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## Systematic review: the consequences of psychosocial effects of inflammatory bowel disease on patients' reproductive health

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## Summary

Background: High levels of voluntary childlessness and pregnancy-related fears have been reported amongst inflammatory bowel disease (IBD) patients.

Aims: To investigate what factors determine IBD patients' childbearing decisions; and to examine psychosocial consequences of IBD on various aspects of patients' reproductive health.

Methods: Six electronic databases were searched in a pre-specified and structured manner.

Results: A total of 41 articles with data on 7122 patients were included. Between one-fifth to one-third of IBD patients had chosen voluntary childlessness. Around 50% of all IBD patients have poor knowledge of pregnancy-related issues in IBD. Poor knowledge of pregnancy-related issues in IBD was associated with voluntary childlessness. Observational studies have found preconception counselling is associated with patients choosing parenthood. Pregnancy-related fears and concerns are multifaceted, stemming partly from lack of knowledge of pregnancy-related issues in IBD. Many female patients are considered at increased risk for pregnancy because between one-fifth to one-third of patients do not use contraception. Research evidence for sexual dysfunction after disease diagnosis and treatment is inconsistent. There are limited data on patients' pregnancy, postpartum and parenting experiences. A few shortcomings of the literature are evident; sample sizes were small, participation rates were low, use of non-validated questionnaires was common, and few studies included men and/or ethnic minority groups. The design of intervention studies is also weak.

Conclusion: This review recommends pre-conception counselling for all IBD patients of childbearing age to tackle poor knowledge and allow patients to make an informed decision on their reproductive health.

The Handling Editor for this article was Professor Jonathan Rhodes, and this uncommissioned review was accepted for publication after full peer-review.

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## 1 | INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic disease with a relapsing and remitting course and includes Crohn's disease (CD) and ulcerative colitis (UC). In the UK, the prevalence of CD is about 145 per 100 000<sup>1</sup> and UC is around 240 per 100 000.<sup>2</sup> IBD usually affects patients in their childbearing years and the highest incidence of IBD is among patients aged 20-29 years old.<sup>3</sup>

High levels of voluntary childlessness and having fewer children have been reported in this population. A review of non-surgical IBD studies found that within CD female patients, there was a 17%-44% reduction in fertility compared with controls. This was linked to voluntary childlessness, with no evidence of biological causes of infertility. A large population-based study with 9639 women with IBD and 2 131 864 women without IBD, found women with CD experienced slightly lower birth rates (45.3 live births per 1000 person-years), compared to those with UC (47.6 live birth per 1000 person-years), or women from the general population (49.3 live births per 1000 person-years). These rates were further impaired following active disease or surgery.

High rates of voluntary childlessness or having fewer children can only be partially explained by existing research on biomedical factors. For example, active CD, certain types of surgery and certain medications for male patients may affect fertility and fecundity, and patients are advised to conceive in remission. Exacerbation of disease during pregnancy is often linked with adverse pregnancy outcomes, such as increased risk of preterm delivery and low birth weight. Moreover, women with IBD (regardless of phenotype) are more likely to experience poor maternal and infant outcomes, such as severe pre-eclampsia, low 5 minute Apgar score, and (for CD) major congenital abnormality in offspring, than women without IBD. 11

Given this evidence of increased risks of pregnancy complications, it is perhaps unsurprising that IBD patients report high levels of pregnancy-related fears and anxieties, which include the fear of IBD affecting pregnancy, worries regarding medication use, fear of poor pregnancy outcomes, and fear of disease inheritance. 5,6,12,13 Patients also have poor knowledge of pregnancy-related issues in IBD.6 Knowledge of pregnancy-related issues is most commonly tested by the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) score which contains sub-scales on knowledge of inheritance of IBD, conception and medication in the periconceptual period, medication during pregnancy and breastfeeding, mode of delivery and congenital abnormalities in babies to mothers with IBD.6 However, existing reviews on IBD and pregnancy mostly report biomedical aspects of IBD on pregnancy, management of pregnancy, and drug safety. 9,10 Also, practice guidelines such the European Crohn's and Colitis Organisation's (ECCO) consensus document on reproduction in IBD9 provide little guidance on psychosocial factors which may need to be managed during pregnancy. Guidelines on pregnancy in IBD, from the National Institute for Clinical Excellence (NICE), are also limited to providing patients with information on the potential effects of IBD on pregnancy, risks and benefits of treatment on fertility, and ensuring effective communication across specialties.<sup>2,14</sup> Furthermore, there are no provisions of pre-conception counselling for patients in the UK and patients will have to approach their healthcare professionals for any advice. There is no data on how many patients with IBD actually receive pre-conception counselling. Additionally, there is no systematic literature review on the consequences of psychosocial effects of IBD on patient's reproductive health (ie, reproduction, pregnancy, maternity, and birth). Therefore, the aims of this review

- investigate what factors may determine IBD patients choosing parenthood or childlessness; and
- **2.** examine the consequences of psychosocial effects of IBD on patients'
  - a contraceptive decision-making;
  - **b** sexual function;
  - c pregnancy and post-partum experiences.

