**The Impact of Gender Identity in the Inflammatory Bowel Disease Population – An Evidence Review and Practical Steps for Gastroenterologists**

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**ABSTRACT**

There has been greater societal awareness of differences in gender identity and sexual orientation in recent years. The rates of identifying as transgender or gender non-conforming (TGNC) are increasing and is known to be higher in the younger population and will therefore be over-represented in the inflammatory bowel disease (IBD) sub-population. However, despite this there is very little in the literature with regards to those who identify as TGNC and are diagnosed with IBD (TGNC-IBD). Many TGNC individuals have poor experiences when seeking healthcare and many physicians find it a challenging and daunting clinical situation to be faced with. We reviewed the available literature with regards to TGNC-IBD population demographics, physical, mental and sexual health considerations, medication interactions and implications for surgery in this heterogenous group. We have identified areas that need further research and suggested simple and practical steps that can be adopted in order to help healthcare providers improve the experience for TGNC-IBD individuals and the quality of care they provide.

**INTRODUCTION**

In recent years there has been a growing societal awareness of the differences in gender identity particularly amongst younger people. Subsequently, census bureaus have begun to collect data on the number of people with a gender identity different to the sex which they were assigned at birth, grouped as either transgender or gender non-conforming (TGNC).[1] Data from 2021 found 262,000 people (0.55% of the population) identify as TGNC in England and Wales.[1] However, there is very little in the literature regarding the impact of a TGNC identity on chronic diseases including inflammatory bowel disease (IBD).

IBD is a chronic inflammatory condition which can have a profound impact upon patients’ physical, mental, sexual and social wellbeing. It is believed to affect as many as 1 in 123 people in the United Kingdom[2] and has a rising worldwide prevalence.[3] The peak incidence of presentation is in the third decade and it is known that TGNC identity is more common in younger people[1] and TGNC individuals may therefore be over-represented in the IBD population compared to national rates. However, the interplay between gender identity and IBD is unknown with even basic demographic data unavailable. This article reviews the available literature highlighting specific issues relevant to managing these patients.

Definitions and terminology can be problematic in this context sometimes leading to confusion which can alienate the TGNC community. This review uses the words male or female to describe biological sex, based upon genital anatomy at birth. We will use man or woman when describing gender-related characteristics and we will use the terms TGNC to describe a person who has a gender identity different to the sex assigned at birth and cisgender to describe a person who has the same gender identity as that assigned at birth.

**METHOD**

A PubMed search was conducted in October 2023 using keywords in the title, abstract or index terms. Studies published in English that reported on at least one physical or psychosocial element of IBD for the TGNC population were reviewed, search terms can be seen in the supplementary information. The search identified 24 papers which were manually reviewed and 10 papers were found to be clinically relevant to TGNC individuals diagnosed with IBD (TGNC-IBD). The references of these 10 papers were also manually reviewed for utility with regards to this review.

**DISCUSSION**

**What Is the TGNC-IBD Population?**

This has not yet been accurately defined. Our recent work using census data[4] has estimated the size of these populations in the UK suggesting there are approximately 2,700 TGNC-IBD individuals in the UK and similar findings were reported in the United States of America (USA).[5] As discussed earlier, it is likely that the TGNC population is over-represented in the IBD population compared to the national population so these are likely to be under-estimations and there remains a need to obtain accurate demographic data from the TGNC-IBD population.

**Physical Health & Outcomes**

It has been demonstrated that there are higher rates of mental and physical health problems[6][7] in TGNC individuals and that they have poorer health outcomes compared with their cisgender counterparts.[6] There is also some limited data from the National Inpatient Sample in the USA suggesting TGNC-IBD individuals have a higher inpatient mortality and length of hospital stay.[8] Whilst this study only included 177 participants, the mortality difference was statistically significant after propensity matching. Whilst stigma and bias likely play a role, the reasons for these differences are complex and intersectional. Further research to investigate the causes is required but there are some clues in the literature which may be relevant.

One possible factor is that TGNC patients will often avoid interaction with healthcare. Many have experienced being mistreated or becoming frustrated about having to teach healthcare practitioners about the nature and implications of being TGNC individuals.[9] This stigmatisation can lead to delays in diagnosis which is associated with worse outcomes in IBD.[10] Perceived differences in required societal norms in gender response to symptoms may also contribute to a delayed contact with healthcare practitioners. The perceived need to be tough and live with symptoms for men or symptoms being misdiagnosed as menstrual problems or functional disorders in women are common place and may exacerbate delays in seeking healthcare.[11]

