

**Association between remnant cholesterol and the risk of 4
site-specific cancers: evidence from a cross-sectional and Mendelian
randomization study**

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Table S1. Statin use information in the NHANES database

Medication category	Medications	Drug names
C10AA	HMG CoA reductase inhibitors	ATORVASTATIN
C10AA	HMG CoA reductase inhibitors	FLUVASTATIN
C10AA	HMG CoA reductase inhibitors	LOVASTATIN
C10AA	HMG CoA reductase inhibitors	PITAVASTATIN
C10AA	HMG CoA reductase inhibitors	PRAVASTATIN
C10AA	HMG CoA reductase inhibitors	ROSUVASTATIN
C10AA	HMG CoA reductase inhibitors	SIMVASTATIN

Table S2. Participant characteristics at baseline based on RC quartiles

Characteristic	Overall N = 18,067	logRC				P Value
		Q1(<2.64) N = 4,570	Q2(2.64-3.04) N = 4,909	Q3(3.04-3.40) N = 4,177	Q4($\geq$ 3.40) N = 4,411	
Age category, %						<0.001
<60 years	11,732 (74.44%)	3,407 (81.42%)	3,140 (73.90%)	2,486 (70.53%)	2,699 (71.22%)	
$\geq$ 60 years	6,335 (25.56%)	1,163 (18.58%)	1,769 (26.10%)	1,691 (29.47%)	1,712 (28.78%)	
Age, years	47.24 (16.78)	42.75 (16.64)	47.17 (17.06)	49.35 (16.81)	50.17 (15.53)	<0.001
Sex, %						<0.001
Female	9,051 (50.92%)	2,544 (57.10%)	2,503 (52.88%)	2,014 (48.17%)	1,990 (44.70%)	
Male	9,016 (49.08%)	2,026 (42.90%)	2,406 (47.12%)	2,163 (51.83%)	2,421 (55.30%)	
Race, %						<0.001
Mexican American	2,957 (7.52%)	494 (6.09%)	716 (6.96%)	774 (8.12%)	973 (9.11%)	
Non-Hispanic White	8,460 (70.35%)	1,872 (65.79%)	2,254 (69.98%)	2,055 (71.75%)	2,279 (74.34%)	
Non-Hispanic Black	3,581 (10.58%)	1,428 (16.91%)	1,123 (11.97%)	610 (7.52%)	420 (5.13%)	
Other Race	3,069 (11.55%)	776 (11.21%)	816 (11.09%)	738 (12.61%)	739 (11.42%)	
Education level, %						<0.001
Below high school	1,872 (5.11%)	268 (3.10%)	462 (4.84%)	507 (6.08%)	635 (6.67%)	
High school or equivalent	6,683 (34.67%)	1,521 (29.38%)	1,818 (34.74%)	1,589 (36.38%)	1,755 (38.65%)	

Characteristic	Overall N = 18,067	logRC				P Value
		Q1(<2.64) N = 4,570	Q2(2.64-3.04) N = 4,909	Q3(3.04-3.40) N = 4,177	Q4($\geq$ 3.40) N = 4,411	
College or above	9,512 (60.22%)	2,781 (67.52%)	2,629 (60.42%)	2,081 (57.54%)	2,021 (54.68%)	0.027
PIR, %						
<1.3	5,175 (19.78%)	1,207 (18.77%)	1,404 (19.81%)	1,199 (19.72%)	1,365 (20.90%)	
1.3-3.5	7,026 (36.55%)	1,754 (34.85%)	1,893 (36.38%)	1,655 (38.04%)	1,724 (37.15%)	
>3.5	5,866 (43.67%)	1,609 (46.37%)	1,612 (43.81%)	1,323 (42.24%)	1,322 (41.95%)	<0.001
BMI category, %						
Underweight	250 (1.51%)	131 (3.06%)	73 (1.51%)	27 (0.74%)	19 (0.58%)	
Normal	5,001 (29.41%)	1,881 (45.03%)	1,512 (33.18%)	928 (22.95%)	680 (14.53%)	
Overweight	6,133 (33.38%)	1,378 (29.66%)	1,687 (34.03%)	1,440 (33.72%)	1,628 (36.35%)	
Obese	6,683 (35.69%)	1,180 (22.25%)	1,637 (31.27%)	1,782 (42.59%)	2,084 (48.54%)	<0.001
BMI	27.70 (24.10, 32.21)	25.20 (22.45, 29.30)	27.01 (23.70, 31.40)	28.80 (25.20, 33.30)	29.77 (26.60, 34.34)	
Drinking status, %						<0.001
Never	2,306 (10.17%)	576 (10.48%)	633 (10.09%)	526 (9.85%)	571 (10.21%)	
Former	3,450 (15.90%)	705 (12.18%)	909 (15.58%)	854 (17.01%)	982 (19.21%)	
Mild	6,251 (37.10%)	1,646 (38.11%)	1,700 (36.30%)	1,463 (37.63%)	1,442 (36.41%)	

Characteristic	Overall N = 18,067	logRC				P Value
		Q1(<2.64) N = 4,570	Q2(2.64-3.04) N = 4,909	Q3(3.04-3.40) N = 4,177	Q4($\geq$ 3.40) N = 4,411	
Moderate	2,661 (17.15%)	842 (21.25%)	750 (17.68%)	523 (14.07%)	546 (15.06%)	
Heavy	3,399 (19.69%)	801 (17.98%)	917 (20.35%)	811 (21.45%)	870 (19.11%)	
Smoking status, %						<0.001
Never smoker	9,683 (53.25%)	2,803 (61.17%)	2,659 (53.60%)	2,166 (51.19%)	2,055 (46.30%)	
Former smoker	4,721 (26.05%)	1,006 (22.22%)	1,243 (25.39%)	1,135 (26.87%)	1,337 (30.15%)	
Current smoker	3,663 (20.69%)	761 (16.61%)	1,007 (21.01%)	876 (21.94%)	1,019 (23.56%)	
Diabetes, %						<0.001
No	14,723 (86.23%)	4,099 (93.08%)	4,133 (89.41%)	3,275 (83.92%)	3,216 (77.50%)	
Yes	3,344 (13.77%)	471 (6.92%)	776 (10.59%)	902 (16.08%)	1,195 (22.50%)	
Hypertension, %						<0.001
No	9,826 (60.30%)	3,011 (72.75%)	2,761 (63.47%)	2,053 (54.36%)	2,001 (49.01%)	
Yes	8,241 (39.70%)	1,559 (27.25%)	2,148 (36.53%)	2,124 (45.64%)	2,410 (50.99%)	
Statin use, %						<0.001
No	14,742 (83.59%)	3,947 (88.74%)	4,064 (85.16%)	3,282 (81.08%)	3,449 (78.66%)	
Yes	3,325 (16.41%)	623 (11.26%)	845 (14.84%)	895 (18.92%)	962 (21.34%)	

Characteristic	Overall N = 18,067	logRC				P Value
		Q1(<2.64) N = 4,570	Q2(2.64-3.04) N = 4,909	Q3(3.04-3.40) N = 4,177	Q4($\geq$ 3.40) N = 4,411	
Cancer						0.005
No	16,325 (90.49%)	4,198 (92.07%)	4,451 (90.65%)	3,737 (89.83%)	3,939 (89.24%)	
Yes	1,742 (9.51%)	372 (7.93%)	458 (9.35%)	440 (10.17%)	472 (10.76%)	
Breast cancer						0.042
No	17,811 (98.54%)	4,525 (98.97%)	4,840 (98.36%)	4,097 (98.04%)	4,349 (98.74%)	
Yes	256 (1.46%)	45 (1.03%)	69 (1.64%)	80 (1.96%)	62 (1.26%)	
Lung cancer						0.035
No	18,023 (99.78%)	4,565 (99.89%)	4,897 (99.86%)	4,165 (99.75%)	4,396 (99.61%)	
Yes	44 (0.22%)	5 (0.11%)	12 (0.14%)	12 (0.25%)	15 (0.39%)	
Colorectal cancer						0.701
No	17,932 (99.43%)	4,5465 (99.56%)	4,875 (99.36%)	4,140 (99.38%)	4,372 (99.40%)	
Yes	135 (0.57%)	25 (0.44%)	34 (0.64%)	37 (0.62%)	39 (0.60%)	
Prostate cancer						0.391
No	17,789 (98.98%)	4,497 (99.06%)	4,841 (99.11%)	4,110 (98.71%)	4,341 (99.00%)	
Yes	278 (1.02%)	73 (0.94%)	68 (0.89%)	67 (1.29%)	70 (1.00%)	

PIR poverty income ratio; RC Remnant cholesterol, TC Total cholesterol, LDL-C Low-density lipoprotein cholesterol, HDL-C High-density lipoprotein cholesterol; BMI body mass index.

Table S3. Survey-weighted multivariate analysis of RC/TC, RC/LDL and RC/HDL on breast cancer

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
log(RC/TC)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	0.80	0.52, 1.22	0.293	0.79	0.52, 1.22	0.283	0.82	0.53, 1.27	0.361
<i>Q3</i>	1.07	0.68, 1.66	0.780	1.09	0.67, 1.77	0.727	1.13	0.68, 1.90	0.627
<i>Q4</i>	0.79	0.51, 1.21	0.279	0.80	0.51, 1.26	0.343	0.81	0.48, 1.36	0.420
<i>P trend</i>			0.554			0.661			0.726
log(RC/LDL)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.22	0.76, 1.97	0.413	1.18	0.73, 1.91	0.502	1.18	0.72, 1.94	0.504
<i>Q3</i>	1.18	0.75, 1.85	0.481	1.05	0.65, 1.70	0.833	1.06	0.65, 1.73	0.819
<i>Q4</i>	1.03	0.65, 1.63	0.897	0.90	0.55, 1.46	0.666	0.86	0.50, 1.50	0.602
<i>P trend</i>			0.942			0.582			0.533
log(RC/HDL)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	0.88	0.59, 1.32	0.545	0.96	0.63, 1.47	0.845	1.01	0.66, 1.56	0.945

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Q3</i>	1.08	0.69, 1.68	0.746	1.24	0.76, 2.00	0.384	1.35	0.80, 2.26	0.259
<i>Q4</i>	0.58	0.37, 0.91	0.019	0.83	0.51, 1.35	0.453	0.88	0.52, 1.50	0.634
<i>P trend</i>			0.048			0.699			0.907

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S4. Survey-weighted multivariate analysis of RC, RC/TC, RC/LDL and RC/HDL on lung cancer

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
logRC									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.24	0.34, 4.53	0.739	0.95	0.26, 3.40	0.933	0.85	0.24, 3.02	0.797
<i>Q3</i>	2.27	0.71, 7.23	0.163	1.56	0.50, 4.85	0.444	1.37	0.43, 4.38	0.595
<i>Q4</i>	3.54	1.14, 11.0	0.029	2.35	0.74, 7.46	0.147	1.67	0.52, 5.36	0.384
<i>P trend</i>			0.011			0.082			0.261
log(RC/TC)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.92	0.45, 8.18	0.378	1.65	0.40, 6.87	0.491	1.42	0.32, 6.31	0.646
<i>Q3</i>	3.05	0.86, 10.8	0.084	2.36	0.66, 8.36	0.183	1.91	0.50, 7.22	0.340
<i>Q4</i>	3.79	1.07, 13.4	0.039	2.72	0.75, 9.88	0.127	1.76	0.40, 7.74	0.450
<i>P trend</i>			0.021			0.093			0.380
log(RC/LDL)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	3.46	0.59, 20.2	0.167	3.08	0.53, 18.0	0.211	2.79	0.47, 16.8	0.259

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Q3</i>	7.12	1.33, 38.0	0.022	5.44	1.04, 28.5	0.045	4.59	0.83, 25.4	0.080
<i>Q4</i>	5.66	1.09, 29.5	0.040	3.87	0.76, 19.6	0.102	2.55	0.42, 15.4	0.306
<i>P trend</i>			0.021			0.067			0.236
log(RC/HDL)									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	0.50	0.14, 1.84	0.293	0.42	0.11, 1.56	0.193	0.39	0.10, 1.53	0.178
<i>Q3</i>	1.16	0.43, 3.12	0.766	0.93	0.34, 2.52	0.888	0.76	0.26, 2.23	0.609
<i>Q4</i>	2.35	0.94, 5.88	0.067	1.96	0.72, 5.37	0.188	1.43	0.46, 4.41	0.536
<i>P trend</i>			0.018			0.077			0.329

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S5. Survey-weighted multivariate analysis of RC on breast cancer after excluding participants with RC outliers

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
logRC category									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.59	0.94, 2.70	0.083	1.28	0.75, 2.20	0.361	1.33	0.77, 2.27	0.302
<i>Q3</i>	1.91	1.20, 3.04	0.007	1.55	0.94, 2.57	0.088	1.69	1.00, 2.86	0.048
<i>Q4</i>	1.22	0.74, 1.99	0.431	0.94	0.55, 1.61	0.827	1.00	0.58, 1.74	0.990
logRC category									
<i>Q2</i>	—	—		—	—		—	—	
<i>Q1</i>	0.63	0.37, 1.06	0.083	0.78	0.45, 1.33	0.361	0.75	0.44, 1.29	0.302
<i>Q3</i>	1.20	0.76, 1.89	0.436	1.21	0.76, 1.92	0.418	1.28	0.79, 2.07	0.318
<i>Q4</i>	0.76	0.47, 1.24	0.274	0.73	0.45, 1.21	0.223	0.76	0.45, 1.27	0.292
logRC category									
<i>Q3</i>	—	—		—	—		—	—	
<i>Q1</i>	0.53	0.33, 0.85	0.008	0.65	0.39, 1.08	0.097	0.60	0.35, 1.01	0.054

