Preventive Medicine Reports 44 (2024) 102807

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Sex difference in alcohol consumption associated with colorectal cancer risk in Quzhou, China: A nested case-control study

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ARTICLE INFO

Keywords:
Colorectal cancer
Alcohol consumption
Drinking
Nested case-control study
Mass screening
Sex difference

ABSTRACT

Objective: Colorectal cancer (CRC) incidence has been increasing worldwide over time. This study investigated whether drinking was associated with CRC risk.
Methods: We designed a case-control study nested in a mass CRC screening program in Quzhou, China. Cases were newly diagnosed CRC in 2020–2022. Controls were randomly sampled using frequency match. Drinking variables included drinking status, frequency, duration, and others. Logistic regressions were used to estimate odds ratio (OR) and 95 % confidence interval (CI).
Results: The crude OR (cOR) (95 % CI) of drinking between 153 cases and 650 controls was 1.46 (0.99, 2.16) in current drinkers, 3.31 (1.44, 7.60) in former drinkers, 1.82 (1.21, 2.74) in drinking 6–7 days/week, and 3.48 (1.29, 9.37) in drinking 1–19 years. Stratifying by sex, all drinking variables in women but not all in men were consistently associated with CRC risk. The adjusted OR (aOR) (95 % CI) was 1.01 (0.59, 1.74) in current drinking men, 2.27 (0.78, 6.64) in former drinking men, and 4.24 (1.61, 11.13) in current drinking women. The aOR (95 % CI) of drinking whisky was 0.19 (0.04, 0.83), 1.89 (0.86, 4.17), 2.25 (1.05, 4.83), and 1.82 (0.85, 3.92) in men drinking ≤0.5, >0.5–≤1.0, >1.0–≤1.5, and >1.5 Liter/week (P_{trend} = 0.011), and 3.80 (1.03, 14.00) and 9.92 (2.01, 49.00) in women drinking ≤0.5 and >0.5 Liter/week (P_{trend} = 0.001), respectively.
Conclusions: There was sex difference in drinking associated with increased risk of CRC which association was stronger in women than that in men. Men's association between drinking whisky and CRC risk was J-shaped.

1. Introduction

Colorectal cancer (CRC) has become a common cancer and its incidence is continuously increasing worldwide over time (Sung et al, 2021; Zhu et al, 2023; IARC, 2021; Wild, 2020; Cao and Chen, 2021; Xun et al, 2023; Zhang et al, 2022). According to the International Agency for Research on Cancer, there were over 1.88 million new CRC cases diagnosed in the world in 2020, which incidence was ranked third among 36 cancers; and there were about 0.92 million deaths of CRC, which mortality was ranked second among 36 cancers (Sung et al, 2021; IARC, 2021; Wild, 2020). CRC incidence has been increasing in China (Zhu et al, 2023; Cao and Chen, 2021; Xun et al, 2023; Zhang et al, 2022). There were about 555,000 new cases and 286,000 deaths of CRC in China in 2020 (Sung et al, 2021; Cao and Chen, 2021; Xun et al, 2023; Zhang et al, 2022), where age standardized incidence and mortality was 23.9/100,000 and 12.0/100,000, higher than the world average rate (19.5/100,000 and 9.0/100,000), respectively.

In order to reduce CRC incidence and mortality, it is important to study its risk factors. The etiology of CRC is not completely understood. Many factors (Sung et al, 2021; Zhu et al, 2023; Thanikachalam and Khan, 2019; Lancet, 2017; Hua et al, 2023; Sifaki-Pistolla et al, 2022; Danial et al, 2022; Cai et al, 2003), including family history of CRC, physical inactivity, unhealthy diet, obesity, being sedentary for too long, smoking and drinking have been reported to be associated with CRC

Abbreviations: CRC, colorectal cancer; OR, odds ratio; CI, confidence interval; HRFQ, high-risk-factors questionnaire; FIT, faecal immunochemical test.

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https://doi.org/10.1016/j.pmedr.2024.102807
Received 23 January 2024; Received in revised form 26 June 2024; Accepted 27 June 2024
Available online 28 June 2024

incidence. But the conclusions of their causal relationships remain inconclusive. The association of drinking with CRC risk is still controversial (Sung et al, 2021; Zhu et al, 2023; Thanikachalam and Khan, 2019; Lancet, 2017; Hua et al, 2023; Sifaki-Pistolla et al, 2022; Danial et al, 2022; Cai et al, 2003; Chen et al, 2004; Lim and Park, 2008; Tverdal et al, 2021; Fedirko et al, 2011; Choi et al, 2018; McNabb et al, 2020; Gu et al, 2018): Some studies have found drinking is associated with increase in CRC risk (Sung et al, 2021; Thanikachalam and Khan, 2019; Lancet, 2017; Hua et al, 2023; Sifaki-Pistolla et al, 2022; Danial et al, 2022; Tverdal et al, 2021; Fedirko et al, 2011; Choi et al, 2018; McNabb et al, 2020; Gu et al, 2018); some have reported drinking is associated with decrease in CRC risk (Cai et al, 2003; McNabb et al, 2020); and some have reported no association between them (Chen et al, 2004; Lim and Park, 2008).

