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Importance of ideal cardiovascular health metrics in the risk of colorectal cancer among people aged 50 years or older: a UK Biobank cohort study

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ABSTRACT

Objective To explore the correlation between the ideal cardiovascular health metrics (ICVHMs) and the incidence of colorectal cancer (CRC) among people aged 50 years or older.

Design Prospective cohort study.

Setting The UK Biobank, a prospective cohort of middle-aged participants recruited between 2006 and 2010.

Participants The study included 342 226 participants from the UK Biobank aged 50 years or older without prevalent cancer.

Exposure The ICVHMs consist of four behavioural factors (abstinence from smoking, ideal body mass index (BMI), physical activity at goal and consumption of healthy diet) and three cardiometabolic factors (untreated total cholesterol <200 mg/dL, untreated blood pressure <120/80 mm Hg and untreated fasting plasma glucose <100 mg/dL).

Main outcomes The outcome was ascertained by linkage to cancer and death registries using the International Classification of Diseases, Tenth codes C18–C20.

Results During a median follow-up time of 8.72 years, 3060 CRC cases were identified. Compared with the reference (participants with ICVHMs ≤2), the multivariable-adjusted HRs for subgroups with 3, 4, 5 and ≥6 ICVHM factors were 0.98 (95% CI 0.85 to 1.12), 0.90 (95% CI 0.77 to 1.02), 0.85 (95% CI 0.71 to 0.98) and 0.69 (95% CI 0.48 to 0.90), respectively. Among the seven ICVHM factors, lower BMI, healthier diet and ideal fasting plasma glucose were significantly associated with lower risk of CRC (HR: 0.86, 95% CI 0.78 to 0.95; HR: 0.92, 95% CI 0.84 to 0.99; HR: 0.90, 95% CI 0.80 to 0.99).

Conclusions Adherence to the ICVHMs was associated with a lower risk of CRC among people aged 50 years or older. Among the seven ICVHM factors, BMI, diet and fasting plasma glucose played a more critical role in the prevention of CRC. These findings imply that adherence to ICVHMs should be encouraged to reduce the burden of cardiovascular disease as well as CRC.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study was based on a prospective cohort with a long follow-up period and large sample size.
⇒ Outcomes were ascertained through linkage to comprehensive cancer and death registries.
⇒ We could not capture the long-term trajectories of the ideal cardiovascular health metrics due to unavailability of data sets.
⇒ Some relevant factors, such as psychosocial factors and genetic susceptibility, were not included in the model for further adjustment, which could lead to residual confounding.
⇒ Due to the low response rate in the UK Biobank, the study findings may be biased by the 'healthy volunteer' effect.

INTRODUCTION

Prevention of chronic diseases is essential in improving population health and reducing the global disease burden.[1] Colorectal cancer (CRC) and cardiovascular disease (CVD) are the two significant public health concerns affecting human health worldwide. CVD remains a major cause of death and disability globally,[2] while CRC is the second leading cause of cancer deaths and the fourth most commonly diagnosed cancer in the world.[3]

Although they are usually regarded as two independent diseases, emerging evidence has manifested many similarities and interactions between the two. In terms of pathophysiology, they may commonly share potential pathogenic mechanisms, such as chronic inflammation, oxidative stress and altered telomere length.[4 5] Some traditional cardiovascular risk factors (such as smoking, obesity, hypertension, dyslipidaemia, etc) may lead to oxidative stress and chronic inflammation of the organism, thus promoting the incidence of CVD and CRC.[6–8]

In 2010, the American Heart Association (AHA) proposed the concept of 'ideal cardiovascular health metrics (ICVHMs)', defined as (1) the simultaneous presence of four favourable health behaviours (abstinence from smoking, ideal body mass index (BMI), physical activity at goal and consumption of

a dietary pattern that promotes cardiovascular health); and (2) the simultaneous presence of three favourable health factors (untreated total cholesterol <200 mg/dL, untreated blood pressure <120/80 mm Hg and untreated fasting plasma glucose <100 mg/dL).[9] Several studies have shown that ICVHMs played an essential role in preventing CVD.[10–12] However, few studies have elucidated their effect on cancer, especially on CRC. Previous research showed that adherence to ICVHMs was associated with a lower incidence of cancer, except for non-melanoma skin cancer.[13] To further explore the correlation between ICVHMs and CRC, more evidence from large population cohorts is needed. This study aimed to explore the relationship between ICVHMs and the incidence of CRC through the UK Biobank cohort.

