Greater resveratrol intake is associated with a lower risk of colorectal cancer among Chinese population

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Acknowledgements: Natural Science Foundation of China (No. 81973020)

Disclosure: No conflict of interests

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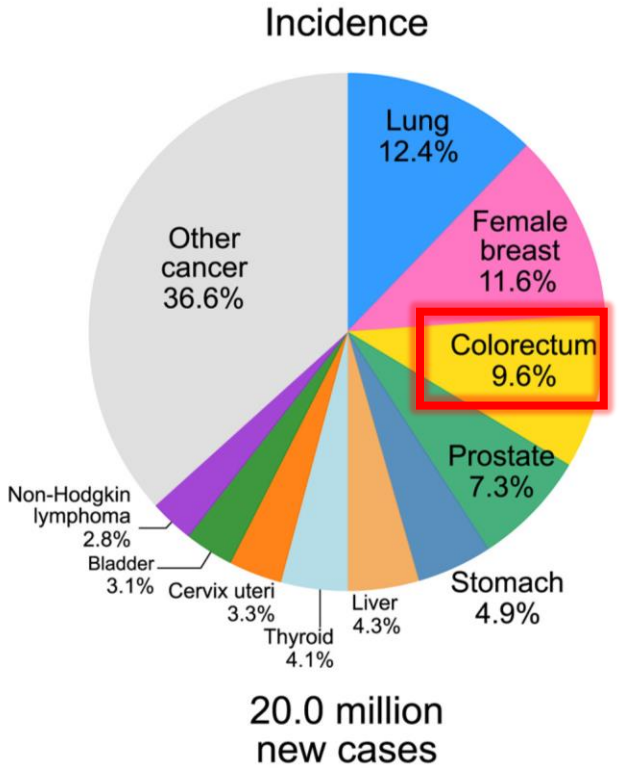
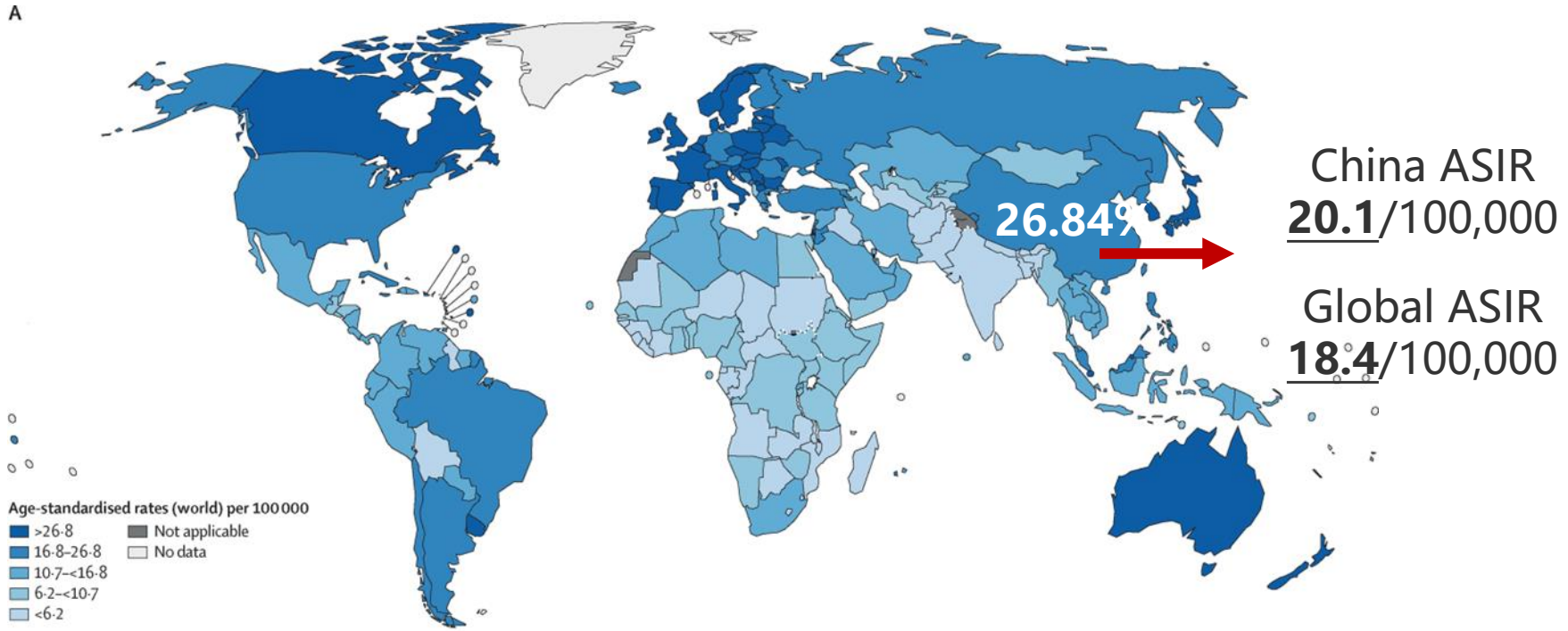
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Prevalence of colorectal cancer