Drinking prevalence is increasing over time and varies in sex, age and city in China (Huang et al, 2020; Li et al, 2022; Yan et al, 2019; Xie et al, 2020; Liu et al, 2021). The drinking prevalence in residents aged 15 years or older was 35.1 %, 39.6 %, and 68.6 % in men and 2.6 %, 4.5 % and 42.6 % in women in China in 1991, 2002, and 2016, respectively (Huang et al, 2020). The drinking prevalence in adults reached 50.13 % in Guangdong city where drinking prevalence in men (66.71 %) was much higher than that in women (32.59 %) and drinking prevalence in the urban (53.96 %) was much higher than that in the rural (41.61 %) in 2018 (Li et al, 2022); the drinking prevalence was 47.58 % in Heilongjiang province (Yan et al, 2019) and 41.81 % in Beijing city (Xie et al, 2020). In Shanghai, the drinking prevalence in a working population aged 18–59 years old was 31.86 % in men and 5.22 % in women in 2013 (Liu et al, 2021).

We believe increasing drinking prevalence in China (Huang et al, 2020; Li et al, 2022) could help explain part of the increase in CRC incidence in the past decades. In order to obtain more scientific evidence, this study investigated whether drinking was associated with CRC risk in a population aged 40–74 years.

2. Methods

2.1. Study design and participants

We designed a case-control study nested in an ongoing mass CRC screening program in Quzhou, China. Residents aged 50–74 years old in the community were invited. All participants had signed the consent form and had cost free high-risk-factors questionnaire (HRFQ) evaluation, faecal immunochemical test (FIT) and colonoscopy. Those who had a history of colorectal cancer and severe diseases of liver, heart, kidney, lung, brain, and mental health were excluded at the baseline. The study has been approved by the Ethics Committees of our institutions.

Cases were defined as primary CRC (ICD-10 code: C18-20) diagnosed through colonoscopy and confirmed by histopathological examinations. A total of 153 new cases diagnosed from 2020 to 2022 were included in this study. Controls were participants without any colorectal diseases confirmed by colonoscopy at the same time period. A total of 650 controls were randomly selected by frequency matching with a sampling ratio of about 4 controls per case.

2.2. Study outcomes and risk factors

The primary outcome was CRC, and the secondary outcome was the association between drinking and CRC risk. Main study factor was drinking that was defined as drinking at least once per week continuously for at least 6 months. Drinking data were based on self-reported standardized questionnaire which had been validated. They included drinking status (never, current and former), age at start drinking, frequency, duration, type of alcohol beverage (beer, wine/yellow wine (a wine made of rice in China), and whisky), beer frequency and amount in bottles per week, whisky frequency and amount in Liter/week, whisky alcohol degree (<40 %, 40–50 %, and ≥50 %), wine/yellow wine frequency and amount in Liter/week and years stop drinking.

Other adjusted factors included age (<55, 55–59, 60–64, 65–69, and ≥70 years old), sex (woman and man), education (<6 and ≥6 years), marriage status (married: still in the first marriage and others including never married, widowed, and divorced), smoking status (never, current and former), body mass index (BMI) group defined using the international standard (underweight: <18.5 defined as), normal:18.5–<25, overweight: 25–<30, and obese: ≥30), physical activity in the past year (<3 times/month, 1–2 times/week, 3–5 times/week, and 6–7 times/week), diet habit (healthy food was defined based on frequency of fresh vegetables, fruit, full grains and white meat (fish, chicken, and duck) and unhealthy food was defined based on frequency of red meat, pickled, processed and fried food), history of cancer in family members (never and ever), history of cancer in relatives (never and ever), history of intestinal disease (never and ever), history of chronic diseases (never and ever), history of medication (never and ever), and results of high-risk-factors questionnaire (HRFQ) (high-risk score (defined based on either history of colorectal polyps/adenoma, or history of colorectal polyps/adenomas in the first-degree family members, or high risk score ≥5 (score estimated based on age: 0 for 50–54, 1 for 55–64 and 2 for 65–74 years old; sex: 0 for woman and 1 for man; history of colorectal cancer in the first-degree family members: 0 for no and 1 for yes; smoking: 0 for never and 1 for ever; and BMI: 0 for <23 and 1 for ≥23 kg/m^2), medium risk (scored 1–4) and low (scored 0), faecal immunochemical test (FIT) (negative and positive), history of colonoscopy (never and ever), and others.