METHODS

Study population

The UK Biobank is a prospective cohort holding unprecedented data on about 500 000 participants, recruited between 2006 and 2010. The current study initially included 384 627 participants aged 50 years or older. Before data analyses, 42 401 participants with prevalent cancer were excluded. Participants were followed until the first diagnosis date of CRC, death, loss to follow-up or 10 February 2022, whichever came first. The flow chart of the study is shown in figure 1.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

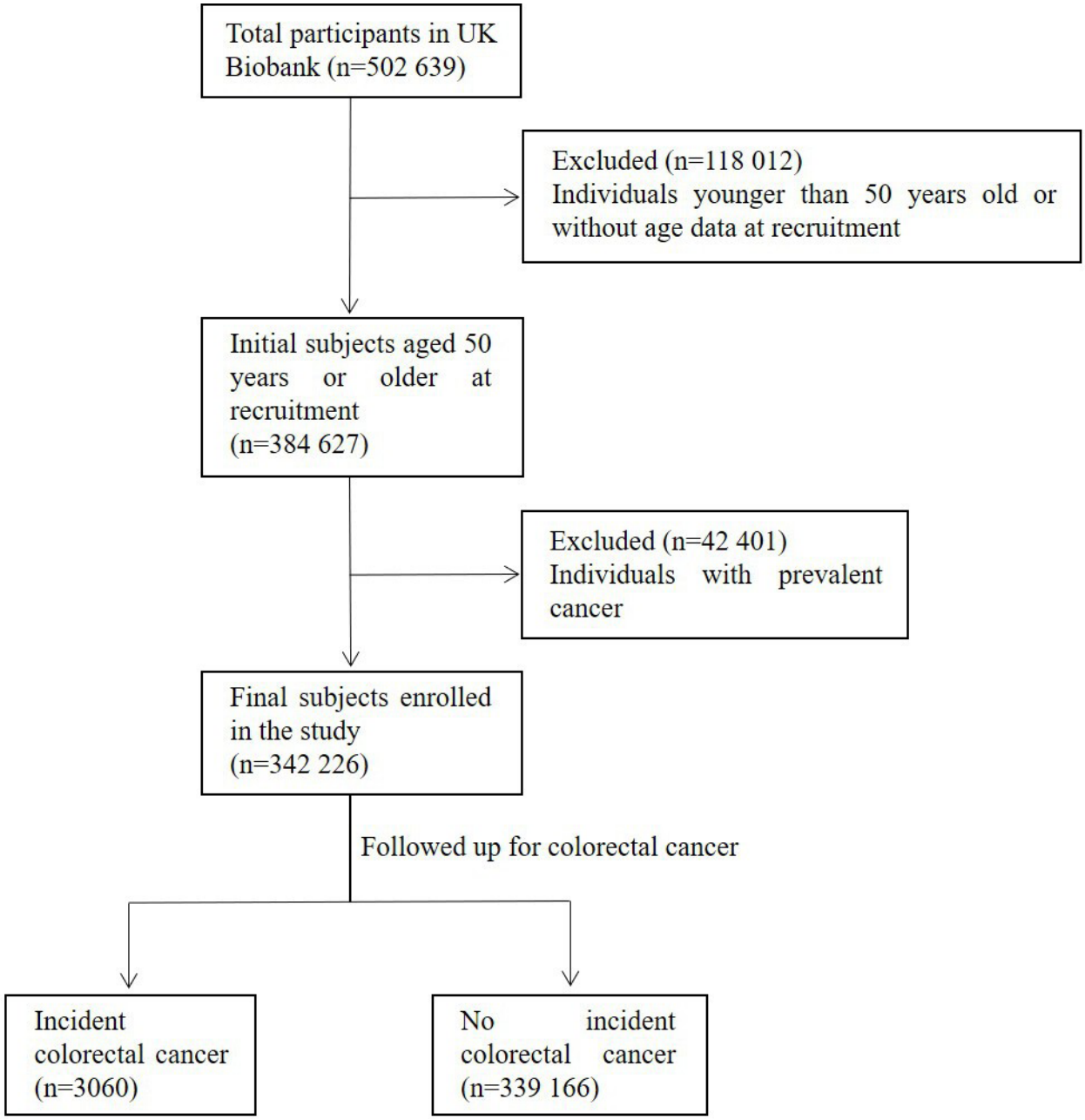

Figure 1 Flow chart of the study.