### 2 | METHOD

## 2.1 | Registration

The review has been registered with PROSPERO—CRD42017078787.

## 2.2 Information sources and searches

Six electronic databases which publish gastroenterology-related research (CINAHL, PsycINFO, EMBASE, PubMed, Web of Science, ScienceDirect) were searched. No time, language, or publication restrictions were applied. See Table S1 for search strategy.

#### 2.3 Study selection and eligibility criteria

After removing duplicates using bibliographic software (Refworks), titles, abstracts, and full-texts were screened independently for eligibility by two reviewers (SP and SC). Any disagreements were resolved by discussion and agreement between the two reviewers was recorded to confirm the validity of the screening process. Bibliographies of all identified eligible studies were searched to identify other potentially eligible (published and unpublished) studies. We contacted experts for unpublished research and reviewed conference abstracts. See Table S1 for eligibility criteria.

## 2.4 Data collection process and data items

The Joanna Briggs Institute Reviewers' Manual 2015<sup>15</sup> was utilised to extract data. All members of the team were involved in independent data extraction and any discrepancies were resolved by discussion. Data extracted included (a) study characteristics (authors, year of publication, country of origin, study duration, research aims/

questions, study population, inclusion, and exclusion criteria); (b) Methodology (sampling method, recruitment, and details of data collection), analysis procedure, and study type (observational, qualitative, mixed-methods, or intervention); (c) study outcomes and outcome measurements; and (d) key findings and main conclusions.

## 2.5 | Quality assessment and risk of bias

All authors were involved in quality assessment. Different quality assessment tools, <sup>16–18</sup> depending on the study design, were used. No study was excluded based on quality, but we report and discuss study quality below. Using the quality assessment tools, study quality was classified as 3-high; 2-moderate; or 1-poor. See Table S2 for quality assessment system and Table S2 for study quality scoring.

## 3 | RESULTS

In total, 3596 records were identified through electronic databases and 5 records through hand searching and contacting authors of conference abstracts (a total of 20 authors were contacted). After duplicates were removed, 1807 titles were screened and 242 abstracts were reviewed. Of the 242 abstracts, 79 full text articles were examined in full and 41 articles were included in the review (see Figure 1 for PRISMA flow chart). Agreement between SP and SC through screening was high (>90% agreement on titles, abstracts and full text).

## 3.1 Study characteristics

The 41 included articles reported data on 7122 patients (Table S2). The majority of studies (k = 30/41) were cross-sectional surveys, three were non-randomised intervention studies,  $^{19-21}$  of which one<sup>21</sup> used no comparison group and only measured one group before and after an educational intervention. Four studies used content analysis and performed interviews and coded responses numerically converting the data into quantitative.  $^{13,22-24}$  There were two qualitative studies.  $^{25,26}$  Only one cross-sectional survey study had a 100% male sample,  $^{27}$  all remaining studies included women (k = 24) or female and male samples (k = 15). The study locations were mostly in countries with majority White populations (k = 37/41). A total of k = 12 studies reported participants' ethnicity, and of these, k = 11 reported overwhelming White samples (on average 80% of the samples were White vs 20% other ethnic groups combined) and only one included 100% British South Asian patients.  $^{26}$ 

## 3.2 | Quality

As can be seen from Table S2, study quality varied. Nineteen studies were scored as poor, 16 as moderate and only six as high. Reasons for low scores included small samples size (k = 20, 50% of studies have sample sizes n  $\leq$  143) and low response rates (k = 29 studies report response rates, average 25%). Some studies used retrospective clinic data, <sup>28,29</sup> or included retrospective accounts. <sup>30</sup> Twenty

studies used non-standardised and/or not validated outcome measurements (see Table S2). Knowledge of IBD (Crohn's and Colitis Knowledge Questionnaire)<sup>31</sup> was examined in two studies,  $^{32,33}$  while the remaining studies (k = 7/16) examined the more specific knowledge of pregnancy-relating issues to IBD (Crohn's and Colitis Pregnancy Knowledge score). Studies which assessed sexual function, particularly after surgery, also predominantly used standardised and validated measurements (k = 6). For sexual function six studies used the International Index of Erectile Function (IIEF) $^{35}$  and the Female Sexual Function Index (FSFI) $^{36}$ ; however, these measures have not been validated within the IBD population. See Table S2 for full listings of questionnaires and measurements used in the literature.