2.3. Quality assurance and quality control

All personnel including medical doctors who participated in this mass screening program were required to get well-trained and must have obtained training certificates before they started working for this screening program. Medical doctors worked in the community health service centers used face to face method to collect questionnaire data and to evaluate whether participants are HRFQ positive (+) or negative (−) and did FIT tests which were free to participants. Those with either HRFQ+ or FIT+ were invited to get a free colonoscopy in the hospitals in the counties or the city. All information, including questionnaire data, FIT results, colonoscopy and histopathological results, was recorded into the system named “the Zhejiang Province Cancer Screening Information Platform” which has an intelligent examination function that can help correct errors in it.

2.4. Statistical analysis

Numerical variables such as age were expressed as mean ± SD (standard deviation) and *t* test was used to compare them between the case and control groups. Categorical and ordered variables were expressed as frequency number (n) and percentage (%) and χ^2 test was used to compare them between the two groups. Logistic regression was used to estimate odds ratio (OR) and 95 % confidence interval (CI) for the association between drinking and CRC. In the final multivariable models, age was defined as 0 = <55, 1 = 55–59, 2 = 60–64, 3 = 65–69, and 4 = 70–74 years old; physical activity was defined as 0 = 0–3 times/month, 1 = 1–5 times/week, and 2 = 6–7 times/week); and ever having chronic diseases was defined as 0 = never and 1 = ever. All adjusted variables were used as dummy variables and required to have a *P* value ≤ 0.10 in order to be included in the final models. *P* value for the trend of the association between drinking and CRC risk was estimated by a χ^2 trend test (i.e., Cochran-Armitage trend test). All statistical tests were two-tailed. A *P* value ≤0.05 was defined as statistically significant; 0.05 < *P* value ≤0.10 was defined as statistically marginally significant, and a *P* value > 0.10 was defined as statistically insignificant. STATA/SE 15.1 software was used to analyze the data.

3. Results

Information of characteristics between cases and controls is presented in Table 1. There were overall significant differences in age ($P < 0.001$), drinking status ($P = 0.004$) and HRFQ positive or negative ($P < 0.001$) between the case and control groups. Due to limited space, some factors which were insignificant not shown in Table 1.

The drinking proportion was 56.79 % in cases and 55.12 % in controls in men and 16.67 % in cases and 3.17 % in controls in women, respectively. The average age at start drinking was 23.67 years old (SD: 7.17) in men and 34.6 years old (16.37) in women. The average drinking duration, frequency, cumulative amount, and whisky amount were 21.24 years (20.70), 3.31 days/week (3.23), 127.61 (135.79) days/week-years, and 0.45 Liter/week (1.61) in men and 1.55 years (7.49), 0.24 days/week (1.13), 6.97 days/week-years (37.41), and 0.02 Liter/week (0.10) in women, respectively.

Using never drinking in their lifetime as a common reference for all drinking variables in the analysis, the crude OR (cOR) (95 % CI) of drinking status between cases and controls was 1.46 (0.99, 2.16) in current drinkers and 3.31 (1.44, 7.60) in former drinkers and their adjusted OR (aOR) (95 % CI) was 1.33 (0.89, 2.01) in current drinkers and 2.86 (1.18, 6.95) in former drinkers (Table 2). When stratifying by sex, the cOR (95 % CI) of drinking status between cases and controls was 1.00 (0.60, 1.66) in current drinking men and 1.81 (0.69, 4.79) in former drinking men (Table 3), and 4.58 (1.82, 11.53) in current drinking women shown in Table 4 (only three women were former drinkers). The aOR (95 % CI) was 1.01 (0.59, 1.74) in current drinking men and 2.27 (0.78, 6.64) in former drinking men (Table 3), and 4.24 (1.61, 11.13) in current drinking women (Table 4).

The aOR (95 % CI) was 1.52 (0.64, 3.66), 0.84 (0.45, 1.57), and 1.18 (0.45, 3.21) in age at start drinking <20, 20–29, and ≥30 years old in men (Table 3) and 3.01 (0.93, 9.75) and 9.25 (1.55, 55.18) in age at start drinking ≤35 and >35 years old in women (Table 4) (most drinking variables for women were categorized into 2 categories due to low drinking prevalence in women), respectively.

The aOR (95 % CI) of drinking frequency between cases and controls was 0.89 (0.24, 3.24), 1.42 (0.68, 2.95), and 1.55 (1.01, 2.38) in drinking 1–2, 3–5, and 6–7 days/week, respectively, with a $P_{trend} = 0.038$ (Table 2). When stratifying by sex, their aOR (95 % CI) was 0.36 (0.04, 3.03), 0.91 (0.36, 2.32), and 1.22 (0.71, 2.13) in men drinking 1–2, 3–5, and 6–7 days/week with a $P_{trend} = 0.458$ (Table 3), and 4.03 (1.24, 13.12) and 7.40 (1.88, 29.15) in women drinking 1–4 and 5–7 days/week with a $P_{trend} = 0.001$ (Table 4), respectively.

