

Supplementary Material

Diabetes, plasma glucose and incidence of colorectal cancer in Chinese adults:

a prospective study of 0.5 million people

Journal of Epidemiology and Community Health

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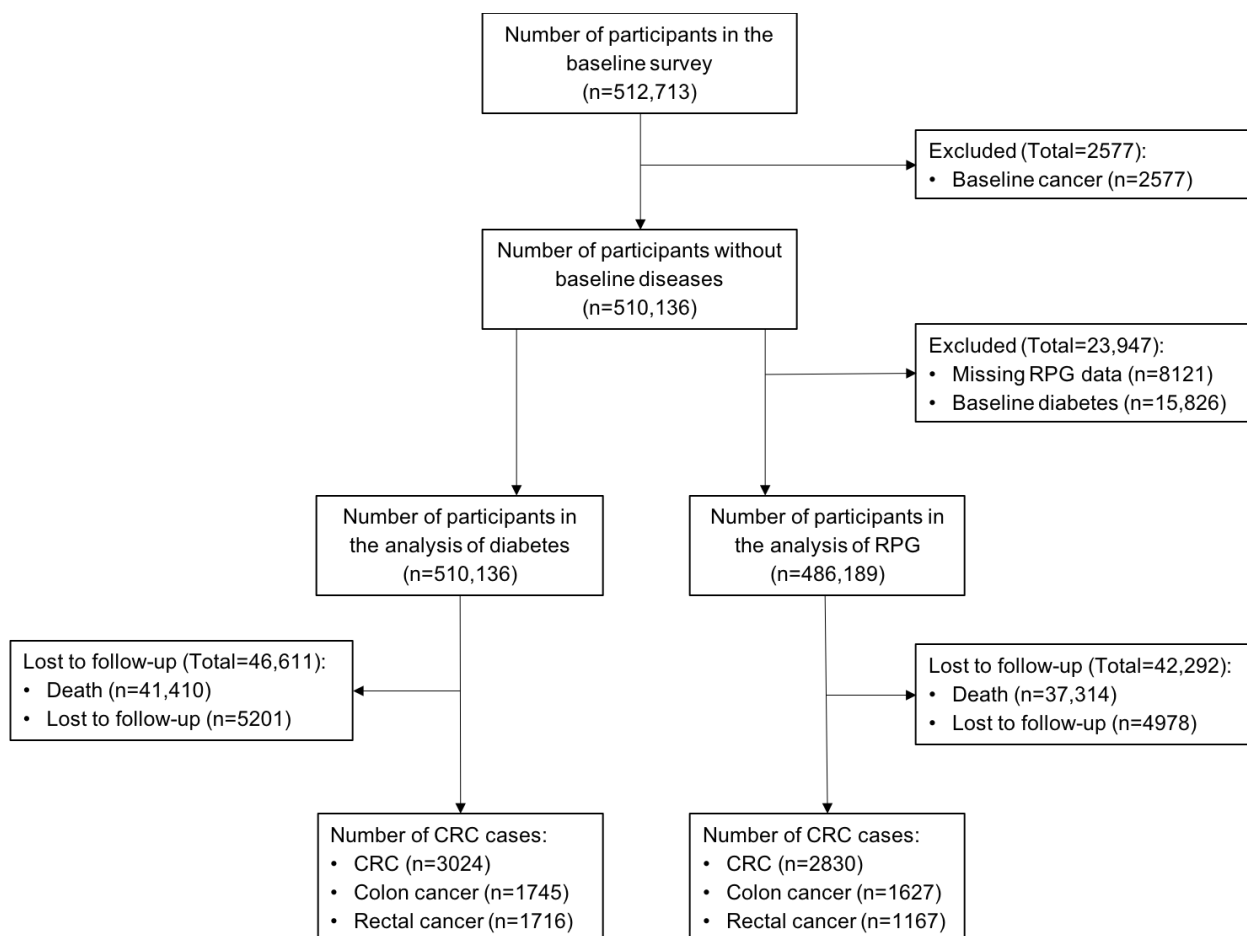
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Supplementary Figure 1. Flow chart