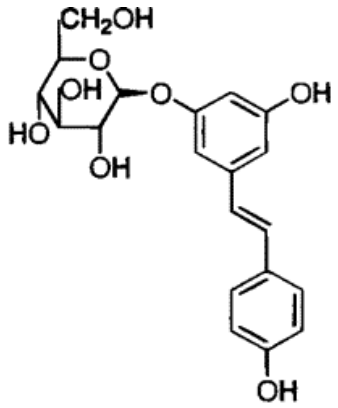
- In 2022, the number of **new CRC cases** worldwide reached 1.9 million, ranking **third** among all cancer
- The number of new cases in **China** accounted for 26.84%, with an age-standardized incidence rate (ASIR) **higher** than the global average



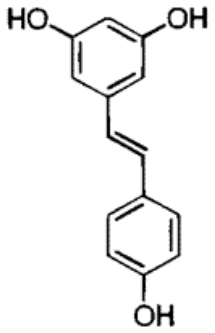


[1] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263. doi:10.3322/caac.21834

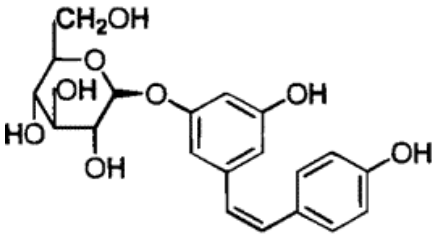
Introduction of resveratrol



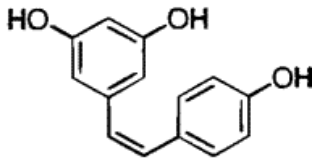
trans-Piceid



trans-Resveratrol



cis-Piceid



cis-Resveratrol

- 3, 5, 4′-trihydroxystilbene, a naturally occurring **polyphenolic** compound belonging to the group of **stilbenes**
- Found in a variety of **plant foods**: grapes, peanuts, berries, red wine, etc
- Resveratrol has been reported to exert multiple biological activities

[2] Halls, C.; Yu, O. Potential for metabolic engineering of resveratrol biosynthesis. Trends Biotechnol 2008, 26, 77-81.
[3] Regev-Shoshani, G.; Shoseyov, O.; Bilkis, I.; Kerem, Z. Glycosylation of resveratrol protects it from enzymic oxidation. Biochem J 2003, 374, 157-163.

Current status of research

Animal experiments

- In *Apc*^{Min} mice receiving a high-fat diet, dietary achievable doses of resveratrol halt tumor progression in mice through induction of AMPK and senescence and that these effects translate to human tissue

Population epidemiological studies

- Two previous nested case-control studies concluded that pre-diagnostic plasma resveratrol levels were not associated with colon cancer risk

[6] Cai H, et al. (2015). Cancer chemoprevention: Evidence of a nonlinear dose response for the protective effects of resveratrol in humans and mice. Sci Transl Med.
[7] Murphy, et al. (2018). A prospective evaluation of plasma polyphenol levels and colon cancer risk. International Journal of Cancer.
[8] Mori, N. , et al. (2022). Prediagnostic plasma polyphenol concentrations and colon cancer risk: The JPHC nested case-control study. Clinical Nutrition.