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Q2</i>	0.83	0.53, 1.32	0.436	0.83	0.52, 1.31	0.417	0.78	0.48, 1.27	0.318
<i>Q4</i>	0.64	0.41, 1.00	0.048	0.61	0.39, 0.95	0.031	0.59	0.37, 0.94	0.028
logRC category									
<i>Q4</i>	—	—		—	—		—	—	
<i>Q1</i>	0.83	0.51, 1.36	0.465	1.08	0.63, 1.83	0.787	1.01	0.58, 1.75	0.975
<i>Q2</i>	1.31	0.81, 2.12	0.274	1.36	0.83, 2.24	0.224	1.32	0.78, 2.22	0.293
<i>Q3</i>	1.57	1.00, 2.45	0.048	1.65	1.05, 2.59	0.031	1.69	1.06, 2.69	0.028
<i>P trend</i>			0.318			0.988			0.773

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S6. Unweighted multivariate analysis of RC on breast cancer

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
logRC category									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.43	0.99, 2.10	0.062	1.16	0.82, 1.64	0.408	1.17	0.80, 1.73	0.422
<i>Q3</i>	1.96	1.37, 2.86	<0.001	1.49	1.07, 2.11	0.021	1.51	1.03, 2.25	0.038
<i>Q4</i>	1.43	0.98, 2.12	0.068	1.09	0.76, 1.58	0.626	1.10	0.72, 1.68	0.664
logRC category									
<i>Q2</i>	—	—		—	—		—	—	
<i>Q1</i>	0.70	0.48, 1.01	0.062	0.87	0.61, 1.22	0.408	0.85	0.58, 1.25	0.422
<i>Q3</i>	1.37	0.99, 1.90	0.058	1.29	0.96, 1.74	0.087	1.29	0.93, 1.80	0.131
<i>Q4</i>	1.00	0.71, 1.41	>0.999	0.95	0.69, 1.30	0.735	0.94	0.65, 1.34	0.722
logRC category									
<i>Q3</i>	—	—		—	—		—	—	
<i>Q1</i>	0.51	0.35, 0.73	<0.001	0.67	0.47, 0.94	0.021	0.66	0.44, 0.97	0.038

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Q2</i>	0.73	0.53, 1.01	0.058	0.77	0.58, 1.04	0.087	0.77	0.55, 1.08	0.131
<i>Q4</i>	0.73	0.52, 1.02	0.065	0.73	0.54, 0.99	0.044	0.73	0.51, 1.02	0.064
logRC category									
<i>Q4</i>	—	—		—	—		—	—	
<i>Q1</i>	0.70	0.47, 1.02	0.068	0.91	0.63, 1.31	0.626	0.91	0.60, 1.38	0.664
<i>Q2</i>	1.00	0.71, 1.42	>0.999	1.06	0.77, 1.45	0.735	1.07	0.75, 1.53	0.722
<i>Q3</i>	1.37	0.98, 1.92	0.065	1.37	1.01, 1.85	0.044	1.38	0.98, 1.94	0.064
<i>P trend</i>			0.023			0.363			0.427

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S7. AIC and BIC results of 5 imputation models (logRC and breast cancer)

	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5
AIC	2699.80	2699.45	2699.81	2701.16	2701.35
BIC	2876.28	2875.93	2876.29	2877.64	2877.83

All adjusted by model 3. AIC: Akaike information criterion, BIC: Bayesian Information Criterion.

Table S8. Survey-weighted multivariate logistic regression based on PSM

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
logRC category									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.23	0.60, 2.52	0.562	1.22	0.59, 2.53	0.584	1.32	0.62, 2.80	0.462
<i>Q3</i>	2.13	1.05, 4.35	0.037	2.10	1.02, 4.32	0.044	2.37	1.13, 5.00	0.024
<i>Q4</i>	1.01	0.55, 1.88	0.964	1.00	0.51, 1.94	0.998	1.22	0.56, 2.67	0.610
logRC category									
<i>Q2</i>	—	—		—	—		—	—	
<i>Q1</i>	0.81	0.40, 1.66	0.562	0.82	0.39, 1.69	0.584	0.76	0.36, 1.60	0.462
<i>Q3</i>	1.73	0.84, 3.56	0.134	1.71	0.84, 3.50	0.137	1.80	0.89, 3.64	0.102
<i>Q4</i>	0.82	0.45, 1.49	0.513	0.82	0.45, 1.48	0.500	0.92	0.47, 1.80	0.816
logRC category									
<i>Q3</i>	—	—		—	—		—	—	
<i>Q1</i>	0.47	0.23, 0.96	0.037	0.48	0.23, 0.98	0.044	0.42	0.20, 0.89	0.024

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
<i>Q2</i>	0.58	0.28, 1.19	0.134	0.58	0.29, 1.19	0.137	0.56	0.27, 1.13	0.102
<i>Q4</i>	0.48	0.25, 0.90	0.022	0.48	0.25, 0.90	0.024	0.51	0.26, 1.00	0.051
logRC category									
<i>Q4</i>	—	—		—	—		—	—	
<i>Q1</i>	0.99	0.53, 1.83	0.964	1.00	0.52, 1.94	0.998	0.82	0.38, 1.79	0.610
<i>Q2</i>	1.22	0.67, 2.20	0.513	1.22	0.68, 2.22	0.500	1.08	0.55, 2.11	0.816
<i>Q3</i>	2.10	1.11, 3.98	0.022	2.10	1.11, 3.98	0.024	1.94	1.00, 3.79	0.051
<i>P trend</i>			0.548			0.606			0.335

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S9. Survey-weighted multivariate logistic analysis after multiple interpolation for missing data

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
logRC category									
<i>Q1</i>	—	—		—	—		—	—	
<i>Q2</i>	1.48	1.07, 2.07	0.020	1.25	0.92, 1.69	0.153	1.27	0.91, 1.77	0.161
<i>Q3</i>	1.82	1.32, 2.55	<0.001	1.41	1.04, 1.92	0.028	1.43	1.02, 2.01	0.039
<i>Q4</i>	1.47	1.05, 2.07	0.026	1.15	0.83, 1.59	0.398	1.17	0.82, 1.67	0.399
logRC category									
<i>Q2</i>	—	—		—	—		—	—	
<i>Q1</i>	0.68	0.48, 0.94	0.020	0.80	0.59, 1.08	0.153	0.79	0.57, 1.10	0.161
<i>Q3</i>	1.23	0.92, 1.65	0.160	1.13	0.87, 1.47	0.361	1.13	0.85, 1.51	0.411
<i>Q4</i>	0.99	0.73, 1.34	0.968	0.92	0.70, 1.22	0.563	0.92	0.68, 1.25	0.600
logRC category									
<i>Q3</i>	—	—		—	—		—	—	
<i>Q1</i>	0.55	0.39, 0.76	<0.001	0.71	0.52, 0.96	0.028	0.70	0.50, 0.98	0.039

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
<i>Q2</i>	0.81	0.61, 1.09	0.160	0.88	0.68, 1.15	0.361	0.89	0.66, 1.18	0.411
<i>Q4</i>	0.81	0.60, 1.09	0.162	0.81	0.62, 1.07	0.140	0.82	0.61, 1.10	0.180
logRC category									
<i>Q4</i>	—	—		—	—		—	—	
<i>Q1</i>	0.76	0.48, 1.20	0.230	0.93	0.58, 1.50	0.764	0.89	0.55, 1.46	0.653
<i>Q2</i>	1.11	0.72, 1.70	0.635	1.18	0.76, 1.82	0.467	1.16	0.73, 1.83	0.527
<i>Q3</i>	1.31	0.89, 1.93	0.163	1.36	0.93, 1.98	0.108	1.37	0.93, 2.00	0.110
<i>P trend</i>			0.012			0.294			0.286

Model 1: unadjusted.

Model 2: adjusted for age, sex, race, PIR and education level.

Model 3: adjusted for age, sex, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S10. Association of RC with breast cancer in the female population stratified by age

Characteristic	Sample size (Patients/Total)	OR	95% CI	<i>P</i> value
Total female	255/9051			
Q1		—	—	
Q2		1.34	0.78, 2.29	0.289
Q3		1.71	1.01, 2.88	0.045
Q4		1.01	0.58, 1.74	0.981
<i>P trend</i>				0.766
<60 years	56/5905			
Q1		—	—	
Q2		0.75	0.32, 1.80	0.520
Q3		1.67	0.69, 4.03	0.255
Q4		0.95	0.35, 2.56	0.925
<i>P trend</i>				0.678
≥60 years	199/3146			
Q1		—	—	
Q2		1.76	0.91, 3.42	0.094
Q3		1.88	1.03, 3.45	0.041
Q4		1.14	0.62, 2.10	0.661
<i>P trend</i>				0.627
<i>P interaction</i>				0.595

Analysis in total female population adjusted for age, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Analysis stratified by age in female population adjusted for race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S11. Association of RC with prostate cancer in the male population stratified by age

Characteristic	Sample size (Patients/Total)	OR	95% CI	P value
Total male	278/9016			
Q1		—	—	
Q2		0.81	0.48, 1.36	0.427
Q3		1.07	0.65, 1.75	0.785
Q4		0.88	0.55, 1.41	0.588
<i>P trend</i>				0.889
<60 years	15/5827			
Q1		—	—	
Q2		0.43	0.05, 3.37	0.419
Q3		0.15	0.01, 1.86	0.139
Q4		0.95	0.14, 4.80	0.823
<i>P trend</i>				0.577
≥60 years	263/3189			
Q1		—	—	
Q2		0.86	0.52, 1.43	0.556
Q3		1.22	0.76, 1.96	0.409
Q4		0.87	0.55, 1.36	0.529
<i>P trend</i>				0.918
<i>P interaction</i>				0.418

Analysis in total male population adjusted for age, race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Analysis stratified by age in male population adjusted for race, PIR, education level, BMI, smoking status, drinking status, diabetes, hypertension, and statins.

Table S12. Detailed information of data sources

Variables	Consortium	Cases (n)	Controls (n)	Sample size (n)	GWAS ID in IEU	Source
<i>Exposure data</i>						
Remnant cholesterol	UK Biobank	NA	NA	115082	ebi-a-GCST90092943	PMID 35213538
<i>Outcome data</i>						
Breast cancer	BCAC	122977	105974	228951	ieu-a-1126	PMID 29059683
Lung cancer	ILCCO	11348	15861	27209	ieu-a-966	PMID 24880342
Colorectal cancer	A meta-analysis of GWAS	19948	12124	32072	NA	PMID 30510241
Prostate cancer	PRACTICAL	79148	61106	140254	ieu-b-85	PMID 29892016
<i>Outcome data (Replication)</i>						
Breast cancer	FinnGen R10	18786	182927	201713	NA	https://www.finnngen.fi/en/access_results
Lung cancer		6340	314193	320533		
Colorectal cancer		6847	314193	321067		
Prostate cancer		15199	131266	146465		
<i>Lipids and Cholesterol data</i>						
TC	NA	NA	NA	437878	ebi-a-GCST90025953	PMID 34226706
LDL-C	UK Biobank	NA	NA	440546	ieu-b-110	PMID 32203549
HDL-C	UK Biobank	NA	NA	403943	ieu-b-109	PMID 32203549
TG	UK Biobank	NA	NA	441016	ieu-b-111	PMID 32203549
<i>Other confounders</i>						
Smoking initiation	GSCAN	311629	321173	607291	ieu-b-4877	PMID 30643251
Alcoholic drinks per week	GSCAN	NA	NA	335394	ieu-b-73	PMID 30643251
Body mass index	GIANT	NA	NA	681275	ieu-b-40	PMID 30124842
Type 2 diabetes	NA	61714	1178	655666	ebi-a-GCST006867	PMID 30054458

Table S13. Excluding SNPs associated with confounding factors identified by phenoscanner in primary MR analysis

SNP	Gwas Trait	Effect Allele	Other Allele	Beta	<i>P</i> value	PMID
rs112875651	Body mass index	A	G	0.0126	2.00E-09	34594039
rs58542926	Type 2 diabetes	C	T	0.089	5.00E-25	32541925

Table S14. Instrumental variables strongly associated with RC

SNP	EA	OA	Beta	Eaf	SE	Pval	R2	F
rs472495	T	G	0.0314252	0.649121	0.0042923	2.50E-13	0.00046555	53.60044761
rs7534572	G	C	0.0558037	0.64747	0.00428598	9.40E-39	0.001470886	169.5189145
rs11206517	G	T	0.0908334	0.033012	0.011479	2.50E-15	0.0005438	62.61458145
rs1293261	T	A	0.023626	0.525176	0.00410118	8.40E-09	0.00028829	33.18602148
rs553427	T	C	0.0286973	0.517037	0.00410145	2.60E-12	0.000425221	48.95529647
rs11591147	T	G	-0.308882	0.017457	0.0156254	5.60E-87	0.003384101	390.7647374
rs12740374	T	G	-0.0961513	0.221064	0.00493378	1.40E-84	0.003289368	379.7897267
rs693	A	G	0.0769739	0.520889	0.00410273	1.60E-78	0.003049351	351.9926223
rs12620918	C	T	0.0295835	0.173985	0.00542051	4.80E-08	0.000258761	29.78593654
rs4299376	T	G	-0.047141	0.676277	0.00439223	7.10E-27	0.000999967	115.1913549
rs35633876	T	G	-0.0238608	0.481858	0.00411923	6.90E-09	0.000291477	33.55292375
rs4665972	C	T	-0.0359412	0.604609	0.00421805	1.60E-17	0.000630493	72.60293069
rs4704834	G	A	0.0412619	0.644028	0.00427763	5.10E-22	0.000807855	93.04316239
rs1500188	G	A	-0.0240193	0.450404	0.00412981	6.00E-09	0.00029385	33.82618364
rs12916	C	T	0.0580953	0.400341	0.00418643	8.70E-44	0.001670555	192.5691804
rs72843670	C	T	0.0352589	0.138368	0.00592019	2.60E-09	0.000308124	35.46979518
rs72848251	A	G	0.0484938	0.194675	0.00531677	7.50E-20	0.000722363	83.18961981
rs3777411	T	C	-0.0483808	0.150735	0.00573293	3.20E-17	0.000618467	71.21726072
rs532754706	G	A	-0.0955271	0.023055	0.0161499	3.30E-09	0.00030393	34.98694036
rs10260606	C	G	0.0337973	0.182652	0.0052964	1.80E-10	0.000353705	40.7187945
rs2737245	T	G	-0.0279349	0.278602	0.00458436	1.10E-09	0.000322544	37.13036901
rs6601299	C	T	0.044935	0.899281	0.0068214	4.50E-11	0.000376922	43.39252383
rs2326077	T	C	-0.027081	0.663229	0.00434692	4.70E-10	0.000337142	38.81133233
rs115478735	T	A	0.0594489	0.183304	0.00530499	3.80E-29	0.001090028	125.5772475