The aOR (95 % CI) of drinking duration between cases and controls was 4.18 (1.41, 12.43), 1.88 (1.08, 3.27), and 1.03 (0.62, 1.72) in drinking 1–19, 20–39, and ≥40 years, respectively, with a $P_{trend} = 0.281$ (Table 2). When stratifying by sex, their aOR (95 % CI) was 2.33 (0.42, 13.03), 1.55 (0.76, 3.15), 0.85 (0.45, 1.59) in men drinking 1–19, 20–39, and ≥40 years with a $P_{trend} = 0.908$ (Table 3), and 6.44 (1.73, 23.97) and 4.35 (1.28, 14.71) in women drinking 1–29 and ≥30 years with a $P_{trend} = 0.002$ (Table 4), respectively.

The aOR (95 % CI) of drinking whisky type between cases and controls was 0.94 (0.24, 3.64), 1.41 (0.75, 2.66), and 1.11 (0.56, 2.21) in men drinking whisky with <40 %, 40–50 %, and >50 % alcohol in it with a $P_{trend} = 0.508$ (Table 3), and 12.99 (2.90, 58.15) and 4.02 (0.76, 21.16) in women drinking whisky with <40 % and 40–50 % alcohol in it with a $P_{trend} = 0.001$ (Table 4), respectively. The aOR (95 % CI) of drinking whisky amount between cases and controls was 0.19 (0.04, 0.83), 1.89 (0.86, 4.17), 2.25 (1.05, 4.83), and 1.82 (0.85, 3.92) in men drinking whisky amount of ≤0.5, >0.5–≤1.0, >1.0–≤1.5, and >1.5 Liter/week with a $P_{trend} = 0.011$ (Table 3), and 3.80 (1.03, 14.00) and 9.92 (2.01, 49.00) in women drinking whisky amount ≤0.5 and >0.5 Liter/week with a $P_{trend} = 0.001$ (Table 4), respectively.

The cOR (95 % CI) of cumulative drinking amount between cases and controls was 1.49 (0.69, 3.24), 1.27 (0.63, 2.55), 1.32 (0.74, 2.35) and 2.54 (1.44, 4.50) in < 100, 100–<200, 200–<300, and ≥300 days/

Table 1
Characteristics between cases and controls in a case-control study nested in a mass colorectal cancer screening program in Quzhou, China, 2020–2022.

Characteristic		Case group (n = 153)	Control group (n = 650)	Pearson *P* value
Sex, n (%)	Woman	72 (47.06)	347 (53.38)	
	Man	81 (52.94)	303 (46.62)	0.159
Age in years, mean (SD)		65.5 (6.42)	61.0 (7.21)	<0.001
Education, n (%)	<6 years	106 (69.28)	398 (61.23)	
	≥6 years	47 (30.72)	252 (38.77)	0.064
Marriage[a], n (%)	Married	137 (89.54)	602 (92.62)	
	Others	16 (10.46)	48 (7.38)	0.207
Smoking status, n (%)	Never	95 (62.09)	435 (66.92)	
	SHS[b]	11 (7.19)	45 (6.92)	
	Quitted	8 (5.23)	40 (6.15)	0.493
	Current	39 (25.49)	130 (20.00)	
Drinking status, n (%)	Never	95 (62.09)	472 (72.62)	
	Current	48 (31.37)	163 (25.08)	
	Quitted	10 (6.54)	15 (2.31)	0.004
Physical activity, n (%)	<once/week	124 (81.05)	488 (75.08)	
	1–5 times/week	15 (9.80)	74 (11.38)	
	6–7 times/week	14 (9.15)	88 (13.54)	0.255
Body Mass Index (BMI)[c] in kg/m^2, n (%)	18.5–<25	90 (58.82)	343 (52.77)	
	<18.5	7 (4.58)	25 (3.85)	
	25–<30	53 (34.64)	266 (40.92)	
	≥30	3 (1.96)	16 (2.46)	0.499
Healthy food[d], n (%)	6–7 times/week	7 (4.58)	58 (8.92)	
	3–5 times/week	81 (52.94)	317 (48.77)	
	1–2 times/week	62 (40.52)	258 (39.69)	
	<once/week	3 (1.96)	17 (2.62)	0.313
Unhealthy food[e], n (%)	<once/week	55 (35.95)	237 (36.46)	
	1–2 times/week	83 (54.25)	347 (53.38)	
	3–5 times/week	12 (7.84)	52 (8.00)	
	6–7 times/week	3 (1.96)	14 (2.15)	0.997
HRFQ[f], n (%)	Negative	20 (13.07)	180 (27.69)	
	Positive	133 (86.93)	470 (72.31)	<0.001

(*continued on next page*)

Table 1 (*continued*)