Supplementary Table 1. Distribution and classification of colorectal and small intestine cancer by ICD-10 code

ICD-10 code	Descriptions	No. of cases
C18.0	Caecum	63
C18.1	Appendix	15
C18.2	Ascending colon	135
C18.3	Hepatic flexure	37
C18.4	Transverse colon	45
C18.5	Splenic flexure	8
C18.6	Descending colon	34
C18.7	Sigmoid colon	276
C18.8	Overlapping lesion of colon	29
C18.9	Colon, unspecified	1474
C18.0-5	Proximal colon	294
C18.6, C18.7	Distal colon	308
C18	Colon	1745
C19	Rectosigmoid junction	152
C20	Rectum	1716
C18-C20	Colorectum	3024

Supplementary Table 2. Adjusted HRs for colorectal cancer by diabetes status after excluding early years of follow-up*

	No. events	Rate, Per 100,000	Excluding first 2 years of follow-up HR (95% CI)	No. events	Rate, Per 100,000	Excluding first 5 years of follow-up HR (95% CI)
Colorectal cancer						
No diabetes	2391	498.0	Reference	1632	340.0	Reference
Diabetes	252	839.8	1.13 (0.99, 1.30)	165	549.9	1.13 (0.96, 1.33)
Colon cancer						
No diabetes	1371	285.6	Reference	918	191.2	Reference
Diabetes	152	506.6	1.14 (0.96, 1.36)	93	309.9	1.10 (0.88, 1.36)
Rectal cancer						
No diabetes	1348	280.8	Reference	914	190.4	Reference
Diabetes	129	429.9	1.08 (0.90, 1.30)	93	309.9	1.19 (0.96, 1.49)

* Estimates were stratified by stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, total physical activity, and BMI.

Supplementary Table 3. Adjusted HRs for colorectal cancer mortality by diabetes and levels of RPG among individuals without previously diagnosed diabetes

	No. events	Rate, Per 100,000	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Colorectal cancer				
Diabetes				
No	866	180.4	Reference	Reference
Yes	95	316.6	1.18 (0.95, 1.47)	1.17 (0.94, 1.45)
RPG				
≤ 5.5	373	153.7	1.00 (0.90, 1.12)	1.00 (0.90, 1.12)
5.6 - 6.7	317	200.3	1.10 (0.99, 1.23)	1.10 (0.99, 1.22)
6.8 - 7.7	99	193.9	0.97 (0.80, 1.19)	0.97 (0.79, 1.18)
≥ 7.8	108	316.9	1.48 (1.22, 1.80)	1.47 (1.21, 1.79)
Effects per 1 mmol/L	897	185.6	1.04 (1.01, 1.07)	1.04 (1.01, 1.07)
<i>p for trend</i>			<0.001	0.01
Colon cancer				
Diabetes				
No	379	78.9	Reference	Reference
Yes	50	166.6	1.29 (0.95, 1.74)	1.27 (0.94, 1.71)
RPG				
≤ 5.5	147	60.6	1.00 (0.84, 1.19)	1.00 (0.84, 1.19)
5.6 - 6.7	147	92.9	1.30 (1.11, 1.52)	1.29 (1.10, 1.51)
6.8 - 7.7	44	86.2	1.11 (0.82, 1.50)	1.10 (0.82, 1.49)
≥ 7.8	60	176.1	2.20 (1.69, 2.85)	2.17 (1.67, 2.82)
Effects per 1 mmol/L	398	81.9	1.07 (1.04, 1.11)	1.07 (1.04, 1.11)
<i>p for trend</i>			<0.001	<0.001
Rectal cancer				
Diabetes				
No	475	98.9	Reference	Reference
Yes	43	143.3	1.07 (0.78, 1.47)	1.06 (0.77, 1.46)
RPG				
≤ 5.5	222	91.5	1.00 (0.87, 1.15)	1.00 (0.87, 1.15)
5.6 - 6.7	163	103.0	0.96 (0.82, 1.11)	0.96 (0.82, 1.11)
6.8 - 7.7	54	105.8	0.89 (0.68, 1.17)	0.89 (0.68, 1.16)
≥ 7.8	46	135.0	1.03 (0.77, 1.38)	1.02 (0.76, 1.37)
Effects per 1 mmol/L	485	99.8	1.00 (0.96, 1.05)	1.00 (0.95, 1.05)
<i>p for trend</i>			0.98	0.96

Model 1: stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, total physical activity, and fasting time (for RPG).