SNP	EA	OA	Beta	Eaf	SE	Pval	R2	F
rs102275	C	T	-0.0453463	0.34979	0.00428851	3.90E-26	0.000970603	111.805537
rs12804228	G	A	0.0522524	0.08472	0.00742254	1.90E-12	0.00043044	49.55641082
rs964184	C	G	-0.0710628	0.86726	0.00604505	6.60E-32	0.001199378	138.1902137
rs1169292	T	C	0.030447	0.310497	0.00444764	7.60E-12	0.000407048	46.86215023
rs653178	T	C	0.0247731	0.516036	0.00410821	1.60E-09	0.000315872	36.36201093
rs6602911	T	C	0.0245499	0.360028	0.00427046	9.00E-09	0.00028709	33.04780281
rs72694391	C	T	0.0226707	0.482108	0.00411579	3.60E-08	0.000263573	30.3400224
rs633695	G	A	0.0546603	0.292354	0.00452543	1.40E-33	0.001266096	145.8870597
rs261290	C	T	-0.0759505	0.654645	0.0043224	4.10E-69	0.002675718	308.7477617
rs11854242	T	C	-0.0317694	0.275074	0.00462128	6.20E-12	0.000410495	47.25915065
rs34042070	G	C	0.0411867	0.186978	0.00528041	6.20E-15	0.000528374	60.83747145
rs247616	T	C	-0.0608862	0.324699	0.00438395	7.40E-44	0.001673292	192.8852453
rs77542162	G	A	0.149245	0.022666	0.0137929	2.80E-27	0.001016341	117.0794997
rs56325564	A	G	0.0303526	0.482691	0.00413217	2.10E-13	0.000468624	53.95452691
rs72631343	G	C	-0.0429508	0.129021	0.00611975	2.20E-12	0.000427841	49.25696003
rs77960347	G	A	0.134647	0.013234	0.0179189	5.70E-14	0.0004904	56.46289267
rs4939883	C	T	0.0309854	0.819142	0.00532421	5.90E-09	0.000294218	33.8685273
rs118147862	A	G	-0.354908	0.045764	0.0101119	1.00E-200	0.01059094	1231.851901
rs117310449	T	C	0.177991	0.011985	0.0189492	5.80E-21	0.00076608	88.22807004
rs41289512	G	C	0.0789205	0.042305	0.0101341	6.80E-15	0.000526712	60.64594079
rs12151108	A	G	-0.152836	0.119677	0.00630319	7.00E-130	0.005082882	587.926426
rs2738447	C	A	0.0328659	0.59318	0.00417665	3.60E-15	0.000537767	61.91948633
rs61679753	A	T	-0.349415	0.030645	0.0118993	1.60E-189	0.007436884	862.2490295
rs111278137	A	G	-0.101597	0.021614	0.0145756	3.20E-12	0.000422006	48.58490275
rs1883711	C	G	0.108501	0.031207	0.0120475	2.10E-19	0.000704304	81.10844293

SNP	EA	OA	Beta	Eaf	SE	Pval	R2	F
rs9616847	T	A	0.0250082	0.388272	0.00422751	3.30E-09	0.000303988	34.99355244

Table S15. Excluding outliers identified by Radial MR in primary MR analysis

Exposure	Outcome	SNP
Remnant cholesterol	Breast cancer	rs115478735
	Breast cancer	rs118147862
	Breast cancer	rs2326077
	Breast cancer	rs247616
	Breast cancer	rs4299376
	Breast cancer	rs6601299
	Breast cancer	rs72694391
	Breast cancer	rs964184
Remnant cholesterol	Lung cancer	rs102275
	Lung cancer	rs2737245
	Lung cancer	rs41289512
	Lung cancer	rs653178
Remnant cholesterol	Colorectal cancer	rs102275
	Colorectal cancer	rs12620918
	Colorectal cancer	rs4665972
	Colorectal cancer	rs4704834
	Colorectal cancer	rs553427
	Colorectal cancer	rs653178
	Colorectal cancer	rs72694391
Remnant cholesterol	Prostate cancer	rs12620918
	Prostate cancer	rs1883711
	Prostate cancer	rs2737245
	Prostate cancer	rs2738447
	Prostate cancer	rs472495

Exposure	Outcome	SNP
	Prostate cancer	rs553427
	Prostate cancer	rs653178
	Prostate cancer	rs72848251

Table S16. Harmonization data between RC and breast cancer ultimately used in primary MR analysis

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs102275	C	T	C	T	-0.0453463	-0.0069	0.34979	0.3424	0.00428851	0.0065
rs10260606	C	G	C	G	0.0337973	0.0115	0.182652	0.1938	0.0052964	0.0085
rs111278137	A	G	A	G	-0.101597	0.0168	0.021614	0.0147	0.0145756	0.0322
rs11206517	G	T	G	T	0.0908334	3.00E-04	0.033012	0.0391	0.011479	0.0162
rs11591147	T	G	T	G	-0.308882	-0.0442	0.017457	0.0173	0.0156254	0.0273
rs117310449	T	C	T	C	0.177991	-0.0314	0.011985	0.0104	0.0189492	0.0353
rs11854242	T	C	T	C	-0.0317694	-0.0094	0.275074	0.2731	0.00462128	0.0074
rs12151108	A	G	A	G	-0.152836	0.001	0.119677	0.1128	0.00630319	0.0103
rs12620918	C	T	C	T	0.0295835	-0.0028	0.173985	0.18	0.00542051	0.0081
rs12740374	T	G	T	G	-0.0961513	-0.0073	0.221064	0.2206	0.00493378	0.0075
rs12804228	G	A	G	A	0.0522524	-0.0132	0.08472	0.0904	0.00742254	0.0117
rs12916	C	T	C	T	0.0580953	0.0113	0.400341	0.4097	0.00418643	0.0063
rs1500188	G	A	G	A	-0.0240193	-0.0048	0.450404	0.4431	0.00412981	0.0062
rs1883711	C	G	C	G	0.108501	0.0115	0.031207	0.0373	0.0120475	0.0205
rs261290	C	T	C	T	-0.0759505	-0.0079	0.654645	0.669	0.0043224	0.0068
rs2737245	T	G	T	G	-0.0279349	-0.0105	0.278602	0.2753	0.00458436	0.007
rs2738447	C	A	C	A	0.0328659	0.0115	0.59318	0.5782	0.00417665	0.0063
rs34042070	G	C	G	C	0.0411867	-0.0027	0.186978	0.2073	0.00528041	0.0077
rs35633876	T	G	T	G	-0.0238608	-0.0018	0.481858	0.496	0.00411923	0.0063
rs3777411	T	C	T	C	-0.0483808	-0.0065	0.150735	0.1459	0.00573293	0.0087
rs41289512	G	C	G	C	0.0789205	-0.0261	0.042305	0.0439	0.0101341	0.0172
rs4665972	C	T	C	T	-0.0359412	0.0093	0.604609	0.5991	0.00421805	0.0064
rs4704834	G	A	G	A	0.0412619	-0.003	0.644028	0.641	0.00427763	0.0068

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs472495	T	G	T	G	0.0314252	7.00E-04	0.649121	0.6382	0.0042923	0.0071
rs4939883	C	T	C	T	0.0309854	0.0049	0.819142	0.8279	0.00532421	0.0082
rs553427	T	C	T	C	0.0286973	0.0047	0.517037	0.5347	0.00410145	0.0066
rs56325564	A	G	A	G	0.0303526	0.0134	0.482691	0.4648	0.00413217	0.0063
rs61679753	A	T	A	T	-0.349415	-0.0225	0.030645	0.038	0.0118993	0.017
rs633695	G	A	G	A	0.0546603	0.0037	0.292354	0.2906	0.00452543	0.0069
rs6602911	T	C	T	C	0.0245499	0.0087	0.360028	0.3738	0.00427046	0.0071
rs693	A	G	A	G	0.0769739	0.0102	0.520889	0.499	0.00410273	0.0063
rs72631343	G	C	G	C	-0.0429508	-0.0107	0.129021	0.1454	0.00611975	0.0093
rs72843670	C	T	C	T	0.0352589	0.013	0.138368	0.1453	0.00592019	0.0087
rs72848251	A	G	A	G	0.0484938	-0.0057	0.194675	0.2052	0.00531677	0.0082
rs7534572	G	C	G	C	0.0558037	-0.0097	0.64747	0.7391	0.00428598	0.0076
rs77542162	G	A	G	A	0.149245	0.003	0.022666	0.0194	0.0137929	0.0243
rs77960347	G	A	G	A	0.134647	0.0094	0.013234	0.0128	0.0179189	0.0293
rs9616847	T	A	T	A	0.0250082	0.0124	0.388272	0.3786	0.00422751	0.0065

Table S17. Harmonization data between RC and breast cancer ultimately used in replication MR analysis

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs102275	C	T	C	T	-0.0453463	-0.0143611	0.34979	0.41535	0.00428851	0.0115213
rs10260606	C	G	C	G	0.0337973	0.00267189	0.182652	0.326418	0.0052964	0.0121738
rs111278137	A	G	A	G	-0.101597	0.000764229	0.021614	0.0107894	0.0145756	0.0561248
rs11206517	G	T	G	T	0.0908334	0.0268427	0.033012	0.0442309	0.011479	0.0275014
rs115478735	T	A	T	A	0.0594489	0.0247634	0.183304	0.198773	0.00530499	0.0142406
rs11591147	T	G	T	G	-0.308882	0.0320315	0.017457	0.0363159	0.0156254	0.0307389
rs117310449	T	C	T	C	0.177991	-0.0428341	0.011985	0.0131025	0.0189492	0.0503837
rs118147862	A	G	A	G	-0.354908	-0.0155618	0.045764	0.0290385	0.0101119	0.0337354
rs11854242	T	C	T	C	-0.0317694	-0.0086114	0.275074	0.199027	0.00462128	0.0142254
rs12151108	A	G	A	G	-0.152836	0.0228757	0.119677	0.101753	0.00630319	0.0189244
rs12620918	C	T	C	T	0.0295835	-0.0133856	0.173985	0.181337	0.00542051	0.0147455
rs12740374	T	G	T	G	-0.0961513	-0.00991312	0.221064	0.214244	0.00493378	0.0138897
rs12804228	G	A	G	A	0.0522524	-0.0213957	0.08472	0.152862	0.00742254	0.0158299
rs12916	C	T	C	T	0.0580953	0.0086107	0.400341	0.452701	0.00418643	0.0114313
rs1500188	G	A	G	A	-0.0240193	0.0217744	0.450404	0.486371	0.00412981	0.0113862
rs1883711	C	G	C	G	0.108501	-0.00898343	0.031207	0.0617223	0.0120475	0.0237761
rs2326077	T	C	T	C	-0.027081	-0.00158694	0.663229	0.615103	0.00434692	0.0117115
rs247616	T	C	T	C	-0.0608862	0.00730919	0.324699	0.279384	0.00438395	0.0126786
rs261290	C	T	C	T	-0.0759505	-0.0109031	0.654645	0.619128	0.0043224	0.0117326
rs2737245	T	G	T	G	-0.0279349	0.0108319	0.278602	0.30828	0.00458436	0.0123468
rs2738447	C	A	C	A	0.0328659	0.00485729	0.59318	0.60623	0.00417665	0.0116599
rs34042070	G	C	G	C	0.0411867	-0.026521	0.186978	0.193396	0.00528041	0.0143812
rs35633876	T	G	T	G	-0.0238608	-0.0071116	0.481858	0.566127	0.00411923	0.0114942

