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Association between inflammatory bowel disease and prostate cancer: A large-scale, prospective, population-based study

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Abstract

Inflammatory bowel disease (IBD) is an established risk factor for colorectal cancer. Recent reports suggesting IBD is also a risk factor for prostate cancer (PC) require further investigation. We studied 218 084 men in the population-based UK Biobank cohort, aged 40 to 69 at study entry between 2006 and 2010, with follow-up through mid-2015. We assessed the association between IBD and subsequent PC using multivariable Cox regression analyses, adjusting for age at assessment, ethnic group, UK region, smoking status, alcohol drinking frequency, body mass index, Townsend Deprivation Index, family history of PC and previous prostate-specific antigen testing. Mean age at study entry was 56 years, 94% of the men were white, and 1.1% (n = 2311) had a diagnosis of IBD. After a median follow-up of 78 months, men with IBD had an increased risk of PC (adjusted hazard ratio [aHR] = 1.31, 95% confidence interval [CI] = 1.03–1.67, P = .029). The association with PC was only among men with the ulcerative colitis (UC; aHR = 1.47, 95% CI = 1.11–1.95, P = .0070), and not Crohn's disease (aHR 1.06, 95% CI = 0.63–1.80, P = .82). Results are limited by lack of data on frequency of health care interactions. In a large-scale, prospective cohort study, we detected an association between IBD, and UC specifically, with incident PC diagnosis.

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Travis J. Meyers and Adam B. Weiner shared equally to the first authorship.
Shilajit D. Kundu and John S. Witte shared equally to the senior authorship.

DATA ACCESSIBILITY

UK Biobank is an open-access resource. Bonafide researchers can apply to use UK Biobank data by registering and applying at https://www.ukbiobank.ac.uk/register-apply/.

ETHICS STATEMENT

Each participant provided written informed consent and the UK Biobank's study protocol was approved by the UK North West Multicenter Research Ethics Committee.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPORTING INFORMATION

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

Keywords

cohort study; inflammatory bowel disease; prostate cancer

1 | INTRODUCTION

Prostate cancer (PC) is the second most common noncutaneous malignancy in men globally, accounting for 1.3 million new cases and over 350 000 deaths in 2018 globally.[1] Screening for PC may help reduce PC mortality at the potential cost of overdiagnosis leading to unnecessary exposure to treatment-related morbidities.[2,3] Guidelines in both the United States and Europe acknowledge the benefits of identifying risk factors for PC to better counsel men on the use of prostate-specific antigen (PSA)-based screening.[4,5]

Inflammatory bowel disease (IBD) is a group of debilitating conditions including ulcerative colitis (UC) and Crohn's disease (CD), characterized by chronic gastrointestinal inflammation, with an estimated prevalence of about 6.8 million cases worldwide.[6] IBD incidence is generally stabilizing in the US and Europe while increasing in newly industrialized countries.[7] IBD frequently manifests beyond the gastrointestinal tract and can affect almost any organ system.[8] Furthermore, since inflammation and genome instability underly the "hallmarks of cancer",[9] the role of IBD as a cancer risk factor merits attention. Therefore, in light of the close proximity of the gastrointestinal tract and prostate, it is of interest to evaluate the potential relationship between IBD and PC.

While inflammatory bowel disease is an established risk factor for colorectal cancer,[10] associations between IBD with PC have been reported for some studies[11–17] but not others.[18–20] We thus conducted a prospective study of men from the large-scale, population-based UK Biobank cohort[21] to test this association. Men in the UK historically have low rates of PC screening (an estimated 6.2% of men aged 45–89 with no history of PC were PSA tested in 2007)[22] and PC screening is not currently recommended by the UK National Screening Committee.[23] We hypothesized that men in the UK Biobank with a diagnosis of IBD would experience a higher incidence of subsequent PC diagnosis.

2 | MATERIALS AND METHODS

2.1 | Study population

The UK Biobank is a prospective, population-based study established to investigate genetic and nongenetic risk factors for disease in individuals of middle and advanced age.[21] The details of study design and data collection have previously been described and the complete protocol can be found online.[21,24] In summary, 500 796 participants aged 40 to 69 years registered within the National Health Service (NHS) and living within 40 km of one of 22 assessment centers across England, Scotland, and Wales were recruited between 2006 and 2010. Each participant provided written informed consent and the UK Biobank's study protocol was approved by the UK North West Multicenter Research Ethics Committee. Baseline assessments at entry into the cohort were made for each participant in 90-minute appointments which included questionnaires, sample collections, and health care physical

exams and interviews. Participants are linked to the NHS Central Register to capture IBD status, cancer diagnoses, and deaths.