Model 2: Model 1 plus BMI.

Supplementary Table 4. Adjusted HRs for colorectal cancer by diabetes status

	No. events	Rate, Per 100,000	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Colorectal cancer				
No diabetes	2732	569.1	1.00 (0.96, 1.04)	1.00 (0.96, 1.05)
Previously diagnosed diabetes	144	900.0	0.99 (0.84, 1.18)	0.98 (0.83, 1.16)
Screen-detected diabetes	148	1056.7	1.42 (1.21, 1.67)	1.37 (1.17, 1.61)
Colon cancer				
No diabetes	1570	327.0	1.00 (0.95, 1.06)	1.00 (0.94, 1.06)
Previously diagnosed diabetes	90	562.5	1.03 (0.84, 1.27)	1.00 (0.81, 1.24)
Screen-detected diabetes	85	606.9	1.39 (1.13, 1.72)	1.33 (1.08, 1.65)
Rectal cancer				
No diabetes	1561	325.2	1.00 (0.94, 1.06)	1.00 (0.94, 1.06)
Previously diagnosed diabetes	70	437.5	0.90 (0.71, 1.14)	0.88 (0.70, 1.12)
Screen-detected diabetes	85	606.9	1.46 (1.18, 1.81)	1.42 (1.15, 1.76)

Model 1: stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, and total physical activity.

Model 2: Model 1 plus BMI.

Supplementary Table 5. Adjusted HRs for colon cancer per 1 SD higher in different measures of adiposity by anatomical subsite*

	Total colon	Proximal colon	Distal colon	Distal colon + rectal
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
No. of cases	1745	294	308	2044
Diabetes	1.14 (0.83, 1.56)	0.64 (0.20, 2.09)	0.66 (0.20, 2.15)	1.02 (0.74, 1.40)
RPG per 1 mmol/L	1.03 (0.99, 1.08)	1.01 (0.87, 1.16)	0.99 (0.85, 1.15)	1.03 (0.99, 1.08)

ICD-10: total colon, C18; proximal colon, C18.0-5; distal colon, C18.6, C18.7; distal colon + rectal, C18.6, C18.7, C19, C20.

* Model was stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, total physical activity, and fasting time (for RPG).

Supplementary Table 6. Adjusted HRs for colorectal cancer by levels of RPG among participants without previously diagnosed diabetes

	No. events	Rate, Per 100,000	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Colorectal cancer				
≤ 5.5	1197	493.4	1.00 (0.94, 1.06)	1.00 (0.94, 1.06)
5.6 - 6.7	998	630.7	1.11 (1.05, 1.18)	1.10 (1.04, 1.17)
6.8 - 7.7	338	663.9	1.10 (0.98, 1.22)	1.08 (0.97, 1.20)
≥ 7.8	297	871.6	1.33 (1.18, 1.49)	1.29 (1.15, 1.45)
Effects per 1 mmol/L	2830	582.2	1.04 (1.02, 1.05)	1.03 (1.02, 1.05)
<i>p</i> for trend			<0.001	<0.001
Colon cancer				
≤ 5.5	699	288.1	1.00 (0.92, 1.08)	1.00 (0.92, 1.08)
5.6 - 6.7	575	363.4	1.08 (0.99, 1.17)	1.06 (0.98, 1.15)
6.8 - 7.7	181	355.5	0.98 (0.84, 1.13)	0.95 (0.82, 1.10)
≥ 7.8	172	504.8	1.29 (1.11, 1.50)	1.24 (1.06, 1.44)
Effects per 1 mmol/L	1627	334.7	1.03 (1.01, 1.05)	1.02 (1.00, 1.05)
<i>p</i> for trend			0.01	0.04
Rectal cancer				
≤ 5.5	683	281.5	1.00 (0.92, 1.08)	1.00 (0.92, 1.08)
5.6 - 6.7	562	355.2	1.12 (1.03, 1.21)	1.11 (1.03, 1.20)
6.8 - 7.7	208	408.6	1.22 (1.06, 1.40)	1.20 (1.05, 1.38)
≥ 7.8	161	472.5	1.30 (1.11, 1.52)	1.27 (1.09, 1.49)
Effects per 1 mmol/L	1614	332.0	1.04 (1.02, 1.06)	1.04 (1.02, 1.06)
<i>p</i> for trend			<0.001	<0.001