# 3.3 | Factors that determine IBD patients choosing parenthood or childlessness

Around one-fifth to one-third of IBD patients choose voluntary childlessness; observed percentages ranged from 17%<sup>6</sup>; 19.4%<sup>37</sup>; 29.7%<sup>38</sup> to 38%.<sup>39</sup> CD patients (18%-19%) are more likely to choose voluntary childless than UC patients (14%).<sup>6,39</sup> Births rates are also significantly lower in CD (1 live births per woman) and UC (1.2 live births per woman) than the general population in Australia (1.81 live births per woman).<sup>5</sup> Two inter-related determinants of childbearing decisions emerged from the research literature: (a) poor knowledge of pregnancy-related issues in IBD and this often leads to (b) high levels of pregnancy-related fears and anxieties.

## 3.4 | Knowledge of pregnancy-related issues in IBD

Around 50% of all IBD patients have poor knowledge of pregnancyrelated issues in IBD. Specifically, half of all participants sampled scored between 0 and 7 "poor" on CCPKnow scale<sup>21,34,37,40,41</sup> (scores which range from 0 to 7 = poor knowledge; 8 to 10 = adequate knowledge; 11 to 13 = good knowledge; and >14 = very good knowledge of pregnancy-related issues in IBD). Selinger et al<sup>6</sup> (n = 1324) found knowledge of pregnancy-related issues in IBD remained low even amongst participants who had actively sought support and education through IBD Crohn's and Colitis, UK charity membership (a national charity which provides support, education and funding for IBD patients and clinicians/academics), 50.8% of the sample still scored poor on the CCPKnow scale.40 Poor knowledge of pregnancy-related (22.4% and 10% able to correctly answer the pregnancy knowledge question and 11.2% and 7.9% the male fertility question on the CCknow questionnaire, respectively) issues in IBD are prevalent across different countries and healthcare systems in Republic Korean and Chile. 32,37

Higher levels of pregnancy-related knowledge in IBD were associated with parenthood whereas, lower levels of knowledge were associated with childlessness. Higher levels of pregnancy-related knowledge in IBD were associated with parenthood and lower levels of knowledge are associated with childlessness. Selinger et al<sup>6</sup> conducted a survey with 1324 female UK patients of childbearing age recruited via Crohn's and Colitis UK and using the CCPKnow scale. Poor pregnancy-specific

-Wilfy<sup>⊥</sup>

**TABLE 1** Summary of the different types of pregnancy-related concerns and worries reported in the literature (reported as percentages of participants reporting these concerns)

Study	Study population	Study design	General concerns of the effects of IBD on pregnancy/ baby	Effects of pregnancy on IBD	Pregnancy & birth complications	Inheritance of IBD	Infertility	Medication effects on pregnancy/ child	Ability to look after child	Breastfeeding
Ellul et al <sup>43</sup>	N = 348	Cross- sectional survey	63%		63%	68%	22%	73%	13%	
Gawron et al <sup>13</sup>	N = 129 (n = 73 desiring future pregnancy)	Cohort design. Phone survey		56%	27%	25%	25%	53%	10%	
Marri et al <sup>39</sup>	N = 169 (n = 37 pregnancy related responses)	Cross- sectional survey		76%		73%			70%	
Mountfield et al <sup>5</sup>	N = 255 (n = 48 pregnancy related responses)	Cross- sectional survey			18%	15%	35%	30%		
Selinger et al <sup>38</sup>	N = 145 (n = 96 nulliparous women)	Cross- sectional survey	90%	91%	54%	74%	46%	19%	43%	64%
Selinger et al <sup>6</sup>	N = 1324 (n = 226 voluntary childless women)	Cross- sectional survey		59%	31%	67%			67%	
Toomey & Waldron <sup>42</sup>	N = 31	Cross- sectional survey						68%		
Walldorf et al <sup>44</sup>	Study N = 443 (n = 234 childless women)	Cross- sectional survey		19%	48%	61%	18%	51%	25%	

N = entire study sample; n = sub-sample who were surveyed on their pregnancy related concerns.

disease-related knowledge was significantly associated with voluntary childlessness (P < 0.001). Moreover, female patients with poor CCPKnow scores more likely to be voluntarily childless than women with adequate or higher CCPKnow scores (59.5% vs 42.7%, P = 0.008). Every point increase in CCPKnow score corresponded to 8% lower odds ratio of childlessness. Other factors associated with childlessness included older age (35 years vs 28 years; P < 0.001), being single (34.5% vs 9.3% with children; P < 0.001), older age at diagnosis (25.6 years vs 21.9 years; P < 0.001) and longer disease duration (13 years vs 8 years; P < 0.032), however poor pregnancy-related knowledge was the strongest predictor of childlessness.