Since the present outcome of interest was PC, the analytical cohort was limited to self-reported male participants (n = 228 284). We excluded men if at baseline assessment they had: (a) prior history of a malignant cancer (any site), or timing of malignant cancer diagnosis relative to baseline could not be determined (n = 9902, 4.3%); (b) surgical removal of the prostate (n = 64, <0.1%; NHS procedure codes: OPCS version 3–630-635; OPCS version 4-M61); (c) earlier recorded death date (n = 1, <0.01%). We also excluded 233 (0.1%) individuals whose genetically inferred sex was female. The remaining 218 084 men comprised the study population.

2.2 | Exposure

The exposure of interest was a history of IBD (UC or CD) at the time of baseline assessment. IBD history was considered present if the participant had either a relevant inpatient ICD code or self-reported illness. ICD10 codes for UC and CD were K51 and K50, respectively. ICD9 codes for UC and CD were 556 and 555. Self-reported IBD and the approximate date that a doctor first diagnosed IBD were collected during the baseline assessment interview. If a participant had recorded diagnoses for both UC and CD, then they were still included in the analysis of overall IBD but not in the subtype analyses.

2.3 | Outcome

The outcome of interest was first diagnosis of malignant PC after baseline assessment. PC case status was determined using ICD codes (ICD-9:185, ICD-10: C61). Follow-up data for the UK Biobank cohort was available through the middle of 2015.

2.4 | Covariates

Covariates included in multivariable analyses included age at baseline assessment (continuous), self-reported ethnicity (White, Mixed, South Asian, Chinese, Black or other), region of assessment center (10 cancer registry regions), Townsend Deprivation Index (TDI; quintiles), smoking status (never, former or current), alcohol drinking frequency (never, special occasions only, 1–3 times per month, 1–2 times per week, 3–4 times per week, daily/almost daily), body mass index (BMI; quintiles), family history of PC in biological relatives (yes, no) and history of PSA testing (yes, no). All categorical variables included a category for missingness. The TDI is a measure of material deprivation for a small geographical area based on four census variables: households without a car, overcrowded households, households not owner-occupied and persons unemployed.[25] We adjusted for TDI to account for potential confounding of the IBD-PC association by access to health care services. We also assessed the appropriateness of including history of partial or complete colectomy as a model covariate (OPCS-3 codes: 452, 460, 461, 471, 472; OPCS-4 codes: H4-H11).

2.5 | Statistical analyses

The distributions of covariates were compared between men with no history of IBD to men with any IBD, UC exclusively or CD exclusively. Continuous variables were tested with t tests; categorical variables were tested with chi-square tests. The purpose of these tests was

not for inference, but rather to present descriptive information on the cohort and motivate inclusion of covariates in our Cox regression models.

Person-years were calculated from the date of baseline assessment until diagnosis of PC, or until any of the following non-PC endpoints: diagnosis of a different malignant cancer, noncancer related prostatectomy, death, or end of follow-up, whichever came first. The non-PC endpoints were considered censoring events. If PC diagnosis followed any of the other censoring events within 3 months, then PC was used as the endpoint and the time to PC was included as the follow-up time. The rationale was that the censoring event may have been correlated with PC diagnosis.

Incidence rates for PC were calculated for each baseline group (no IBD, any IBD, UC or CD) from the number of incident PC cases divided by the person-years of follow-up in each group. Kaplan-Meier curves were fit comparing survival for men with IBD (any IBD, UC or CD) at baseline to those without IBD at baseline. The difference in survival by IBD status was compared by the univariate log-rank test.

Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for the association between IBD and PC were calculated using Cox proportional hazards models adjusting for all aforementioned covariates. This analysis was the basis for testing our main hypothesis. We further investigated whether the potential association between IBD and PC varied by: (a) IBD subtype; (b) duration of living with IBD (using 20 years from IBD diagnosis until baseline assessment in UK Biobank as the cut point); (c) age at assessment (using 60 years as the cut point); and (d) obesity status at baseline (BMI > 30 vs ≤30). For Subanalyses 1 and 2, we performed the same regression as the primary analysis except IBD status was categorized as UC, CD or no IBD; and IBD > 20 years, IBD ≤ 20 years or no IBD, respectively. We used a cut point of 20 years to reflect the induction of IBD-related carcinogenesis in colorectal cancer. Specifically, IBD-related colorectal cancer is relatively rare before 20 years after onset of IBD symptoms.[26] We hypothesized that a similar interval would be necessary to observe an association between IBD with PC. For Subanalysis 3, we created a new model which included age categorized as ≤60 or >60 years and an interaction term between this new age variable and IBD status (IBD or no IBD). We used a cut point of 60 years for age at assessment because this approximated the median value. For Subanalysis 4, we stratified the IBD-PC HRs on obesity status at baseline (BMI ≤ 30 or >30) and tested the interaction product term.

To determine the appropriateness of our Cox models, we tested the underlying assumption that the relative incidence of PC between men with and without IBD was constant over time (proportional hazards). Specifically, the correlation between scaled Schoenfeld residuals with follow-up time was tested, based on the univariable Cox model with IBD status as the regressor. All statistical analyses were conducted using R statistical software, version 3.6.0: Kaplan-Meier plots were generated by the “survminer” package; Cox models were conducted using the “survival” package.

3 | RESULTS

3.1 | Study participants

At baseline assessment, there were 2311 men with a history of IBD and 215 773 men without a history of IBD (Table 1). Compared to men without IBD, men with IBD were on average 1 year older (57.3 vs 56.5; P < .05), were more likely to be White (95.3% vs 93.8%; P < .05), were more likely to be former smokers (49.5% vs 37.7%) than current smokers (8.9% vs 12.6%), and had a lower average BMI (27.5 vs 27.8; *P* < .05). All participants were similar with respect to average TDI (No IBD: −1.25; IBD: −1.19; negative values reflect relative affluence), family history of PC (both 7.7%) and history of PSA testing (No IBD: 27.6%; IBD: 26.9%). Of those with IBD, 1488 exclusively had UC and 643 exclusively had CD. Compared to men with CD, men with UC were on average 1 year older (57.7 vs 56.4; *P* < .05), had a lower TDI (−1.33 vs −0.88; *P* < .05), were more likely to be former smokers (51.2% vs 47.6%) than current smokers (6.7% vs 13.7%), and had a higher average BMI (27.7 vs 27.1, *P* < .05).

3.2 | PC incidence based on inflammatory bowel disease status

After a median follow-up of 78 months (over 1.3 million person-years for men without IBD and 14 379 years for men with IBD), there were 4681 new cases of PC in men without IBD and 66 in men with IBD (Table 2). Men with IBD demonstrated a shorter time to developing PC (Log-rank, *P* = .018; Figure 1). The assumption of proportional hazards was satisfied for each univariate model for baseline status of any IBD, UC or CD. The incidence rates for PC (cases per 100 000 person-years) were 343 for non-IBD and 459 for men with IBD. After adjusting for covariates, IBD was associated with an increased hazard of PC (aHR = 1.31, 95% CI = 1.03–1.67, *P* = .029; Table 2). Further adjusting for history of partial or complete colectomy did not meaningfully change the HR so it was not included in the final models. In addition, we observed a trend for increasing HR across years since IBD diagnosis (≤20 years, aHR = 1.22; >20 years, aHR = 1.49; *P*-trend = .018; Table 3).

3.3 | PC incidence based on inflammatory bowel disease subtype

The person-years for men with exclusively one IBD subtype were comprised of 9201 for men with UC and 4021 for men with CD (Table 2). A total of 49 men with UC and 14 men with CD developed PC. While men with UC developed PC more rapidly than men without IBD (Log-rank *P* = .0023, 533 cases per 100 000 person-years), those with CD did not (Log-rank *P* = .95; 348 cases per 100 000 person-years; Figure 2). The same associations were noted on adjusted analysis (UC: aHR = 1.47, 95% CI = 1.11–1.95, *P* = .0070; CD: aHR = 1.06, 95% CI = 0.63–1.80, *P* = .82; Table 2). For the UC subtype, increasing HR was also noted across years since diagnosis (≤20 years, aHR = 1.29; >20 years, aHR = 1.87; *P*-trend = .0022; Table 3).

