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Risk of colorectal cancer incidence and mortality after removals of polyps: a cohort study using the UK Biobank

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Abstract

Background Colorectal cancer (CRC) is a leading cause of cancer death worldwide, however, the risk of newly-diagnosed CRC and its related mortality after polypectomy have not been conclusively determined.

Methods Prospective cases with polypectomy were identified in the UK Biobank. The age- and sex-standardized incidence ratio (SIR) and standardized mortality ratio (SMR) were calculated to assess the risk of CRC between the removal group and both the non-index-colonoscopy group (no record of diagnostic colonoscopy) from the UK Biobank and the general population in England. We also estimated the effect of removal compared with the polyp-free group using a competing risk model.

Results During a median follow up of 10 (1-44) years (51,136 person-years), 78 incident CRCs (153/100,000 person-years), and 16 CRC-specific deaths (31/100,000 person-years) were identified in the removal group. Compared with the general population in England, the removal group had a similar risk of incident CRC (SIR 0.81, 95% confidence interval [CI] 0.64-1.01; P=0.060), whereas the CRC-specific mortality was 52% lower (SMR 0.48, 95%CI 0.28-0.78; P=0.004). Compared with the non-index-colonoscopy group, CRC-specific deaths after polyp removal were not significantly different (SMR 1.64, 95%CI 0.94-2.66; P=0.050). Compared with the polyp-free group, the risks of incidence and mortality in the removal group were both greater (incidence: adjusted hazard ratio [HR] 6.17, 95%CI 4.36-8.74; P<0.001; mortality: adjusted HR 3.25, 95%CI 1.65-6.41; P<0.001).

Conclusion Polypectomy reduced but not eliminated the risk of CRC for polyp-positive participants to the level of the general population, reinforcing the importance of procedural quality and tailored surveillance strategies.

Keywords Polypectomy, colorectal cancer, incidence, mortality, UK Biobank

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Conflict of Interest: None

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Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death worldwide and the third most commonly diagnosed cancer [1]. The burden of CRC has been steadily rising for years [2]. Early screening is critical, to reduce CRC incidence and mortality by detecting and removing precursor lesions at early or even pre-cancer stages [3]. Most CRC lesions arise from neoplastic polyps that have acquired somatic gene mutations, such as *APC* and *BRAF* [4]. Pre-cancerous polyps, particularly adenomas, account for 60-70% of all colorectal polyps, which can evolve into cancers via several pathways [5]. Therefore, patients diagnosed with colorectal

polyps are strongly recommended to have the lesions removed (polypectomy) [6,7].

However, risk estimates of newly-diagnosed CRC and its related mortality after polypectomy have not been conclusively determined [8]. Studies showed the risk of incident CRC remained high compared with the general population or the non-adenoma group. A Swedish nationwide study prospectively investigated 178,377 patients with polyps removed from 1993-2016, and observed a higher risk of newly-diagnosed CRC by 1.11-3.82 times for all morphological subtypes, compared with their matched reference population (n=864,831) [9]. A Polish observational study of 236,089 participants found that the high-risk adenoma group still had a 4-6 times higher risk of newly-diagnosed CRC than the non-adenoma group, and twice the risk of the general population [10].

For the risk of CRC-specific death (also called fatal CRC), clinical cohorts have shown inconsistent outcomes. A prospective American cohort, with 2602 patients who underwent polypectomy between 1980 and 1990, showed that CRC-specific death was 50% lower compared with the general population during a median follow up of 15.8 years [11]. However, a Norwegian study, with 40,826 patients who had polypectomy between 1993 and 2007, observed a greater risk of CRC mortality among participants who had high-risk adenomas removed, compared with their general population, during a median follow up of 7.7 years [12]. Differences in the length of follow up, sample size and study period could account for these inconsistent findings.

In the United Kingdom (UK), polypectomy has been routinely performed during colonoscopy for any visible polyp [6,13]. Results from a Northern Irish cohort with 6,972 patients found that, despite removal, patients with adenomas still had approximately 3 times higher risk of incident CRC than the general population [14]. The clinical effects of removal have not been revealed in any other larger British cohort. To address the effects of removal and resolve such discrepancies in findings, we aimed to explore whether polypectomy mitigates the risk of incident and fatal CRC. To achieve this, we utilized the UK Biobank, which has recruited more than 500,000 participants and provides a larger sample with long-term follow-ups.

Materials and methods

Data sources

The UK Biobank comprises over 0.5 million participants aged from 40-69 at recruitment, and prospectively follows their wellbeing. The present study was conducted under application number 100787 from the UK Biobank. The detailed study design of the UK Biobank has been described elsewhere [15]. Ethical approval and informed consent were provided by the UK Biobank study. Patients or the public were involved in the design, conduct, reporting or dissemination plans of our research.

Participants

The total number of individuals was 502,166 at enrollment, after the exclusion of 205 withdrawals from the project at the beginning of our attempt at investigation. Notably, the UK Biobank did not disclose any report of colonoscopy. Therefore, we inferred the clinical course from patients' diagnoses and operations. Codes for the main phenotypes are provided in Supplementary Table 1.

We first identified individuals who had records of diagnostic colonoscopy (mainly code H22 following OPCS4) to avoid ambiguous diagnoses of colorectal polyps. A total of 116,997 individuals had at least 1 record of diagnostic colonoscopy. We further excluded 16,640 individuals who had the following conditions diagnosed before or at the time of diagnostic colonoscopy: 1) colorectal polyps or adenoma or neoplasia; 2) any cancer other than non-melanoma skin cancer; 3) hereditary nonpolyposis colon cancer; 4) adenomatous polyposis coli; 5) inflammatory bowel disease; 6) volvulus; 7) radiation proctitis or colitis; 8) bowel

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resection; and 9) operation of colorectal removals [8,16]. We consequently identified 100,357 participants who underwent diagnostic colonoscopy.

The other 385,169 individuals did not have any record of diagnostic colonoscopy. These comprised the non-index-colonoscopy group (the first control group). We excluded individuals who had any of the above personal histories at recruitment (n=17,436). We further excluded individuals with a diagnosis of any types of colorectal polyps or adenomas (n=24,153), or with operations for removal (n=1006) at any time. Finally, the non-index-colonoscopy group consisted of 342,574 individuals.

Colorectal polyps and polypectomy

Colorectal polyps included polyps of colon (code K63.5 following ICD-10) and rectal polyps (code K62.1) for all types. Colorectal adenomas were defined as benign neoplasms of the colon and rectum (code D12). To avoid under-identified cases, we included diagnoses of either polyps or adenomas, and we identified 21,172 prospective cases diagnosed with colorectal polyps or adenomas after diagnostic colonoscopy. The other 79,185 participants thus had no detected colorectal polyps or adenomas. Excluding 1103 individuals with records of removal at any time, the other 78,082 individuals composed the second control group (the polyp-free group).

Removal of colorectal polyps or adenomas was defined as excision of lesions of the colon or large intestine with code H20 for OPCS4 and code 466 for OPCS3. We only included participants who had operations for removal within 180 days after the diagnostic colonoscopy [9]. We excluded 7273 participants who had no record of operation on their colorectal polyps or adenomas. We further excluded participants who had operations for removal before their diagnosis (n=640; the diagnoses might have been missed) or beyond 180 days (n=7942). Ultimately, we identified 5317 participants who had undergone excision of lesions with prior diagnoses of colorectal polyps or adenomas based on colonoscopy (the removal group).

