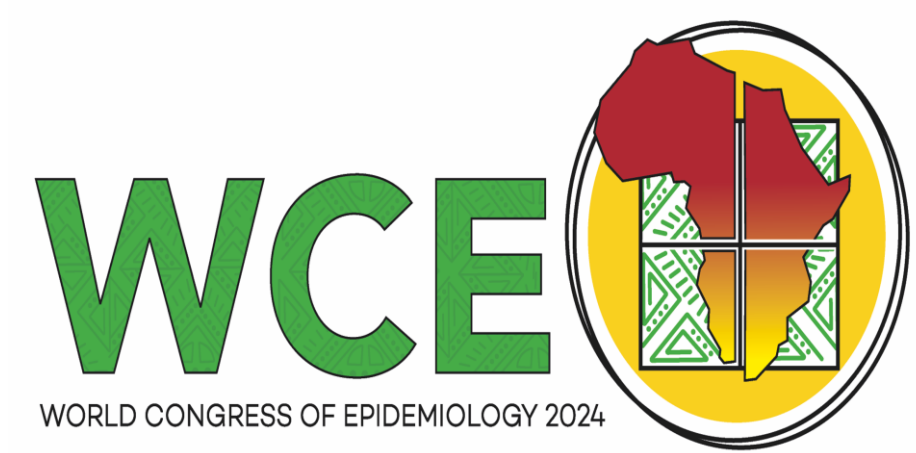




## : a nested case-control study within the National Health Insurance Service-Health Screening Cohort



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### - Background

- **Early-onset colorectal cancer (EoCRC)** refers to the diagnosis of colorectal cancer in individuals under the age of 50
- The incidence of EoCRC has been rising globally, though the causes remain unclear
- **We aimed to investigate the risk factors for EoCRC among the Korean population**

### - Methods

#### Data source

- **National Health Insurance Service-Health Screening Cohort (NHIS-HEALS)**
- A cohort of 514,866 individuals was randomly selected from 10% of health screening program participants, aged 40-79, in 2002-2003 by the NHIS, with the data shown below:
- ① **Eligibility data:** socio-economic status (sex, age, residence, insurance type, premium, etc.), death date, and cause of death
- ② **Claim data:** information on the diagnoses, utilization of medical services, and prescriptions (e.g.) identification of medical history
- ③ **Health screening data:** results based on examinations and questionnaires (e.g.) body mass index (BMI), lifestyle habits (smoking, alcohol consumption, physical activity, etc.)

#### Study design & Study population

- **Nested case-control study**
- **Colorectal cancer cases**
- ICD-10 codes (C18-C20) for hospitalization between 2004-2019
- ① **Early-onset colorectal cancer (EoCRC):** 40-49 years old (N=285)
- ② **Late-onset colorectal cancer (LoCRC):** 50+ years old (N=9,317)
- **Controls** were matched on birth-year, sex, and year of health screening at a ratio of 15:1 to cases

#### Modifiable risk factors

- ① **Lifestyle**
- BMI, smoking, alcohol consumption, and physical activity
- ② **Medical history**
- Diabetes, ischemic heart disease, cerebrovascular disease (CVA), other cancers, metabolic syndrome (MetS), and dyslipidemia

#### Statistical analyses

- ① **Assessment of modifiable risk factors**
- Multivariable conditional logistic regression
- Stratification by sex
- ② **Evaluation of population attributable risk fraction (PAF)**
- Relative risk was estimated using the adjusted odds ratio (aOR)
- Prevalence from 2002-2019 was obtained from the NHIS-HEALS
- PAF was calculated using minimum, median, maximum prevalence (median value was marked with symbols: EoCRC, ●; LoCRC, ◆)

### - Conclusion

- **Assessment of modifiable risk factors:** we found **BMI, smoking, alcohol consumption, diabetes, and other cancer** increase the risk of EoCRC in **both males and females**
- **Evaluation of PAF:** **BMI** was examined as the risk factor for EoCRC compared to LoCRC in **both sexes**
- Only the **MetS and dyslipidemia** were shown to be risk factors for **female EoCRC** based on the estimation of aOR and PAF
- To prevent EoCRC, lifestyle modifications targeting BMI, metabolic-related diseases, and healthy habits may be necessary