Purpose of the study

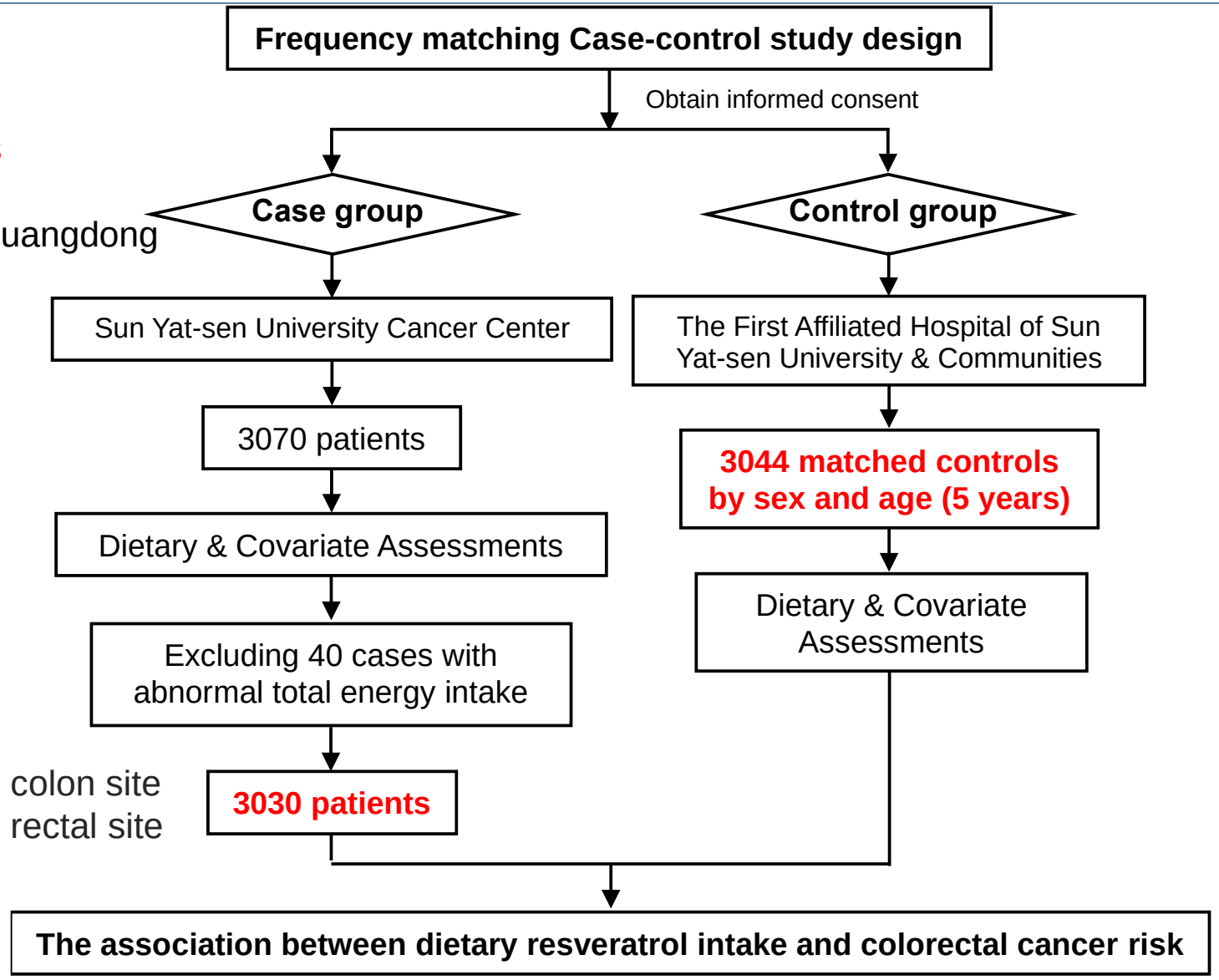
- The beneficial effects of **dietary resveratrol** on colorectal cancer **have yet to be confirmed in population-based studies**
- Habitual dietary intake is likely to better reflect long-term exposure compared to biomarkers