Control groups

We compared the removal group with 2 different control groups in the UK Biobank, in accordance with a previous study [17]: (1) the non-index-colonoscopy group (the first control group), consisting of individuals without any record of diagnostic colonoscopy; (2) the polyp-free group (the second control group), a low-risk reference group, defined as individuals who had no diagnosis of colorectal polyps or adenomas after diagnostic colonoscopy. We also compared the removal group with the general population from cancer registration statistics in England in 2017 (most participants in the UK Biobank were born in England) [18].

Covariates

In the comparisons between the removal group and the 2 control groups we incorporated covariates of sex, year of birth, smoking status, body mass index (BMI), number of diagnostic colonoscopies, age at removal (last diagnostic colonoscopy for the polyp-free), family history of digestive cancers, and regular use of aspirin or ibuprofen, given their possible effect on CRC [19]. For cases of adenoma, we extracted the locations according to ICD-10 subcodes. However, the location of non-adenoma polyps, as well as their number, size and histology, were not available from the UK Biobank.

Outcomes

The clinical outcome was incident CRC. We identified cases of CRC with codes C18-C20 following ICD-10. We retrieved the cause of death as the primary cause of death coded by ICD-10, with corresponding dates (field ID 40001). As in a previous study [20], we excluded individuals with follow-ups of less than 1 year (n=1589) to ensure a sufficient observation period. We also excluded CRC cases that were diagnosed within 180 days of the baseline removal of polyps or adenoma, or the start of follow up (n=3040).

Statistical analysis

We represented descriptive variables as numbers and percentages, and continuous variables as means and their respective standard deviations. To compare the removal group with both the non-index-colonoscopy group and the general population, we calculated the standard incidence ratio (SIR) and standard mortality ratio (SMR), to assess the risks of developing CRC and death from CRC. Person-years for each individual were calculated from the date of recruitment, or the last diagnostic colonoscopy, to the date of diagnosis of events, death, loss to follow up, or end of follow up (censored at November 30, 2023, for participants from England and Wales, or December 31, 2023, for participants from Scotland), whichever came first. The expected number of CRC cases was calculated by multiplying the observed person-years stratified by sex and 5-year age groups by the corresponding incidence (or CRC-specific death) in the non-index-colonoscopy group or in the general population. We then expressed the ratio of observed to expected cases as an SIR or SMR, with 95% confidence intervals (CIs), under the assumption of an exact Poisson distribution.

To compare the removal group with the polyp-free group, we matched controls to individuals in the removal group by sex, year of birth (±2 years), same number of diagnostic colonoscopies, year of the first diagnostic colonoscopy (±1 year), and year of the last diagnostic colonoscopy (±1 year) without replacement in the ratio of 1:5. The ratio was chosen in order to increase precision and to control bias [21]. A standardized mean difference (SMD) of <0.1 indicates no significance imbalance

between groups [22]. To assess the representativeness of cases and controls after matching, we compared their clinical features before and after matching. The follow up began at the date of the last diagnostic colonoscopy and ended at death from any cause or censoring. The primary outcomes were the cumulative incidence of CRC and the mortality of CRC (CRC-specific death). We estimated the effect of removal on the cumulative incidence and mortality of CRC using a competing risk model, regarding any non-CRC death as a competing risk event. We estimated the effect of removal using Cox regression and estimated the hazard ratios (HRs) and 95%CIs with adjustment for sex, age at removal (last diagnostic colonoscopy), number of diagnostic colonoscopies, year of birth, age at first diagnostic colonoscopy, smoking status, family history of digestive cancers, ethnic background and education level. Missing data were marked as not available (NA). Random forest imputation was performed to deal with missing values (under the R package *mice*) when conducting Cox regression.

All analyses were performed using R programming v4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Sensitivity analysis

We conducted several sensitivity analyses to ensure the robustness of our findings: we first restricted analyses to cases who had their last colonoscopy after recruitment; second, to avoid time gaps between diagnostic and therapeutic colonoscopy, we only included cases that had both procedures on the same day (possibly the same colonoscopy), which is the common clinical course; third, we excluded cases that had family histories of digestive cancers at baseline assessment [23]; fourth, we conducted Cox regression to estimate the effect of removal compared with the non-index-colonoscopy group.

Results

Baseline characteristics

We identified 4880 participants in the removal group, 74,491 in the polyp-free group and 341,973 in the non-index-colonoscopy group. The details of inclusion and exclusion were described in the Methods section and are presented in Fig. 1.

The mean age at recruitment was 56±8 years for all included participants, and 189,887 (45%) participants were men. The mean BMI was 27.34±4.78 kg/m^2. Regarding the country of birth, most participants (77%) were born in England. In ethnic background, the majority (94%) were white. Regarding education, college or above, high school or equivalent, and less than high school, each accounted for 1/3 of the participants. More than half (56%) had never smoked, while the others (44%) were either previous or current smokers. There were 122,226 (29%) participants who regularly took aspirin or ibuprofen. Baseline characteristics were not balanced among groups (Table 1), necessitating subsequent matching and adjustment.

Removal vs. the non-index-colonoscopy group

In the removal group, 78 incident CRCs and 16 CRC-specific deaths were diagnosed during 51,136 person-years of follow up (median follow up of 10 years, range 1-44), resulting in an incidence of 153 events and a mortality of 31 CRC-specific deaths per 100,000 person-years. In the non-index-colonoscopy group, 1424 incident CRCs and 653 CRC-specific deaths were diagnosed during 4,919,591 person-years of follow up (median follow up 15 years, range 1-18), resulting in an incidence of 29 events and a mortality of 13 CRC-specific deaths per 100,000 person-years. Adjusted for sex and age, CRC incidence after polyp removal was significantly higher than that in the non-index-colonoscopy group (SIR 3.85, 95%CI 3.05-4.81; P<0.001; Table 2); however, CRC-specific deaths in the removal group were not significantly different from those in the non-index-colonoscopy group (SMR 1.64, 95%CI 0.94-2.66; P=0.050; Table 2). The age- and sex-stratified SIR and SMR are illustrated in Fig. 2A,B.

In the sensitivity analysis, given the large range of time at removal, we scaled cases in the removal group down to 2006-2010 (n=1061 with a median follow up of 15 years, range 1-18, and 15,023 person-years) to match the start of follow up in the non-index-colonoscopy group. The SIR was in the same direction of significance (5.84, 95%CI 4.04-8.16). The risk of fatal CRC was significantly greater compared with the non-index-colonoscopy group (SMR 2.87, 95%CI 1.24-5.66). The adjusted HRs were 5.36 for incident CRCs (95%CI 4.24-6.79; P<0.001) and 2.35 for mortality (95%CI 1.40-3.95; P<0.001; Supplementary Table 2).

Removal vs. the general population

We obtained data for the general population from the cancer registration statistics in England in 2017. Incident CRC cases in the removal group were not significantly different from those in the general population (SIR 0.81, 95%CI 0.64-1.01; P=0.060; Table 2); the CRC-specific mortality was even lower than that in the general population, with statistical significance (SMR 0.48, 95%CI 0.28-0.78; P=0.004; Table 2). The age- and sex-stratified SIR and SMR are illustrated in Fig. 2C,D.