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs3777411	T	C	T	C	-0.0483808	0.000357416	0.150735	0.125726	0.00573293	0.0171439
rs41289512	G	C	G	C	0.0789205	-0.0361315	0.042305	0.0555754	0.0101341	0.0252037
rs4299376	T	G	T	G	-0.047141	-0.002008	0.676277	0.784864	0.00439223	0.0138607
rs4665972	C	T	C	T	-0.0359412	-0.0153039	0.604609	0.625268	0.00421805	0.0117768
rs4704834	G	A	G	A	0.0412619	-0.00454142	0.644028	0.670066	0.00427763	0.0121288
rs472495	T	G	T	G	0.0314252	-0.021922	0.649121	0.575277	0.0042923	0.0115465
rs4939883	C	T	C	T	0.0309854	-0.0269619	0.819142	0.824104	0.00532421	0.0149218
rs553427	T	C	T	C	0.0286973	0.017691	0.517037	0.560058	0.00410145	0.0114674
rs56325564	A	G	A	G	0.0303526	0.0185058	0.482691	0.458746	0.00413217	0.0114552
rs61679753	A	T	A	T	-0.349415	-0.0150117	0.030645	0.0210506	0.0118993	0.0393136
rs633695	G	A	G	A	0.0546603	-0.0138714	0.292354	0.305329	0.00452543	0.0123625
rs6601299	C	T	C	T	0.044935	0.0195424	0.899281	0.843457	0.0068214	0.0156983
rs6602911	T	C	T	C	0.0245499	-0.0102036	0.360028	0.363376	0.00427046	0.0119638
rs693	A	G	A	G	0.0769739	-0.0105777	0.520889	0.418866	0.00410273	0.0115207
rs72631343	G	C	G	C	-0.0429508	-0.0046975	0.129021	0.143735	0.00611975	0.0163196
rs72694391	C	T	C	T	0.0226707	0.0114055	0.482108	0.378508	0.00411579	0.0117647
rs72843670	C	T	C	T	0.0352589	-0.010339	0.138368	0.128592	0.00592019	0.0170063
rs7534572	G	C	G	C	0.0558037	-0.00677344	0.64747	0.73611	0.00428598	0.0129407
rs77542162	G	A	G	A	0.149245	0.133923	0.022666	0.00675517	0.0137929	0.0702893
rs77960347	G	A	G	A	0.134647	-0.0402536	0.013234	0.00726318	0.0179189	0.0656835
rs9616847	T	A	T	A	0.0250082	0.00990847	0.388272	0.416059	0.00422751	0.0115392
rs964184	C	G	C	G	-0.0710628	-0.00313118	0.86726	0.855775	0.00604505	0.0161792

Table S18. Harmonization data between RC and lung cancer ultimately used in primary MR analysis

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs10260606	C	G	C	G	0.0337973	-0.0033787	0.182652	0.201567	0.0052964	0.023911
rs111278137	A	G	A	G	-0.101597	-0.106921	0.021614	0.0172735	0.0145756	0.070639
rs11206517	G	T	G	T	0.0908334	-0.0229299	0.033012	0.0403094	0.011479	0.045139
rs115478735	T	A	T	A	0.0594489	-0.01403	0.183304	0.220984	0.00530499	0.021152
rs1169292	T	C	T	C	0.030447	0.0295035	0.310497	0.32105	0.00444764	0.020035
rs117310449	T	C	T	C	0.177991	-0.00150313	0.011985	0.00765599	0.0189492	0.098571
rs118147862	A	G	A	G	-0.354908	0.0718973	0.045764	0.0384231	0.0101119	0.054776
rs11854242	T	C	T	C	-0.0317694	0.000870621	0.275074	0.270094	0.00462128	0.020509
rs12151108	A	G	A	G	-0.152836	0.0250467	0.119677	0.115856	0.00630319	0.028392
rs12620918	C	T	C	T	0.0295835	-0.0153096	0.173985	0.177449	0.00542051	0.023094
rs12740374	T	G	T	G	-0.0961513	-0.0205181	0.221064	0.226442	0.00493378	0.020808
rs12804228	G	A	G	A	0.0522524	-0.0294463	0.08472	0.0917027	0.00742254	0.029771
rs12916	C	T	C	T	0.0580953	-0.0172805	0.400341	0.410017	0.00418643	0.017787
rs1500188	G	A	G	A	-0.0240193	-0.0064719	0.450404	0.44507	0.00412981	0.017944
rs2326077	T	C	T	C	-0.027081	-0.00859991	0.663229	0.643124	0.00434692	0.018703
rs247616	T	C	T	C	-0.0608862	0.00103546	0.324699	0.320561	0.00438395	0.019459
rs261290	C	T	C	T	-0.0759505	-0.00542227	0.654645	0.661887	0.0043224	0.018993
rs2738447	C	A	C	A	0.0328659	-0.0236062	0.59318	0.569377	0.00417665	0.018521
rs34042070	G	C	G	C	0.0411867	0.0122269	0.186978	0.210445	0.00528041	0.022117
rs35633876	T	G	T	G	-0.0238608	-0.0114331	0.481858	0.496585	0.00411923	0.017879
rs3777411	T	C	T	C	-0.0483808	-0.0388635	0.150735	0.146374	0.00573293	0.024474
rs4299376	T	G	T	G	-0.047141	0.0164709	0.676277	0.684302	0.00439223	0.019077
rs4665972	C	T	C	T	-0.0359412	0.00446797	0.604609	0.575478	0.00421805	0.018818

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs4704834	G	A	G	A	0.0412619	-0.0140765	0.644028	0.619845	0.00427763	0.018761
rs472495	T	G	T	G	0.0314252	0.0109518	0.649121	0.638623	0.0042923	0.019846
rs4939883	C	T	C	T	0.0309854	0.00014401	0.819142	0.83205	0.00532421	0.0235
rs553427	T	C	T	C	0.0286973	0.00385141	0.517037	0.535484	0.00410145	0.018049
rs56325564	A	G	A	G	0.0303526	0.00297756	0.482691	0.431131	0.00413217	0.019841
rs61679753	A	T	A	T	-0.349415	0.0213377	0.030645	0.0340636	0.0118993	0.051633
rs633695	G	A	G	A	0.0546603	-0.0127641	0.292354	0.288007	0.00452543	0.019472
rs6601299	C	T	C	T	0.044935	-0.0294345	0.899281	0.903709	0.0068214	0.030025
rs693	A	G	A	G	0.0769739	0.00312588	0.520889	0.49598	0.00410273	0.017851
rs72631343	G	C	G	C	-0.0429508	-0.00915175	0.129021	0.141888	0.00611975	0.027465
rs72694391	C	T	C	T	0.0226707	0.0229291	0.482108	0.470189	0.00411579	0.019213
rs7534572	G	C	G	C	0.0558037	-0.036518	0.64747	0.686192	0.00428598	0.0199
rs77542162	G	A	G	A	0.149245	0.0448529	0.022666	0.0174656	0.0137929	0.078907
rs77960347	G	A	G	A	0.134647	0.0703121	0.013234	0.0124778	0.0179189	0.084876
rs9616847	T	A	T	A	0.0250082	0.00872384	0.388272	0.384199	0.00422751	0.019062
rs964184	C	G	C	G	-0.0710628	-0.0369942	0.86726	0.859074	0.00604505	0.026308

Table S19. Harmonization data between RC and lung cancer ultimately used in replication MR analysis

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs10260606	C	G	C	G	0.0337973	0.00283224	0.182652	0.326094	0.0198914	0.0052964
rs111278137	A	G	A	G	-0.101597	-0.0484537	0.021614	0.0108376	0.0900349	0.0145756
rs11206517	G	T	G	T	0.0908334	0.0690593	0.033012	0.0444632	0.0437416	0.011479
rs115478735	T	A	T	A	0.0594489	-0.00198455	0.183304	0.198593	0.0232788	0.00530499
rs11591147	T	G	T	G	-0.308882	0.0563924	0.017457	0.0361512	0.0506329	0.0156254
rs1169292	T	C	T	C	0.030447	0.00538335	0.310497	0.354006	0.0196212	0.00444764
rs117310449	T	C	T	C	0.177991	0.0239302	0.011985	0.0134019	0.0786308	0.0189492
rs118147862	A	G	A	G	-0.354908	0.0674313	0.045764	0.0292198	0.0534027	0.0101119
rs11854242	T	C	T	C	-0.0317694	0.00370553	0.275074	0.199196	0.0230664	0.00462128
rs12151108	A	G	A	G	-0.152836	-0.0105549	0.119677	0.101498	0.0311457	0.00630319
rs12620918	C	T	C	T	0.0295835	-0.0066907	0.173985	0.181132	0.0239042	0.00542051
rs12740374	T	G	T	G	-0.0961513	0.00057718	0.221064	0.214364	0.0225937	0.00493378
rs12804228	G	A	G	A	0.0522524	-0.0321689	0.08472	0.152968	0.0257581	0.00742254
rs12916	C	T	C	T	0.0580953	-0.00168278	0.400341	0.452956	0.0185891	0.00418643
rs1500188	G	A	G	A	-0.0240193	0.00549854	0.450404	0.486786	0.0185011	0.00412981
rs1883711	C	G	C	G	0.108501	-0.0353547	0.031207	0.0620296	0.0384194	0.0120475
rs2326077	T	C	T	C	-0.027081	0.0175033	0.663229	0.615248	0.019092	0.00434692
rs247616	T	C	T	C	-0.0608862	-0.00335658	0.324699	0.278798	0.0206029	0.00438395
rs261290	C	T	C	T	-0.0759505	0.00223982	0.654645	0.61946	0.0190697	0.0043224
rs2737245	T	G	T	G	-0.0279349	-0.00707807	0.278602	0.308483	0.0200843	0.00458436
rs2738447	C	A	C	A	0.0328659	0.000598699	0.59318	0.606799	0.018925	0.00417665
rs34042070	G	C	G	C	0.0411867	0.00470859	0.186978	0.19436	0.0232748	0.00528041
rs35633876	T	G	T	G	-0.0238608	-0.0214164	0.481858	0.565826	0.0187525	0.00411923

SNP	Effect_allele .exposure	Other_allele .exposure	Effect_allele .outcome	Other_allele .outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs3777411	T	C	T	C	-0.0483808	-0.0148008	0.150735	0.126165	0.0277892	0.00573293
rs41289512	G	C	G	C	0.0789205	-0.0686488	0.042305	0.0557202	0.0413479	0.0101341
rs4299376	T	G	T	G	-0.047141	0.0436162	0.676277	0.784573	0.0224515	0.00439223
rs4665972	C	T	C	T	-0.0359412	0.0220175	0.604609	0.624376	0.0191472	0.00421805
rs4704834	G	A	G	A	0.0412619	-0.00621747	0.644028	0.671267	0.0197476	0.00427763
rs472495	T	G	T	G	0.0314252	-0.00066107	0.649121	0.575915	0.0188039	0.0042923
rs4939883	C	T	C	T	0.0309854	0.0414619	0.819142	0.824078	0.0241096	0.00532421
rs553427	T	C	T	C	0.0286973	0.0286634	0.517037	0.559556	0.0185806	0.00410145
rs56325564	A	G	A	G	0.0303526	0.0225314	0.482691	0.458394	0.0185713	0.00413217
rs61679753	A	T	A	T	-0.349415	0.0108498	0.030645	0.0210261	0.0628389	0.0118993
rs633695	G	A	G	A	0.0546603	0.00525982	0.292354	0.305757	0.0201191	0.00452543
rs6601299	C	T	C	T	0.044935	-0.0319551	0.899281	0.843251	0.0256752	0.0068214
rs6602911	T	C	T	C	0.0245499	0.00246594	0.360028	0.363427	0.019413	0.00427046
rs693	A	G	A	G	0.0769739	0.00984618	0.520889	0.419354	0.0187554	0.00410273
rs72631343	G	C	G	C	-0.0429508	0.0472547	0.129021	0.143459	0.026568	0.00611975
rs72694391	C	T	C	T	0.0226707	-0.00872488	0.482108	0.378349	0.0190895	0.00411579
rs72843670	C	T	C	T	0.0352589	0.00579231	0.138368	0.129346	0.0276323	0.00592019
rs7534572	G	C	G	C	0.0558037	-0.0250834	0.64747	0.736224	0.0210361	0.00428598
rs77542162	G	A	G	A	0.149245	0.0743991	0.022666	0.00677193	0.11244	0.0137929
rs77960347	G	A	G	A	0.134647	0.0836832	0.013234	0.0072121	0.107427	0.0179189
rs9616847	T	A	T	A	0.0250082	-0.0217518	0.388272	0.416379	0.0188063	0.00422751
rs964184	C	G	C	G	-0.0710628	-0.0138017	0.86726	0.855519	0.0262733	0.00604505

Table S20. Harmonization data between RC and colorectal cancer ultimately used in primary MR analysis

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs10260606	C	G	C	G	0.0337973	-0.012736564	0.182652	0.2175383	0.0052964	0.021642613
rs111278137	A	G	A	G	-0.101597	0.052880952	0.021614	0.014857694	0.0145756	0.067910356
rs11206517	G	T	G	T	0.0908334	0.003505959	0.033012	0.040850705	0.011479	0.04382929
rs11591147	T	G	T	G	-0.308882	0.034078498	0.017457	0.012280361	0.0156254	0.072386223
rs1169292	T	C	T	C	0.030447	0.027635358	0.310497	0.367997881	0.00444764	0.017850685
rs117310449	T	C	T	C	0.177991	0.007216714	0.011985	0.009449004	0.0189492	0.082477212
rs118147862	A	G	A	G	-0.354908	-0.098309521	0.045764	0.031585218	0.0101119	0.049599285
rs11854242	T	C	T	C	-0.0317694	-0.015282952	0.275074	0.280980117	0.00462128	0.018850116
rs12151108	A	G	A	G	-0.152836	-0.053785089	0.119677	0.103029552	0.00630319	0.026066146
rs12740374	T	G	T	G	-0.0961513	-0.001058135	0.221064	0.187389866	0.00493378	0.020836633
rs12804228	G	A	G	A	0.0522524	0.019096476	0.08472	0.103659231	0.00742254	0.029684795
rs12916	C	T	C	T	0.0580953	0.003566142	0.400341	0.426768993	0.00418643	0.017184443
rs1500188	G	A	G	A	-0.0240193	0.007622026	0.450404	0.462143077	0.00412981	0.017186762
rs1883711	C	G	C	G	0.108501	-0.059734891	0.031207	0.030224648	0.0120475	0.054725424
rs2326077	T	C	T	C	-0.027081	0.004951401	0.663229	0.689271336	0.00434692	0.017923773
rs247616	T	C	T	C	-0.0608862	0.009221904	0.324699	0.291815376	0.00438395	0.018390533
rs261290	C	T	C	T	-0.0759505	-0.034947318	0.654645	0.66303355	0.0043224	0.018095738
rs2737245	T	G	T	G	-0.0279349	-0.025341894	0.278602	0.252665743	0.00458436	0.019855313
rs2738447	C	A	C	A	0.0328659	-0.020384701	0.59318	0.587900117	0.00417665	0.017210902
rs34042070	G	C	G	C	0.0411867	0.021552761	0.186978	0.231657915	0.00528041	0.020731385
rs35633876	T	G	T	G	-0.0238608	-0.000271514	0.481858	0.448393117	0.00411923	0.017147813
rs3777411	T	C	T	C	-0.0483808	0.024374826	0.150735	0.193597764	0.00573293	0.02296701
rs41289512	G	C	G	C	0.0789205	-0.068471213	0.042305	0.033780466	0.0101341	0.046947475