3.4 | Effect measure modification by age at study assessment and obesity

We did not detect interaction by age at study assessment for any IBD, UC or CD on PC incidence (Table S1). While CD was marginally associated with PC in obese men (HR = 2.21, 95% CI = 0.92–5.33, *P* = .077), the same was not observed in nonobese men (aHR =

0.82, 95% CI = 0.42–1.57, *P* = .55; *P* for interaction = .079; Table 4). We did not observe interaction between obesity and any IBD (P-interaction = .66) or UC (*P*-interaction = .80).

4 | DISCUSSION

IBD is a chronic inflammatory condition with a growing prevalence, affecting at least 0.3% of individuals in developed countries.[7] In a large, prospective cohort of men in the UK, where PC screening is low, we found a positive association between IBD and PC. This association was driven by an approximate 50% increase in PC risk among men with UC. These findings suggest that even outside the setting of routine PC screening, men with IBD are at an increased risk of PC.

The limited research into IBD and PC has demonstrated conflicting results. In a recent, large, retrospective study at a single medical center, men with IBD undergoing PC screening had a greater than fourfold increase in incident PC and high-grade PC compared to men without IBD.[13] In a case-control study within a shared, equal-access healthcare system, men with IBD had a 70% increased risk of PC.[11] In contrast, other studies and a meta-analysis found no clear association between IBD and PC.[18–20] Three studies reported the positive association in UC but not CD,[12,16,17] as we observed in the present study. A pair of studies observed the association for both CD[14] and UC,[15] although the associations were attenuated when cancers diagnosed within the first year after IBD diagnosis were excluded. Much of this prior research included men younger than 50 and thus at low risk of PC,[12,16,17,19,20] which may explain why two of these studies reported no IBD-PC association.[19,20] In contrast, the UK Biobank was designed to study age-related diseases.[24]

Our observed association between IBD with PC may indicate either a causal biological effect or noncausal factors for which we have not accounted. Chronic inflammation is a risk factor for cancer development in various solid tumors and is thought to play a role in the well-established association between IBD and colorectal cancer.[10] In addition, chronic inflammation may contribute to prostate tumorigenesis by inducing DNA damage and promoting carcinogenic epigenetic alterations.[27] However, it is unknown whether chronic gut inflammation leads to changes in the prostatic inflammatory milieu. We observed a stronger association between IBD (UC) with PC in men having IBD for longer than 20 years compared to less than 20 years. This fits with a hypothesis that chronic inflammation induces carcinogenesis in the prostate, similar to the changes over time in the colorectum.

Consideration for the association between IBD and PC should account for the distinct clinical and pathologic features between IBD subtypes.[28] For example, transmission of gut inflammation to the prostate may occur via local inflammation in the rectum, which is nearly universal in UC and less frequently observed in CD.[29] While local inflammation may help to explain our observation and prior reports that UC, not CD, is associated with PC, further research is warranted, in particular the documentation of adjacent rectal-prostatic inflammation in patients with UC vs CD. Besides local inflammation, elevated serum (systemic) inflammatory markers which are known to occur in IBD[30] may play a role in PC development and progression.[27]

As for noncausal factors, immunomodulatory medications commonly used in IBD have been associated with several extra-intestinal malignancies,[18,31] suggesting immunosuppression may also be responsible for prostate tumorigenesis or progression. Moreover, shared underlying genetics may explain the IBD-PC association, although preliminary evidence across common gene variants has not detected genetic correlations for either UC or CD with PC.[32]

The potential link between IBD and PC has important implications for screening and detection of PC. While recommendations are controversial, some guideline panels have supported more aggressive screening in high-risk populations.[4,5] Older age, African ancestry, and family history of PC have been consistently identified as risk factors for PC development.[33] Our study suggests that IBD may be an independent risk factor for PC, but future study is needed to determine how to appropriately apply this finding to patient screening practices.