### - Results

Table 1. The assessment of risk factors in male colorectal cancer

	EOCRC				LOCRC			
	Case N (N=192)	Control N (N=2,880)	aOR*	95% CI	Case N (N=6,128)	Control N (N=91,920)	aOR**	95% CI
<b>Health screening</b>								
<b>BMI (kg/m<sup>2</sup>)</b>								
<25	113	1,835	1.00	Ref.	4,036	61,625	1.00	Ref.
25≤	79	1,044	1.31	0.96-1.77	2,090	30,257	1.06	1.00-1.12
Missing	0	1	-	-	2	38	0.76	0.18-3.16
<b>Smoking duration (year)</b>								
Never	64	1,035	1.00	Ref.	2,499	41,303	1.00	Ref.
<20	59	792	1.23	0.84-1.80	709	11,461	1.03	0.94-1.12
20≤	59	879	1.05	0.72-1.53	2,734	36,419	1.19	1.13-1.27
Missing	10	174	0.95	0.47-1.91	186	2,737	1.06	0.89-1.25
<b>Alcohol consumption (times/week)</b>								
0	101	1,467	1.00	Ref.	3,032	48,575	1.00	Ref.
1~2	53	967	0.83	0.58-1.18	1,538	23,937	1.04	0.98-1.12
3≤	38	405	1.26	0.84-1.89	1,508	18,693	1.26	1.18-1.35
Missing	0	41	-	-	50	715	1.02	0.74-1.41
<b>Physical activity (times/week)</b>								
0	139	2,093	0.79	0.47-1.35	3,401	49,023	1.10	1.03-1.18
1~2	31	489	0.86	0.47-1.60	1,016	16,502	0.99	0.91-1.07
3≤	19	240	1.00	Ref.	1,487	23,571	1.00	Ref.
Missing	3	58	0.57	0.16-2.02	224	2,824	1.30	1.10-1.55
<b>Medical history</b>								
<b>Diabetes mellitus</b>								
Yes	20	274	1.03	0.63-1.69	2,170	30,622	1.08	1.02-1.14
No	172	2,606	1.00	Ref.	3,958	61,298	1.00	Ref.
<b>Ischemic heart disease</b>								
Yes	11	160	0.90	0.47-1.73	1,309	20,479	0.93	0.87-0.99
No	181	2,720	1.00	Ref.	4,819	71,441	1.00	Ref.
<b>Cerebrovascular disease</b>								
Yes	8	84	1.38	0.64-2.95	1,275	19,430	0.96	0.90-1.03
No	184	2,796	1.00	Ref.	4,853	72,490	1.00	Ref.
<b>Other cancers***</b>								
Yes	20	72	4.93	2.87-8.46	996	11,488	1.39	1.29-1.49
No	172	2,808	1.00	Ref.	5,132	80,432	1.00	Ref.
<b>Metabolic syndrome</b>								
Yes	27	384	1.00	0.64-1.56	2,523	37,885	0.99	0.93-1.04
No	165	2,496	1.00	Ref.	3,605	54,035	1.00	Ref.
<b>Dyslipidemia</b>								
Yes	24	360	0.94	0.59-1.50	2,363	35,969	0.97	0.91-1.02
No	168	2,520	1.00	Ref.	3,765	55,951	1.00	Ref.

\*Adjusted for income level and history of other cancers. \*\*Adjusted for income level, history of other cancers, smoking duration, alcohol consumption, and physical activity. \*\*\*Other cancers include any type of cancer except for colorectal cancer.

Table 2. The assessment of risk factors in female colorectal cancer

	EOCRC				LOCRC			
	Case N (N=93)	Control N (N=1,395)	aOR*	95% CI	Case N (N=3,189)	Control N (N=47,835)	aOR**	95% CI
<b>Health screening</b>								
<b>BMI (kg/m<sup>2</sup>)</b>								
<25	64	1,053	1.00	Ref.	2,000	30,543	1.00	Ref.
25≤	29	342	1.42	0.88-2.29	1,188	17,264	1.05	0.98-1.14
Missing	0	0	-	-	1	28	0.48	0.07-3.56
<b>Smoking duration (year)</b>								
Never	88	1,323	1.00	Ref.	3,028	45,855	1.00	Ref.
<20	2	33	0.54	0.11-2.60	42	489	1.26	0.92-1.74
20≤	1	1	4.93	0.20-123.94	59	677	1.24	0.95-1.63
Missing	2	38	0.62	0.14-2.84	60	814	1.12	0.86-1.47
<b>Alcohol consumption (times/week)</b>								
0	79	1,215	1.00	Ref.	2,930	43,998	1.00	Ref.
1~2	11	135	1.26	0.63-2.53	152	2,500	0.92	0.78-1.09
3≤	2	24	0.94	0.19-4.58	61	735	1.21	0.93-1.58
Missing	1	21	0.66	0.08-5.17	46	602	1.11	0.70-1.76
<b>Physical activity (times/week)</b>								
0	71	1,069	1.07	0.52-2.21	2,110	31,330	1.10	1.00-1.22
1~2	11	150	1.14	0.45-2.89	419	6,047	1.11	0.98-1.27
3≤	10	144	1.00	Ref.	530	8,582	1.00	Ref.
Missing	1	32	0.43	0.05-3.65	130	1,876	1.11	0.87-1.41
<b>Medical history</b>								
<b>Diabetes mellitus</b>								
Yes	11	104	1.46	0.73-2.92	1,170	16,559	1.08	1.00-1.16
No	82	1,291	1.00	Ref.	2,019	31,276	1.00	Ref.
<b>Ischemic heart disease</b>								
Yes	3	65	0.73	0.22-2.40	763	11,400	0.98	0.90-1.07
No	90	1,330	1.00	Ref.	2,426	36,435	1.00	Ref.
<b>Cerebrovascular disease</b>								
Yes	3	49	0.75	0.22-2.53	852	12,516	1.01	0.92-1.10
No	90	1,346	1.00	Ref.	2,337	35,319	1.00	Ref.
<b>Other cancers***</b>								
Yes	19	49	6.92	3.80-12.60	525	4,752	1.79	1.62-1.98
No	74	1,346	1.00	Ref.	2,664	43,083	1.00	Ref.
<b>Metabolic syndrome</b>								
Yes	17	155	1.37	0.75-2.50	1,576	24,313	0.91	0.84-0.98
No	76	1,240	1.00	Ref.	1,613	23,522	1.00	Ref.
<b>Dyslipidemia</b>								
Yes	15	137	1.44	0.76-2.72	1,468	22,702	0.92	0.85-0.99
No	78	1,258	1.00	Ref.	1,721	25,133	1.00	Ref.