**Anatomy and Surgery**

Along with the rising incidence of TGNC identity, rates of gender-affirming surgeries have increased significantly in recent years with one national estimate in the USA showing a near three-fold increase between 2016 and 2019[12] with similar figures in Europe and the UK.[13] A wide variety of surgical procedures may be utilised such as thyrochondroplasty, vaginoplasty, breast augmentation for feminisation and masculinising chest surgery (so called ‘top surgery’), scrotoplasty or phalloplasty for masculinisation. The exact type of surgery performed varies and depends upon patient preference, surgical skill, restrictions in public health systems and anatomical considerations.[14]

For those TGNC individuals who also suffer from IBD the surgery becomes more complicated. Many medications commonly used for IBD can negatively impact wound healing, such as recurrent or chronic steroid use,[15] and increase the likelihood of post-operative infections.[16][17] Perianal Crohn’s disease can result in poor healing, fistulae and abscess formation post-operatively[19] and previously active disease can lead to scarring and distortion of anatomy making surgery more challenging and dangerous. This can make genital surgery unfeasible which limits the individual’s ability to have genitalia concordant with their gender identity negatively affecting their mental health, further discussed below. In order to achieve favourable outcomes and reduce post-operative complications, this group of patients require pre-operative optimisation, as previously described,[18] with good disease control, early escalation to advanced therapies, optimal nutrition, steroid avoidance and close co-ordination between the Surgical and Gastroenterology teams.

Gender-affirming surgery can also have long-term consequences for TGNC-IBD individuals. A case report is illustrative and describes a transfeminine patient who had undergone vaginoplasty using her sigmoid colon 10 years prior and later presented with diarrhoea, rectal bleeding and blood-stained vaginal discharge. Examination revealed macroscopic and histological changes consistent with ulcerative colitis within the neo-vagina, matching those from the colonic biopsies.[20] Whilst a rare occurrence, this case underscores the complex interactions between IBD and gender-affirming surgery and need for greater understanding amongst IBD physicians and surgeons about TGNC-IBD patients.

 **Mental Health in the TGNC-IBD population**

Both identifying as TGNC and being diagnosed with IBD are known to be independent risk factors for mental health disorders[21][22][23] and it is established that there is a bi-directional relationship between mental health disorders, stress and IBD activity.[24] Psychological comorbidity in TGNC individuals is largely due to the influence of minority stress which is known to increase low mood and anxiety.[25] Therefore, it is reasonable to assume that having both a TGNC identity and IBD may further increase the mental health burden and with an already higher rate of suicidal ideation, parasuicide, suicide and self-harm amongst TGNC individuals[26] this is a potentially concerning combination.

The chronic and intermittent nature of IBD can pose long-term challenges for patients and their mental health. With the TGNC-IBD population they also face further difficulties such as the process of either changing their identity or showing their true identity to the world, sometimes referred to as ‘coming out’, which can be a particularly difficult time and will often have negative implications for their mental and physical health. Understanding and recognising this is crucial in making TGNC-IBD patients feel welcome and supported by their healthcare provider and able to discuss physical and mental health openly.

Body image dissatisfaction is high in both those identifying as TGNC[27] and patients with IBD, more so in females than males,[28][29] and surgical complications can exacerbate this impacting upon relationships and daily activities.[31] Examples of this in TGNC-IBD individuals include stomas and scars following colorectal surgery, post-operative chest scars or residual breast tissue in transmasculine individuals and emergency stomas following complications from genital reconstructive surgery.[30]

Access to psychiatric and psychological support is an essential part of holistic care for TGNC-IBD individuals but provision is often poor. In the UK, the most recent IBD national standards report published by Crohn’s and Colitis UK found that only 2% of teams were sufficiently staffed with psychologists[32].

There are several free resources available that patients can access such as the British Association for Counselling and Psychotherapy, self-referral to NHS talking therapies, Local Minds (<https://www.mind.org.uk/information-support/local-minds/>) and Stonewall (<https://www.stonewall.org.uk/young-futures/lgbtq-support/mental-health>). Alongside greater knowledge of the available support resources for TGNC-IBD individuals is a requirement for greater understanding of the journeys these patients go through which can pose challenges to their mental wellbeing. Where possible healthcare practitioners should routinely screen for mental health disease, especially anxiety and depression, during consultations amongst all patients with IBD but particularly TGNC-IBD individuals.

**Sexual Health**

Sexual health is an area that is often poorly addressed by IBD healthcare practitioners and sexual dysfunction is common.[33] IBD, particularly if poorly controlled, can have detrimental effects on libido and fertility.[34] Sexual dysfunction amongst TGNC individuals is also known to be high, with a 2019 study identifying up to 32% experiencing either difficulties seeking contact, low libido or difficulties achieving arousal or orgasm.[35] Whilst this can improve with gender-affirming surgery,[36] as the individual has a body more congruent with their sexual identity, the combination of IBD and TGNC identity poses a further challenge with regards to sexual health.