- In this **hospital-based large-scale case-control study**, we aimed to investigate the association between **dietary resveratrol intake** and the risk of colorectal cancer

Technology Frame

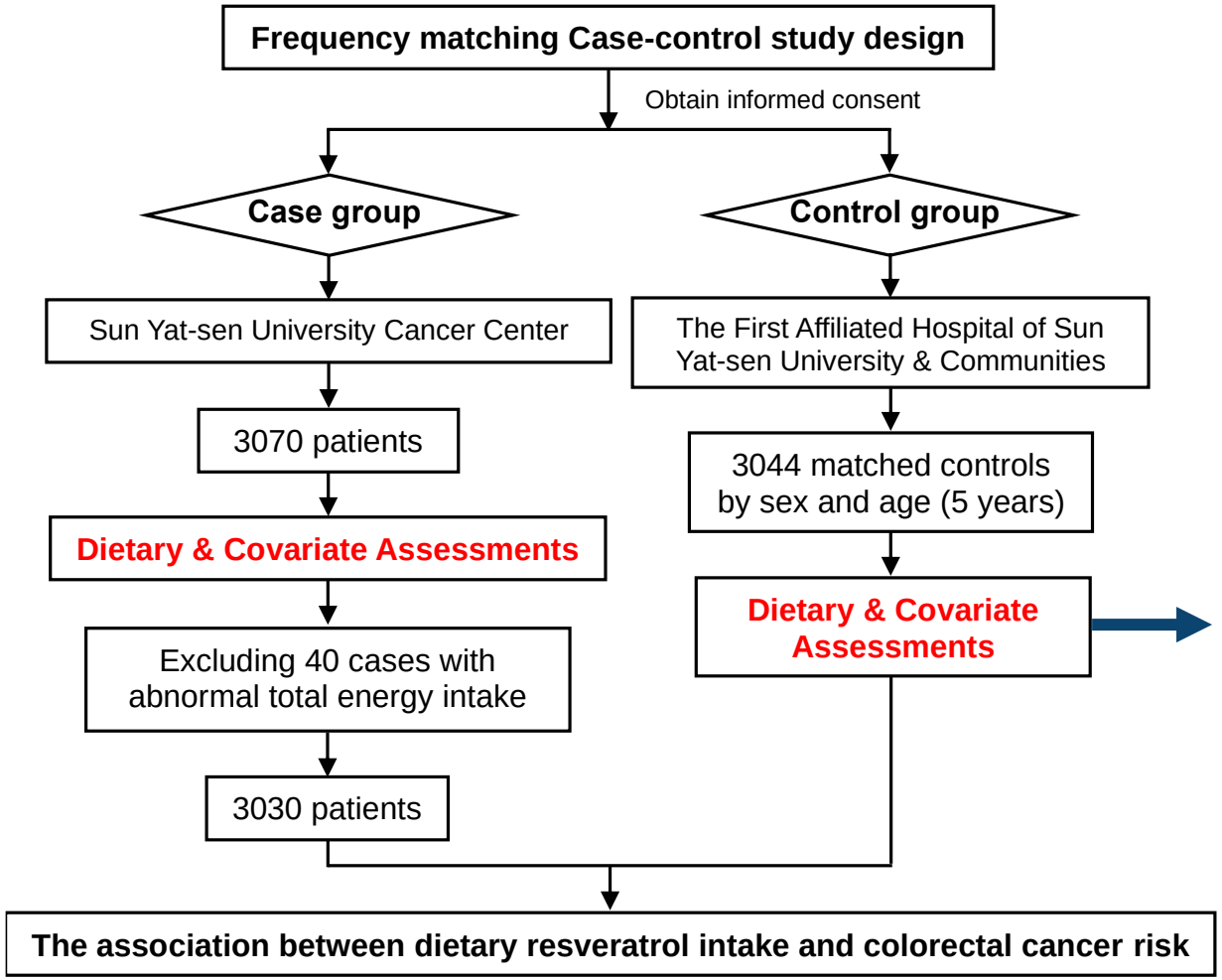
July 2010 to January 2024

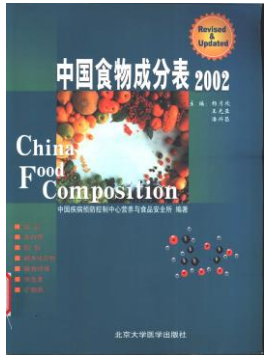
- Newly diagnosed cases
- 30-75 years
- Local or have lived in Guangdong for ≥5 years