Characteristic		Case group (n = 153)	Control group (n = 650)	Pearson *P* value
Having intestinal disease, n (%)	Never	141 (92.61)	583 (89.6)	
	Ever	12 (7.84)	67 (10.31)	0.357
Having chronic disease, n (%)	Never	112 (73.20)	465 (71.54)	
	Ever	41 (26.80)	185 (28.46)	0.680

[a] Married was defined as married (means still in the first marriage) and others included never married, widowed, and divorced.
[b] secondhand smoke.
[c] was defined as weight in Kilogram divided by (height in meter)^2.
[d] was defined as frequency of fresh vegetables, fruit, tofu, full grain food, and sea food.
[e] was defined as frequency of red meat, fried food, pickled food, processed food and dried food.
[f] HRFQ, high-risk-factors questionnaire.

week-years (drinking frequency in days/week times drinking duration in years), respectively, with a $P_{trend} = 0.003$. Their aOR (95 % CI) was 1.78 (0.78, 4.07), 1.34 (0.65, 2.78), 1.39 (0.76, 2.54) and 1.49 (0.82, 2.70) in <100, 100–<200, 200–<300, and ≥300 days/week-years, respectively, with a $P_{trend} = 0.096$ (data not shown in Table).

After stratifying by sex, the cOR (95 % CI) of cumulative drinking amount between cases and controls was 0.62 (0.20, 1.90), 0.68 (0.28, 1.65), 0.85 (0.43, 1.69), and 2.15 (1.12, 4.11) in men drinking <100, 100–<200, 200–<300, and ≥300 days/week-years, respectively, with a $P_{trend} = 0.133$, and their aOR (95 % CI) was 0.85 (0.27, 2.72), 0.77 (0.30, 1.95), 0.91 (0.44, 1.88), and 1.43 (0.72, 2.85) in men drinking <100, 100–<200, 200–<300, and ≥300 days/week-years, respectively, with a $P_{trend} = 0.509$; their cOR (95 % CI) was 5.60 (1.57, 19.93) and 6.53 (2.12, 20.11) in women drinking <100 and ≥100 days/week-years, respectively, with a $P_{trend} < 0.001$, and their aOR (95 % CI) was 5.33 (1.38, 20.56) and 5.14 (1.58, 16.75) in women drinking <100 and ≥100 days/week-years, respectively, with a $P_{trend} = 0.001$ (Table 4).

We did cross analysis between drinking frequency, duration, and age at start drinking. Only results in women are shown in Table 4 due to limited space. Beer frequency and amount in week, wine/yellow wine frequency and amount in week and years stop drinking were not significantly associated with CRC risk with or without adjusting for other risk factors in all, men, and women, respectively (data were not shown).

4. Discussions

This nested case-control study discovered some novel findings: 1) This study found the association of drinking with increased risk of CRC in women was much stronger than that in men; 2) Our findings strengthen the association of drinking with increased risk of CRC in different study setting which population in our study is a Chinese population aged 50–74 years; 3) In addition, our study found the consistency of the association of increased risk of CRC with all drinking variables for all or women no matter adjusting for other risk factors but not all for men; and 4)This study found a J-shaped relationship between drinking whisky and CRC risk in men.

Our study found all drinking variables were consistently associated with increased risk in CRC, which is supported by some studies (Sung et al, 2021; Thanikachalam and Khan, 2019; Lancet, 2017; Hua et al, 2023; Sifaki-Pistolla et al, 2022; Danial et al, 2022; Tverdal et al, 2021; Fedirko et al, 2011; Choi et al, 2018; McNabb et al, 2020; Gu et al, 2018) and is ecologically supported by the facts of increasing drinking prevalence and the average alcohol consumption amount in adults in China (Huang et al, 2020; Li et al, 2022) which helps explain part of the increase in CRC incidence over time. That studies (Chen et al, 2004; Lim and Park, 2008) have reported no association between drinking and CRC risk was based on drinking status without information of the association of drinking frequency, duration and age at start drinking with CRC risk. Studies have reported drinking beer is associated with decreased risk in CRC in Chinese (Cai et al, 2004), but there are not enough cases drinking beer in our study (which association in this population can be estimated during the follow-ups when more cases are diagnosed in this mass screening program). Former drinkers showed higher OR than current drinkers in our study which could be explained by more heavy drinkers in former drinkers.

Table 2
Odds ratios (OR) and 95% confidence intervals (CI) of drinking between cases and controls in a case-control study nested in a mass colorectal cancer screening program in Quzhou, China, 2020–2022.