Surgical management of IBD can also cause challenges with sexual health and behaviour. A survey of patients undergoing colorectal and pelvic floor surgery found that 79% of respondents disagreed that they were given sufficient pre-operative advice regarding the impact of the surgery on their sexual activity.[37] Negative post-operative impacts on sexual preferences, activity and body confidence were also common.

There is no data regarding the impact on sexual health of IBD-related surgery in TGNC individuals and none looking at those individuals who have also undergone gender-affirming surgery. What is known is that the interaction between identifying as TGNC and sexual orientation, and therefore sexual health, is complex and many healthcare providers find it a challenging and confusing area to discuss with their patients.[38] Greater education and awareness to build confidence and normalise the importance of a sexual history as part of an IBD consultation is needed.

**Medication Interactions**

Patients diagnosed with IBD are often treated with corticosteroids such as Prednisolone, Hydrocortisone or Methylprednisolone. The long term impacts of these medications are well known amongst Gastroenterologists[39][40] but data has also shown a link between corticosteroid use and hypogonadism in males[41][42] and suppression of gonadotrophin levels in females.[43] There is however no data investigating the interaction between recurrent or prolonged corticosteroid use and gender-affirming hormone therapy. This is discussed in greater detail below but with regards to those TGNC-IBD individuals who require recurrent corticosteroid courses we advocate switching to an alternative therapy as early as possible, monitor for features suggesting inadequate efficacy of hormonal therapy such as recurrence of physical features that were present prior to initiation of treatment and monitoring of serum hormonal levels with referral to Endocrinology if indicated.

Gender-affirming hormone therapy is often an important facet of treatment for TGNC individuals either in isolation or with surgical procedures to masculinise or feminise the body further. The mainstay of therapy for transfeminine people is oestrogen which is usually given in combination with androgen suppression such as a GnRH analogue in the UK or Spironolactone or Cypoterone acetate elsewhwere. Transmasculine people use testosterone and this may be supplemented by progestins to block menstrual activity. In adolescence puberty may be arrested using a GnRH analogue in isolation before sex steroid treatment is given. There is no research in TGNC-IBD individuals on interactions between these medications and IBD however there is some data from the cisgender population.

Data suggests that exposure to the combined oral contraceptive pill is associated with an increased risk of Crohn’s disease and ulcerative colitis (UC)[44] although no correlation was seen with the use of the progestogen-only pill and Crohn’s disease and only a small increased risk for UC was observed. The pathogenesis is unclear but it has been hypothesised that exogenous oestrogen has impacts upon immunomodulation, intestinal wall function and the gut microbiome increasing the risk of developing IBD. Furthermore, a retrospective study from the Chicago IBD clinic[46] examined the impact of hormone replacement therapy (HRT) and found no different in disease activity pre- and post-menopause but did find those on HRT had reduced disease activity suggesting that long-term oestrogen therapy can impact upon IBD. With regards to testosterone therapy, previous studies have not shown an increased risk of developing IBD or worsening of the condition once it is established and normalising serum testosterone in hypogonadal males has actually been shown to have a positive outcome on the clinical course of IBD.[45] However, care needs to be taken in extrapolating these data to the TGNC population given the endocrine physiology may differ from the cisgender population and further research into the impact of gender-affirming hormone therapy on IBD is required.

Patients with IBD, particularly those with active disease or those admitted to hospital, are known to be at risk of VTE due to the inflammatory nature of their disease.[47] Some of the newer small molecule medications, such as JAK inhibitors (JAKi), may be associated with an increased VTE risk and it is currently advised that patients with other risk factors for VTE should avoid these agents.[48] Oestrogen therapy is known to be a risk factor for VTE but the bulk of this data comes from HRT in post-menopausal women.[49] There is conflicting data for transfeminine individuals with a meta-analysis from 2021 demonstrating that, in transfeminine people under the age of 38 who were taking oestrogen feminizing therapy, the VTE risk is not significantly increased.[50] However, a 2021 cohort study with 2842 transfeminine participants taking gender-affirming hormones found the overall ischaemic stroke and VTE risk is 2–4 times the background risk.[51] Further dedicated research evaluating VTE and cardiovascular risks in the TGNC-IBD population is required. Given this, caution is advised, particularly with regards to JAKi use.