Removal vs. the polyp-free group

After matching, 4827 cases in the removal groups were matched with 23,717 controls in the polyp-free group with balance (SMD for all controlled variables <0.01). In the removal group, the cumulative incidences of CRC were 0.9% (95%CI 0.7-1.2%) at 5 years, 1.3% (95%CI 1.0-1.7%) at 10 years and 2.3% (95%CI 1.7-2.9%) at 15 years (Table 3). In the matched polyp-free control group, the cumulative incidences of CRC were 0.11% (95%CI 0.08-0.17%) at 5 years, 0.21% (95%CI 0.16-0.29%) at 10 years, and 0.35% (95%CI 0.26-0.46%) at 15 years (Table 3). The Cox regression indicated that the removal group

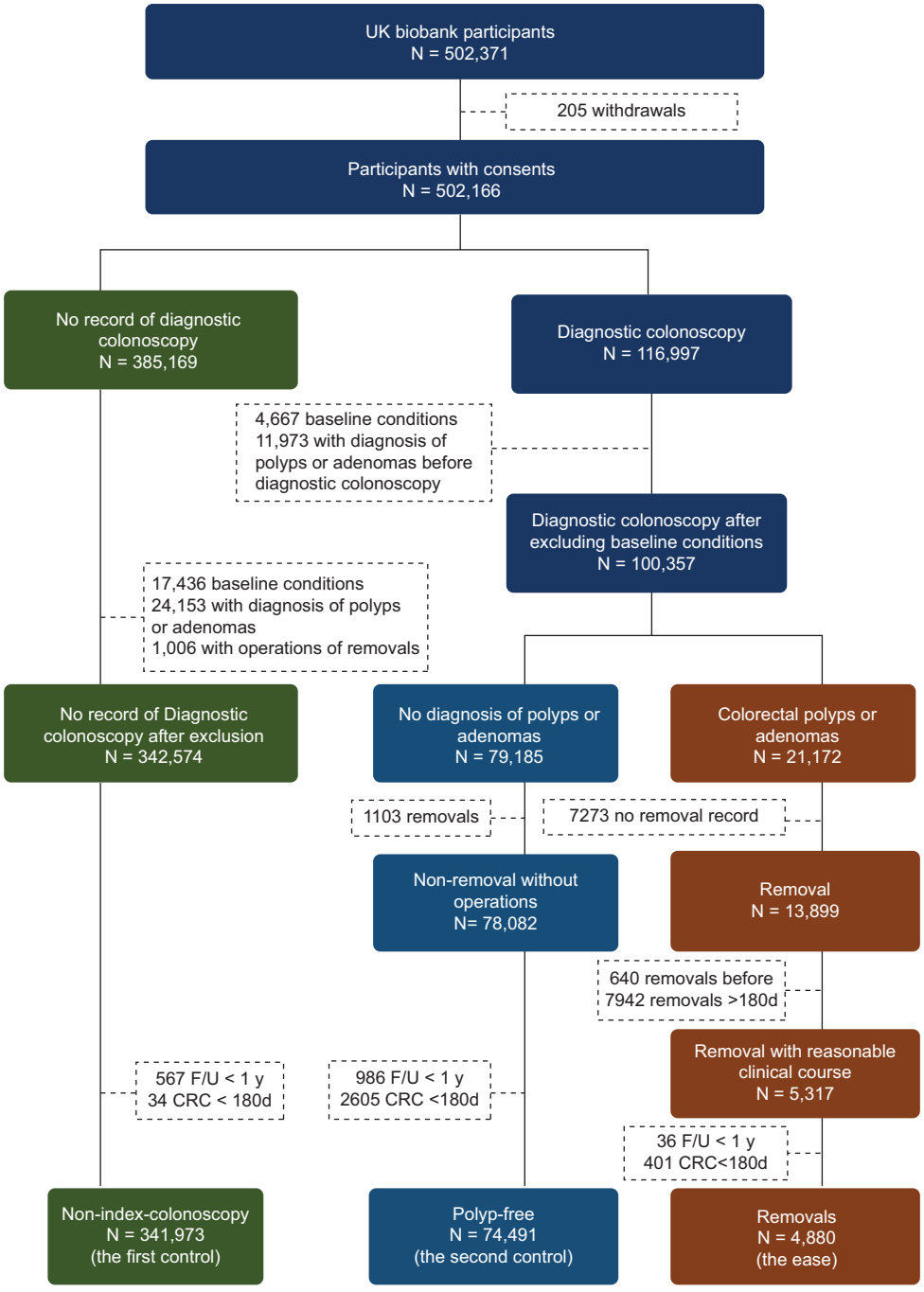

Figure 1 Flow chart of participant inclusion and exclusion. We identified 4,880 participants in the removal group, 74,491 in the polyp-free group, and 341,973 in the non-index-colonoscopy group.
UK, United Kingdom; F/U, follow up; CRC, colorectal cancer

was an independent factor that increased the risk of incident CRC cases (HR 6.17, 95%CI 4.36-8.74; P<0.001; Fig. 3A). Age (HR 1.01, 95%CI 0.90-1.15; P=0.820) and sex (HR 0.99, 95%CI 0.70-1.40; P=0.940) were not associated with the risk of incidence (Supplementary Table 3).

For CRC-specific death, the cumulative mortality rates of CRC in the removal group were 0.11% (95%CI 0.04-0.26%) at 5 years, 0.25% (95%CI 0.13-0.45%) at 10 years and 0.44% (95%CI 0.23-0.77%) at 15 years (Table 3). In the polyp-free group, the rates were 0.01% (95%CI 0.00-0.24%), 0.07% (95%CI 0.04-0.11%) and 0.16% (95%CI 0.09-0.26%), respectively (Table 3). The Cox regression indicated that operation for removal and age at removal were 2 independent factors that increased the risk of CRC-specific death (operation for removal

Table 1 Baseline characteristics of participants in UK Biobank

Characteristics	Overall	Non-index-colonoscopy	Diagnostic colonoscopy		P-value
			Polyp-free	Removal	
N	421344	341973	74491	4880	
Male sex (%)	189887 (45.1)	159027 (46.5)	28199 (37.9)	2661 (54.5)	<0.001
Age (mean±SD)	56.09±8.15	55.77±8.21	57.33±7.80	59.91±6.81	<0.001
BMI (mean±SD)	27.34±4.78)	27.29±4.73	27.51±5.00	28.40±4.93	<0.001
Education level (%)					<0.001
College or above	138189 (32.8)	114906 (33.6)	22058 (29.6)	1225 (25.1)	
High school or equivalent	136806 (32.5)	111476 (32.6)	23743 (31.9)	1587 (32.5)	
Less than high school	141795 (33.7)	111989 (32.7)	27808 (37.3)	1998 (40.9)	
NA	4554 (1.1)	3602 (1.1)	882 (1.2)	70 (1.4)	
Birthplace (%)					<0.001
England	326557 (77.5)	264218 (77.3)	58549 (78.6)	3790 (77.7)	
Wales	18510 (4.4)	15484 (4.5)	2808 (3.8)	218 (4.5)	
Scotland	33942 (8.1)	27421 (8.0)	6016 (8.1)	505 (10.3)	
Northern Ireland	2531 (0.6)	2044 (0.6)	464 (0.6)	23 (0.5)	
Republic of Ireland	3912 (0.9)	3052 (0.9)	790 (1.1)	70 (1.4)	
Elsewhere	34362 (8.2)	28478 (8.3)	5623 (7.5)	261 (5.3)	
NA	1530 (0.4)	1276 (0.4)	241 (0.3)	13 (0.3)	
Smoking status (%)					<0.001
Never	235339 (55.9)	192271 (56.2)	41011 (55.1)	2057 (42.2)	
Previous	140891 (33.4)	112293 (32.8)	26509 (35.6)	2089 (42.8)	
Current	42686 (10.1)	35480 (10.4)	6498 (8.7)	708 (14.5)	
NA	2428 (0.6)	1929 (0.6)	473 (0.6)	26 (0.5)	
Ethnicity (%)					<0.001
White	395340 (93.8)	320353 (93.7)	70289 (94.4)	4698 (96.3)	
Asian or Asian British	8695 (2.1)	7112 (2.1)	1512 (2.0)	71 (1.5)	
Black or Black British	7131 (1.7)	6072 (1.8)	1016 (1.4)	43 (0.9)	
Mixed	1368 (0.3)	2061 (0.6)	432 (0.6)	19 (0.4)	
Chinese	2512 (0.6)	1162 (0.3)	199 (0.3)	7 (0.1)	
Other ethnic group	3956 (0.9)	3283 (1.0)	650 (0.9)	23 (0.5)	
NA	2342 (0.6)	1930 (0.6)	393 (0.5)	19 (0.4)	
Regular taking of aspirin or ibuprofen (%)	122226 (29.0)	96889 (28.3)	23662 (31.8)	1675 (34.3)	<0.001
Aspirin	62465 (14.8)	48202 (14.1)	13132 (17.6)	1131 (23.2)	
Ibuprofen	68753 (16.3)	55732 (16.3)	12361 (16.6)	660 (13.5)	
Family history of bowel cancer (%)	43470 (10.3)	31094 (9.1)	11380 (15.3)	996 (20.4)	<0.001
Location (%)					
Non-adenoma polyps				2376 (48.7)	
Distal				704 (14.4)	
Proximal				949 (19.4)	
Rectum				321 (6.6)	
NOS				530 (10.9)	