Variable (number of cases/controls)		In all	
		cOR (95 % CI)[a]	aOR (95 % CI)[b]
Drinking status	Never (95/472)	1.00 (common reference)	1.00 (common reference)
	Current (48/163)	1.46 (0.99, 2.16)	1.33 (0.89, 2.01)
	Former (10/15)	3.31 (1.44, 7.60)	2.86 (1.18, 6.95)
Age start drinking in years old	<20 (11/27)	2.02 (0.97, 4.22)	1.81(0.83, 3.91)
	20–29 (25/107)	1.16 (0.71, 1.89)	1.04 (0.63, 1.73)
	≥30 (12/29)	2.06 (1.01, 4.17)	2.00 (0.95, 4.22)
Drinking frequency in days/week	1–2 (3/17)	0.88 (0.25, 3.05)	0.89 (0.24, 3.24)
	3–5 (11/41)	1.33 (0.66, 2.69)	1.42 (0.68, 2.95)
	6–7 (44/120)	1.82 (1.21, 2.74)	1.55 (1.01, 2.38)
	P for trend	0.004	0.038
Drinking duration in years	1–19 (7/10)	3.48 (1.29, 9.37)	4.18 (1.41, 12.43)
	20–39 (23/86)	1.33 (0.80, 2.21)	1.88 (1.08, 3.27)
	≥40 (28/82)	1.70 (1.05, 2.75)	1.03 (0.62, 1.72)
	P for trend	0.021	0.281
Whisky type in alcohol percentage	<40 % (3/19)	0.78 (0.23, 2.70)	0.82 (0.23, 2.97)
	40–50 % (32/66)	2.41 (1.50, 3.88)	1.99 (1.20, 3.29)
	≥50 % (20/67)	1.48 (0.86, 2.56)	1.40 (0.79, 2.47)
	P for trend	0.004	0.027
Whisky amount in Liter/week	≤500 (7/52)	0.68 (0.30, 1.55)	0.60 (0.26, 1.39)
	>500–≤1000 (15/38)	2.01 (1.06, 3.79)	2.10 (1.07, 4.10)
	>1000–≤1500 (17/34)	2.54 (1.37, 4.73)	2.49 (1.28, 4.83)
	>1500 (16/28)	2.90 (1.51, 5.57)	2.04 (1.04, 4.03)
	P for trend	<0.001	0.001

[a] Crude OR.
[b] Adjusted OR adjusting for age in groups (0 = <55, 1 = 55–59, 2 = 60–64, 3 = 65–69, and 4 = ≥70 years old), physical activity in the past year (0 = <once/month, 1 = 1–3 times/month, 2 = 1–2 times/week, 3 = 3–5 times/week, and 4 = 6–7 times/day), and chronic disease status (0 = never and 1 = ever) (other variables were not significant in the final model).

Table 3
Odds ratios (OR) and 95 % confidence intervals (CI) of drinking between cases and controls in men aged 40–74 years in a case-control study nested in a mass colorectal cancer screening program in Quzhou, China, 2020–2022.

Variable (number of cases/controls)		All men	
		cOR (95 % CI)[a]	aOR (95 % CI)[b]
Drinking status	Never (35/136)	1.00 (reference)	1.00 (reference)
	Current (39/152)	1.00 (0.60, 1.66)	1.01 (0.59, 1.74)
	Former (7/15)	1.81 (0.69, 4.79)	2.27 (0.78, 6.64)
Age start drinking in years old	<20 (10/26)	1.49 (0.66, 3.39)	1.52 (0.64, 3.66)
	20–29 (22/101)	0.85 (0.47, 2.72)	0.84 (0.45, 1.57)
	≥30 (7/25)	1.09 (0.43, 2.72)	1.18 (0.45, 3.21)
	P for trend	0.281	0.812
Drinking frequency in days/week	1–2 (1/13)	0.30 (0.04, 2.36)	0.36 (0.04, 3.03)
	3–5 (7/38)	0.72 (0.29, 1.74)	0.91 (0.36, 2.32)
	6–7 (38/116)	1.27 (0.76, 2.14)	1.22 (0.71, 2.13)
	P for trend	0.389	0.458
Drinking duration in years	1–19 (2/7)	1.11 (0.22, 5.58)	2.33 (0.42, 13.03)
	20–39 (19/82)	0.90 (0.48, 1.68)	1.55 (0.76, 3.15)
	≥40 (25/78)	1.25 (0.69, 2.23)	0.85 (0.45, 1.59)
	P for trend	0.606	0.908
Whisky type in alcohol percentage	<40 % (3/17)	0.69 (0.19, 2.47)	0.94 (0.24, 3.64)
	40–50 % (25/63)	1.54 (0.85, 2.79)	1.41 (0.75, 2.66)
	≥50 % (17/64)	1.03 (0.54, 1.97)	1.11 (0.56, 2.21)
	P for trend	0.515	0.508
Whisky amount in Liter/week	≤0.5 (2/47)	0.19 (0.04, 0.81)	0.19 (0.04, 0.83)
	>0.5–≤1.0 (13/35)	1.64 (0.79, 3.41)	1.89 (0.86, 4.17)
	>1.0–≤1.5 (15/34)	1.95 (0.96, 3.95)	2.25 (1.05, 4.83)
	>1.5 (15/28)	2.37 (1.15, 4.88)	1.82 (0.85, 3.92)
	P for trend	0.003	0.011

[a] Crude OR.
[b] Adjusted OR adjusting for age in groups (0 = <55, 1 = 55–59, 2 = 60–64, 3 = 65–69, and 4 = ≥70 years old), physical activity in the past year (0 = <once/month, 1 = 1–3 times/month, 2 = 1–2 times/week, 3 = 3–5 times/week, and 4 = 6–7 times/day), and chronic disease status (0 = never and 1 = ever) (other variables were not significant in the final model).