Model 1: stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, total physical activity, and fasting time.

Model 2: Model 1 plus BMI.

Supplementary Table 7. Adjusted HRs for colorectal cancer by diabetes status

	No. events	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Colorectal cancer			
No diabetes	2732	Reference	Reference
Diabetes	292	1.18 (1.04, 1.33)	0.85 (0.64, 1.11)
Colon cancer			
No diabetes	1570	Reference	Reference
Diabetes	175	1.19 (1.01, 1.39)	0.96 (0.68, 1.35)
Rectal cancer			
No diabetes	1561	Reference	Reference
Diabetes	155	1.14 (0.96, 1.35)	0.67 (0.45, 1.00)

Model 1: stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, and total physical activity.

Model 2: Model 1 plus diabetes medication.

Supplementary Table 8. Adjusted HRs for colorectal cancer by diabetes medications*

	No. events	HR (95% CI)
Colorectal cancer		
No diabetes	2732	1.00 (0.95, 1.05)
No medication	31	1.03 (0.73, 1.47)
Metformin	71	0.94 (0.75, 1.19)
Insulin	19	1.29 (0.82, 2.02)
Metformin and insulin	1	0.31 (0.04, 2.23)
Colon cancer		
No diabetes	1570	1.00 (0.94, 1.07)
No medication	19	1.04 (0.66, 1.63)
Metformin	46	1.03 (0.77, 1.38)
Insulin	15	1.65 (0.99, 2.75)
Metformin and insulin	0	--
Rectal cancer		
No diabetes	1561	1.00 (0.94, 1.07)
No medication	13	0.81 (0.47, 1.40)
Metformin	36	0.87 (0.63, 1.21)
Insulin	7	0.95 (0.45, 1.99)
Metformin and insulin	1	0.58 (0.08, 4.11)

* Estimates were stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, and total physical activity.

Supplementary Table 9. Adjusted HRs for colorectal cancer by treated and untreated diabetes*

	No. events	Rate, Per 100,000	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Colorectal cancer				
No diabetes	2732	569.1	1.00 (0.96, 1.05)	1.00 (0.96, 1.05)
Treated diabetes	91	568.8	0.98 (0.80, 1.20)	0.95 (0.78, 1.17)
Untreated diabetes	179	1278.0	1.34 (1.15, 1.55)	1.29 (1.12, 1.49)
Colon cancer				
No diabetes	1570	327.0	1.00 (0.94, 1.06)	1.00 (0.94, 1.06)
Treated diabetes	61	381.3	1.10 (0.85, 1.41)	1.06 (0.83, 1.37)
Untreated diabetes	104	742.6	1.31 (1.08, 1.59)	1.26 (1.04, 1.52)
Rectal cancer				
No diabetes	1561	325.2	1.00 (0.94, 1.06)	1.00 (0.94, 1.06)
Treated diabetes	44	275.0	0.88 (0.65, 1.18)	0.86 (0.64, 1.16)
Untreated diabetes	98	699.7	1.32 (1.09, 1.61)	1.29 (1.06, 1.57)

* Treated diabetes includes previously diagnosed diabetes on medication, while untreated includes screen-detected and previous diagnosed not on medication.

Model 1: stratified by age-at-risk, sex, and region, and adjusted for age at baseline, education, smoking, alcohol, and total physical activity.

Model 2: Model 1 plus BMI.