BMI, body mass index; NA, not available; NOS, not otherwise specified; SD, standard deviation; UK, the United Kingdom

HR 3.25, 95%CI 1.65-6.41; P<0.001; Fig. 3B: age at removal HR 1.19, 95%CI 1.03-1.38; P=0.021; Supplementary Table 3). Sex was not associated with the risk of mortality (HR 1.42, 95%CI 0.71-2.85; P=0.270).

In the sensitivity analysis, we did not find any significant alteration in the trend of results, including cases that were strictly prospective, cases without family history, and cases that had removal at the same time as diagnosis. For representativeness, there was no significant difference in baseline characteristics between the matched removal group and the whole (Supplementary Table 4). When cases not diagnosed within 180 days were excluded, the 1-, 3- and 6-month CRC incidences in the removal group were twice those in the polyp-free group (Supplementary Table 5). In the subgroup analysis, regular taking of aspirin showed a protective trend for lowering CRC risk in the removal group (HR 0.62,

Table 2 Standardized incidence/mortality ratio of the removal group compared with the non-index-colonoscopy from the UK Biobank and with the general population in England

Age group	Sex	Removal (Observed)			Non-index-colonoscopy (UK Biobank observed)			SIR	P SIR	SMR	P SMR
		Person-years	Incident cases	Fatal cases	Person-years	Incident cases	Fatal cases				
20	Female	-	-	-	-	-	-	-	-	-	-
	Male	2.4	0	0	-	-	-	-	-	-	-
25	Female	-	-	-	-	-	-	-	-	-	-
	Male	5.0	0	0	-	-	-	-	-	-	-
30	Female	3.5	0	0	-	-	-	-	-	-	-
	Male	15.9	0	0	-	-	-	-	-	-	-
35	Female	26.9	0	0	0.3	0	0	-	-	-	-
	Male	50.3	0	0	4.5	0	0	-	-	-	-
40	Female	151.0	1	0	48532.5	2	0	160.71 (4.06-895.40)	<0.001	-	-
	Male	166.2	0	0	43716.0	2	0	0.00 (0.00-485.11)	<0.001	-	-
45	Female	425.3	0	0	176277.5	10	3	0.00 (0.00-152.90)	0.002	0.00 (0.00-509.67)	<0.001
	Male	448.8	1	0	150700.0	9	5	37.31 (0.94-207.90)	0.004	0.00 (0.00-247.76)	<0.001
50	Female	1095.0	0	0	318523.3	39	16	0.00 (0.00-27.52)	0.318	0.00 (0.00-67.07)	0.058
	Male	1156.6	2	0	264302.9	30	16	15.24 (1.85-55.03)	<0.001	0.00 (0.00-52.69)	0.104
55	Female	2189.0	3	0	423920.6	72	24	8.07 (1.66-23.58)	<0.001	0.00 (0.00-29.77)	0.285
	Male	2213.2	1	0	343878.8	72	29	2.16 (0.05-12.02)	0.957	0.00 (0.00-19.76)	0.468
60	Female	3669.5	6	1	486320.6	90	44	8.84 (3.24-19.23)	<0.001	3.01 (0.08-16.78)	0.771
	Male	3980.9	4	0	397713.0	106	36	3.77 (1.03-9.65)	0.018	0.00 (0.00-10.24)	0.816
65	Female	5032.2	10	2	512127.9	126	44	8.08 (3.87-14.85)	<0.001	4.63 (0.56-16.71)	0.104
	Male	6200.6	9	2	439690.6	145	70	4.40 (2.01-8.36)	<0.001	2.03 (0.25-7.32)	0.606
70	Female	5579.0	6	2	414758.3	174	89	2.56 (0.94-5.58)	0.039	1.67 (0.20-6.03)	0.782
	Male	7056.3	8	3	370371.1	185	84	2.27 (0.98-4.47)	0.034	1.87 (0.39-5.48)	0.477
75	Female	3965.8	7	0	218573.1	125	63	3.09 (1.24-6.36)	0.005	0.00 (0.00-3.23)	0.548
	Male	5053.9	19	5	199870.0	152	85	4.94 (2.98-7.72)	<0.001	2.33 (0.76-5.43)	0.109
80	Female	1222.2	1	0	56847.9	42	22	1.11 (0.03-6.17)	0.672	0.00 (0.00-7.80)	0.969
	Male	1428.7	0	1	52155.1	43	23	0.00 (0.00-3.13)	0.532	1.59 (0.04-8.84)	0.870
85	Female	15.0	0	0	702.4	0	0	-	-		-
	Male	14.4	0	0	604.5	0	0	-	-		-
Sum		51167.5	78	16	4919591.0	1424	653	3.85 (3.05-4.81)	<0.001	1.64 (0.94-2.66)	0.050

Age group	Sex	Removal (Observed)			General population (Expected)			SIR	P SIR	SMR	P SMR
		Person-years	Incident cases	Fatal cases	Person-years	Incident cases	Fatal cases				
20	Female	-	-	-	-	0	0	-	-	-	-
	Male	2.4	0	0	2.4	0	0	-	-	-	-
25	Female	-	-	-	-	0	0	-	-	-	-
	Male	5.0	0	0	5.0	0	0	-	-	-	-

(*Contd...*)

Table 2 (*Continued*)