Some 40%-68% of patients do not discuss family planning with their healthcare professionals. 41,42 Patients who received pre-

conception counselling from healthcare professionals were less likely to be voluntarily childless. <sup>6,41,43</sup> Multivariate logistic regression analysis estimated that discussing family planning with a physician corresponded to 56% lower odds of having a poor CCPKnow score and 72% lower odds of voluntary childlessness. <sup>41</sup> Specifically, the adjusted OR (for current age and marital status) is 0.28 (95% CI 0.057-1.3) for the effect of having discussed family planning with a healthcare professionals on voluntary childlessness among childless women. <sup>41</sup>

Socio-demographic factors were associated with knowledge. White ethnicity ( $\beta$  = 0.223, P = 0.01; White CCPKnow mean score 8.6 vs non-White CCPKnow mean score 6.34), membership of IBD charity ( $\beta$  = 0.200, P = 0.02; charity member CCPKnow mean score

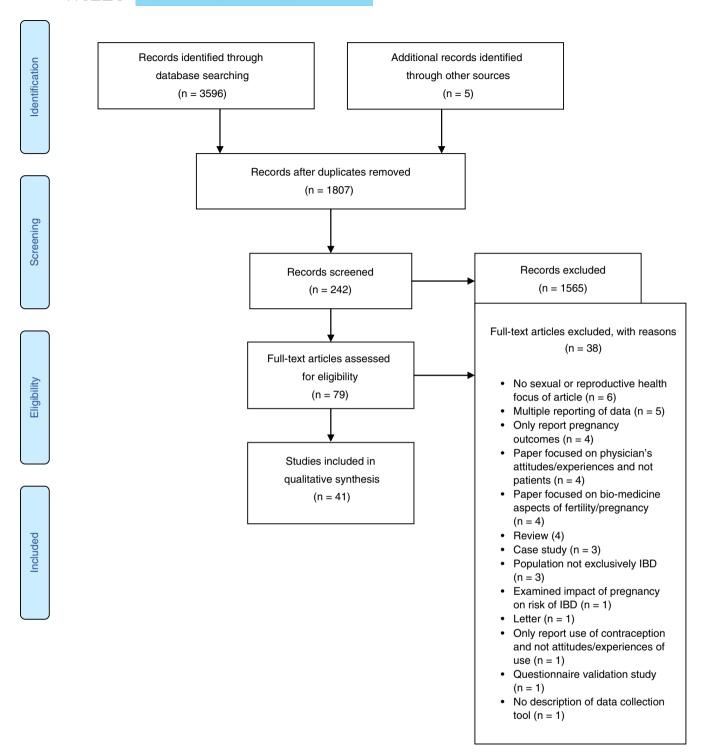


FIGURE 1 Prisma flow diagram

10.18 vs non-member CCPKnow mean score 7.62) and diagnosis of CD ( $\beta$  = 0.223, P < 0.001; CD CCPKnow mean score 9.6 vs UC CCPKnow mean score 7.2) were significant independent predictors of better pregnancy-related knowledge.<sup>34</sup> University education ( $\beta$  = 0.292, P < 0.0001; University education CCPKnow mean score 8 vs secondary school education CCPKnow mean score 6), having spoken to healthcare professional about pregnancy ( $\beta$  = 0.317, P < 0.0001; yes CCPKnow mean score 8.75 vs no CCPKnow mean

score 5.82) and younger age at IBD diagnosis ( $\beta$  = 0.274, P < 0.003) were all significant, independent predictors of higher knowledge. Other factors significantly associated with higher knowledge included working full-time (CCPKnow score 7.18 vs unemployment CCPKnow score 6.12), being in a long-term relationship (CCPKnow 7.60 vs being single CCPKnow score 6.26), CD diagnosis (CCPKnow score 7.51 vs UC diagnosis CCPKnow score 6.97), and having children after IBD diagnosis or planning to have children (CCPKnow

7.71 vs having children prior to IBD diagnosis or being infertile or planning to remain childless CCPKnow 7.05).

Two studies tested educational interventions designed to improve knowledge. Mayberry<sup>20</sup> developed an information booklet on pregnancy and asked patients and nurses to review its usefulness. Participants (patients and nurses), overwhelmingly found the information booklet helpful (87%) and 71 out of the 102 participants were prepared to buy the booklet, indicating the need for pregnancy-related information. Mountfield et al<sup>21</sup> provided a one-off group education session to 155 patients and measured their knowledge before and after the session using the CCPKnow scale. Knowledge was low at baseline (65.1% scored "poor") and increased significantly post-education (P < 0.0001). Importantly, knowledge regarding medication during pregnancy improved: 33.5% of the participants initially thought they should avoid all medication during pregnancy, but after the education session, this dropped to 1.2% (P < 0.0001) indicating attempts to improve knowledge can be successful.