Ascertainment of CRC

The outcome was ascertained by linkage to cancer and death registries using the International Classification of Diseases, Tenth codes C18–C20. More detailed information about the outcome definition is shown in online supplemental table 1.

Assessment of ICVHMs

Based on the recommendations of the Goals and Metrics Committee of the Strategic Planning Task Force of the AHA,[9] the ICVHMs were defined as four behavioural factors (abstinence from smoking, ideal BMI, physical activity at goal and consumption of healthy diet that promotes cardiovascular health) and three cardiometabolic factors (untreated total cholesterol <200 mg/dL, untreated blood pressure <120/80 mm Hg and untreated fasting plasma glucose <100 mg/dL). Smoking status was categorised as current or never/previous smoking, and abstinence from smoking was defined as never/previous smoking. BMI was calculated by dividing the body weight (kg) by the square of height (m^2), and ideal BMI was defined as 25 kg/m^2. Having at least 75 min/week of vigorous activity, or 150 min/week of moderate activity, or equivalent combination was identified as physical activity at goal. The ideal diet focused on at least four of seven ideal food groups according to the dietary recommendations for cardiometabolic health.[14] More detailed information about the definition of the ICVHMs is shown in online supplemental table 2. Each factor in the ICVHMs was classified into two categories: 'ideal' or 'not ideal'. 'Ideal' is scored 1 point and 'not ideal' 0 points. Therefore, the ICVHM score ranges from 0 (the unhealthiest) to 7 (the healthiest).

Weighted standardised ICVHMs

Assuming that each factor in the ICVHMs has the same effect on the outcome may not be an optimal method. Therefore, we introduced weighted standardised ICVHMs in this study, where each factor was weighted by its association with the outcome. Weighted standardised scores were constructed using the β coefficient for each factor in the Cox proportional hazards model, taking account of other potential confounders, including age, sex, ethnic origin, education, income, Townsend index, chronic illnesses, long-standing disability or infirmity, family history of CRC, medicine use, drinking status, and mutual adjustment for other ICVHM factors. The original binary variable was multiplied by the absolute value of the β coefficient and then divided by the sum of seven absolute β values. Then, the weighted standardised ICVHMs can be obtained by adding the weighted standardised score of each factor. The weighted standardised ICVHMs ranged from 0 (the unhealthiest) to 1 (the healthiest). According to the four quantiles of the weighted standardised ICVHMs, the population was divided into five levels, with higher levels indicating healthier status.

Assessment of covariates

Covariates for this study included age (years), sex (male or female), ethnic origin (white or non-white), education (university degree or non-university degree), income (less than £18 000, £18 000–£30 999, £31 000–£51 999, £52 000–£100 000, or greater than £100 000), Townsend index (continuous), chronic illnesses (yes or no), long-standing disability or infirmity (yes or no), family history of CRC (yes or no), medicine use (yes or no), menopausal status (yes or no), hormone replacement therapy (never used or ever used), and drinking status (never drinking, previous drinking or current drinking) recorded at baseline. The Townsend index is a comprehensive indicator that measures the socioeconomic status of the community, evaluating the degree of unemployment, car-free, house-free and family overcrowding in the UK.[15] Chronic illnesses included diabetes, CVD (heart attack, angina, stroke and high blood pressure), and severe liver and kidney diseases. Family history of CRC was defined as whether the father, mother, brothers or sisters had CRC. Medicine use referred to use of aspirin/ibuprofen or not. More detailed definitions of the covariates are shown in online supplemental table 3.

Statistical analyses

Continuous variables were expressed as mean (SD), and categorical variables were described as number (percentage). Cox proportional hazards models were used to estimate the HR and 95% CI for the association between the ICVHMs and CRC. The proportional hazards assumption was checked using Schoenfeld residuals.[16 17] In the multivariable models, we adjusted for age (years), sex (male or female) and ethnic origin (white or non-white) in model 1. In model 2, we further adjusted for education (university degree or non-university degree), income (less than £18 000, £18 000–£30 999, £31 000–£51 999, £52 000–£100 000, or greater than £100 000) and Townsend index (continuous). In model 3, we further adjusted for chronic illnesses (yes or no), long-standing disability or infirmity (yes or no), family history of CRC (yes or no), medicine use (yes or no), and drinking status (never drinking, previous drinking or current drinking). When exploring the effect of each factor in the ICVHMs, the other factors were mutually adjusted. In addition, we conducted subgroup analyses by age (≥50 years and <60 years vs ≥60 years) and sex (male vs female). To test the interaction between continuous ICVHMs and grouping variables, we calculated the p values for the product terms included in the Cox proportional hazards models. We also performed the following sensitivity analyses to test the robustness of the results: (1) using threefold cross-validation[18] to generate and validate the weighted standardised ICVHMs; (2) excluding CRC cases within the first 2 years of follow-up; and (3) excluding participants with CVD (heart attack, angina, stroke and high blood pressure). Multiple imputation[19] was used in all analyses to minimise sample size reduction due to missing values. Imputation model included survival status, follow-up