There are several important limitations of our study. First, we were unable to account for frequency of healthcare encounters in our analysis of incident PC. Men with IBD have more frequent healthcare encounters,[34] are more likely to undergo rectal examinations, and may be subject to opportunistic screening. Our analysis was adjusted for whether the participant had a PSA test prior to entry into the UK Biobank, however, we were unable to account for number of prior PSA tests or digital rectal examinations. Nevertheless, in a sensitivity analysis, we observed that in men with no history of a PSA test, the hazard ratios were greater by 10% and 12% for IBD and UC, respectively, compared to the models including all men and with PSA test as a covariate. Second, we had access to inpatient ICD codes and self-reported IBD but not outpatient ICD codes. Although we would have more confidence in outpatient ICD codes to capture first diagnosis of IBD, self-reported IBD is expected to be relatively accurate. A recent study reported good agreement between self-reported and medically recorded diagnoses of UC (positive predictive value [PPV] = 64%) and CD (PPV = 100%).[35] Third, the release of the UK Biobank data at the time we performed the analysis did not provide information regarding cancer grade or stage; thus, we were unable to differentiate between low-risk and clinically significant cancer. This limitation is of particular relevance in men with a chronic illness who may be subjected to opportunistic screening and thus over-detection of low-risk disease. Fourth, given the relatively few cancer diagnoses overall, we report incidence of PC diagnosis, but not morbidity or mortality related to diagnosis and treatment. Fifth, we had limited statistical power to detect an interaction between IBD and obesity on PC incidence. However, our preliminary evidence for a CD-PC association specifically in obese men merits follow-up in a larger sample. Finally, selection bias must be considered as a potential source of bias in this observational study. The incidence of PC in our follow-up period—334 cases per 100 000 IBD-free men per year over an average of 6.5 years—is higher than the estimated 208 cases per 100 000 men per year in the UK,[36] as has been reported previously.[37] As for IBD, the prevalence in our study population at baseline was 1071 cases per 100 000 PC-free men, higher than the estimated 2017 prevalence of 450 cases per 100 000 people in the UK.[6] Since the UK Biobank includes more men with increased likelihood of both PC and IBD compared to the UK population, we cannot rule out that our estimated hazard ratios may overestimate the expected association in the general male population.

In conclusion, in this large-scale cohort study outside the setting of widespread PC screening, men with IBD had an increased risk of incident PC compared to men without IBD. Future work is needed to validate this association accounting for PC screening and other covariates, and to determine potential mechanisms of prostate tumorigenesis in men with IBD. Ultimately, this work could provide an avenue for incorporating information about IBD into screening decisions for PC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

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aHR	adjusted hazard ratio
CD	Crohn’s disease
CI	confidence interval
IBD	inflammatory bowel disease
NHS	UK National Health Service
PC	prostate cancer
PSA	prostate-specific antigen
TDI	Townsend Deprivation Index
UC	ulcerative colitis

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What's new?

Inflammatory bowel disease (IBD) is associated with colorectal cancer risk, but what about prostate cancer? Some reports suggest there could be a link. IBD is characterized by chronic debilitating inflammation, and includes Crohn's disease and ulcerative colitis. Here, the authors studied the association between IBD and prostate cancer in 218 084 men from the UK Biobank cohort, where prostate cancer screening is not widespread. They found that men with ulcerative colitis specifically had an increased risk of prostate cancer. Further work is warranted to confirm the association, but incorporating IBD status into cancer screening protocols could be worth considering.