## Pregnancy-related fears and concerns

Pregnancy-related fears and concerns are multifaceted and stem from lack of knowledge and awareness. Unlike for knowledge, there are no validated or standardised measures of pregnancy-related fears and concerns. Within the research literature, there is limited evidence of factors associated with pregnancy and disease related concerns or the exact nature of these concerns. Selinger et al<sup>38</sup> argued that poor disease-related knowledge predicts fears that are inconsistent with medical evidence. One study found nearly 53% of IBD patients reported that disease-related concerns affected their decision-making regarding pregnancy, with CD patients were significantly more likely to report disease-related concerns (62%) than those with UC (38%) (P = 0.01). Additionally, 14% of childless patients reported their decision not to have children was a direct result of IBD.<sup>5</sup> In one study with amongst exclusively male IBD participants nearly two-thirds desired to become fathers (68.4% out of 154), but still 24% of these reported experiencing some hesitation regarding having children due to IBD, but the researchers did not further investigate the exact nature of the hesitations.<sup>27</sup> Further, some of these studies relied on retrospective reports and there was a lack of prospective evidence regarding the predictive effect of these high levels of pregnancy-related concerns on childbearing decisions.

The most common pregnancy-related fears and concerns reported by patients are presented in Table 1. Studies have found that patients often report several pregnancy-related concerns simultaneously, with concerns regarding general concerns over the effects of pregnancy on IBD (percentages of patients reporting this ranged from 21%-79%—see Table 1) and IBD on pregnancy (63%-90%). Nearly all of 96 nulliparous female patients from Australia worried about the general effect of IBD on pregnancy (90%) and about the effects of pregnancy on IBD (91%), but the specific nature of these concerns were not noted.<sup>38</sup> In a survey of 348 female patients from six Mediterranean countries [Malta, Greece, Israel, Italy, Portugal, and Spain] the reasons for voluntary childlessness included fear that IBD could cause harm to the baby (63%),43 Furthermore, 59% of 226 voluntary childless women reported concerns about the effect of pregnancy on IBD,6 with specific concerns over the effect of pregnancy on disease activity. 13 or that pregnancy may worsen their disease (76% of 37).39

Specific concerns regarding the effects of IBD on pregnancy were noted with concerns regarding birth and pregnancy complications which ranged from 18% to 63%. 6,13,43,44 For example, 63% feared IBD would lead to a complicated pregnancy.<sup>43</sup> In a survey of 443 German IBD women, 234 were childless, and of those 61% were concerned with risk of miscarriage, and 44.6% of women aged 18-25 years wanted more information on pregnancy.<sup>44</sup> Other concerns included worry that IBD may cause infertility or difficulties conceiving, 13,38,44 and concerns over breastfeeding while on medication.38

Many patients were also concerned about passing on IBD to their offspring.<sup>5</sup> The percentage of women reporting this concerns ranged from moderate to high-59%44; 67%,6 68%43; 74%38; and 73%.<sup>39</sup> However, it is unknown whether patients are more likely to fear transmitting IBD to their offspring in families where IBD is prevalent, as many studies have not collected this data. Over a third of all patients reported concerns over the effects of IBD medication on children during pregnancy. 5,13,38,42-44 A survey of 31 IBD patients found high levels of misconceptions and worries about the effect of medication during pregnancy<sup>42</sup>; 68% reported anxiety about the effect their IBD drugs could have on a pregnancy, a third believed all drugs should be ceased during pregnancy, 19% said they would stop their medications even if advised to continue them and 35% believed an IBD flare-up is less harmful than continuing medication.

Patients reported concerns about raising a child ranged from 10% to 70%.6,38,39,43 Around 70% of 37 voluntary childless patients<sup>39</sup> and 13% of 348 female patients<sup>43</sup> reported concern they might be unable to care for a child. Whereas, 152 out of 226 voluntary childless women had concerns about their ability to cope with raising a child<sup>6</sup> and some nulliparous (42.9% of n = 96) women reported specific concerns that their disease would negatively impact on their ability to look after their child.<sup>38</sup>

#### Psychosocial effects of IBD on reproductive 3.6 health

The effect of IBD on patients' reproductive health is a complex interaction of biological, psychological, and socio-cultural factors. The research literature has mainly examined contraceptive use and sexual functioning. Research on pregnancy and post-pregnancy experiences and attitudes is very limited and there is considerable variability in study aims. A summary is presented in Data S1

#### 3.7 Contraceptive use

Although high levels of voluntary childlessness have been reported in IBD populations, paradoxically, a number of studies using non-

#### TABLE 2 Recommendations for healthcare professionals based upon the research evidence

#### General recommendations

Knowledge of pregnancy-related issues in inflammatory bowel disease (IBD)

Health care professionals should be aware that

- Up to 50% of all IBD patients will have poor knowledge about how their IBD affects fertility and pregnancy.
- Poor knowledge of pregnancy-related issues in IBD are associated with voluntary childlessness.
- Patients who received pre-conception counselling from healthcare professionals were less likely to be voluntarily childless.