time, all explanatory factors and covariates. Five data sets without missing values were generated after imputation, each of which followed the same analyses. Finally, the results were pooled using Rubin's rules.[19] All statistical analyses were performed using R software (V.4.0.3). The rms package was used to build Cox proportional hazards models and the mice package for multiple imputation. All p values were two-sided, with statistical significance defined at p<0.05.

RESULTS

Baseline characteristics of the participants

A total of 342 226 subjects were enrolled in the study, comprising 3060 CRC cases and 339 166 non-cases. The median follow-up year was 8.72, with an IQR of 1.23. The baseline characteristics of the participants are shown in table 1.

Association between ICVHMs and incident CRC

Compared with the reference (participants with ICVHMs ≤2), the multivariable-adjusted HRs for the subgroups with 3, 4, 5 and ≥6 ICVHM factors were 0.98 (95% CI 0.85 to 1.12), 0.90 (95% CI 0.77 to 1.02), 0.85 (95% CI 0.71 to 0.98) and 0.69 (95% CI 0.48 to 0.90), respectively. When continuous ICVHMs were included in the model, the negative association between the number of ICVHMs and the risk of CRC remained significant (HR: 0.93, 95% CI 0.90 to 0.96). Among the seven ICVHM factors, ideal BMI, ideal diet and ideal fasting plasma glucose were significantly related to a lower risk of CRC (HR: 0.86, 95% CI 0.78 to 0.95; HR: 0.92, 95% CI 0.84 to 0.99; HR: 0.90, 95% CI 0.80 to 0.99). The results of model 2 and model 1 were consistent with those of model 3 (table 2).

Subgroup analyses

Consistent results were observed when analyses were stratified by age (≥50 years and <60 years vs ≥60 years) (p value for interaction=0.750) (figure 2). The inverse association between the ICVHMs and the risk of CRC might be more significant among men than women (p value for interaction=0.055) (figure 2).

Sensitivity analyses

When using weighted standardised ICVHMs, the inverse association between ICVHMs and risk of CRC remained unchanged (online supplemental table 4). Consistent results were observed when we further excluded the cases during the first 2 years of follow-up (online supplemental table 5). Finally, the results were stable after excluding participants with CVD (online supplemental table 6).

DISCUSSION

This prospective study found an inverse correlation between ICVHMs and risk of CRC over a follow-up of 8.72 years. The ICVHMs proved to successfully prevent not only CVD,[10 12 20 21] but also the incidence of CRC.

The inverse association between the ICVHMs and the incidence of CRC was salient in this study. Participants with ≥6 ICVHM factors had 31% lower risk of CRC than those with ≤2 ICVHM factors. Rasmussen-Torvik *et al*[13] had previously examined if adherence to ICVHMs was associated with incident cancers among 13 253 participants (aged 45–64 years at baseline) over 17–19 years of follow-up. They adjusted age, sex, race and study centre in the Cox model and found that ICVHMs might reduce the risk of CRC, with which our findings were consistent. We made further adjustments in our models (eg, education, income, family history of CRC and medicine use) and explored which ICVHM factors played a part in the relationship of interest. Moreover, the majority of patients with CRC were over 50 years old,[22] and most screenings for CRC are recommended to start at the age of 50.[23] We included participants aged 50 years or older to target high-risk groups, emphasising the importance of adhering to the ICVHMs in this population.