- 1961 colon site
- 1069 rectal site

Face-to-face interviews





- **Dietary data:** Use a validated FFQ to collect dietary information from the previous year
- **Energy and resveratrol intake:** Based on the Chinese Food Composition Table (2002) and the Chinese Food Composition Table Standard Edition
- Other covariates

Statistical Analysis

Data reprocessing

- Dietary intakes were log-transformed and adjusted for total energy using the residual method
- Study subjects were divided into five groups by sex

Association analysis

- Multivariable unconditional logistic regression models: estimate the odds ratios and 95% confidence intervals
  - Sex-stratified analysis
  - Subgroup analysis of cancer sites
  - Sensitivity analysis

Nonlinear relationship

- Restricted cubic spline (RCS) analysis

Characteristics and selected risk factors

Characteristics	Cases (*n*=3030)	Controls (*n*=3044)	*P*
Age (years), mean ± *SD*	56.92 ± 10.19	56.87 ± 9.79	0.727
Men, *n* (%)	1716 (56.63)	1723 (56.60)	0.981
Married, *n* (%)	2874 (94.85)	2774 (91.13)	<0.001
Rural, *n* (%)	1085 (35.81)	692 (22.73)	<0.001
Education, *n* (%)			<0.001
Primary school or below	928 (30.63)	673 (22.11)	
Middle school	876 (28.91)	783 (25.72)	
High school/technical school	725 (23.93)	827 (27.17)	
College or above	501 (16.53)	758 (24.90)	
Unknown	0 (0.00)	3 (0.10)	
Occupation, *n* (%)			0.006
Administrator/other white-collar	428 (14.13)	520 (17.08)	
Blue-collar worker	697 (23.00)	682 (22.40)	
Farmer/others	1905 (62.87)	1842 (60.51)	
Household income (Yuan/month), *n* (%)			<0.001
<2000	405 (13.37)	404 (13.27)	
2001–5000	984 (32.48)	1203 (39.52)	
5001–8000	891 (29.41)	894 (29.37)	
>8001	750 (24.75)	543 (17.84)	

- **The mean age of participants was 57 years, and 57% were male**

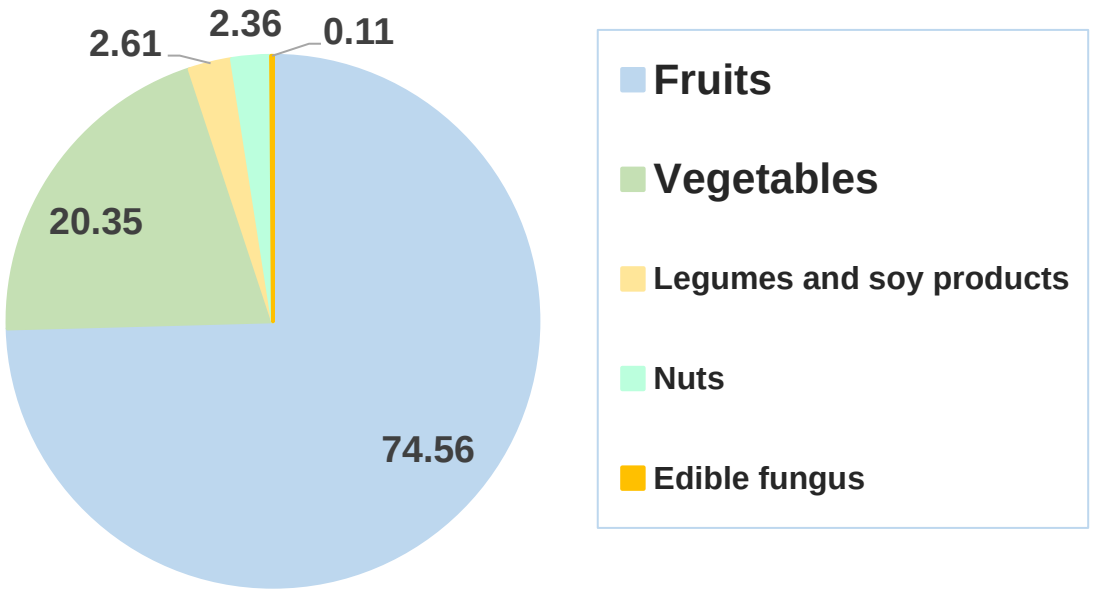
Characteristics and selected risk factors

