is the integration of the gender dimension into research and innovation content.^{55–57} This objective builds on insights from a Horizon report from 2020, *Gendered Innovations 2*, which argues how integrating sex and gender aspects into research and innovation, in terms of data, analysis, research methodologies, dissemination, and clinical translation, can generate innovative approaches such as new personalised therapies and preventive strategies.¹⁶

The Nordic governments and government-supported institutions

Nordic countries generally rank highly in population health. Still, social health inequalities persist and might even be increasing.⁵⁸ A Norwegian report from 2023 on women's health concludes that despite political ambitions, the lack of a systematic approach to sex and gender in the health sector prevents health equality for all.⁵⁹ Although Nordic governments and universities have well established strategies for gender equality, the integration of the gender dimension in research is sporadic, and intersectional approaches in research policy and practice are at the very earliest stages of becoming an integral part of a broader understanding of equality.^{60,61} Some government and non-government funding agencies have

adopted a proactive approach by requiring applicants to account for the relevance of sex and gender analysis in their proposed research.¹⁹ The Nordic governments' organisation, NordForsk, supports Nordic cooperation on research by providing funding for Nordic research and research infrastructure. NordForsk requires research institutions to have a gender equality plan before signing a contract with them, and also publishes reports on gender balance and the implementation of a gender perspective on the research themes annually.⁶²

Medical journals

Medical journals play a part in promoting gendered innovation, such as through advancing the publication of sex-specific and gender-specific data. The SAGER guidelines assist authors and editors in promoting the reporting and assessment of sex and gender in research.¹⁸ However, adherence to these guidelines seems to be limited. Of 100 highly cited medical journals investigated in a cross-sectional review, only seven recommended the use of the SAGER checklist in their author instructions.⁶³

Professional associations

Professional associations are largely aware of their role in promoting equity among patients and professionals. The Nordic gastroenterological associations are actively engaged in United European Gastroenterology (UEG), which aims to improve the prevention and care of digestive diseases, striving for equal opportunity and inclusion among researchers, particularly regarding age, sex and gender, and nationality. Their *Equality and Diversity Plan* provides a framework for implementing diversity and inclusion initiatives.⁶⁴ UEG aims to increase awareness of gender in research and in scientific and educational output by ensuring that gender aspects are included in the content of activities whenever relevant. The organisation aims to provide researchers with appropriate methods to explore and understand how sex and gender differences could affect the design and implementation of research projects. In addition, UEG aims to develop guidelines on how to include sex and gender analysis in research, reporting, and evaluation and peer-review. Progress is monitored by an indicator measuring the number of research projects, educational contents, and guidelines in which a gender dimension is included.

In the USA, the American Gastroenterological Association (AGA) and the American College of Gastroenterology (ACG) are working to reduce gender disparities. In 2024, the AGA introduced its Gender Equity Project, which outlines six key domains: bias and gender disparities, leadership and career advancement, wellness and balance, professional recruitment and retention, mentorship and sponsorship, and recognition. This project was discussed at Digestive Disease Week, where a panel of diverse speakers highlighted the current state of gender disparities in gastroenterology and

the desired future for women in this field. The panel also outlined strategies to achieve these goals. The AGA also acknowledges the challenges that women face in the field, and is committed to addressing them directly. To this end, the AGA offers Women in GI regional workshops, which are aimed at fostering both the professional and personal growth of women in gastroenterology.

The ACG has established a Diversity, Equity, and Inclusion Committee, which not only collaborates with other committees to ensure that educational, research, and community engagement activities conducted by the ACG are approached through a health equity lens, but also advocates for inclusive representation in ACG leadership.

Patient associations

Engaging patients in health and self-care management is an important but largely unexplored aspect in the care of individuals with IBD.^{65,66} Including perspectives from relevant interest groups in research is increasingly recognised to improve its representativeness, validity, and relevance. For example, the UK LGBT Foundation published guidelines to help health-care professionals to support people with minoritised sexual and gender identities.⁶⁷ The Nordic IBD patient associations collaborate at a European level under the European Patients Forum and the European Federation of Crohn's & Ulcerative Colitis Associations, which includes patient associations such as *Crohn's og Colitis Ulcerosa samtökin* (Iceland), *Mage-tarmforbundet* (Norway), *Colitis-Crohn Foreningen* (Denmark), *Magtarmförbundet* (Sweden), and *Tarm-uro-och stomiförbundet* (Sweden). These patient associations address gender aspects by “encouraging gender balance in leadership, offering gender-responsive support services, advocating for gender-equitable policies, and conducting gender-related research”.⁶⁸ In relation to research, patient associations can discuss how to reach more patients, such as those who are not within patient associations and might not regularly attend medical providers.