Bone health is another area of concern for TGNC-IBD individuals and their responsible physicians. Patients with IBD are at risk of osteopenia and osteoporosis due to the impact on bone metabolism of cytokines and other pro-inflammatory molecules, steroid use and malabsorption. TGNC individuals are known to have reduced bone mineral density before starting therapies.[52] Hormone replacement to adult hormone levels maintains bone mineralisation however in the young person’s cohort it is unclear whether bone density recovers fully after puberty blockade.[53] Additionally, TGNC individuals will often need to be on lifelong therapy and during this time will need ongoing assessment of their bone health as per national guidelines and IBD healthcare practitioners should be aware of this risk and have a lower threshold to assess bone density.

Further study as well as multi-disciplinary working between gastroenterologists, endocrinologists, rheumatologists, pharmacists and TGNC-IBD individuals is key to successfully manage the nuances and complexities of TGNC-IBD medical treatment in this group.

**RECOMMENDATIONS FOR PRACTICE**

There is often anxiety amongst physicians when managing TGNC patients[54] and this impacts upon the doctor-patient relationship and patient care. There are several simple strategies, which do not require any additional time in a short clinic appointment, that can be employed to help rectify this and create a safe and stigma-free consultation environment (Figure 1). These include avoiding assumptions and instead asking about a patient’s preferred pronouns, asking who companions are rather than using phrases such as ‘husband’ or ‘wife’ and using gender-neutral terms initially. Including these preferred pronouns and preferred names in clinic letters given the difficult and challenging process of changing their name held on NHS records – a process which the recent Cass review[55] specifically identified as needing to change – can also help to avoid ‘dead-naming’ patients.

Discussing with patients about where they feel most comfortable when changing for or recovering from a procedure or investigation is also important to welcome and reassure TGNC-IBD individuals. There is not a mandatory training module for NHS staff with regards to TGNC identity but there are free online modules available from the National LGBTQIA+ Health Education Centre in the USA.[56] Incorporating UK versions of these modules into the mandatory training curriculum would help to raise awareness, remove stigma and encourage open and honest discussions between healthcare practitioners and patients.

Adapting the clinical environment to improve TGNC-IBD care is a more substantial challenge. Poster resources are available from charities such as Stonewall which can be erected in waiting rooms and the UK charity *Mindout* has published helpful guidance on how to create a more welcoming clinical environment.[57] Creation of gender-neutral bathrooms and changing facilities is also a long-term strategy that can improve TGNC-IBD patient experience.

**THE FUTURE**

Given the size of the TGNC-IBD population, providing an evidence-based answer to many of the questions raised will be challenging. The Cass review[55], which recently reported into the changes required to improve TGNC care in the UK, also noted this for the wider TGNC population and recommended a centralised approach to research to create a sufficient knowledge base for safe and effective treatment. However, given the size and heterogeneity of the TGNC-IBD population this may still be insufficient. International collaboration and including gender identity and sex assigned at birth questions in population-based IBD studies, a practice recently adopted by the National Institute for Health and Care Research IBD Bioresource,[58] would increase the potential research participant pool and volume of available data and strengthen the validity of recommendations.

**CONCLUSION**

Whilst the TGNC-IBD population is relatively small, it presents a complex clinical challenge with little in the literature to guide practice. Creating a more welcoming clinical environment, increased understanding by clinicians of the challenges these individuals can face and improved psychological support are key facets to improving care. Further work is required to determine the optimal management of TGNC-IBD individuals, the interactions between IBD medications and gender-affirming medications, optimal surgical strategies and the impact of IBD on the physical, mental and sexual health of TGNC-individuals.

**KEY POINTS**

* The TGNC-IBD population has yet to be accurately defined.
* TGNC-IBD individuals are at a higher risk of mental health problems including body image dissatisfaction.
* TGNC individuals will often delay seeking or completely avoid healthcare. Stigma plays a significant role and education of healthcare providers is required to ensure a safe and welcoming environment to these patients. Simple changes to practice such as asking for preferred pronouns, gender neutral language and minor modification to the clinical environment as well as providing appropriate support materials can be effective initial steps in addressing this.
* Sexual health is poorly addressed by IBD healthcare providers and dysfunction can be more complex for TGNC-IBD patients. Open questioning and clear discussions can help to address this.
* Close co-ordination between medical specialties with regards to timing of both IBD and gender-affirming surgery, pre-operative optimisation and post-operative management is required.
* Further good quality study into the experience of TGNC-IBD individuals as well as best practice with regards to medication management, surgery and supporting mental and sexual health is required.

**COMPETING INTERESTS**

The authors do not have any competing interests to declare.

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AP and MC were involved in the conception. MC was responsible for the initial drafting. All authors were involved in reviewing and finalising the article. The authors have all made contributions to the writing of the manuscript. All authors have read and agreed upon the submitted version of this paper and bear responsibility for the content.

**ETHICAL APPROVAL STATEMENT**

No ethical approval is required given the nature of this review.

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