Health care professionals are recommended to

- Use the validated Crohn's and Colitis Pregnancy Knowledge (CCPKnow) tool<sup>34</sup> on childbearing aged patients to screen patients with poor/adequate knowledge of pregnancy-related issues in IBD (scores between which range from 0 to 10 on CCPKnow).
- Healthcare professionals should educate patients with poor/adequate knowledge of pregnancy-related issues on the impact of IBD on pregnancy and fertility and the impact of pregnancy and breastfeeding on IBD.
- Consider providing patients with educational resources developed by some IBD charities which offers patient-friendly and evidence-led
  materials to patients (e.g., https://www.crohnsandcolitis.org.uk/).
- Offer patients the opportunity to voice their pregnancy and fertility related concern and respond to these concerns with patient-specific advice.

#### Contraception

Healthcare professionals should be aware that

 Between one-fifth to one-third of female patients do not use contraception and patients with a history of IBD-related surgery or past biologic therapy use are more likely not to use contraception.

Healthcare professionals are recommended to

- Record the use of contraceptive for all childbearing aged patients in their clinic file.
- Identify patients who are a 'high' pregnancy risk.
- Healthcare professionals are advised to provide 'high' pregnancy risk patients with appropriate advice on contraception and preconception counselling to prepare for unplanned pregnancy.

#### Sexual functioning

Healthcare professionals should be aware that

• For some patients, IBD (particularly during active disease) and surgery has a negative impact on patient's sexual function and satisfaction.

Healthcare professionals are recommended to

- Offer patients the opportunity to discuss sexual function and satisfaction, particularly during active disease or before and after surgery.
   Refer patients identified by the International Index of Erectile Function (IIEF)<sup>35</sup> for men and the Female Sexual Function Index (FSFI)<sup>36</sup>; as
- Refer patients identified by the International Index of Erectile Function (IIEF)<sup>35</sup> for men and the Female Sexual Function Index (FSFI)<sup>36</sup>; a experiencing sexual dysfunction to specialist services such as psychological services, specialists in pelvic floor dysfunction or gynaecologists, as appropriate and if available.

## Medication

Healthcare professionals should be aware that

- A significant number of patients report concerns over the safety of IBD medication during pregnancy and breastfeeding.
- Some studies have reported that around one-fifth of patients stop taking their medication during pregnancy without medical advice or believed medication should be stopped.
- The evidence on breastfeeding is mixed and limited.

Health care professionals are recommended to

- Advise patients who are pregnant or postpartum on the effects of medication on pregnancy and breastfeeding.
- Offer patients the opportunity to discuss their concerns regarding medication and respond to patients fears and concerns.
- Healthcare professionals should highlight the importance of patients staying healthy during pregnancy and postpartum period and the benefits of breastfeeding and the role of medication in this, if appropriate.
- Ask about medication adherence using non-judgemental, open questions during pregnancy and record medication adherence.

validated measurements have found significant numbers of female patients may also be considered at 'high-risk' for pregnancy. Ellul et al<sup>43</sup> found that more than half of all pregnancies (57.4%) were unplanned. Between one-fifth to one-third of female patients did not use any contraception (percentage ranged from 18%,<sup>39</sup> 23%,<sup>45</sup> and

31.8%<sup>13,22</sup>), with the definitions of contraception being reasonably consistent between the studies. Ellul et al<sup>43</sup> found that only 27% of 348 patients used contraceptive methods and that patients who had received counselling from healthcare professionals regarding the use of contraception were no more likely to use contraception.

Participants with a history of IBD-related surgery (P < 0.03) or past biologic therapy use (P < 0.05) were less likely to use any contraceptive method compared to those without prior surgery or biologic use.<sup>45</sup> Education attainment of high school or less was also associated with no contraceptive use (P < 0.03). Documentation of contraceptive method was poorly documented at the gastroenterology visit, in only 29.2% of cases,<sup>29</sup> and only 19% of participants were provided with reproductive health counselling by their physicians.<sup>29</sup>

## 3.8 | Sexual function

A number of studies have investigated the impact of disease and its treatment on various aspects of patient's sexual lives (particularly women), investigating mostly sexual function and dysfunction, but also sexual frequency and occasionally, sexual satisfaction. The rates of sexual dysfunction in the literature are inconsistent and variable because of significant heterogeneity in study aims, definition of sexual dysfunction, design and samples between the studies.