Research teams

Diversity among researchers is increasingly recognised as substantially affecting research outcomes and impact.⁶⁹ Researchers with diverse backgrounds might be more likely to include diversity considerations in study design, address biases, and deliver research reflecting population diversity, improving the applicability of research outcomes.¹⁹ However, robust data on the effect of researcher diversity on research outcomes are still lacking.

Sex and gender in the NORDTREAT study

The Nordic NORDTREAT study is a good example of how sex and gender can shape research in IBD. The aims of NORDTREAT are to assess whether a biomarker-based top-down treatment strategy can improve treatment outcomes in patients with IBD and to identify markers that can improve diagnostic and prognostic accuracy among patients referred to hospital with suspected IBD.

In 2020, at the beginning of the NORDTREAT project, a workshop was conducted between the Gender Equality Team at the University of Southern Denmark (Odense, Denmark) and the NORDTREAT Executive Committee. This workshop looked at diversity and inclusivity, focusing on addressing these considerations within the research content and research team organisation, and started valuable discussions among the researchers regarding sex and gender aspects in relation to IBD outcomes.

In terms of research content, the workshop gave rise to a thorough examination of matters such as the formulation of survey questions and communication materials. People of different sexes and genders might reply to survey questions differently depending on varying factors, such as how the questions have been phrased or cultural norms (eg, relating to food items or portion sizes). For the sake of comparability, we were not able to modify the standard survey used, but the workshop led to a modification of the illustrations and language used in general communication materials. The workshop led to a modification in the reporting of gender so that respondents can identify as men, women, or other. For those who choose other, there is an opportunity to further specify gender identity. However, we acknowledge that this approach might still not accurately register some patients with diverse gender identities. In terms of communication images and texts, efforts are being made to avoid replicating stereotypical gender roles and interactions, such as ensuring that the genders of doctors, nurses, and patients in these communication materials do not over-represent one gender versus others. Additionally, as a result of this workshop the decision was made to analyse how lifestyle and gender interact in IBD outcomes according to SAGER recommendations.¹⁸

Concerning research organisation, active efforts are being made to increase awareness and embrace diversity within the NORDTREAT research group to improve the quality of output through inclusivity. These efforts include having group work, brainstorming, and written reflections during meetings to help to ensure that all perspectives are heard and considered in decision making. Regular discussions held by NORDTREAT contribute to maintaining constant awareness of these efforts.

Additionally, an online workshop was held by NORDTREAT in November, 2023, with the participation of clinicians, researchers, patients with IBD, and gender experts. It focused on gender, IBD, and patient quality of life to prepare clinicians and researchers to respond in more adequate and personalised ways to various patient presentations. The workshop also focused on patient experiences of gender aspects in relation to their interactions with the health system and how this affected their daily life and quality of life. Although patients reported that they did not observe gender disparities in individual meetings with their health professionals outside of the NORDTREAT study, this is not necessarily

For more on *Crohn's og Colitis Ulcerosa samtökin* see <https://www.ccu.is/>

For more on *Mage-tarmforbundet* see <https://magetarm.no/hjem>

For more on *Colitis-Crohn Foreningen* see <https://ccf.dk/>

For more on *Magtarmförbundet* see <https://magotarm.se/>

For more on *Tarm-uro-och stomiförbundet* see <https://www.ilco.nu/>

Panel 2: Examples of how sex and gender considerations can shape research

What is investigated: research content

Research ideas phase

- Have you considered how assessments of sex and gender, including stereotypes about what is considered female or male, can affect what you want to investigate, what questions you ask, and how to answer them?
- Are sex and gender important for understanding the event, topic, or issue you will investigate, and, if so, how? Are there other dimensions that can be considered in relation to sex and gender, such as age, ethnicity, education, income, occupation, geographical location, or health literacy?
- Have you reviewed literature and other sources relating to sex and gender in the research field?

Proposal phase

- Do the project's research topics and methods account for sex and gender? Does the proposal explain how sex and gender will be handled?
- Are researchers trained in gender studies included in the research group?
- Have you considered whether the results of the research can have different effects by gender identity? Can the research contribute to the advancement of gender equality?

Research phase

- Are research methods (eg, questionnaires and focus groups) designed in a way that considers possible sex and gender differences? Will data differentiated by sex and gender be collected? Are samples, test groups, or others involved in the project diverse in terms of sex and gender, age, and other background variables?
- Will sex and gender be variables in the analysis?
- Are unconscious (stereotypical) assumptions about sex and gender implicit in the interpretation of data? Are there dimensions other than sex and gender that are important to consider?

Dissemination phase

- Is the sex and gender dimension included in the presentation of findings?
- If the sex and gender dimension is included, is it done in a way that does not reproduce stereotypical notions about sex and gender but also looks at variations within the sex and gender categories?
- Have you considered that dissemination of the research findings can be directed towards networks, institutions, journals, and conferences that address gender issues?