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs4299376	T	G	T	G	-0.047141	0.025329959	0.676277	0.727725068	0.00439223	0.018334655
rs472495	T	G	T	G	0.0314252	-0.020457737	0.649121	0.643917345	0.0042923	0.017430675
rs4939883	C	T	C	T	0.0309854	-0.021054257	0.819142	0.83048607	0.00532421	0.022955927
rs61679753	A	T	A	T	-0.349415	0.021248036	0.030645	0.041089936	0.0118993	0.044662905
rs633695	G	A	G	A	0.0546603	0.007603835	0.292354	0.344073722	0.00452543	0.018538343
rs6601299	C	T	C	T	0.044935	0.028628115	0.899281	0.922337321	0.0068214	0.030894094
rs6602911	T	C	T	C	0.0245499	-0.019807401	0.360028	0.387981783	0.00427046	0.01892438
rs693	A	G	A	G	0.0769739	0.032868336	0.520889	0.408119057	0.00410273	0.017073034
rs72631343	G	C	G	C	-0.0429508	-0.007034122	0.129021	0.191870041	0.00611975	0.024796512
rs72843670	C	T	C	T	0.0352589	0.037593127	0.138368	0.184045824	0.00592019	0.02308284
rs72848251	A	G	A	G	0.0484938	0.024489348	0.194675	0.232249506	0.00531677	0.021607383
rs7534572	G	C	G	C	0.0558037	0.020953308	0.64747	0.699759296	0.00428598	0.018347343
rs77542162	G	A	G	A	0.149245	0.110878149	0.022666	0.013594549	0.0137929	0.079359285
rs77960347	G	A	G	A	0.134647	0.011710012	0.013234	0.011110344	0.0179189	0.076309816
rs9616847	T	A	T	A	0.0250082	-0.028541028	0.388272	0.414222017	0.00422751	0.017624786
rs964184	C	G	C	G	-0.0710628	-0.013030701	0.86726	0.83954438	0.00604505	0.023920044

Table S21. Harmonization data between RC and colorectal cancer ultimately used in replication MR analysis

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs10260606	C	G	C	G	0.0337973	0.0327467	0.182652	0.326234	0.0052964	0.0189409
rs111278137	A	G	A	G	-0.101597	0.105477	0.021614	0.0108736	0.0145756	0.0853446
rs11206517	G	T	G	T	0.0908334	-0.0425294	0.033012	0.0443505	0.011479	0.0421587
rs115478735	T	A	T	A	0.0594489	-0.00252097	0.183304	0.198598	0.00530499	0.0221789
rs11591147	T	G	T	G	-0.308882	0.0606488	0.017457	0.0361556	0.0156254	0.0482954
rs117310449	T	C	T	C	0.177991	0.0697088	0.011985	0.0134084	0.0189492	0.0757078
rs118147862	A	G	A	G	-0.354908	-0.0480156	0.045764	0.0291469	0.0101119	0.0514499
rs11854242	T	C	T	C	-0.0317694	0.0141689	0.275074	0.199212	0.00462128	0.0220177
rs12151108	A	G	A	G	-0.152836	-0.0142532	0.119677	0.101498	0.00630319	0.029602
rs12620918	C	T	C	T	0.0295835	0.025498	0.173985	0.18122	0.00542051	0.0228459
rs12740374	T	G	T	G	-0.0961513	-0.00553501	0.221064	0.214354	0.00493378	0.0215178
rs12804228	G	A	G	A	0.0522524	-0.00299766	0.08472	0.152994	0.00742254	0.0246544
rs12916	C	T	C	T	0.0580953	-0.00115325	0.400341	0.452939	0.00418643	0.017721
rs1500188	G	A	G	A	-0.0240193	0.0155421	0.450404	0.486837	0.00412981	0.0176371
rs1883711	C	G	C	G	0.108501	-0.0427237	0.031207	0.0619941	0.0120475	0.0369163
rs2326077	T	C	T	C	-0.027081	-0.00650455	0.663229	0.615108	0.00434692	0.018185
rs247616	T	C	T	C	-0.0608862	0.0199955	0.324699	0.278896	0.00438395	0.0196575
rs261290	C	T	C	T	-0.0759505	-0.00770176	0.654645	0.6194	0.0043224	0.0181843
rs2737245	T	G	T	G	-0.0279349	-0.0240908	0.278602	0.308439	0.00458436	0.0191373
rs2738447	C	A	C	A	0.0328659	-0.0037807	0.59318	0.606778	0.00417665	0.0180597
rs34042070	G	C	G	C	0.0411867	-0.00738492	0.186978	0.194307	0.00528041	0.022255
rs35633876	T	G	T	G	-0.0238608	-0.0323906	0.481858	0.565752	0.00411923	0.017859
rs3777411	T	C	T	C	-0.0483808	-0.0492827	0.150735	0.126091	0.00573293	0.0264876

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs41289512	G	C	G	C	0.0789205	-0.0478879	0.042305	0.0557253	0.0101341	0.0395888
rs4299376	T	G	T	G	-0.047141	-0.0171862	0.676277	0.78441	0.00439223	0.0214476
rs4665972	C	T	C	T	-0.0359412	0.0281306	0.604609	0.624423	0.00421805	0.0182769
rs4704834	G	A	G	A	0.0412619	-0.00477869	0.644028	0.67125	0.00427763	0.0188392
rs472495	T	G	T	G	0.0314252	-0.00573364	0.649121	0.575884	0.0042923	0.0179202
rs4939883	C	T	C	T	0.0309854	0.00463072	0.819142	0.823994	0.00532421	0.0230387
rs553427	T	C	T	C	0.0286973	-0.00597436	0.517037	0.559404	0.00410145	0.0177624
rs56325564	A	G	A	G	0.0303526	0.0226077	0.482691	0.458397	0.00413217	0.0177101
rs61679753	A	T	A	T	-0.349415	0.0657821	0.030645	0.0210509	0.0118993	0.0599058
rs633695	G	A	G	A	0.0546603	0.0156288	0.292354	0.305791	0.00452543	0.0191748
rs6601299	C	T	C	T	0.044935	0.0297192	0.899281	0.843411	0.0068214	0.0244949
rs6602911	T	C	T	C	0.0245499	-0.00361732	0.360028	0.363368	0.00427046	0.0185325
rs693	A	G	A	G	0.0769739	-0.00800436	0.520889	0.419252	0.00410273	0.0178789
rs72631343	G	C	G	C	-0.0429508	0.00566863	0.129021	0.14337	0.00611975	0.0253483
rs72694391	C	T	C	T	0.0226707	-0.0186202	0.482108	0.378291	0.00411579	0.0182112
rs72843670	C	T	C	T	0.0352589	0.0264916	0.138368	0.129403	0.00592019	0.0262647
rs7534572	G	C	G	C	0.0558037	-0.0125138	0.64747	0.736231	0.00428598	0.0200251
rs77542162	G	A	G	A	0.149245	-0.0665967	0.022666	0.00675429	0.0137929	0.107165
rs77960347	G	A	G	A	0.134647	0.0200639	0.013234	0.0072079	0.0179189	0.10149
rs9616847	T	A	T	A	0.0250082	0.00760812	0.388272	0.416487	0.00422751	0.0179086
rs964184	C	G	C	G	-0.0710628	0.0139401	0.86726	0.855576	0.00604505	0.0250016

Table S22. Harmonization data between RC and prostate cancer ultimately used in primary MR analysis

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs102275	C	T	C	T	-0.0453463	-7.00E-04	0.34979	0.3508	0.00428851	0.0084
rs10260606	C	G	C	G	0.0337973	-0.0077	0.182652	0.2006	0.0052964	0.0107
rs111278137	A	G	A	G	-0.101597	-0.0151	0.021614	0.015	0.0145756	0.0397
rs11206517	G	T	G	T	0.0908334	-0.0157	0.033012	0.0386	0.011479	0.021
rs115478735	T	A	T	A	0.0594489	0.0067	0.183304	0.2226	0.00530499	0.0098
rs11591147	T	G	T	G	-0.308882	-0.0561	0.017457	0.0191	0.0156254	0.0322
rs1169292	T	C	T	C	0.030447	0.0089	0.310497	0.3215	0.00444764	0.0086
rs117310449	T	C	T	C	0.177991	-9.00E-04	0.011985	0.0104	0.0189492	0.0427
rs118147862	A	G	A	G	-0.354908	0.0206	0.045764	0.039	0.0101119	0.0217
rs11854242	T	C	T	C	-0.0317694	0.0047	0.275074	0.2665	0.00462128	0.0096
rs12151108	A	G	A	G	-0.152836	0.0091	0.119677	0.1133	0.00630319	0.0131
rs12740374	T	G	T	G	-0.0961513	-0.0085	0.221064	0.2212	0.00493378	0.0097
rs12804228	G	A	G	A	0.0522524	0.023	0.08472	0.0976	0.00742254	0.0143
rs12916	C	T	C	T	0.0580953	0.0136	0.400341	0.4109	0.00418643	0.0081
rs1500188	G	A	G	A	-0.0240193	-0.0075	0.450404	0.448	0.00412981	0.008
rs2326077	T	C	T	C	-0.027081	-0.0022	0.663229	0.6521	0.00434692	0.0085
rs247616	T	C	T	C	-0.0608862	0.0024	0.324699	0.3154	0.00438395	0.0087
rs261290	C	T	C	T	-0.0759505	0.004	0.654645	0.6622	0.0043224	0.0087
rs34042070	G	C	G	C	0.0411867	0.0057	0.186978	0.2049	0.00528041	0.01
rs35633876	T	G	T	G	-0.0238608	-0.0042	0.481858	0.4985	0.00411923	0.008
rs3777411	T	C	T	C	-0.0483808	-0.0133	0.150735	0.1477	0.00573293	0.0112
rs41289512	G	C	G	C	0.0789205	-9.00E-04	0.042305	0.0446	0.0101341	0.0218
rs4299376	T	G	T	G	-0.047141	0.0116	0.676277	0.7004	0.00439223	0.0091

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs4665972	C	T	C	T	-0.0359412	-0.0164	0.604609	0.6019	0.00421805	0.0082
rs4704834	G	A	G	A	0.0412619	0.005	0.644028	0.6438	0.00427763	0.0087
rs4939883	C	T	C	T	0.0309854	0.0156	0.819142	0.825	0.00532421	0.0104
rs532754706	G	A	G	A	-0.0955271	-0.0182	0.023055	0.0148	0.0161499	0.045
rs56325564	A	G	A	G	0.0303526	0.0047	0.482691	0.4648	0.00413217	0.0081
rs61679753	A	T	A	T	-0.349415	-0.0124	0.030645	0.0363	0.0118993	0.0225
rs633695	G	A	G	A	0.0546603	0.0094	0.292354	0.2934	0.00452543	0.0089
rs6601299	C	T	C	T	0.044935	-0.0033	0.899281	0.896	0.0068214	0.0132
rs6602911	T	C	T	C	0.0245499	0.0092	0.360028	0.3723	0.00427046	0.0091
rs693	A	G	A	G	0.0769739	-0.0021	0.520889	0.4909	0.00410273	0.0082
rs72631343	G	C	G	C	-0.0429508	-0.025	0.129021	0.1416	0.00611975	0.0121
rs72694391	C	T	C	T	0.0226707	0.0013	0.482108	0.4648	0.00411579	0.0085
rs72843670	C	T	C	T	0.0352589	8.00E-04	0.138368	0.1439	0.00592019	0.0113
rs77542162	G	A	G	A	0.149245	0.0124	0.022666	0.0169	0.0137929	0.0328
rs77960347	G	A	G	A	0.134647	-0.0071	0.013234	0.0129	0.0179189	0.0371
rs9616847	T	A	T	A	0.0250082	0.0074	0.388272	0.3871	0.00422751	0.0083
rs964184	C	G	C	G	-0.0710628	0.0133	0.86726	0.8598	0.00604505	0.0117

Table S23. Harmonization data between RC and prostate cancer ultimately used in replication MR analysis