Most male and female IBD patients were sexually active, with 30.6% reported weekly and 28.7% reported more frequent than weekly sexual activity. 46 However, sexual frequency was reduced by IBD (flare-up) with over half patients (57.6%) reporting this decrease in frequency, and more females (females 66.3% vs males 40.5%, P < 0.0001), and participants with history of surgery (68.5% vs 50.4%/non-operated, P = 0.0113) reporting a decreased frequency of sexual activity. Without a control group from the general population it is difficult to judge whether these rates of sexual activity are comparable or reduced. More recently a qualitative study, with n = 18CD and n = 14 UC British South Asian participants, provides some context to patient's experiences.<sup>26</sup> Using semi-structured interviews. most of the married participants reported supportive partners but, some spoke of how having IBD had at times put a strain on their relationship. This included being too ill to be interested in sex with one participant reporting "At the beginning when it was... it was all really bad... I, it was really hard in the bedroom just to be sexually active, it was so hard... I couldn't make him understand that, you know, I was having stomach pain, we were arguing constantly because he'd think I've had something bad to eat".

Some patients experience sexual dysfunction; but due to conflicting results and variability between the studies it is difficult to establish the percentages of patients reporting sexual dysfunction. Using a modified but previously validated questionnaire sexual dysfunction amongst 50 women with UC and 100 men with CD/UC was investigated and compared to a control group. <sup>47</sup> Frequency of patient's sexual intercourse and rates of sexual dyspareunia was comparable to the control group. However, a number of other studies have examined the impact of IBD treatments, especially surgery, on sexual functioning and the findings were inconsistent and contradictory. For example, immunomodulator or biologic agent therapy has not been found to impact on female or male sexual functioning using FSFI or IIEF. <sup>48</sup> Studies looking at the effect of surgery have largely focused on colectomy and pouch surgery, where potential

disturbances to the function of the pelvic floor are greatest. In contrast, there is a lack of data on patients without surgery and small bowel Crohn's disease surgery. Dyspareunia was experienced by a small number of women (n = 8/15) and disturbed erection and or eiaculation was experienced by 15 (out of 71) male ileostomists who had undergone colectomies.<sup>23</sup> However, this study did not use a validated measure of sexual functioning. More recently, Harnoy et al<sup>49</sup> assessed sexual dysfunction in n = 43 male and n = 45 female UC patients after ileal pouch-anal anastomosis (IPAA) using FSFI or IIEF and presented notably higher levels of sexual dysfunction after surgery. Half of the female sample met the criteria for sexual dysfunction (FSFI score 26) and 29% of men were evaluated as suffering from moderate to severe erectile dysfunction (IIEF-5 score 21). Further, fear of anal leakage interfered in male and female enjoyment of sexually activity, however between 55% and 80% of respondents perceived no change or improved sexual function after surgery.<sup>50</sup>

Reports of sexual dysfunction after surgery were inconsistent with some reporting deterioration and some reporting improvement. For example, in a longitudinal study that assessed perceptions of relationships and sexual parameters in 37 male and female patients with UC *before* and *after* an ileostomy or an IPAA surgery,<sup>51</sup> it was found that quality of life improved significantly after surgery. There were partial changes in sexual satisfaction (improvement in female patients but not male patients) and sexual function (improvement in male patients but not female) suggesting that changes in sexual function do not necessarily coincide with changes in sexual satisfaction. These findings are consistent with other studies which have indicated surgery does not have an adverse effect on male and female sexual functioning,<sup>24,52</sup> and quality of life significantly improves 6 and 12 months post-operatively.<sup>53</sup>

In childhood or adolescent UC (n = 25) patients undergoing J-pouch ileoanal anastomosis, compared to a control group (n = 38), there was no evidence that surgery was detrimental to participants sexual function. Similarly, no significant differences were seen in a case-controlled study, comparing the sexual function of patients with pouch failure (n = 36) to an age and sex matched-control group with no pouch failure (n = 72). However, the pouch failure group scored significantly worse perceptions of body image than the control group.  $^{55}$ 

## 4 | DISCUSSION

The incidence and prevalence of IBD is rising worldwide,<sup>3</sup> so the number of patients who require reproductive healthcare and education will increase. This is the first, comprehensive systematic review on the psychosocial effects of IBD on patients' reproductive health. This review provides rich insight into the psychological reproductive health of IBD patients and should be read alongside existing reviews on biomedical aspects of IBD on pregnancy and fertility.<sup>9,10</sup> First, we report high levels of voluntary childlessness amongst IBD populations with around one-fifth to one-third of IBD patients reported voluntary childlessness. <sup>6,37–39</sup> This is consistent with Tavernier et