There was sex difference in the association strength between alcohol consumption and CRC risk in this study. All drinking variables for women were consistently shown to be strongly (ORs > 5.0 except few) associated with increased risk of CRC no matter whether other risk factors were adjusted or not, which indicates that women may be more sensitive to alcohol than men in alcohol carcinogenesis in CRC or just because this subgroup of women tended to be heavy drinkers. In addition, only age group was significantly included in the final multivariable model for women, which indicates women's association of alcohol

Table 4
Odds ratios (OR) and 95 % confidence intervals (CI) of drinking between cases and controls in women aged 40–74 years in a case-control study nested in a mass colorectal cancer screening program in Quzhou, China, 2020–2022.

Variable (number of cases/controls)		All women	
		cOR (95 % CI)[a]	aOR (95 % CI)[b]
Drinking status	Never (60/336)	1.00 (reference)	1.00 (reference)
	Current (9/11)	4.58 (1.82, 11.53)	4.24 (1.61, 11.13)
	Former (3/0)	–	–
Age start Drinking (years old)	≤35 (5/9)	3.11 (1.01, 9.60)	3.01 (0.93, 9.75)
	>35 (4/2)	11.20 (2.01, 62.51)	9.25 (1.55, 55.18)
	P for trend	<0.001	0.001
Drinking duration (years)	1–29 (6/5)	6.72 (1.99, 22.72)	6.44 (1.73, 23.97)
	≥30 (6/6)	5.60 (1.75, 17.94)	4.35 (1.28, 14.71)
	P for trend	<0.001	0.002
Weekly frequency (days/week)	1–4 (6/7)	4.80 (1.56, 14.78)	4.03 (1.24, 13.12)
	5–7 (6/4)	8.40 (2.30, 30.66)	7.40 (1.88, 29.15)
	P for trend	<0.001	0.001
Amount in days/week-years (days/week times years)	<100 (5/5)	5.60 (1.57, 19.93)	5.33 (1.38, 20.56)
	≥100 (7/6)	6.53 (2.12, 20.11)	5.14 (1.58, 16.75)
	P for trend	<0.001	0.001
Whisky type of different % alcohol	<40 % (0/2)	–	–
	40–50 % (7/3)	13.07 (3.29, 51.94)	12.99 (2.90, 58.15)
	>50 % (3/3)	5.60 (1.10, 28.40)	4.02 (0.76, 21.16)
	P for trend	<0.001	0.001
Whisky amount (Liter/week)	≤0.5 (5/5)	5.47 (1.54, 19.45)	3.80 (1.03, 14.00)
	>0.5 (5/3)	9.11 (2.12, 39.11)	9.92 (2.01, 49.00)
	P for trend	<0.001	0.001
Cross of days per week (d/w) and duration in years (y)	1–4d/w & <30y (2/4)	2.80 (0.50, 15.63)	2.33 (0.38, 14.30)
	1–4d/w & ≥30y (4/3)	7.47 (1.63, 34.21)	6.20 (1.25, 30.66)
	5–7d/w & <30y (4/1)	22.40 (2.46, 203.88)	26.44 (2.56, 272.88)
	5–7d/k & ≥30y (2/3)	3.73 (0.61, 22.82)	2.61 (0.40, 17.11)
Cross of age start in years old (yo) and days per week (d/w)	≤35yo & 1–4d/w	4.48 (1.17, 17.16)	4.52 (1.10, 18.65)
	≤35 yo & 5–7d/w	1.40 (0.15, 12.74)	1.27 (0.13, 12.35)
	>35 yo & 1–4d/w	2.80 (0.25, 31.37)	1.74 (0.15, 20.09)
	>35 yo & 5–7d/w	–	–
Cross of age start in years old (yo) and duration in years (y)	≤35 yo & <30 y	–	–

(*continued on next page*)

Table 4 (*continued*)

Variable (number of cases/controls)		All women	
		cOR (95 % CI)[a]	aOR (95 % CI)[b]
	≤35yo & ≥30y	4.67 (1.38, 15.78)	3.88 (1.09, 13.77)
	>35yo & <30y	8.40 (1.37, 51.34)	7.49 (1.15, 48.63)
	>35yo & ≥30 y	–	–

[a] Crude OR.
[b] Adjusted OR adjusting for age in groups (0 = <55, 1 = 55–59, 2 = 60–64, 3 = 65–69, and 4 = ≥70 years old) (all other variables were not significant in the final model).

consumption with CRC risk was independent of other important risk factors such as smoking, physical activity, diet, family history and history of chronic diseases. It is possible that this group of women tend to have the similar exposure status of the other risk factors between cases and controls. These findings need to be confirmed by follow-ups with this mass screening program and other studies.