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs102275	C	T	C	T	-0.0453463	-0.0236847	0.34979	0.41743	0.00428851	0.0135683
rs10260606	C	G	C	G	0.0337973	0.0242294	0.182652	0.325408	0.0052964	0.0143849
rs111278137	A	G	A	G	-0.101597	-0.0260436	0.021614	0.0109549	0.0145756	0.0646075
rs11206517	G	T	G	T	0.0908334	0.000528875	0.033012	0.0449405	0.011479	0.0321002
rs115478735	T	A	T	A	0.0594489	0.0200703	0.183304	0.199036	0.00530499	0.016811
rs11591147	T	G	T	G	-0.308882	0.0407007	0.017457	0.035834	0.0156254	0.0368494
rs117310449	T	C	T	C	0.177991	0.00143249	0.011985	0.0137158	0.0189492	0.0569681
rs118147862	A	G	A	G	-0.354908	0.0127134	0.045764	0.0297081	0.0101119	0.038818
rs11854242	T	C	T	C	-0.0317694	0.00687192	0.275074	0.200096	0.00462128	0.0166707
rs12151108	A	G	A	G	-0.152836	0.0236899	0.119677	0.101327	0.00630319	0.0223909
rs12740374	T	G	T	G	-0.0961513	-0.00241236	0.221064	0.214075	0.00493378	0.0163607
rs12804228	G	A	G	A	0.0522524	0.0255077	0.08472	0.153087	0.00742254	0.0186057
rs12916	C	T	C	T	0.0580953	0.0213967	0.400341	0.454088	0.00418643	0.0134178
rs1500188	G	A	G	A	-0.0240193	0.010675	0.450404	0.488101	0.00412981	0.0133709
rs1883711	C	G	C	G	0.108501	0.00265501	0.031207	0.0625681	0.0120475	0.0277546
rs2326077	T	C	T	C	-0.027081	-0.0180742	0.663229	0.615376	0.00434692	0.013712
rs247616	T	C	T	C	-0.0608862	0.00436366	0.324699	0.278572	0.00438395	0.0149143
rs2737245	T	G	T	G	-0.0279349	-0.00855752	0.278602	0.308512	0.00458436	0.014426
rs2738447	C	A	C	A	0.0328659	-0.00112287	0.59318	0.606905	0.00417665	0.0136822
rs34042070	G	C	G	C	0.0411867	-0.0201767	0.186978	0.195169	0.00528041	0.0168071
rs35633876	T	G	T	G	-0.0238608	0.0118806	0.481858	0.565681	0.00411923	0.0135618
rs3777411	T	C	T	C	-0.0483808	-0.000772704	0.150735	0.127059	0.00573293	0.0200373
rs41289512	G	C	G	C	0.0789205	-0.0446144	0.042305	0.0551528	0.0101341	0.0301503

SNP	Effect_allele. exposure	Other_allele. exposure	Effect_allele. outcome	Other_allele. outcome	Beta. exposure	Beta. outcome	Eaf. exposure	Eaf. outcome	Se. exposure	Se. outcome
rs4299376	T	G	T	G	-0.047141	0.0236918	0.676277	0.783693	0.00439223	0.0162036
rs4665972	C	T	C	T	-0.0359412	-0.010326	0.604609	0.622734	0.00421805	0.0138334
rs4704834	G	A	G	A	0.0412619	-0.0192897	0.644028	0.672151	0.00427763	0.0142865
rs472495	T	G	T	G	0.0314252	-0.00133255	0.649121	0.576566	0.0042923	0.0135843
rs4939883	C	T	C	T	0.0309854	0.0319413	0.819142	0.822991	0.00532421	0.0173655
rs553427	T	C	T	C	0.0286973	0.0041278	0.517037	0.558896	0.00410145	0.0134722
rs56325564	A	G	A	G	0.0303526	-0.0111998	0.482691	0.458218	0.00413217	0.0133984
rs61679753	A	T	A	T	-0.349415	0.0746404	0.030645	0.0212603	0.0118993	0.0452809
rs633695	G	A	G	A	0.0546603	0.00941731	0.292354	0.305979	0.00452543	0.0145415
rs653178	T	C	T	C	0.0247731	0.0196173	0.516036	0.585045	0.00410821	0.013602
rs6601299	C	T	C	T	0.044935	0.00660776	0.899281	0.844093	0.0068214	0.0185458
rs6602911	T	C	T	C	0.0245499	0.00248267	0.360028	0.364276	0.00427046	0.0140354
rs693	A	G	A	G	0.0769739	0.0163857	0.520889	0.420977	0.00410273	0.0135584
rs72631343	G	C	G	C	-0.0429508	-0.00622256	0.129021	0.142373	0.00611975	0.0192585
rs72694391	C	T	C	T	0.0226707	-0.00916622	0.482108	0.378467	0.00411579	0.0138345
rs72843670	C	T	C	T	0.0352589	0.0119594	0.138368	0.130262	0.00592019	0.0199063
rs7534572	G	C	G	C	0.0558037	-0.027486	0.64747	0.735832	0.00428598	0.0151675
rs77542162	G	A	G	A	0.149245	-0.0362712	0.022666	0.0068903	0.0137929	0.0801722
rs77960347	G	A	G	A	0.134647	-0.0516974	0.013234	0.00713504	0.0179189	0.0774559
rs9616847	T	A	T	A	0.0250082	-0.0239561	0.388272	0.416946	0.00422751	0.0135659
rs964184	C	G	C	G	-0.0710628	0.00383889	0.86726	0.855192	0.00604505	0.0189881

Table S24. The results of primary analysis in univariate MR analysis

Exposure	Outcome	Methods	Number of SNPs	<i>P</i> value	OR (95% CI)	Heterogeneity			Pleiotropy			Global Test <i>P</i> value	Power
						Q	Q_df	Q_P	Egger intercept	SE	<i>P</i> value		
Remnant cholesterol	Breast cancer	Inverse variance weighted	38	9.51E-04	1.08 (1.03-1.12)	37.08	37	0.465	0.004	0.004	0.094	0.498	0.95
		Maximum likelihood	38	8.94E-04	1.08 (1.03-1.12)								
		MR Egger	38	5.22E-01	1.02 (0.95-1.10)								
		Weighted Median	38	4.41E-02	1.07 (1.00-1.14)								
		MR-PRESSO	38	2.12E-03	1.08 (1.03-1.12)								
		MR-Raps	38	8.25E-04	1.08 (1.03-1.13)								
Remnant cholesterol	Lung cancer	Inverse variance weighted	39	4.55E-01	0.96 (0.86-1.07)	27.17	38	0.904	0.005	0.006	0.356	0.907	0.12
		Maximum likelihood	39	4.63E-01	0.96 (0.86-1.07)								
		MR Egger	39	2.39E-01	0.89 (0.74-1.07)								
		Weighted Median	39	3.74E-01	0.93 (0.78-1.10)								
		MR-PRESSO	39	3.83E-01	0.96 (0.87-1.05)								

[illegible]

Exposure	Outcome	Methods	Number of SNPs	<i>P</i> value	OR (95% CI)	Heterogeneity			Pleiotropy			Global Test <i>P</i> value	Power
						Q	Q_df	Q_P	Egger intercept	SE	<i>P</i> value		
		MR-Raps	40	1.56E-01	(0.99-1.09) 1.04 (0.99-1.09)								

[illegible]

Exposure	Outcome	Methods	Number of SNPs	<i>P</i> value	OR (95% CI)	Heterogeneity			Pleiotropy			Global Test <i>P</i> value
						Q	Q_df	Q_P	Egger intercept	SE	<i>P</i> value	
		MR-Raps	44	3.96E-01	(0.90-1.06) 0.96 (0.89-1.05)							

[illegible]

Exposure	Outcome	Methods	Number of SNPs	<i>P</i> value	OR (95% CI)	Heterogeneity			Pleiotropy			Global Test <i>P</i> value
						Q	Q_df	Q_P	Egger intercept	SE	<i>P</i> value	
		MR-Raps	120	6.99E-01	(0.99-1.01) 1.00 (0.99-1.01)							

Table S27. Multivariate MR analysis effect estimates of remnant cholesterol on 4 site-specific cancer adjusted for each confounder

Outcome	Adjustment	Number of SNPs	OR (95%CI)	P value
Breast cancer	TC	40	0.94 (0.83-1.06)	0.313
	LDL-C	39	1.02 (0.85-1.23)	0.814
	HDL-C	25	1.05 (0.98-1.12)	0.187
	TG	37	1.03 (0.97-1.10)	0.283
	TC+LDL-C+HDL-C+TG	28	1.03 (0.84-1.25)	0.797
	Smoking initiation	43	1.04 (0.97-1.11)	0.304
	Alcoholic drinks per week	43	1.02 (0.96-1.09)	0.525
	Body mass index	17	1.04 (0.95-1.14)	0.376
	Type 2 diabetes	24	1.06 (0.95-1.19)	0.308
Lung cancer	TC	39	1.20 (0.89-1.61)	0.240
	LDL-C	36	1.28 (0.88-1.86)	0.204
	HDL-C	24	1.07 (0.89-1.29)	0.445
	TG	35	1.07 (0.89-1.28)	0.466
	TC+LDL-C+HDL-C+TG	28	1.34 (0.88-2.03)	0.173
	Smoking initiation	40	1.10 (0.96-1.28)	0.173
	Alcoholic drinks per week	40	1.11 (0.96-1.28)	0.175
	Body mass index	16	1.09 (0.91-1.29)	0.361
	Type 2 diabetes	25	1.13 (0.93-1.37)	0.230
Colorectal cancer	TC	41	0.91 (0.68-1.22)	0.529
	LDL-C	40	1.18 (0.81-1.70)	0.389
	HDL-C	24	1.18 (0.98-1.42)	0.075
	TG	35	0.93 (0.79-1.10)	0.394
	TC+LDL-C+HDL-C+TG	29	0.89 (0.60-1.32)	0.563
	Smoking initiation	43	1.09 (0.94-1.26)	0.262

Outcome	Adjustment	Number of SNPs	OR (95%CI)	P value
Prostate cancer	Alcoholic drinks per week	45	1.10 (0.94-1.29)	0.244
	Body mass index	16	1.03 (0.86-1.25)	0.733
	Type 2 diabetes	25	1.26 (1.05-1.51)	0.014
	TC	41	0.88 (0.73-1.06)	0.183
	LDL-C	41	0.91 (0.71-1.16)	0.457
	HDL-C	26	1.02 (0.94-1.11)	0.614
	TG	37	1.04 (0.97-1.11)	0.283
	TC+LDL-C+HDL-C+TG	29	1.05 (0.82-1.35)	0.693
	Smoking initiation	45	1.05 (0.97-1.13)	0.237
	Alcoholic drinks per week	45	1.06 (0.96-1.17)	0.247
	Body mass index	17	1.09 (0.98-1.21)	0.103
	Type 2 diabetes	24	1.10 (0.99-1.22)	0.093