Age group	Sex	Removal (Observed)			General population (Expected)			SIR	P SIR	SMR	P SMR
		Person-years	Incident cases	Fatal cases	Person-years	Incident cases	Fatal cases				
30	Female	3.5	0	0	3.5	0	0	-	-	-	-
	Male	15.9	0	0	15.9	0	0	-	-	-	-
35	Female	26.9	0	0	26.9	0	0	-	-	-	-
	Male	50.3	0	0	50.3	0	0	-	-	-	-
40	Female	151.0	1	0	151.0	0	0	48.34 (1.22-269.33)	0.001	-	-
	Male	166.2	0	0	166.2	0	0	0.00 (0.00-160.82)	0.002	-	-
45	Female	425.3	0	0	425.3	0	0	0.00 (0.00-43.15)	0.156	0.00 (0.00-173.48)	0.001
	Male	448.8	1	0	448.8	0	0	9.73 (0.25-54.22)	0.215	0.00 (0.00-114.17)	0.009
50	Female	1095.0	0	0	1095.0	0	0	0.00 (0.00-9.79)	0.841	0.00 (0.00-35.09)	0.223
	Male	1156.6	2	0	1156.6	1	0	3.95 (0.48-14.26)	0.163	0.00 (0.00-27.03)	0.325
55	Female	2189.0	3	0	2189.0	1	0	2.36 (0.49-6.91)	0.275	0.00 (0.00-11.70)	0.742
	Male	2213.2	1	0	2213.2	2	1	0.56 (0.01-3.09)	0.822	0.00 (0.00-7.12)	0.980
60	Female	3669.5	6	1	3669.5	3	1	1.76 (0.65-3.83)	0.259	1.29 (0.03-7.16)	0.753
	Male	3980.9	4	0	3980.9	6	2	0.68 (0.18-1.73)	0.561	0.00 (0.00-2.24)	0.372
65	Female	5032.2	10	2	5032.2	6	2	1.74 (0.84-3.20)	0.117	1.15 (0.14-4.16)	0.858
	Male	6200.6	9	2	6200.6	12	4	0.73 (0.33-1.38)	0.418	0.54 (0.07-1.96)	0.534
70	Female	5579.0	6	2	5579.0	9	3	0.65 (0.24-1.42)	0.379	0.69 (0.08-2.48)	0.809
	Male	7056.3	8	3	7056.3	19	6	0.42 (0.18-0.84)	0.017	0.49 (0.10-1.43)	0.287
75	Female	3965.8	7	0	3965.8	9	3	0.74 (0.30-1.52)	0.521	0.00 (0.00-1.06)	0.111
	Male	5053.9	19	5	5053.9	17	7	1.10 (0.66-1.71)	0.781	0.74 (0.24-1.72)	0.620
80	Female	1222.2	1	0	1222.2	4	2	0.28 (0.01-1.54)	0.267	0.00 (0.00-2.17)	0.357
	Male	1428.7	0	1	1428.7	6	3	0.00 (0.00-0.58)	0.020	0.32 (0.01-1.77)	0.354
85	Female	15.0	0	0	15.0	0	0	-	-	-	-
	Male	14.4	0	0	14.4	0	0	-	-	-	-
Sum		51167.5	78	16	51167.5	96	33	0.81 (0.64-1.01)	0.060	0.48 (0.28-0.78)	0.004

SIR, standardized incidence ratio; SMR, standardized mortality ratio; sum, age-group- and sex- standardized ratios; UK, the United Kingdom

95%CI 0.37-1.04; P=0.069), but not in the general population or the polyp-free group.

Discussion

Our investigation based on the UK Biobank observed that the risk of CRC incidence and mortality after removal is similar to or even significantly lower than that of the general population in England. However, patients who had polyps removed had a higher risk of newly-diagnosed CRC and related death, compared with participants who had no index colonoscopy and polyp-free patients.

Polypectomy reduced the risk of CRC for polyp-positive participants to the general level. When we referred to the general population from the cancer registration statistics in England in 2017, the risks of incidence and mortality were lower by 20% and 50%, respectively. The CRC incidence (153/100,000) we obtained in the removal group was parallel to previous UK results (140/100,000 for low-risk group) [24] and previous US results (91/100,000 for nonadvanced adenoma and 200/100,000 for advanced adenoma) [19]. A reduction in mortality was also reported in an American study [11]. Polypectomy fulfils its clinical benefit of long-term prevention from CRC deaths compared with the general population.

But polypectomy does not eliminate the risk of CRC, or reduce it to that associated with a negative colonoscopy.

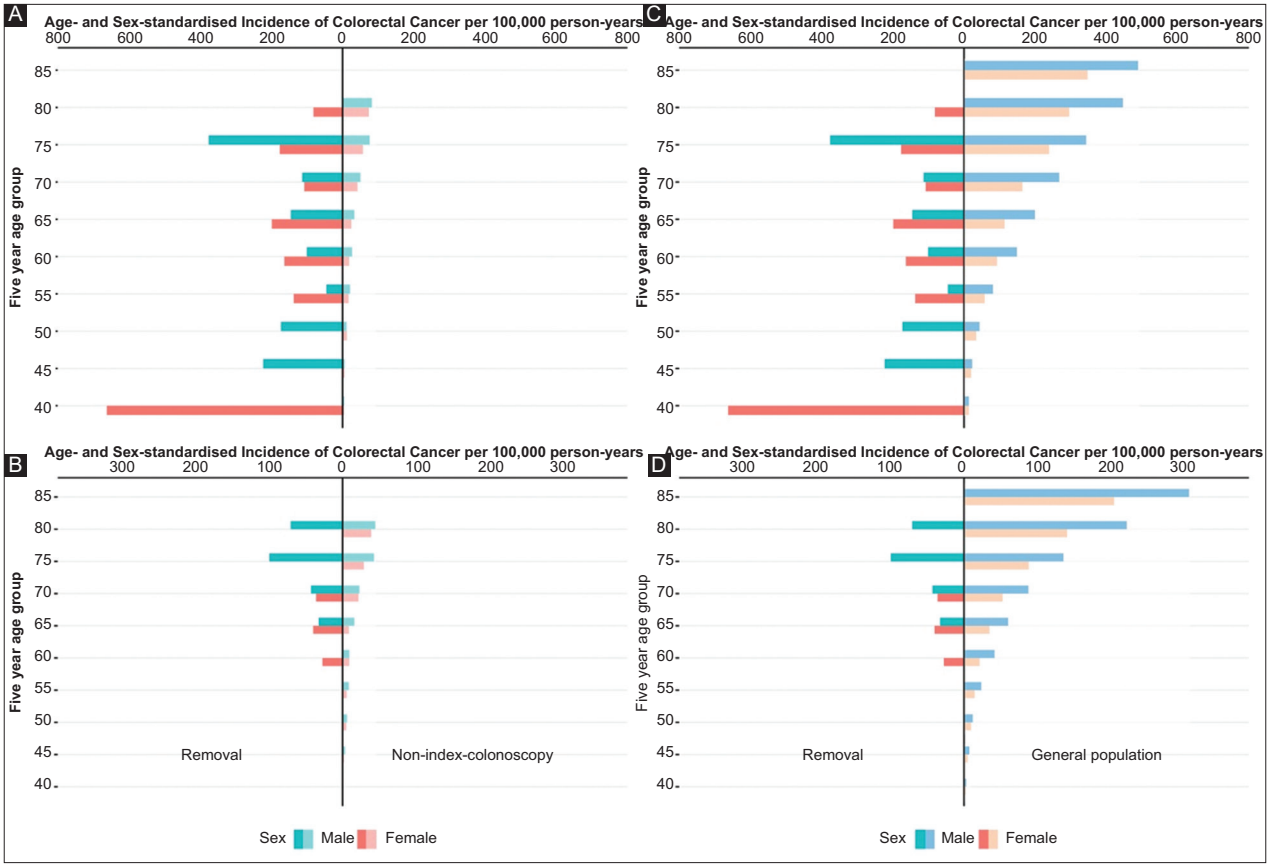

Figure 2 Age- and sex-standardized incidence and mortality of colorectal cancer. Adjusted for sex and age, the colorectal cancer incidence after polyp removal was significantly higher than that in the general population group (SIR 3.85, 95%CI 3.05-4.81; P<0.001); however, colorectal cancer-specific deaths were not significantly different (SMR 1.64, 95%CI 0.94-2.66; P=0.05)
CI, confidence interval; SIR, standardized incidence ratio; SMR, standardized mortality ratio; sum, age-group- and sex- standardized ratios

Table 3 Cumulative incidence and mortality rates of colorectal cancer (polyp-free group vs. removal)

Characteristics	Year 5 (%)	Year 10 (%)	Year 15 (%)	P-value
Incidence				<0.001
Polyp-free	0.11 (0.08–0.17)	0.21 (0.16–0.29)	0.35 (0.26–0.46)	
Removal	0.90 0.65–1.2)	1.30 (1.00–1.70)	2.30 (1.70–2.90)	
Mortality				<0.001
Polyp-free	0.01 (0.00–0.04)	0.07 (0.04–0.11)	0.16 (0.09–0.26)	
Removal	0.11 (0.04–0.26)	0.25 (0.13–0.45)	0.44 (0.23–0.77)	