Who does the research: research organisation

- Is there balanced sex and gender representation in the project?
- Is there balanced sex and gender representation in the project leadership group and in different working groups, and are diverse backgrounds represented across various nationalities, ages, and professional fields?
- Is the project ensuring balanced sex and gender representation in recruitment and communication, and in the use of marketing tools? Has the project considered getting help from a local diversity organisation?
- If not, has the project considered taking compensational measures, such as making attempts to collaborate externally, or reach out to additional advisory board members? Have different working groups collaborated to allow for synergies across different tasks?
- Are all individuals involved in the project able to access meetings, with consideration given to the location and timing of meetings?
- Does the project have experts on sex and gender in relation to inflammatory bowel disease involved, and can they be included if not?

Panel 2 was adapted from Korsvik and Rustad,⁷² by permission of Kilden genderresearch.no.

Search strategy and selection criteria

We searched PubMed using the combined or singular search terms “sex”, “gender”, “inequality”, “disparity”, “gendered innovations”, “Crohn’s disease”, “inflammatory bowel disease”, “ulcerative colitis”, “personalised medicine”, “pharmacology”, “incidence”, “prevalence”, and “quality of life” between Jan 1, 2022, and Dec 31, 2023. In addition, a backward citation search was completed on the included references. Articles were also identified by searches of the first authors’ files. Only papers published in English were reviewed. The final reference list was generated based on originality and relevance to the broad scope of this Review.

indicative of the absence of systemic gender disparities. Notably, a top priority for patients was to have consultations with the same doctor during their interactions with

the hospital. Extended contact and a deeper knowledge between patients and health-care professionals will help mitigate bias, and thus mitigate negative gendered impact. Overall, the workshop underscored that differences in health outcomes between sexes and genders are complex and incompletely understood.

However, limitations also have to be recognised. For instance, the prospective NORDTREAT study of 250–300 individuals has finite power to analyse data from small groups. Hence, information on sex and gender and other intersecting factors, such as age, ethnicity, education, and socioeconomic status, might not be included as the individual groups would become too small to allow analyses. Other studies, such as registry and retrospective studies, often do not have information on gender and thus have restricted options for gendered analyses. Consequently, addressing the sex and gender dimension requires large-scale collaboration and substantial

resources. These limitations might be mitigated through considering sex and gender during the study design phase, ensuring sufficient sample size to enable gendered analyses. Panel 2 shows examples of how sex and gender considerations can shape the research process based on principles from panel 1 and actionable guidelines.^{52,70–72} Collectively, such approaches will ultimately improve research outcomes that can be more effectively translated and applied in clinical work.

Conclusions and future directions

This Review highlights the scarcity of data on sex-based and gender-based IBD knowledge, but also shows the potential of applying a systematic approach to integrating sex, gender, and intersectionality in IBD research. Integrating these elements enhances the validity, relevance, and applicability of research outcomes. Also known as gendered innovation, this approach holds potential in advancing personalised medicine approaches for people with IBD and improving their quality of life. Understanding the biological differences of all sexes could potentially lead to sex-tailored prevention and treatment strategies. Recognising how gender norms influence health behaviours (eg, diet, exercise, substance misuse, and health-care seeking habits) could help to tailor interventions to encourage healthier lifestyles or mitigate barriers preventing people from accessing timely health care. Identifying and understanding sex-based and gender-based disparities in IBD care, and gender bias from professionals caring for people with IBD, might facilitate and encourage the implementation of actionable steps to ensure equity in health-care access and quality. Gendered innovations and mainstreaming, with the consideration of sex and gender in research content and organisation, support from international stakeholders, and widespread endorsement of SAGER by journals can only benefit people with IBD.

Contributors

ESM and VA conceptualised the work. VA wrote the first draft. LBP, ESM, and HHZ contributed specialised gender knowledge, practices, and wording. VSP, BB, MJ, AC, ML, and ES contributed knowledge of patient associations. All authors critically revised the paper for important intellectual content and approved the final version before submission.

Declaration of interests

JH has served as a speaker or advisory board member for AbbVie, Aqilion, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Hospira, Index Pharma, Janssen, Meda Pharmaceuticals, Medivir, Novartis, Pfizer, Prometheus Laboratories, Sandoz, Shire, Takeda, Thermo Fisher Scientific, Tillotts Pharma, Vifor Pharma, and Union Chimique Belge, and has received grant support from Janssen, Merck Sharpe & Dohme, and Takeda. VA has served as an advisory board member for Merck Sharpe & Dohme. MDJ has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Tillotts Pharma, Takeda, Norgine, and Olympus. MR reports consulting fees from Janssen as part of a half-day advisory meeting concerning the use of a medication in clinical gastroenterology and payment from AbbVie as compensation for one lecture during Swedish Gastro Week on quality management within IBD; compensation for both was administrated as part of his job as a consultant of gastroenterology and hepatology.

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