\*Adjusted for income level and history of other cancers. \*\*Adjusted for income level, history of other cancers, and smoking duration. \*\*\*Other cancers include any type of cancer except for colorectal cancer.

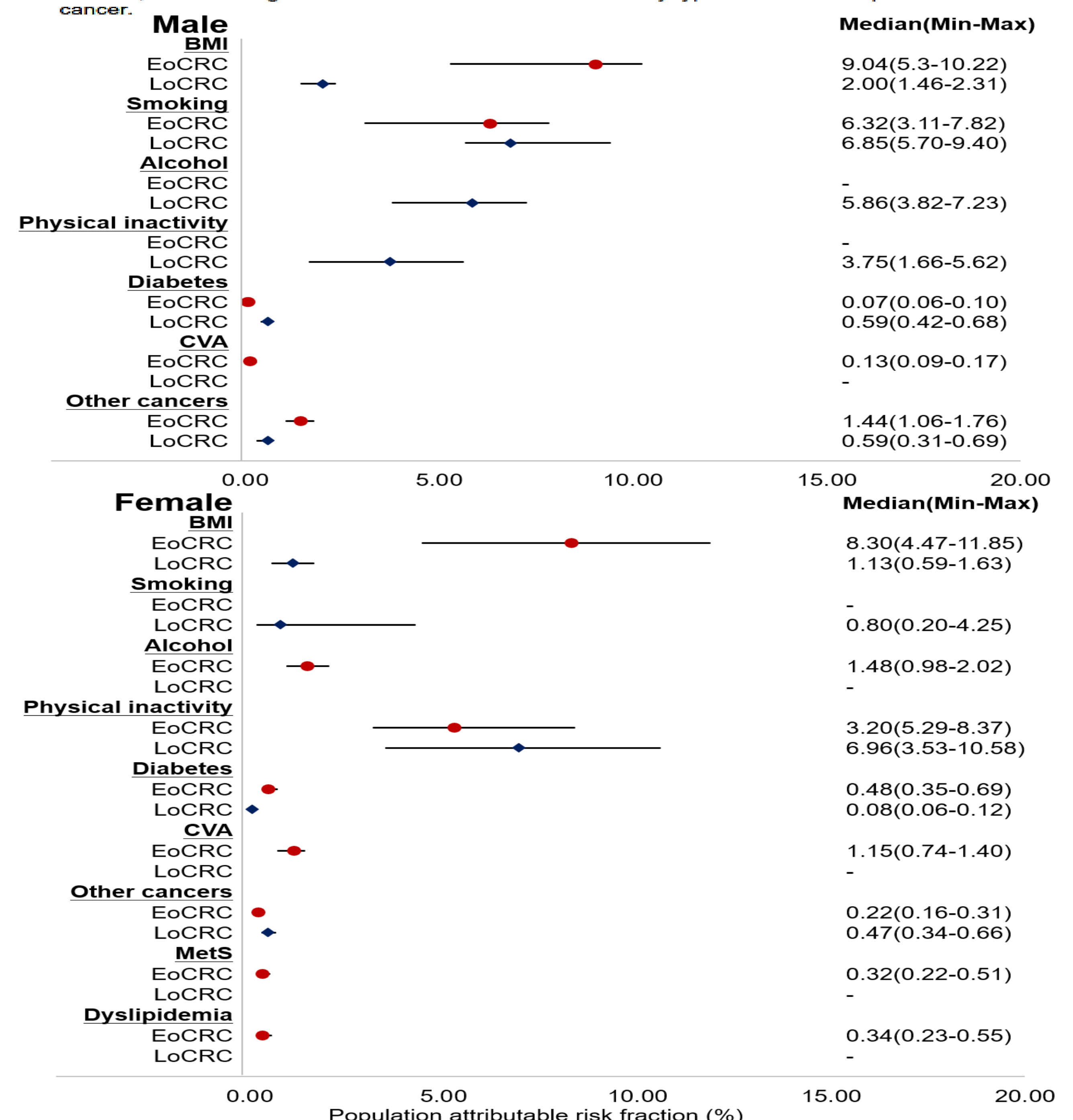


Figure 1. Population attributable risk fraction by sex