We still observed 4-6 times higher risk of incident CRC compared with participants who had no index colonoscopy or a negative one. These estimates were slightly higher than those of previous studies [10,25]. First, participants were from the UK and most of them might have 2-yearly highly sensitive fecal immunochemical testing, following the bowel cancer screening program. If negative and symptomless, participants are highly likely not to be invited for colonoscopy, i.e., the non-index group. Therefore, the removal group was likely to have a selection bias towards participants with higher risk of CRC. Second, patients with polyps are typically subject to more aggressive screening and closer follow up after removal than those without. In particular, they are likely to have repeated surveillance colonoscopies. This would lead to earlier detection of CRC and possibly inflate the incidence—which may paradoxically increase CRC detection in the removal group. Third, the quality of colonoscopy could be another reason for its effect to be less than expected. We realized that a considerable number of CRC cases were diagnosed within 180 days after removal, twice as many as in the polyp-free group. This raises a concern about the poor quality of colonoscopy, the possibility of incomplete resection, missed synchronous lesions, and a decrease in the adenoma detection rate (ADR). The ADR, widely accepted as an indicator of colonoscopy quality, was negatively associated

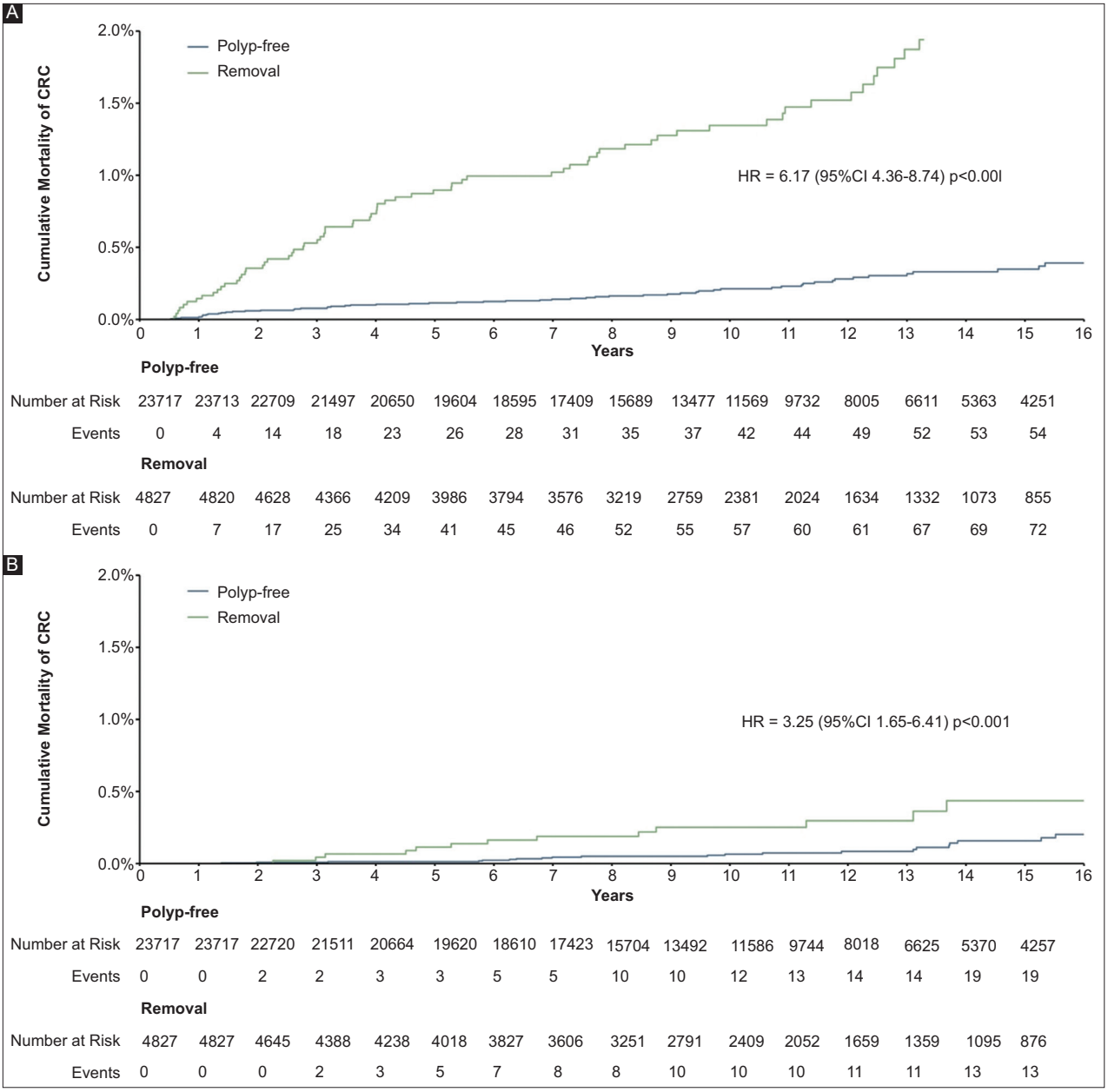

Figure 3 Cumulative incidence and mortality rate of CRC for the removal and the polyp-free. (A) The risk for incident CRC in removal group was significantly higher than that in the polyp-free group (HR 6.17, 95%CI 4.36-8.74; P<0.001). (B) The risk for CRC-specific death was also significantly higher than that in the polyp-free group (HR 3.25, 95%CI 1.65-6.41; P<0.001)
CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio

with the risk of incident and fatal CRC [26]. Thus, low-quality colonoscopy could have affected the clinical benefits we observed.

Our observations for the UK Biobank demonstrate that polypectomy shows a clear benefit, achieving a CRC incidence the same as the level of the general population, while CRC mortality is reduced by half. Therefore, polypectomy is necessary and beneficial for patients with polyps, as has been recommended in clinical practice. Regular aspirin use showed a trend towards a protective effect in the removal group. However, long-term follow-up data from the ASPREE trial indicated that low-dose aspirin was not associated with CRC incidence in older adults [27]. Therefore, its overall impact on cancer warrants further investigation, particularly through the identification of populations that may benefit or be harmed. We also realized that the risk is not eliminated to

the level associated with a negative colonoscopy. The reasons could be selection bias towards a high-risk population, poor quality of colonoscopy, the possibility of incomplete resection, and inadequate surveillance. These are increasingly recognized as critical procedural and clinical features in reducing the risk of CRC.

The number of participants in the non-index-colonoscopy group was about 70% of the total number. However, the representativeness of this group in relation to the general population in the UK was not certain. Physicians could believe this group to be at low risk of CRC, and thus not refer them for a diagnostic colonoscopy. Moreover, the UK Biobank does not fully represent the UK population, introducing a participation bias [28]. It was found that participants in the UK Biobank were more likely to have a healthy lifestyle [29]. The overall cancer incidence in the Biobank was lower by 10-20% in those aged 70-74 than in the general population [29].

We are fully aware of the limitations of this study. First, given the limited clinical data, in investigating the stratified risk of CRC we did not account for key polyp-related data, such as size, number, histology and location of lesions. Therefore, we would characterize this study only as an epidemiological complement to prior clinical trials. Second, as mentioned in the Methods, the UK Biobank lacked clear reports of colonoscopy operations. Quality factors are dropped in exploring the risk of CRC. The method of inferring clinical courses from diagnoses and operations also increases the possibility of introducing a bias because of incomplete records. The lack of quality of the colonoscopy, as well as the details of polyp features, would also limit the applicability of our study. Third, the fecal immunochemical test is a critical screening test for CRC. Unfortunately, these test results are not available in the UK Biobank.