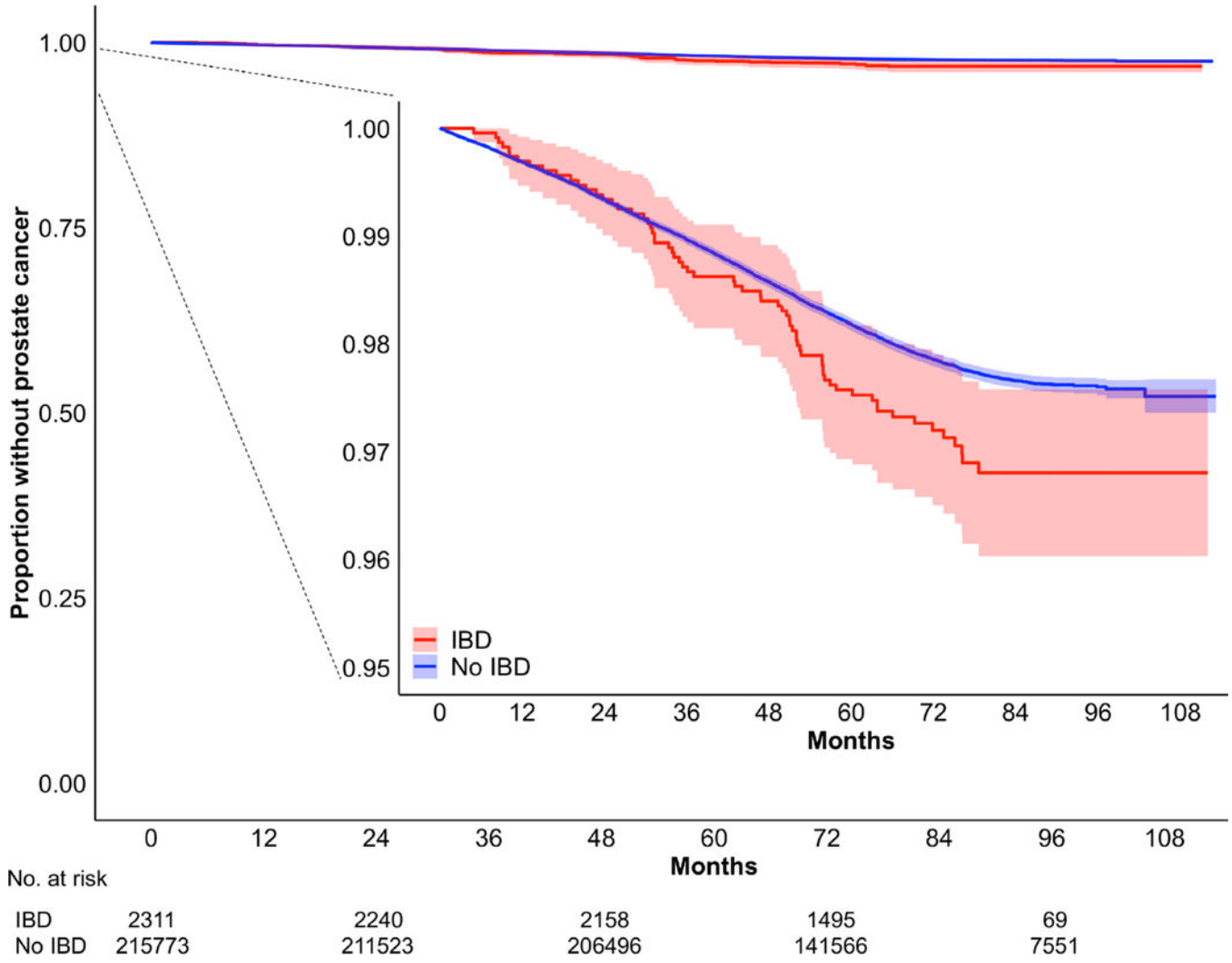
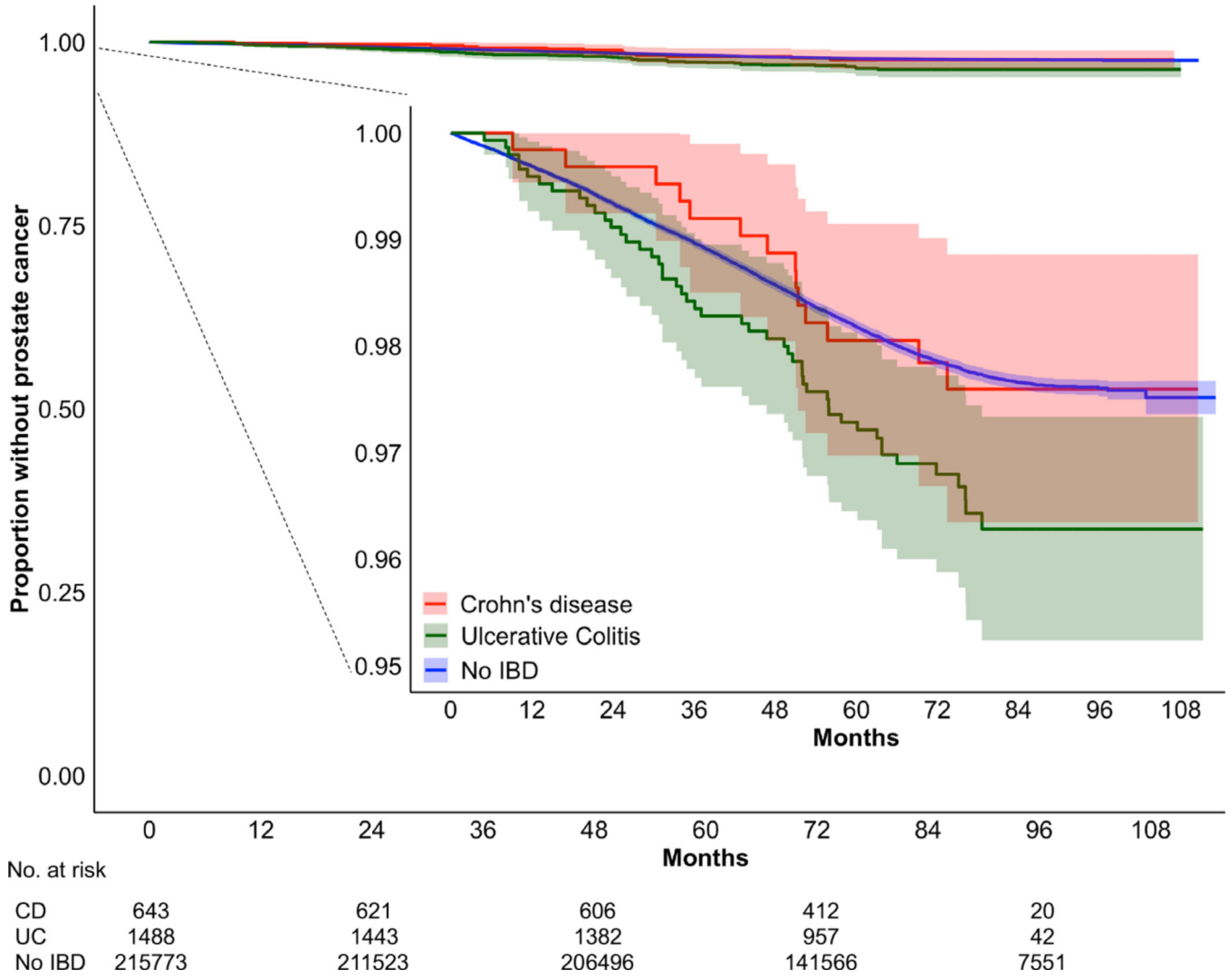