Characteristics	Cases (*n*=3030)	Controls (*n*=3044)	*P*
Ever smokers, *n* (%)	1182 (39.01)	934 (30.68)	<0.001
Passive smoking, *n* (%)	830 (27.39)	895 (29.40)	0.082
Regular drinkers, *n* (%)	546 (18.02)	433 (14.22)	<0.001
Occupational activity, *n* (%)			<0.001
Nonworking	365 (12.05)	1054 (34.63)	
Sedentary	852 (28.12)	615 (20.20)	
Light	845 (27.89)	727 (23.88)	
Moderate	443 (14.62)	291 (9.56)	
Heavy	525 (17.33)	357 (11.73)	
MET (h/week), median (P_{25}–P_{75})	27.00 (8.31–52.50)	34.44 (16.00–56.00)	<0.001
BMI (kg/m^2), mean ± *SD*	23.40 ± 3.31	23.56 ± 3.16	0.030
Family history of cancer in first-degree relatives, *n* (%)	455 (15.02)	255 (8.38)	<0.001

Daily resveratrol intakes

Dietary Intakes	Cases (*n*=3030)	Controls (*n*=3044)
Energy (kcal/day)	1469.91 (1188.86–1808.91)	1551.31 (1261.89–1953.65)
Vegetables (g/day)	388.17 (285.52–516.77)	406.78 (300.98–531.71)
Fruits (g/day)	86.81 (42.39–151.74)	119.28 (65.53–187.48)
Red meat (g/day)	110.84 (73.66–154.93)	91.11 (57.11–131.72)
White meat (g/day)	74.92 (41.58–126.39)	84.23 (49.85–134.08)
Eggs and milk (g/day)	29.06 (12.91–65.40)	51.56 (21.86–126.50)
Legumes and soy products (g/day)	17.42 (6.63–36.62)	19.71 (7.88–42.32)
Edible fungus (g/day)	3.32 (1.19–7.48)	4.61 (1.79–10.10)
Nuts (g/day)	0.85 (0.11–2.94)	1.53 (0.33–5.38)
Resveratrol (μg/day)	**109.57 (60.01–185.27)**	**149.81 (83.77–260.06)**

Percentage of resveratrol intake from different foods (%)