Polypectomy is not the only strategy to decrease CRC incidence. Artificial intelligence is helping to increase ADR, allow earlier detection, and level up the quality of colonoscopy, with its higher accuracy and sensitivity [30,31]. It could serve as a preassessment tool to increase compliance with bowel preparation [32]. Multidisciplinary team discussion would be another strategy to further decrease CRC risk.

In conclusion, the risk of CRC incidence and mortality after removal is similar to or even significantly lower than that of the general population in England. However, patients who had polyps removed had a higher risk of newly-diagnosed CRC and its related death, compared with participants without any index colonoscopy and polyp-free patients. Polypectomy reduced the risk of CRC for polyp-positive participants to the level of the general population. But the risk is not eliminated, reinforcing the importance of procedural quality and tailored surveillance strategies.

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Summary Box

What is already known:

- Patients diagnosed with colorectal polyps are strongly recommended to have lesions removed (polypectomy)
- Risk estimates for newly-diagnosed colorectal cancer (CRC) and its related death after polypectomy have been reported in some large cohorts other than in the United Kingdom (UK)

What the new findings are:

- The clinical effects of removal were revealed in a large UK cohort: the risk of CRC incidence and mortality after polyp removal is similar to or even lower than that of the general population in England
- This risk after polyp removal in the UK Biobank is higher than that in either the non-index-colonoscopy or the negative colonoscopy group

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;**71**:209-249.
2. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. *CA Cancer J Clin* 2023;**73**:233-254.
3. Davidson KW, Barry MJ, Mangione CM, et al; US Preventive Services Task Force. Screening for colorectal cancer: US preventive services task force recommendation statement. *JAMA* 2021;**325**:1965-1977.
4. Huang D, Sun W, Zhou Y, et al. Mutations of key driver genes in colorectal cancer progression and metastasis. *Cancer Metastasis Rev* 2018;**37**:173-187.
5. Nguyen LH, Goel A, Chung DC. Pathways of colorectal carcinogenesis. *Gastroenterology* 2020;**158**:291-302.

6. Ferlitsch M, Hassan C, Bisschops R, et al. Colorectal polypectomy and endoscopic mucosal resection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2024. *Endoscopy* 2024;**56**:516-545.
7. Taghiakbari M, Kim DHD, Djinbachian R, von Renteln D. Endoscopic resection of large non-pedunculated colorectal polyps: current standards of treatment. *eGastroenterology* 2024;**2**:e100025.
8. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for follow-up after colonoscopy and polypectomy: a consensus update by the US multi-society task force on colorectal cancer. *Gastrointest Endosc* 2020;**91**:463-485.
9. Song M, Emilsson L, Bozorg SR, et al. Risk of colorectal cancer incidence and mortality after polypectomy: a Swedish record-linkage study. *Lancet Gastroenterol Hepatol* 2020;**5**:537-547.
10. Wieszczy P, Kaminski MF, Franczyk R, et al. Colorectal cancer incidence and mortality after removal of adenomas during screening colonoscopies. *Gastroenterology* 2020;**158**:875-883.
11. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med* 2012;**366**:687-696.
12. Løberg M, Kalager M, Holme Ø, Hoff G, Adami HO, Bretthauer M. Long-term colorectal-cancer mortality after adenoma removal. *N Engl J Med* 2014;**371**:799-807.
13. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2017;**49**:270-297.
14. Coleman HG, Loughrey MB, Murray LJ, et al. Colorectal cancer risk following adenoma removal: a large prospective population-based cohort study. *Cancer Epidemiol Biomarkers Prev* 2015;**24**: 1373-1380.
15. Sudlow C, Gallacher J, Allen N, et al. UK Biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;**12**:e1001779.
16. He X, Hang D, Wu K, et al. Long-term risk of colorectal cancer after removal of conventional adenomas and serrated polyps. *Gastroenterology* 2020;**158**:852-861.
17. Holme Ø, Bretthauer M, Eide TJ, et al. Long-term risk of colorectal cancer in individuals with serrated polyps. *Gut* 2015;**64**:929-936.
18. Atkin W, Wooldrage K, Brenner A, et al. Adenoma surveillance and colorectal cancer incidence: a retrospective, multicentre, cohort study. *Lancet Oncol* 2017;**18**:823-834.
19. Click B, Pinsky PF, Hickey T, Doroudi M, Schoen RE. Association of colonoscopy adenoma findings with long-term colorectal cancer incidence. *JAMA* 2018;**319**:2021-2031.
20. Cottet V, Jooste V, Fournel I, Bouvier AM, Faivre J, Bonithon-Kopp C. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. *Gut* 2012;**61**:1180-1186.
21. Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. One-to-many propensity score matching in cohort studies. *Pharmacoepidemiol Drug Saf* 2012;**21** Suppl 2:69-80.
22. Lee SW, Kim SY, Moon SY, et al. Estimating COVID-19 infection and severity risks in patients with chronic rhinosinusitis: a Korean nationwide cohort study. *J Allergy Clin Immunol Pract* 2021;**9**:2262-2271.
23. Liang Q, Mukama T, Sundquist K, et al. Longer interval between first colonoscopy with negative findings for colorectal cancer and repeat colonoscopy. *JAMA Oncol* 2024;**10**:866-873.
24. Cross AJ, Robbins EC, Pack K, et al. Long-term colorectal cancer incidence after adenoma removal and the effects of surveillance on incidence: a multicentre, retrospective, cohort study. *Gut* 2020;**69**:1645-1658.
25. Duvvuri A, Chandrasekar VT, Srinivasan S, et al. Risk of colorectal cancer and cancer related mortality after detection of low-risk or high-risk adenomas, compared with no adenoma, at index colonoscopy: a systematic review and meta-analysis. *Gastroenterology* 2021;**160**:1986-1996.
26. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med* 2014;**370**:1298-1306.
27. Orchard SG, Polekhina G, Zalcberg J, et al. Cancer incidence and mortality with aspirin in older adults: follow-up of the ASPREE Trial. *JAMA Oncol* 2026;**12**:285-294.
28. Schoeler T, Speed D, Porcu E, Pirastu N, Pingault JB, Kutalik Z. Participation bias in the UK Biobank distorts genetic associations and downstream analyses. *Nat Hum Behav* 2023;**7**:1216-1227.
29. Fry A, Littlejohns TJ, Sudlow C, et al. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. *Am J Epidemiol* 2017;**186**:1026-1034.
30. Lin Y, Huang C, Tian H, et al. Improving generalization of polyp detection via conditional StyleGAN augmented training. *NPJ Digit Med* 2026;**9**:113.
31. Kader R, Hassan C, Lanas, et al. A novel cloud-based artificial intelligence for real-time detection of colorectal neoplasia - a randomized controlled trial (EAGLE). *NPJ Digit Med* 2025;**9**:84.
32. Kojima K, Takahashi K, Maruyama H, et al. Artificial intelligence model for automated identification of bowel preparation for colonoscopy (AI-PREPOO): a multicenter study. *J Gastroenterol Hepatol* 2026;**41**:678-685.