FIGURE 1.

Kaplan-Meier analysis of prostate cancer incidence by inflammatory bowel disease status. Shading represents 95% confidence intervals. Log-rank comparing IBD to no IBD $P = .018$. IBD, inflammatory bowel disease



No. at risk

CD	643	621	606	412	20
UC	1488	1443	1382	957	42
No IBD	215773	211523	206496	141566	7551

FIGURE 2.

Kaplan-Meier analysis of prostate cancer incidence by inflammatory bowel disease subtype. Shading represents 95% confidence intervals. Log-rank comparing CD to no IBD $P = .95$ and UC to No IBD $P = .0023$. CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis

TABLE 1

Baseline characteristics of male UK Biobank participants by IBD status at baseline assessment

Characteristic	No IBD (n = 215 773)	IBD (n = 2311)	CD (n = 643)	UC (n = 1488)
Age at assessment, mean (SD)	56.5 (8.2)	57.3 (8.0)[a]	56.4 (8.1)	57.7 (7.9)[a,b]
White, n (%)	202 433 (93.8)	2203 (95.3)[a]	621 (96.6)	1410 (94.8)[a]
Townsend Deprivation Index, mean (SD)	−1.25 (3.2)	−1.19 (3.2)	−0.88 (3.4)[a]	−1.33 (3.1)[b]
Region of assessment center, n (%)		[a]	[a]	[a]
Southern England	64 969 (30.1)	644 (27.9)	186 (28.9)	404 (27.2)
English Midlands	35 126 (16.3)	410 (17.7)	113 (17.6)	278 (18.7)
Northern England	91 886 (42.6)	951 (41.2)	249 (38.7)	632 (42.5)
Wales	8873 (4.1)	106 (4.6)	38 (5.9)	59 (4.0)
Scotland	14 919 (6.9)	200 (8.7)	57 (8.9)	115 (7.7)
Smoking Status, n (%)		[a]	[a]	[a,b]
Never	105 751 (49.0)	956 (41.4)	247 (38.4)	622 (41.8)
Former	81 451 (37.7)	1143 (49.5)	306 (47.6)	762 (51.2)
Current	27 220 (12.6)	205 (8.9)	88 (13.7)	99 (6.7)
Alcohol drinking frequency, n (%)		[a]	[a]	[a,b]
Never	13 568 (6.3)	190 (8.2)	57 (8.9)	116 (7.8)
Special occasions/1-3 times per month	34 899 (16.2)	452 (19.6)	146 (22.7)	274 (18.4)
1-2 times per week/3-4 times per week	112 060 (51.9)	1138 (49.2)	303 (47.1)	737 (49.5)
Daily/almost daily	54 513 (25.3)	526 (22.8)	135 (21.0)	358 (24.1)
Body mass index, mean (SD)	27.8 (4.3)	27.5 (4.3)[a]	27.1 (4.3)[a]	27.7 (4.2)[b]
Family history of prostate cancer, n (%)	16 526 (7.7)	179 (7.7)	50 (7.8)	111 (7.5)
Ever had a PSA test, n (%)	59 585 (27.6)	622 (26.9)[a]	171 (26.6)[a]	409 (27.5)[a]