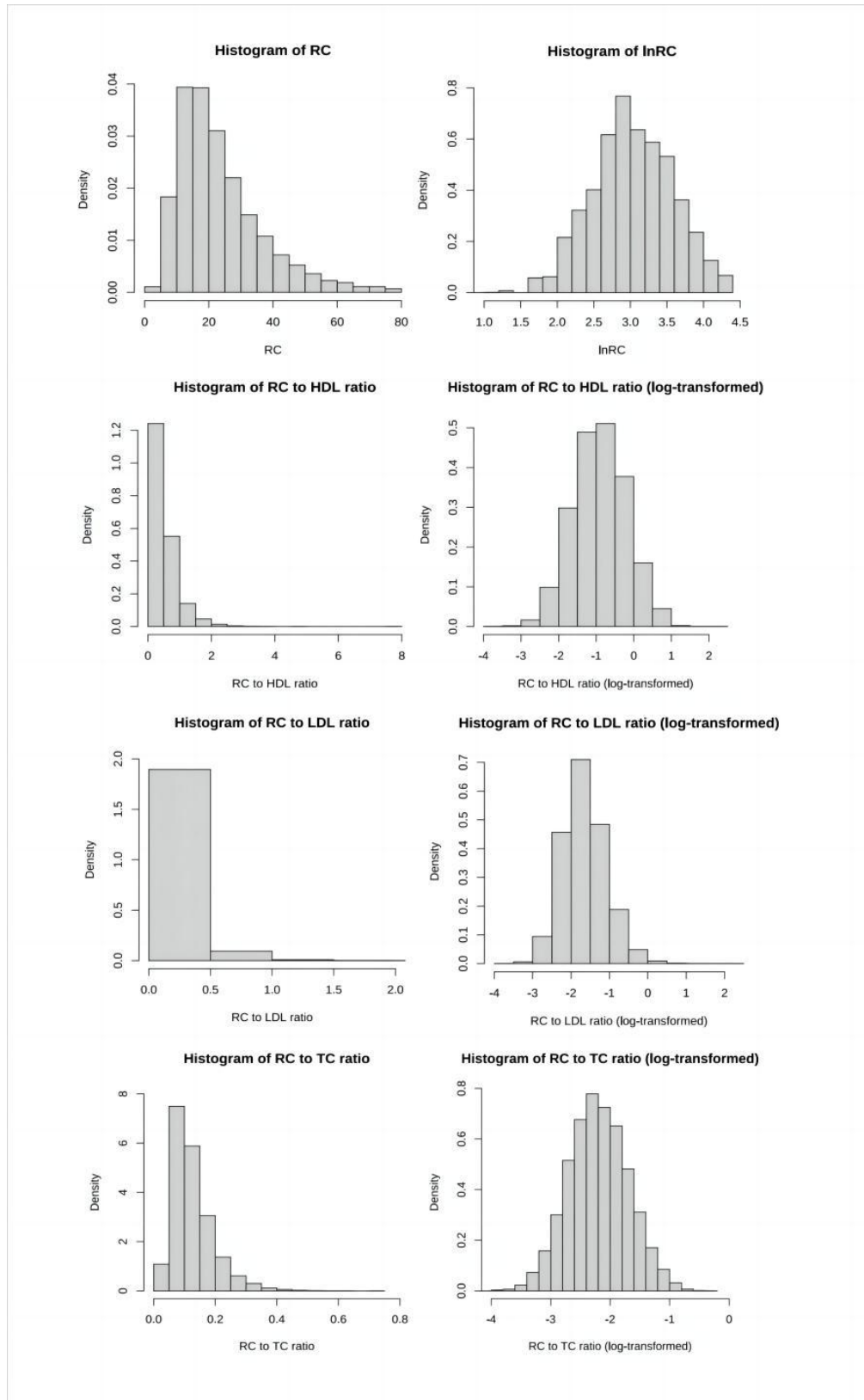


Fig.S1 Histogram of RC, RC/HDL, RC/LDL and RC/TC

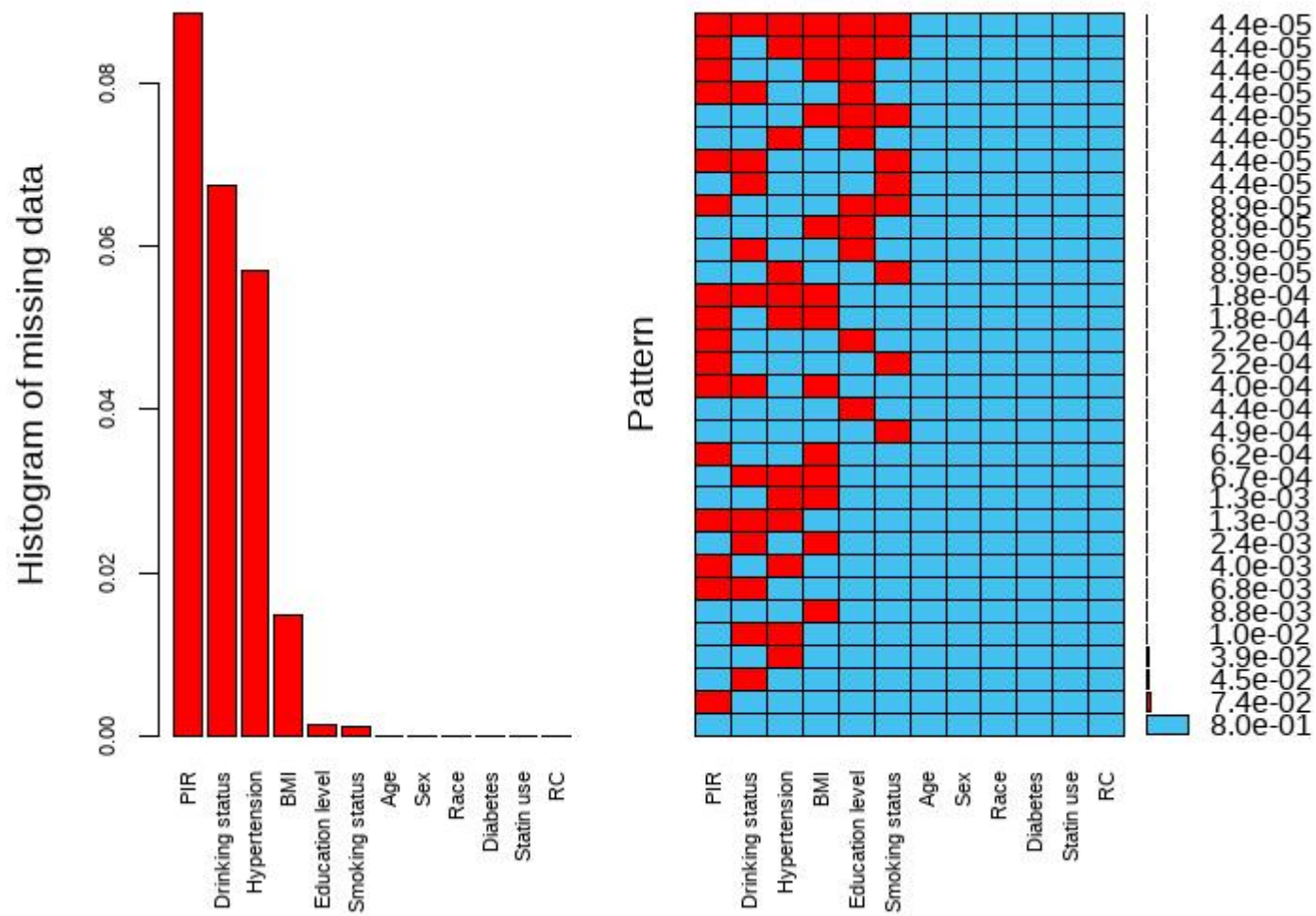


Fig.S2 A visual representation of the missing data distribution for covariables

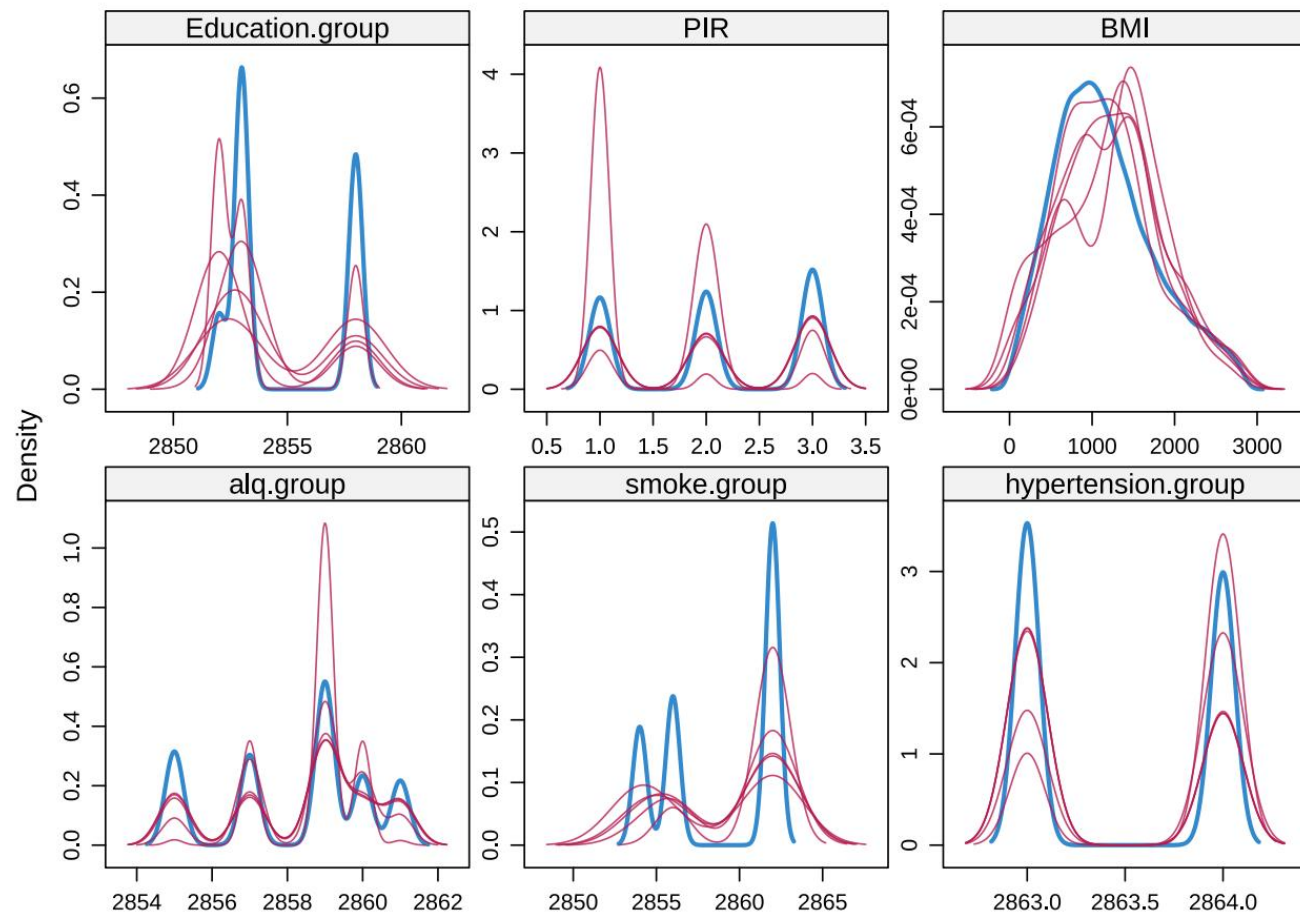


Fig.S3 The distribution of raw data and the corresponding interpolated data

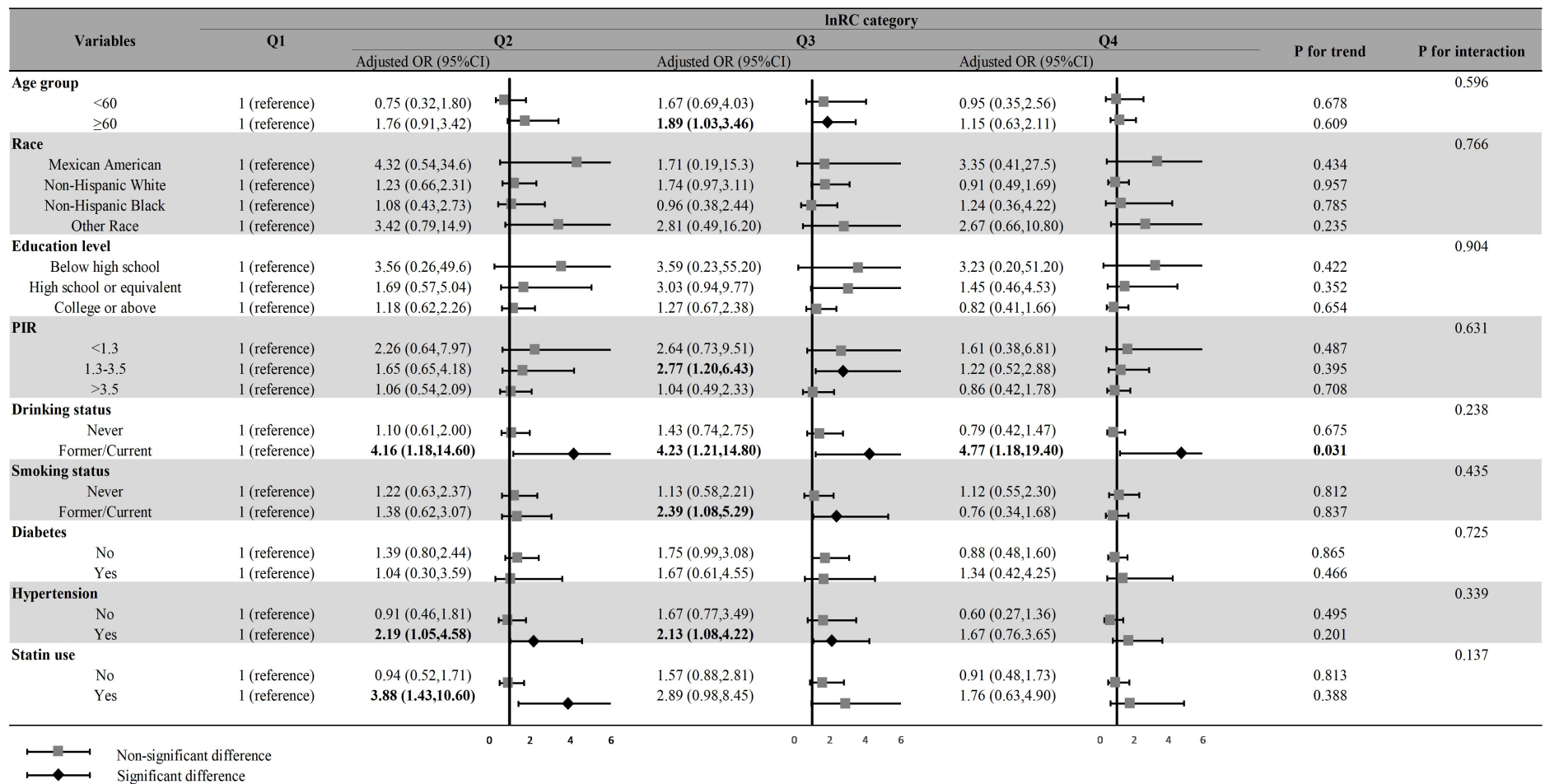


Fig.S4 Forest plot for subgroup analysis

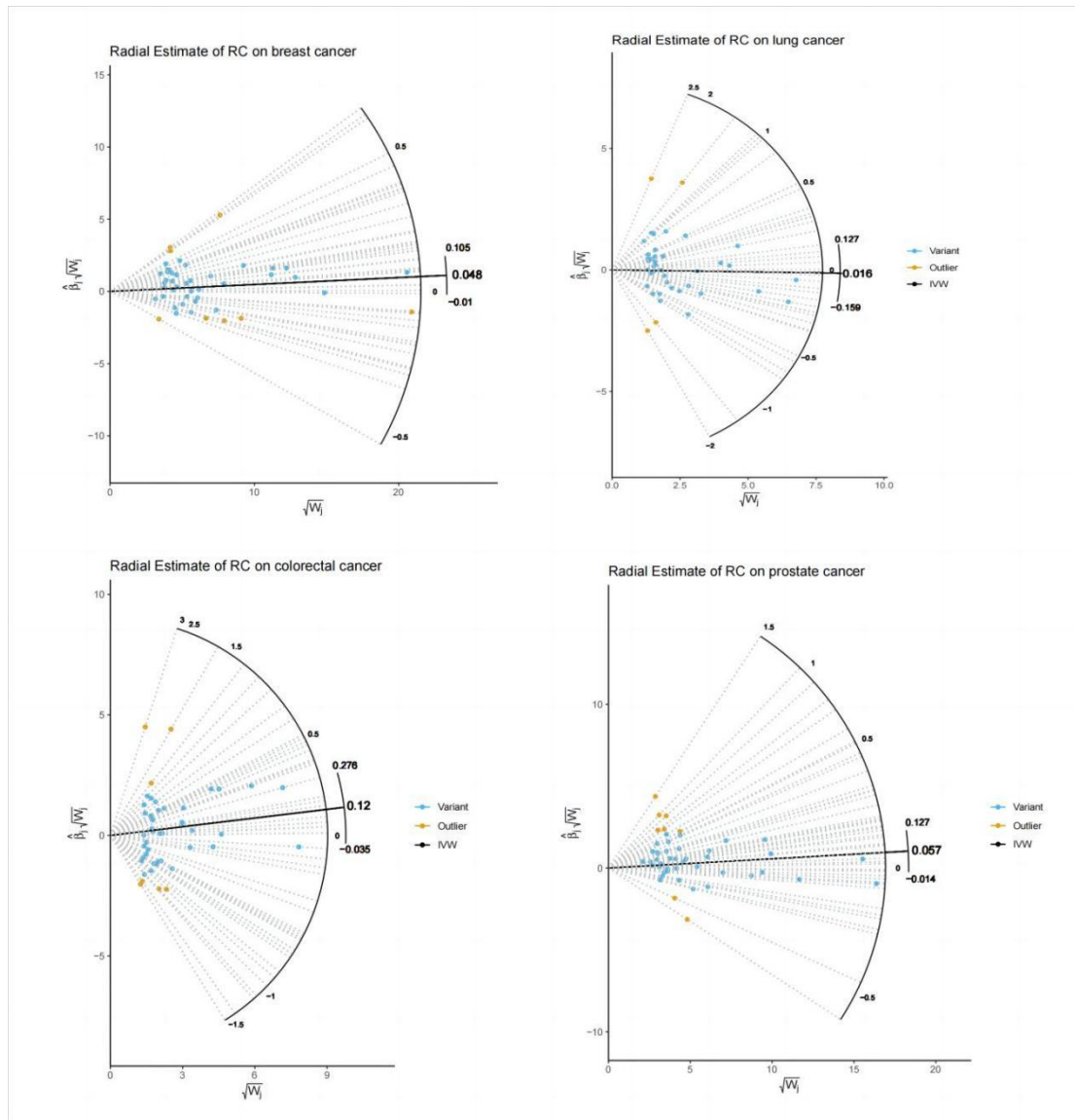