We found that BMI, diet and fasting plasma glucose were the three significant factors independently associated with risk of CRC. Previous epidemiological evidence showed that obesity was positively associated with incident CRC.[24–28] Meta-analyses have demonstrated that a weight gain of 10 kg could result in about 8% increased risk of CRC.[29 30] In contrast, weight loss through bariatric surgery reduced the risk of CRC by approximately 27%.[31 32] Compared with non-obese people, obese people have disordered higher levels of insulin and leptin,[33 34] but lower adiponectin levels.[35] These disordered hormones alone or jointly promote the formation and development of CRC.[36] In addition, adipose tissue mediates low-grade chronic inflammation by releasing various cytokines, including insulin-like growth factor (IGF), interleukin 6, tumour necrosis factor-α and plasminogen activator inhibitor-1,[37] which promotes the proliferation, migration and metastasis signalling of tumour cells.[38 39] Studies have demonstrated that processed meat might increase the risk of CRC,[40 41] while dietary fibre[40 41] and fatty fish[42] were associated with a lower risk of CRC. Moreover, a meta-analysis supported the inverse association between adherence to Mediterranean diet and CRC incidence.[43] Through inflammation pathways or intestinal microbial environment,[44–46] dietary factors notably affect the risk of CRC. Two meta-analyses reported an increased risk of CRC in patients with diabetes compared with those without diabetes (pooled relative risk: 1.26, 95% CI 1.20 to 1.31; pooled relative risk: 1.27, 95% CI 1.21 to 1.34).[47 48] Higher fasting plasma glucose levels were significantly associated with an increased risk of CRC (pooled OR: 1.12, 95% CI 1.06 to 1.18),[49] and the RR of CRC was 1.015 (95% CI 1.012 to 1.019) for each 20 mg/dL increment over the FPG.[50] Hyperglycaemia induces elevated insulin and IGF levels[51] and further activates the IGF-1-PI3K-AKT-mTOR pathway,[51] which promotes tumour growth and invasion.[52] In addition, hyperglycaemia can increase the risk of CRC through epigenetic modifications and gene interactions.[52]