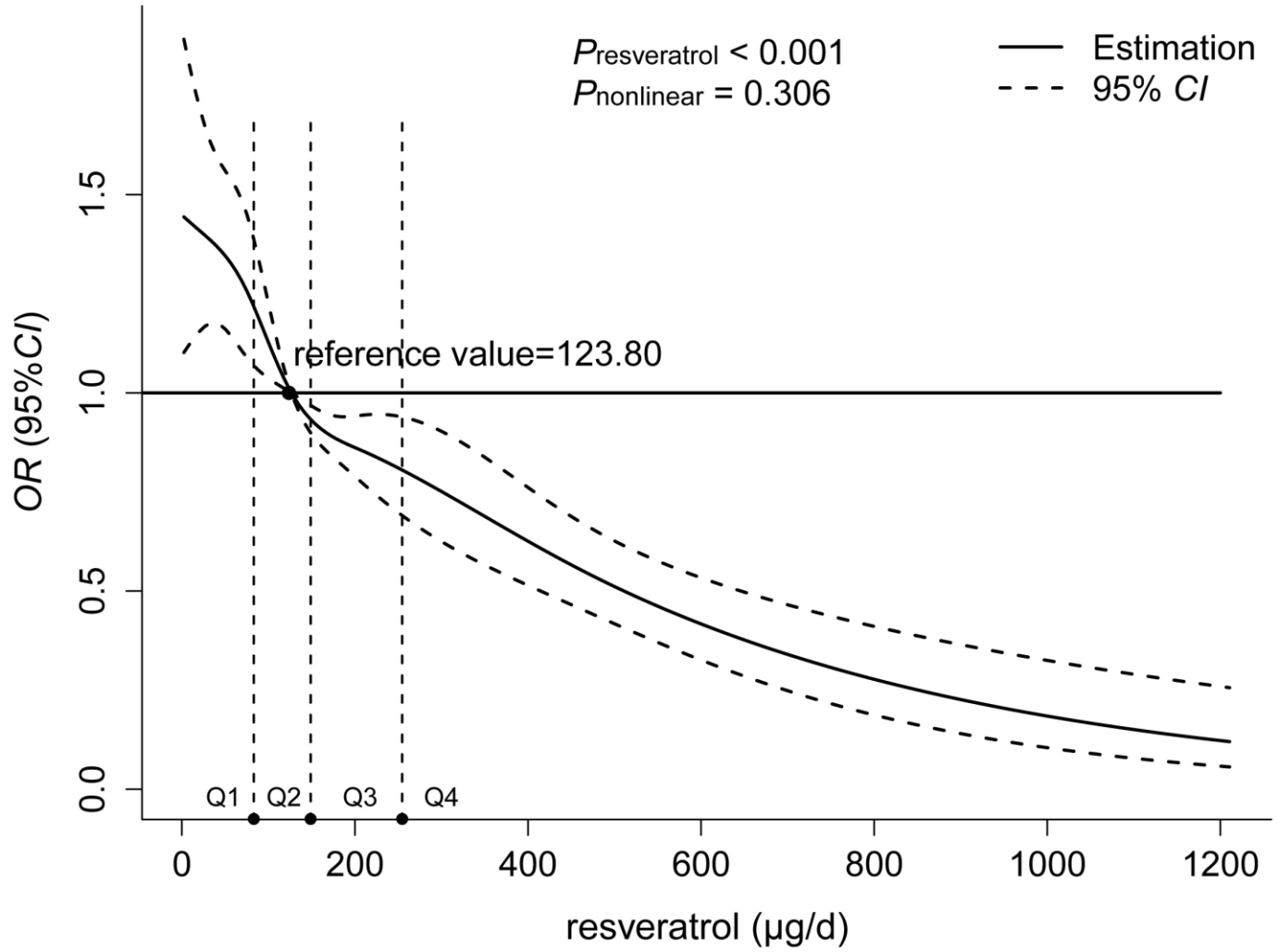


Negative association between dietary resveratrol and CRC risk

	Q1	Q2	Q3	Q4	Q5	P_{trend}
Median (μg/day)	42.35	95.35	147.71	229.62	424.22	
No. of cases/controls	934/610	747/608	566/609	465/608	318/609	
Model1	1.00	0.80 (0.69–0.93)	0.61 (0.52–0.71)	0.50 (0.43–0.59)	0.34 (0.29–0.40)	<0.001
Model2	1.00	0.86 (0.73–1.01)	0.65 (0.55–0.77)	0.54 (0.45–0.64)	0.41 (0.34–0.50)	<0.001
Model3	1.00	0.90 (0.76–1.06)	0.70 (0.59–0.83)	0.59 (0.49–0.71)	**0.47 (0.39–0.57)**	<0.001