al<sup>7</sup> review and rates of voluntary childlessness are often lower among the general population (<10%) in comparison to IBD population.<sup>56</sup> Knowledge of pregnancy-related issues in IBD are consistently poor with half of all patients scoring 'poor' on knowledge scales. Higher levels of pregnancy and fertility knowledge are associated with parenthood and lower levels of pregnancy and fertility knowledge are associated with voluntary childlessness. Several observational studies have found preconception counselling is associated with patients choosing parenthood<sup>6,43</sup> however only a single observational study illustrated a predictive association between preconception counselling and reduced odds of voluntary childlessness.41 Pregnancy-related fears and concerns are multifaceted and often stem from lack of knowledge and, higher levels of pregnancyrelated fears are associated with voluntary childlessness. Second, a significant number of female patients (between one-fifth to onethird) may be considered at "high-risk" for pregnancy because of low use of contraception. Third, the research evidence for sexual dysfunction after disease and treatment is inconsistent, with some studies noting high levels of sexual dysfunction and other studies noting comparable levels to the general population or control groups. Finally, there is limited evidence on patients' pregnancy, postpartum and parenting experiences (see Data S1). Some studies have reported that around one-fifth of patients stop taking their medication during pregnancy without medical advice or believed medication should be stopped. 37,43,57 The evidence on breastfeeding is mixed and limited. 43,58 The quality of evidence is varied and there is limited evidence from intervention, qualitative, and longitudinal studies.

Current guidelines from the ECCO<sup>9</sup> and NICE<sup>2,14</sup> provide little guidance for healthcare professionals on psychological factors that may need addressing in pregnancy and fertility management. Further, knowledge of pregnancy and fertility issues relating to IBD is low across the  $world^{21,32-34,37,40,41}$  and international societies such as ECCO are pivotal in changing these worldwide trends. Research evidence indicates that pre-conception counselling is effective at improving knowledge<sup>21</sup> and reducing voluntary childlessness.<sup>40,41</sup> However, there are no formal provisions of pre-conception counselling in the UK and patients have to approach their healthcare professionals for advice. This could lead to significant variability in quality of advice due to the lack of guidelines. This review lends support to pre-conception counselling for IBD patients to tackle poor knowledge and allow patients to make an informed decision on their reproductive health and childbearing decisions. Based upon research evidence, pre-conception counselling could be tailored for patients which include the recommendations made in Table 2.

We observed that 85% of the studies included in this review have been published in the past decade (since 2008). This suggest that researchers and practitioners' interest on IBD patients' reproductive health is a recent phenomenon and with greater research evidence a better service should follow.

The quality of evidence varied. For example, the quality of research evidence on pregnancy and fertility knowledge was strong because of the use of validated questionnaires (eg, CCPKnow and CCKnow) and large sample sizes.<sup>6</sup> However, the quality of evidence

for research on pregnancy-related fears and anxieties, contraception and sexual function was more mixed, with smaller samples and use of non-validated questionnaires. For example, most of the studies on pregnancy-related fears and anxieties have used non-validated questionnaires<sup>6,13,43,44</sup> and they offer limited contextual explanation to nature of the fears and concerns. However, the picture is complex, despite studies being poor quality (eg, 39) their findings are consistent in indicating high levels of pregnancy-related fears. Studies which measured sexual function were more likely to use validated measures but had select samples, with the post-surgery population being extensively researched but not 'general' IBD groups or other subgroups (eg, peri-anal disease). Further, most studies narrowly focussed on physical aspects of sexual function and ignored other aspect of patient's sexual lives (eg, quality of sexual relationship) and often did not include control groups. Most of the sexual function studies included heterosexual, but not homosexual patients. The exclusion of homosexual patients is a significant oversight because some homosexual patients may experience distress over the disease and treatment on their sexual lives or other aspect of their reproductive health.

Finally, most of the studies have investigated the impact of IBD on exclusively female samples or included female and male samples. There was only one study that solely investigated the impact of IBD on men's reproductive health.<sup>27</sup> So, the findings from this review overwhelming represent women's experiences of IBD, and data on men's experiences and knowledge of pregnancy-related issues is limited. Moreover, the majority of the samples included in the study are White and the findings from this review will, no doubt, over-represent White participants' experiences of IBD and may not be generalisable to different ethnic groups. Response rate was often low, thus questioning the accuracy in representing general IBD patient populations. There was also limited evidence from intervention, qualitative and longitudinal studies. The design of existing intervention studies are also weak as none of the interventions have used randomised controlled trials and some have not used appropriate comparison control groups <sup>20,21</sup> or used unmatched control groups. <sup>19</sup>

Although a number of shortcomings with the research literature have been identified, some clear and consistent evidence emerged. Based upon the research evidence, clinical implications offered from the review recommend pre-conception counselling for childbearing aged IBD patients to provide better psychosocial care during reproductive health management. Further research on patients' pregnancy, postpartum and parenting experiences is warranted. Also, the lack of qualitative, longitudinal and intervention studies needs to be addressed to ensure more comprehensive evidence and a greater methodological rigour in the research literature.

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#### **AUTHORSHIP**

Guarantor of the article: SP & MJB.

Author contributions: SP and SC ran the searches, created the databases, selected the relevant papers and modified the extraction and quality assessment sheets. SP, SC, WCD, CS, HS and MJB developed the study methodology, extracted data and completed quality assessment, co-wrote the manuscript.

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## SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section at the end of the article.

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