Supplementary material

Supplementary Table 1 Codes for main phenotypes

Description	ICD10	ICD9	OPCS4	OPCS3	TouchScreen (Field ID=Code)
Polyps of colon	K63.5				
Polyps of rectum and anus	K62.1	5690			
Colon adenoma	D12.0-D12.7	2113			
Rectal adenoma	D12.8, D12.9	2114			
Inflammatory bowel disease	K50, K51	555			
Radiation proctitis or colitis	K52.0, K62.7				
Volvulus	K56.2	5602			
Colorectal cancer	C18-C20	153, 1540, 1541			
Diagnostic colonoscopy			H22		
Removal of polyps or adenoma			H20	466	
Bowel resection			H04		
Meds; aspirin					6154=1
Meds; ibuprofen					6154=2
Family history: malignant neoplasm of digestive organs	Z80.0	V160			20110=4, 20107=4, 20111=4

Supplementary Table 2 Multivariate analysis for incidence and mortality (non-index-colonoscopy group vs. removal)

Characteristics	N	Incidence			Mortality		
		HR	95%CI	P-value	HR	95%CI	P-value
Group							
Polyp-free	341,973	—	—		—	—	
Removal	4880	5.36	4.24-6.79	<0.001	2.35	1.40-3.95	0.001
Sex							
Female	185,165	—	—		—	—	
Male	161,688	1.27	1.15-1.40	<0.001	1.35	1.16-1.58	<0.001
Education level							
College or above	117,312	—	—	0.2	—	—	
High school or equivalent	114,227	0.93	0.81-1.05	0.034	0.87	0.72-1.06	0.2
Less than high school	115,314	1.14	1.01-1.29		1.26	1.05-1.51	0.014
BMI	346,853	1.02	1.01-1.04	<0.001	1.03	1.02-1.05	<0.001
Regular taking aspirin or ibuprofen							
No	248,289	—	—		—	—	
Yes	98,564	0.98	0.87-1.09	0.7	0.92	0.77-1.09	0.3
Family history							
No	314,763	—	—		—	—	
Yes	32,090	1.28	1.10-1.50	0.002	1.18	0.93-1.51	0.2
Ethnic							
White	326,823	—	—	0.2	—	—	
Mixed	2090	0.56	0.23-1.35	0.004	0.76	0.24-2.35	0.6
Black or Black British	6169	0.44	0.25-0.77	<0.001	0.64	0.32-1.28	0.2
Asian or Asian British	7256	0	0.19-0.62	0.4	0	0.18-0.92	0.031
Chinese	1177	0.64	0.21-1.98	0.056	0	0.00-0.00	<0.001
Other ethnic group	3,338	0	0.23-1.02		1	0.32-1.85	0.6

BMI, body mass index; CI, confidence interval; HR, hazard ratio; NA, not available

Supplementary Table 3 Multivariate analysis for incidence and mortality (polyp-free group vs. removal)

Characteristics	N	Incidence			Mortality		
		HR	95%CI	P-value	HR	95%CI	P-value
Numbers of dscopy	28,544	0.81	0.40-1.64	0.560	0.46	0.11-1.86	0.270
Year of the first dscopy	28,544	0.98	0.87-1.11	0.790	0.87	0.75-1.02	0.092
Group							
Polyp-free	23,717	—	—		—	—	
Removal	4827	6.17	4.36-8.74	<0.001	3.25	1.65-6.41	<0.001
Age at removal	28,544	1.01	0.90-1.15	0.820	1.19	1.03-1.38	0.021
Birth year	28,544	0.94	0.83-1.06	0.330	1.09	0.94-1.27	0.270
Sex							
Female	13,024	—	—		—	—	
Male	15,520	0.99	0.70-1.40	0.940	1.42	0.71-2.85	0.330
Education level							
College or above	8125	—	—		—	—	
High school or equivalent	9064	1.06	0.67-1.68	0.800	1.14	0.39-3.34	0.820
Less than high school	11,355	0.96	0.62-1.49	0.850	2.08	0.80-5.41	0.130
BMI	28,544	0.99	0.95-1.03	0.550	0.95	0.88-1.03	0.250
Regular take Aspirin or Ibuprofen							
No	18,958	—	—		—	—	
Yes	9586	0.7	0.48-1.03	0.072	0.76	0.36-1.60	0.470
Family history							
No	24,073	—	—		—	—	
Yes	4471	1.33	0.88-2.01	0.170	0.93	0.38-2.27	0.880
Ethnic	27,290	—	—	0.001	—	—	<0.001
White	135	7.11	2.19-23.1	<0.001	20.6	4.61-92.0	<0.001
Mixed	324	0	0.00-0.00	<0.001	0	0.00-0.00	<0.001
Black or Black British	523	0	0.00-0.00	<0.001	0	0.00-0.00	<0.001
Asian or Asian British	66	0	0.00-0.00	<0.001	0	0.00-0.00	<0.001
Chinese	206	0	0.00-0.00		0	0.00-0.00	
Other ethnic group							

BMI, body mass index; CI, confidence interval; dscopy, diagnostic colonoscopy; HR, hazard ratio; NA, not available

Supplementary Table 4 Cases included in the matched set compared with the complete cohort

Characteristics	Matched	Total	P-value
N	4827	4880	
Male sex (%)	2634 (54.6)	2661±54.5)	0.985
Age (mean±SD)	59.93±6.81)	59.91±6.81)	0.877
BMI (mean±SD)	28.40±4.93)	28.40±4.93)	0.972
Education level (%)			0.998
College or above	1205 (25.0)	1225 (25.1)	
High school or equivalent	1574 (32.6)	1587 (32.5)	
Less than high school	1980 (41.0)	1998 (40.9)	
NA	68 (1.4)	70 (1.4)	
Birthplace (%)	3755 (77.8)	3790 (77.7)	>0.99
England	215 (4.5)	218 (4.5)	
Wales	494 (10.2)	505 (10.3)	
Scotland	22 (0.5)	23 (0.5)	
Northern Ireland	69 (1.4)	70 (1.4)	
Republic of Ireland	259 (5.4)	261 (5.3)	
Elsewhere	13 (0.3)	13 (0.3)	
NA			
Smoking status (%)			0.999
Never	2032 (42.1)	2057 (42.2)	
Previous	2063 (42.7)	2089 (42.8)	
Current	706 (14.6)	708 (14.5)	
NA	26 (0.5)	26 (0.5)	
Ethnicity (%)			>0.99
White	4645 (96.2)	4698 (96.3)	
Asian or Asian British	71 (1.5)	71 (1.5)	
Black or Black British	43 (0.9)	43 (0.9)	
Mixed	19 (0.4)	19 (0.4)	
Chinese	7 (0.1)	7 (0.1)	
Other ethnic group	23 (0.5)	23 (0.5)	
NA	19 (0.4)	19 (0.4)	
Regular taking of aspirin or ibuprofen (%)	1657 (34.3)	1675 (34.3)	>0.99
Aspirin	1119 (23.2)	1131 (23.2)	>0.99
Ibuprofen	652 (13.5)	660 (13.5)	>0.99
Family history of bowel cancer (%)	976 (20.2)	996 (20.4)	0.835
Location (%)			>0.99
Non-adenoma polyps	698 (14.5)	704 (14.4)	
Distal	523 (10.8)	530 (10.9)	
Proximal	2354 (48.8)	2376 (48.7)	
Rectum	933 (19.3)	949 (19.4)	
NOS	319 (6.6)	321 (6.6)	

BMI, body mass index; NA, not available; NOS, not otherwise specified; SD, standard deviation

Supplementary Table 5 Cumulative incidence and mortality rates of colorectal cancer (polyp-free group vs. removal)

Characteristics	Month 1 (%)	Month 3 (%)	Month 6 (%)	P-value
Incidence				<0.001
Polyp-free	3.3 (3.2-3.5)	3.4 (3.2-3.5)	3.4 (3.3-3.5)	
Removal	6.5 (5.9-7.2)	7.3 (6.6-8.0)	7.6 (6.9-8.3)	