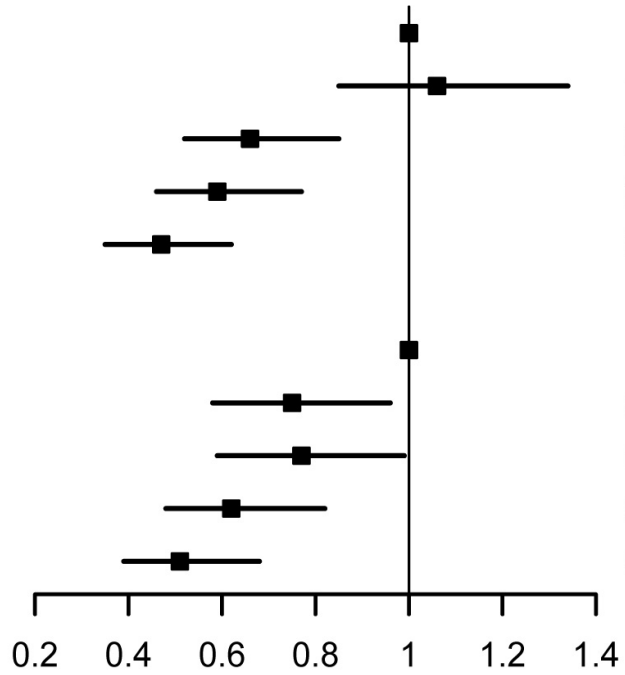
- After adjusting for variables, the highest quintile of resveratrol intake was associated with a 53% reduction in CRC risk compared to the lowest quintile

The linear dose-response relationship



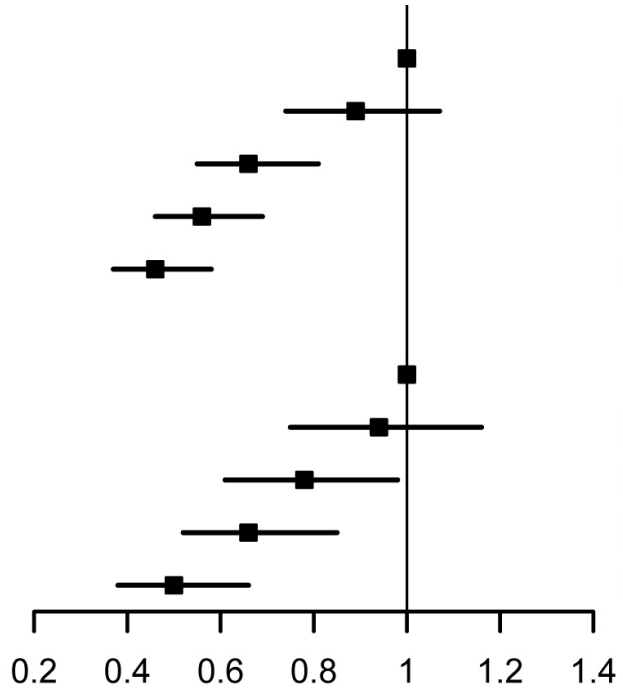
Sex-stratified analysis

Subgroup	No. of Cases	No. of Controls	*OR* (95%*CI*)	P_{trend}	$P_{interaction}$
Sex					0.034
Men				<0.001	
Q1	548	345	1.00		
Q2	477	344	1.06 (0.85–1.34)		
Q3	284	345	0.66 (0.52–0.85)		
Q4	254	344	0.59 (0.46–0.77)		
Q5	153	345	0.47 (0.35–0.62)		
Women				<0.001	
Q1	386	265	1.00		
Q2	270	264	0.75 (0.58–0.96)		
Q3	282	264	0.77 (0.59–0.99)		
Q4	211	264	0.62 (0.48–0.82)		
Q5	165	264	0.51 (0.39–0.68)		



Subgroup analysis of cancer sites

Subgroup	No. of Cases	No. of Controls	OR (95%CI)	P_{trend}	$P_{heterogeneity}$
Subsite					0.210
Colon cancer				<0.001	
Q1	594	610	1.00		
Q2	489	608	0.89 (0.74–1.07)		
Q3	363	609	0.66 (0.55–0.81)		
Q4	297	608	0.56 (0.46–0.69)		
Q5	218	609	0.46 (0.37–0.58)		
Rectal cancer				<0.001	
Q1	340	610	1.00		
Q2	261	608	0.94 (0.75–1.16)		
Q3	200	609	0.78 (0.61–0.98)		
Q4	166	608	0.66 (0.52–0.85)		
Q5	102	609	0.50 (0.38–0.66)		



Conclusion of study

- This study is **the first** to observe the association between dietary resveratrol intake and CRC risk.
- Greater habitual intake of resveratrol is associated with a dose-response reduction in CRC risk in Chinese population.
- The primary contributors to this association were resveratrol found in fruits and edible fungi.

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THANKS

Respondent : Cai-xia Zhang, Professor