Table 1 Baseline characteristics of the participants

Characteristics	Overall	Number of ideal cardiovascular health metrics				
		≤2	3	4	5	≥6
n (%)	342 226 (100.0)	37 402 (10.9)	90 358 (26.4)	120 151 (35.1)	72 227 (21.1)	22 088 (6.5)
Age (years)	59.9 (5.5)	59.4 (5.4)	59.9 (5.4)	60.1 (5.4)	60.1 (5.5)	58.8 (5.6)
Sex, n (%)						
Male	159 754 (46.7)	20 551 (54.9)	46 421 (51.4)	54 908 (45.7)	29 772 (41.2)	8102 (36.7)
Female	182 472 (53.3)	16 851 (45.1)	43 937 (48.6)	65 243 (54.3)	42 455 (58.8)	13 986 (63.3)
Ethnic origin, n (%)						
White	326 071 (95.3)	35 758 (95.6)	86 454 (95.7)	114 422 (95.2)	68 514 (94.9)	20 923 (94.7)
Non-white	16 155 (4.7)	1644 (4.4)	3904 (4.3)	5729 (4.8)	3713 (5.1)	1165 (5.3)
Education, n (%)						
University degree	121 715 (35.6)	11 780 (31.5)	29 498 (32.7)	42 128 (35.1)	28 246 (39.1)	10 062 (45.6)
Non-university degree	220 511 (64.4)	25 622 (68.5)	60 860 (67.3)	78 023 (64.9)	43 981 (60.9)	12 026 (54.4)
Income, n (%)						
Less than £18 000	91 499 (26.8)	11 073 (29.6)	25 081 (27.8)	32 380 (26.9)	18 258 (25.3)	4706 (21.3)
£18 000–£30 999	95 598 (27.9)	9878 (26.4)	25 150 (27.8)	34 226 (28.6)	20 413 (28.3)	5931 (26.9)
£31 000–£51 999	83 244 (24.3)	8745 (23.4)	21 759 (24.1)	29 256 (24.3)	17 838 (24.7)	5646 (25.6)
£52 000–£100 000	57 477 (16.8)	6225 (16.6)	14 871 (16.4)	19 549 (16.3)	12 405 (17.2)	4427 (20.0)
Greater than £100 000	14 408 (4.2)	1481 (4.0)	3497 (3.9)	4740 (3.9)	3313 (4.5)	1378 (6.2)
Townsend index score	−1.4 (3.0)	−1.0 (3.3)	−1.3 (3.1)	−1.5 (3.0)	−1.6 (2.9)	−1.6 (2.9)
Chronic illnesses, n (%)						
Yes	123 939 (36.2)	15 862 (42.4)	35 218 (39.0)	44 211 (36.8)	23 681 (32.8)	4967 (22.5)
No	218 287 (63.8)	21 540 (57.6)	55 140 (61.0)	75 940 (63.2)	48 546 (67.2)	17 121 (77.5)
Long-standing disability or infirmity, n (%)						
Yes	117 239 (34.3)	15 278 (40.9)	32 851 (36.4)	40 413 (33.6)	22 423 (31.1)	6275 (28.4)
No	224 987 (65.7)	22 124 (59.1)	57 507 (63.6)	79 738 (66.4)	49 804 (68.9)	15 813 (71.6)
Family history of colorectal cancer, n (%)						
Yes	25 699 (7.5)	2888 (7.7)	6835 (7.6)	8965 (7.5)	5373 (7.4)	1638 (7.4)
No	316 527 (92.5)	34 514 (92.3)	83 523 (92.4)	111 186 (92.5)	66 854 (92.6)	20 450 (92.6)
Medicine use, n (%)						
Yes	76 711 (22.4)	8290 (22.2)	19 894 (22.0)	26 709 (22.2)	16 589 (23.0)	5228 (23.7)
No	265 515 (77.6)	29 112 (77.8)	70 464 (78.0)	93 442 (77.8)	55 638 (77.0)	16 860 (76.3)
Menopausal status, n (%)						
Yes	140 188 (76.8)	12 675 (75.2)	33 602 (76.5)	50 548 (77.5)	33 131 (78.0)	10 232 (73.2)
No	12 511 (6.9)	1038 (6.2)	2660 (6.0)	4094 (6.3)	2999 (7.1)	1720 (12.3)
Not sure	29 773 (16.3)	3138 (18.6)	7675 (17.5)	10 601 (16.2)	6325 (14.9)	2034 (14.5)
Hormone replacement therapy, n (%)						
Never used	95 867 (52.5)	8700 (51.6)	22 627 (51.5)	33 885 (51.9)	22 616 (53.3)	8039 (57.5)
Ever used	86 605 (47.5)	8151 (48.4)	21 310 (48.5)	31 358 (48.1)	19 839 (46.7)	5947 (42.5)
Drinking status, n (%)						
Never drinking	15 125 (4.4)	1474 (3.9)	3789 (4.2)	5413 (4.5)	3339 (4.6)	1110 (5.0)
Previous drinking	12 638 (3.7)	1490 (4.0)	3272 (3.6)	4248 (3.5)	2675 (3.7)	953 (4.3)
Current drinking	314 463 (91.9)	34 438 (92.1)	83 297 (92.2)	110 490 (92.0)	66 213 (91.7)	20 025 (90.7)

Continued

Table 1 Continued

Characteristics	Overall	Number of ideal cardiovascular health metrics				
		≤2	3	4	5	≥6

Continuous variables are described as mean (SD) and categorical variables are described as n (percentage).

Moreover, we found that the association between the ICVHMs and the incidence of CRC was more significant among men than women, consistent with previous studies.[53 54] This may be related to the biological and behavioural differences between men and women.[55–57] In