The finding of sex difference in drinking in this study is supported by the literature reported in China recently (Huang et al, 2020; Li et al, 2022; Yan et al, 2019; Xie et al, 2020; Liu et al, 2021). Men's drinking prevalence, average alcohol consumption and whisky consumption are all much higher than that in women in our study. The drinking proportion was 56.79 % in CRC cases and 55.12 % in controls in men which was much higher than that in women (16.67 % in CRC cases and 3.17 % in controls), respectively; men was much younger to start drinking than women, and men had much longer drinking duration in years with more frequency in days/week, cumulative amount in days/week-years, and whisky amount than women did in this study, which are comparable with the reported results in the literature (Yan et al, 2019; Xie et al, 2020; Liu et al, 2021).

For men, the association of drinking whisky with CRC risk showed a J-shaped relationship: drinking whisky was associated with decreased risk of CRC when drinking whisky ≤0.5 L/week but drinking whisky turned to be associated with increased risk of CRC when drinking whisky >0.5 L/week. That is to say that the association of drinking whisky with CRC risk in men was determined by the dosage of drinking whisky which can be explained by the phenomenon of J shape curve for the dose–response relationship which is consistent with a meta analysis (McNabb et al, 2019) but not supported by the other two meta analyses (Fedirko, 2011; Choi et al, 2018). Not all studies can find a J shaped relationship because it is possible the studied alcohol consumption level could be not low enough. More research on J-shaped relationship between drinking and CRC risk is warranted.

There are some strengths and limitations in this study. This is a case-control study nested in a mass CRC screening program in a high risk population aged 40–74 years which all questionnaire data were collected before CRC diagnosed, which in general should provide more reliable data than case-control studies which data were retrospectively collected. Cases were newly diagnosed CRC confirmed by histopathological examinations which helps avoid misclassification of CRC. Controls were confirmed by colonoscopy which helps minimize misclassification of controls, but not all normal participants in the mass screening program were included in the analysis which may have some sampling error that has been minimized by using random sampling method. All questionnaire data were based on the participants' self-report but they were collected before CRC diagnosis which helps minimize the reporting bias of drinking and also it may cause the association towards to the null (if any). In addition, the drinking prevalence rates between two sexes in our study which are comparable with the literature which indicates that our questionnaire data are valid. Our results may be limited when generalizing to the other populations such as aged younger than 40 and older than 74 years. Overall, our results are valid but need to be confirmed in studies with more cases.

In conclusion, alcohol consumption was associated with increased risk of CRC in a Chinese population aged 40–74 years. There were sex differences in alcohol consumption and its association with increased risk of CRC. Women showed a stronger association of drinking with increased risk of CRC than men. A J-shaped relationship between drinking whisky dose and CRC risk was found in men. Women should be more cautious than men with regard to drinking alcohol and men should control their whisky dosage for the CRC prevention and control which have significant public health implications.

Disclosure of funding

This research was funded by the Key Project of the Quzhou City Bureau of Science and Technology Grant (Grant No: 2022K77 and 2023K154), and the Key Project of the Zhejiang Chinese Medical University Affiliated Hospital Special Science Research Fund (Grant No.: 2021FSYYZZ11).

CRediT authorship contribution statement

Shi-Ming Lai: Writing – review & editing, Project administration, Funding acquisition, Conceptualization. **Hong-Hong Zhu:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Zhi-Juan Gan:** Writing – original draft, Validation, Funding acquisition, Formal analysis. **Bi-Yun Zheng:** Writing – review & editing, Validation, Formal analysis. **Zhao-Hui Xu:** Writing – review & editing, Validation, Investigation, Funding acquisition. **Zhi-Cheng Wang:** Writing – review & editing, Validation, Funding acquisition. **Xiao-Fang Liao:** Writing – review & editing, Validation, Investigation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

We sincerely thank all medical doctors, nurses and staff who participated in this mass colorectal cancer screening cost free to participants.

Ethics statement

The study was conducted in accordance with relevant guidelines and regulations. The study has been approved by the Ethics Committee at the Quzhou Centers for Disease Prevention and Control and the Zhejiang Chinese Medical University Affiliated Four-Province-Bordering Hospital of Traditional Chinese Medicine (Quzhou Hospital of Traditional Chinese Medicine) (Approval NO: 2022–02-030 and 2023–08-202).

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