Note: Difference of means tested by *t* tests; categorical variables tested by chi-square tests; alcohol drinking frequency tested by chi-square trend test. Percentages do not sum to 100% due to missing data.

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

[a] *P*-value compared to No IBD < .05.

[b] *P*-value compared to CD < .05.

TABLE 2

Cox regressions assessing the association between inflammatory bowel disease and future prostate cancer

IBD status[a]	n	Person-years	PC cases	Incidence/100 000 PYs	Adjusted hazard ratio (95% CI)[b]	*P*
No IBD	215 773	1 365 610	4681	343	1 (Reference)	
Any IBD	2311	14 379	66	459	1.31 (1.03–1.67)	.029
UC	1488	9201	49	533	1.47 (1.11–1.95)	.0070
CD	643	4021	14	348	1.06 (0.63–1.80)	.82

Abbreviations: CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; PC, prostate cancer; PYs, person-years; UC, ulcerative colitis.

[a]Three separate models were tested: Any IBD vs No IBD; UC vs No IBD; and CD vs No IBD.

[b]Models adjusted for age at assessment, ethnic group, UK region, smoking status, alcohol drinking frequency, body mass index, Townsend Deprivation Index, family history of prostate cancer and ever had a PSA test.

TABLE 3

Adjusted hazard ratios and 95% CIs of IBD duration (diagnosis until assessment) and future PC, compared to never having IBD

	n	Person-years	PC cases	aHR (95% CI)[a]	*P*
No IBD	215 773	1 365 610	4681	1 (Reference)	
Any IBD					
≤20 Years	1601	9990	40	1.22 (0.89, 1.66)	.22
>20 years	710	4389	26	1.49 (1.01, 2.19)	.042
P for trend				.018	
UC					
≤20 Years	1076	6679	29	1.29 (0.89, 1.85)	.18
>20 years	412	2521	20	1.87 (1.21, 2.91)	.0052
P for trend				.0022	
CD					
≤20 Years	406	2545	9	1.11 (0.58, 2.14)	.75
>20 years	237	1476	5	0.98 (0.41, 2.37)	.97
P for trend				.89	

Abbreviations: aHR, adjusted hazard ratio; CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; PC, prostate cancer; UC, ulcerative colitis.

[a]Models adjusted for age at assessment, ethnic group, UK region, smoking status, alcohol drinking frequency, body mass index, Townsend Deprivation Index, family history of prostate cancer and ever had a PSA test.

TABLE 4

Adjusted hazard ratios and 95% CIs of IBD and future PC, stratified on obesity status at baseline

	BMI ≤ 30				BMI > 30				
	n	**Person-years**	**PC cases**	**aHR (CI)**	**n**	**Person-years**	**PC cases**	**aHR (CI)**	***P* for interaction**
No IBD	159 722	1 012 093	3640	1 (Reference)	54 495	344 050	1023	1 (Reference)	
Any IBD	1756	10 896	50	1.26 (0.95, 1.66)	535	3367	15	1.44 (0.86, 2.40)	.66
				P = .11				*P* = .16	
UC	1104	6801	38	1.48 (1.07, 2.03)	368	2301	10	1.35 (0.72, 2.51)	.80
				P = .017				*P* = .35	
CD	514	3220	9	0.83 (0.43, 1.59)	125	784	5	2.25 (0.93, 5.41)	.078
				P = .56				*P* = .071	

Note: Models adjusted for age at assessment, ethnic group, UK region, smoking status, alcohol drinking frequency, Townsend Deprivation Index, family history of prostate cancer and ever had a PSA test.

Abbreviations: aHR, adjusted hazard ratio; CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; PC, prostate cancer; UC, ulcerative colitis.