Table 2 HR (95% CI) of incident colorectal cancer according to ICVHMs

Category	Cases	Person-years	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Smoking					
Current smoking	307	278 869	1.00 (reference)	1.00 (reference)	1.00 (reference)
Never or previous smoking	2753	2 666 999	0.92 (0.80 to 1.04)	0.93 (0.81 to 1.05)	0.92 (0.80 to 1.05)
Body mass index					
>25 kg/m^2	2277	2 024 065	1.00 (reference)	1.00 (reference)	1.00 (reference)
≤25 kg/m^2	783	921 803	0.85 (0.77 to 0.94)	0.86 (0.77 to 0.94)	0.86 (0.78 to 0.95)
Physical activity					
<150 min/week mixed (moderate+vigorous) activity	592	534 930	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥150 min/week mixed (moderate+vigorous) activity	2468	2 410 938	0.91 (0.81 to 1.00)	0.91 (0.81 to 1.00)	0.91 (0.82 to 1.00)
Diet					
<4 ideal food groups	1413	1 256 306	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥4 ideal food groups	1647	1 689 562	0.92 (0.84 to 0.99)	0.92 (0.84 to 0.99)	0.92 (0.84 to 0.99)
Total cholesterol					
≥5.18 mmol/L	1942	2 022 426	1.00 (reference)	1.00 (reference)	1.00 (reference)
<5.18 mmol/L	1118	923 442	1.06 (0.98 to 1.13)	1.05 (0.97 to 1.13)	1.05 (0.97 to 1.13)
Blood pressure					
≥120 mm Hg for SBP or ≥80 mm Hg for DBP	2818	2 640 140	1.00 (reference)	1.00 (reference)	1.00 (reference)
<120 mm Hg for SBP and <80 mm Hg for DBP	242	305 728	0.97 (0.83 to 1.11)	0.97 (0.83 to 1.11)	0.98 (0.84 to 1.12)
Fasting plasma glucose					
≥5.56 mmol/L	647	514 132	1.00 (reference)	1.00 (reference)	1.00 (reference)
<5.56 mmol/L	2413	2 431 736	0.89 (0.79 to 0.98)	0.89 (0.79 to 0.99)	0.90 (0.80 to 0.99)
Categorical ICVHMs, number					
≤2	369	318 977	1.00 (reference)	1.00 (reference)	1.00 (reference)
3	888	775 544	0.97 (0.84 to 1.11)	0.98 (0.84 to 1.11)	0.98 (0.85 to 1.12)
4	1073	1 035 319	0.89 (0.76 to 1.01)	0.89 (0.77 to 1.02)	0.90 (0.77 to 1.02)
5	598	624 187	0.84 (0.70 to 0.97)	0.84 (0.71 to 0.98)	0.85 (0.71 to 0.98)
≥6	132	191 841	0.67 (0.46 to 0.88)	0.68 (0.47 to 0.88)	0.69 (0.48 to 0.90)
Continuous ICVHMs	3060	2 945 868	0.92 (0.89 to 0.96)	0.93 (0.89 to 0.96)	0.93 (0.90 to 0.96)

Model 1 was adjusted for age, sex and ethnic origin.
Model 2 was adjusted for age, sex, ethnic origin, education, income and Townsend index.
Model 3 was adjusted for age, sex, ethnic origin, education, income, Townsend index, chronic illnesses, long-standing disability or infirmity, family history of colorectal cancer, medicine use, and drinking status.
When exploring the effect of each factor in the ICVHMs, the other factors were mutually adjusted.
DBP, diastolic blood pressure; ICVHM, ideal cardiovascular health metrics; SBP, systolic blood pressure.

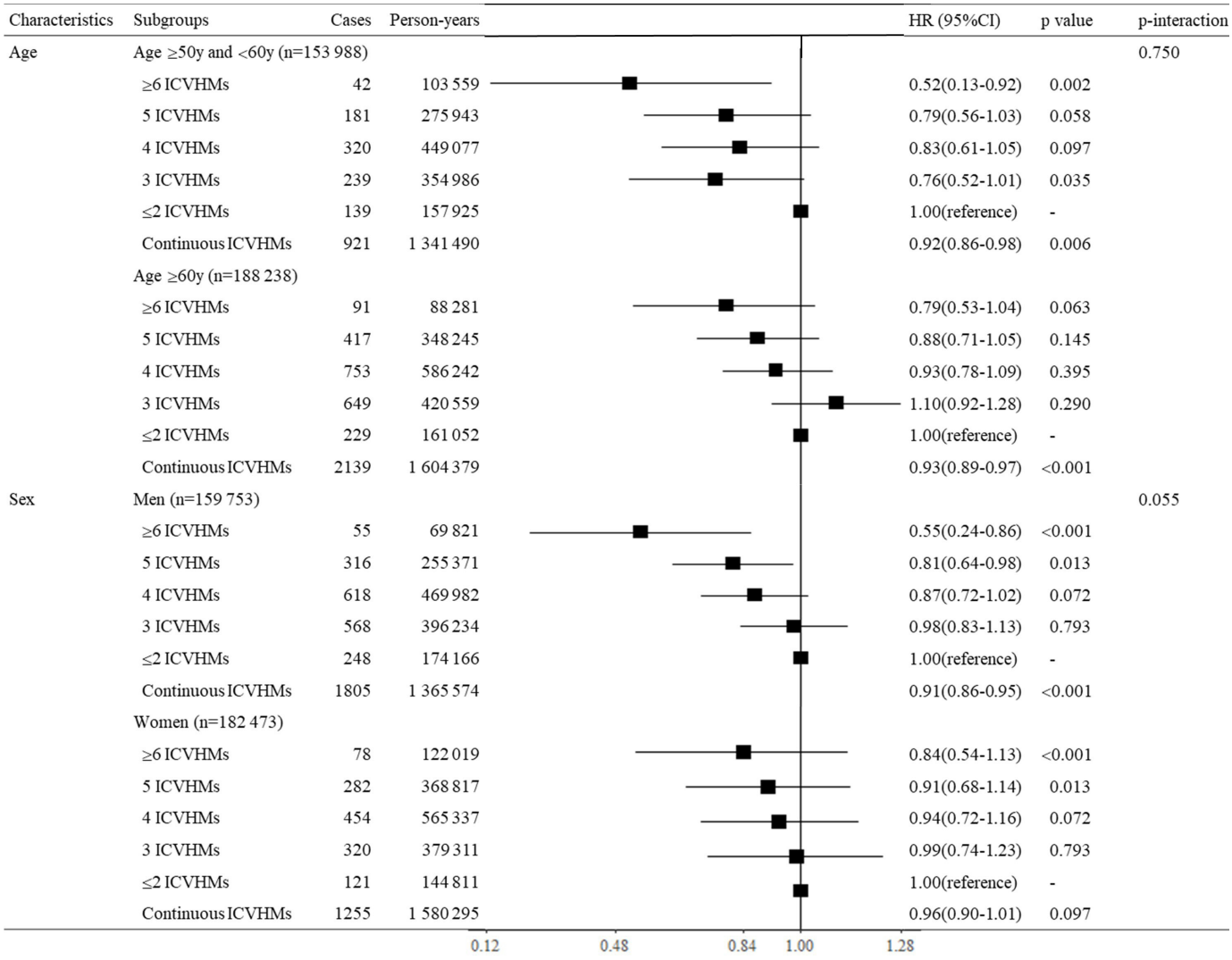

Figure 2 Associations of ideal cardiovascular health metrics (ICVHMs) with incident colorectal cancer risk in age-specific and sex-specific subgroups. The models were adjusted for age, sex, ethnic origin, education, income, Townsend index, chronic illnesses, long-standing disability or infirmity, family history of colorectal cancer, medicine use, drinking status, menopausal status (only in women subgroup), and hormone replacement therapy (only in women subgroup).

this study, the ICVHM factors among men tended to be non-ideal compared with women.

Our research has several advantages. One strength is that it was based on a prospective cohort with a long follow-up period and a large sample size, enhancing the study's representativeness and methodological robustness. In addition, the outcome was ascertained through linkage to cancer and death registries, which are comprehensive and reliable.

However, limitations should be considered. First, this study only explored the relationship between the baseline exposures and the outcome. It did not consider changes in exposure measurements during the follow-up due to unavailability of data sets. Second, some relevant factors, such as psychosocial factors and genetic susceptibility, were not included in the model for further adjustment, which could lead to residual confounding. Third, the AHA recommended defining dietary goals according to 'the Dietary Approaches to Stop Hypertension (DASH)' eating plan, including sodium, sugar-sweetened beverages and so on.[9] However, we did not evaluate adherence to DASH diet since a valid diet recording was difficult in large epidemiological studies. Fourth, due to the low response rate in the UK Biobank, the study findings may be biased by the 'healthy volunteer' effect. However, a previous study has shown that risk factor associations in the UK Biobank seemed to be generalisable despite a very low response rate.[58] Finally, the study participants were mostly white. Therefore, generalisation of the findings to other populations should be cautiously applied due to differences in genetic background and other risk factors among different ethnic groups.

CONCLUSIONS

In this study, we verified that adherence to ICVHMs could reduce the risk of CRC among people aged 50 years or older. Among the seven ICVHM factors, BMI, diet and

fasting plasma glucose played a more critical role in the prevention of CRC. Moreover, the inverse association between the ICVHMs and the risk of CRC might be more significant among men than women. These findings imply that health recommendations related to ICVHMs can be encouraged to reduce the burden of CVD as well as CRC.

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Data availability statement Data are available upon reasonable request. The UK Biobank is an open access resource. Data are available on application to the UK Biobank (www.ukbiobank.ac.uk/). This research has been conducted using the UK Biobank resource under application number 44430. Data and statistical codes used for this paper are available to other researchers on request by email to Hailun Liang (hliang@ruc.edu.cn).

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