Fig.S5 Radial estimates of RC on 4 site-specific cancers in primary analysis

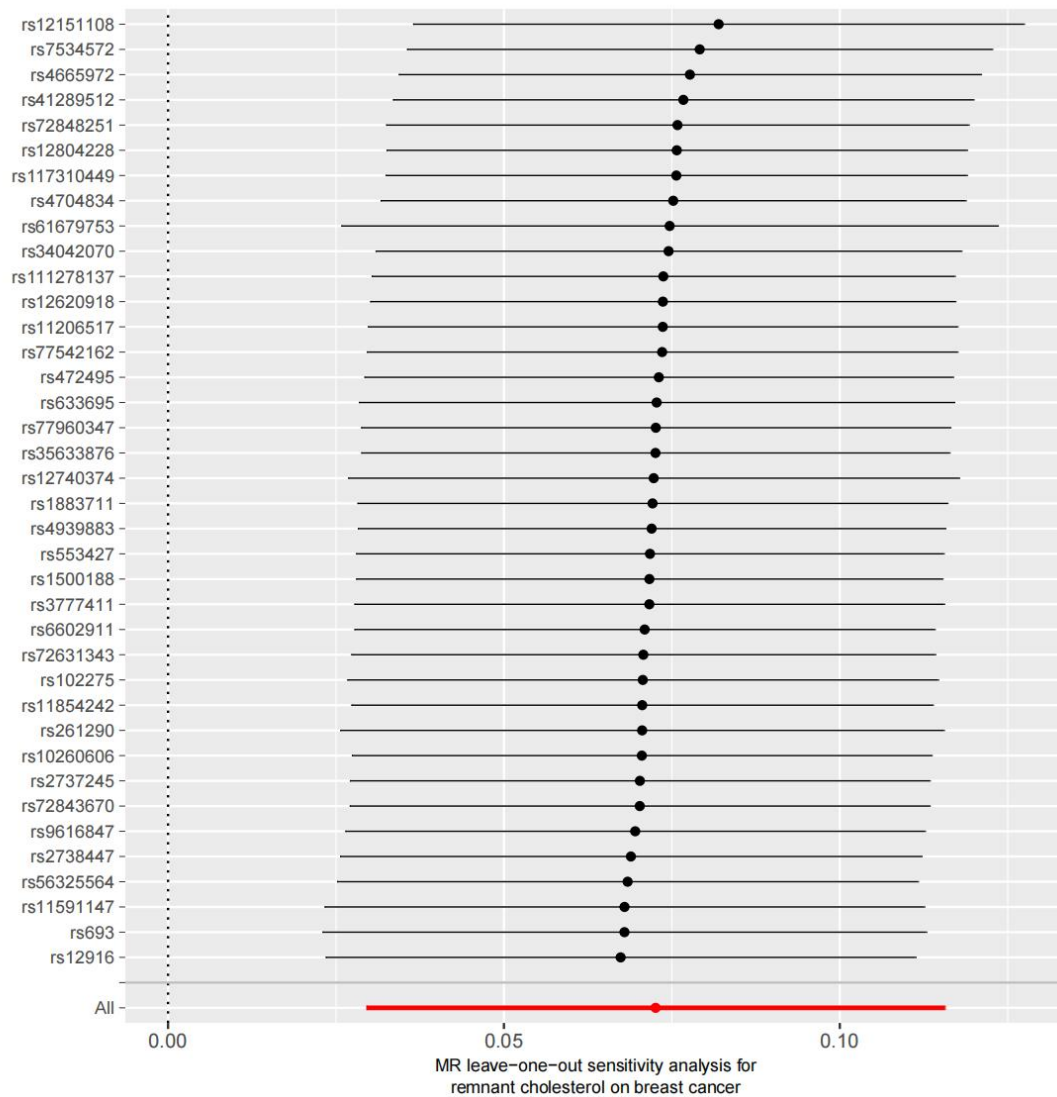


Fig.S6 Leave-one-out sensitivity analysis for remnant cholesterol on breast cancer

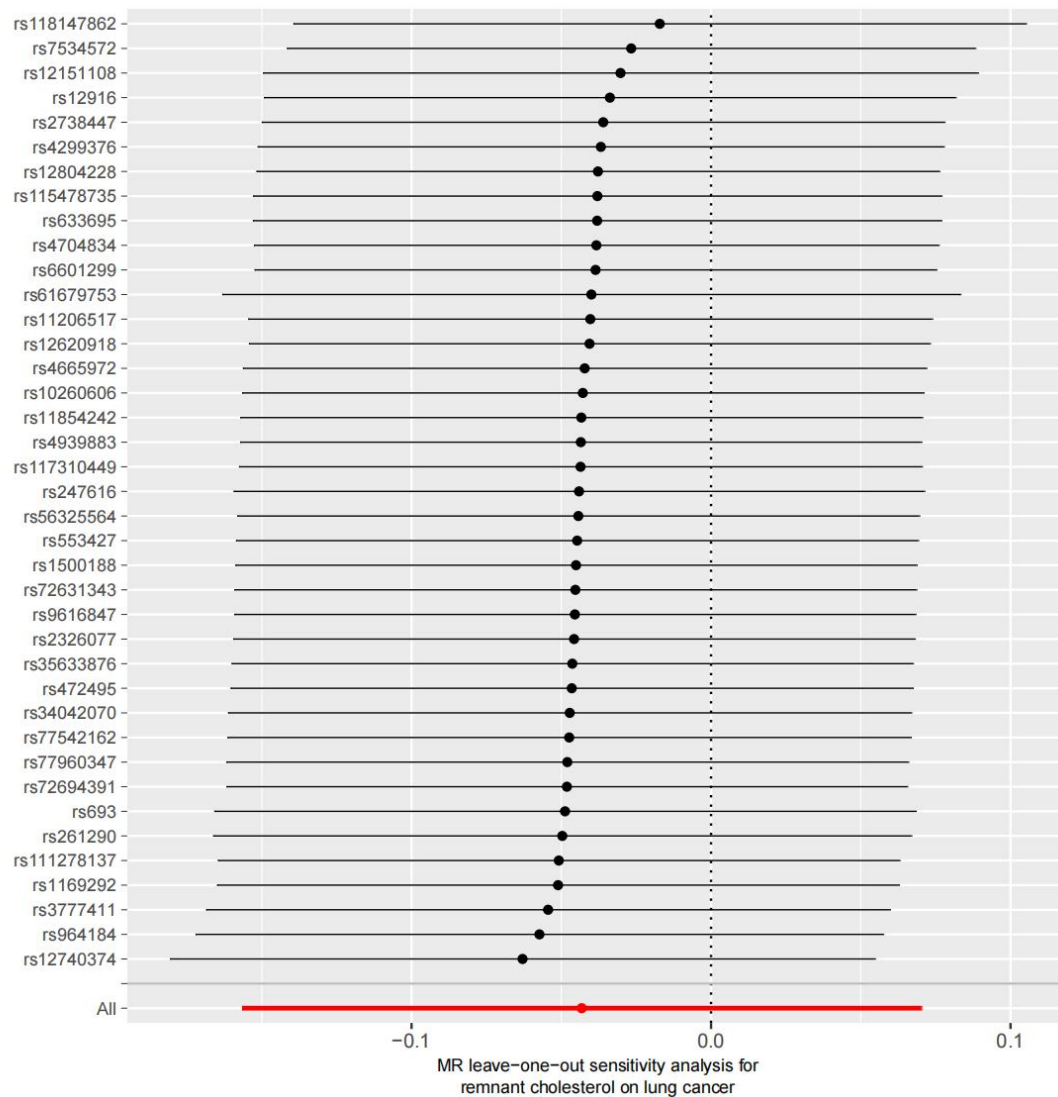


Fig.S7 Leave-one-out sensitivity analysis for remnant cholesterol on lung cancer

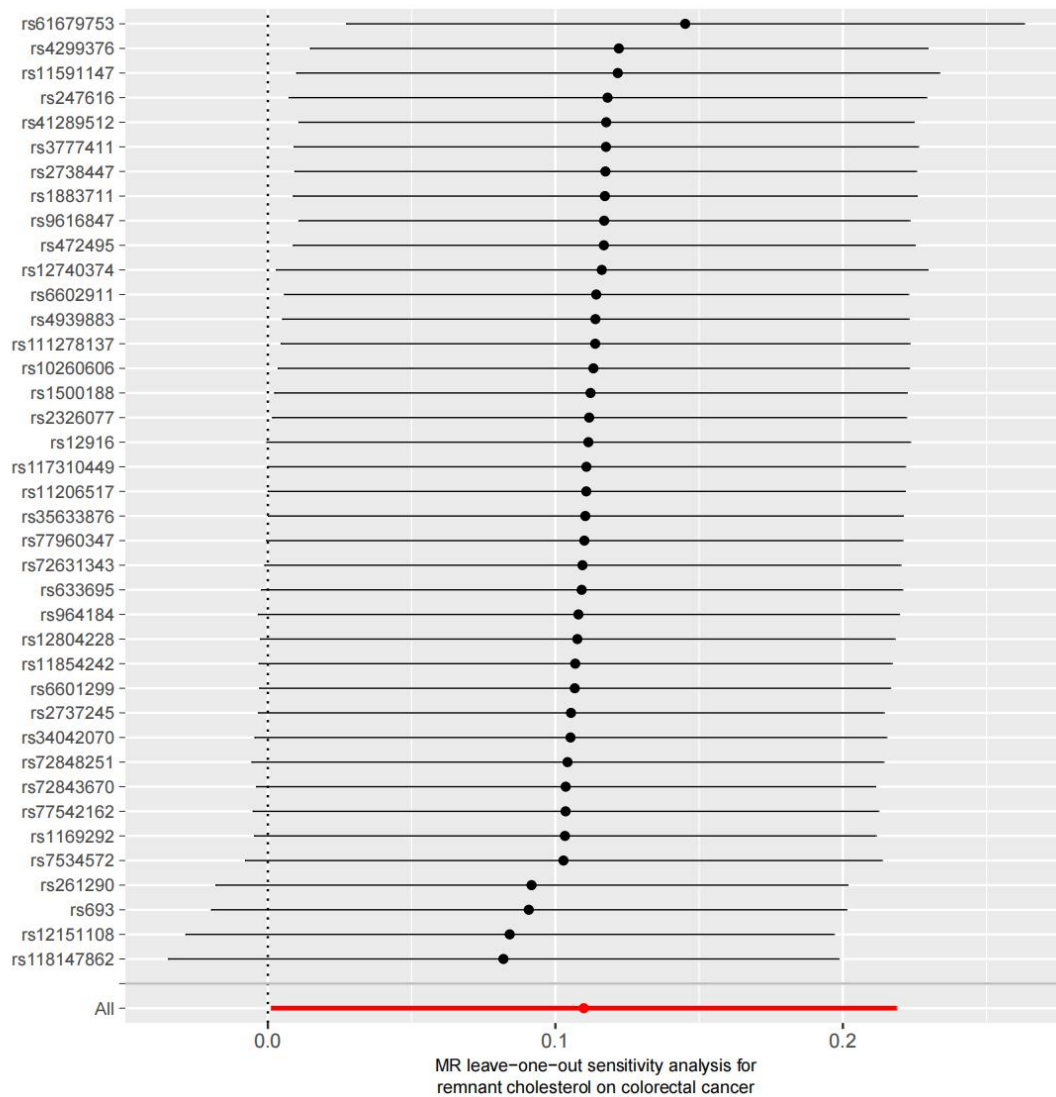


Fig.S8 Leave-one-out sensitivity analysis for remnant cholesterol on colorectal cancer

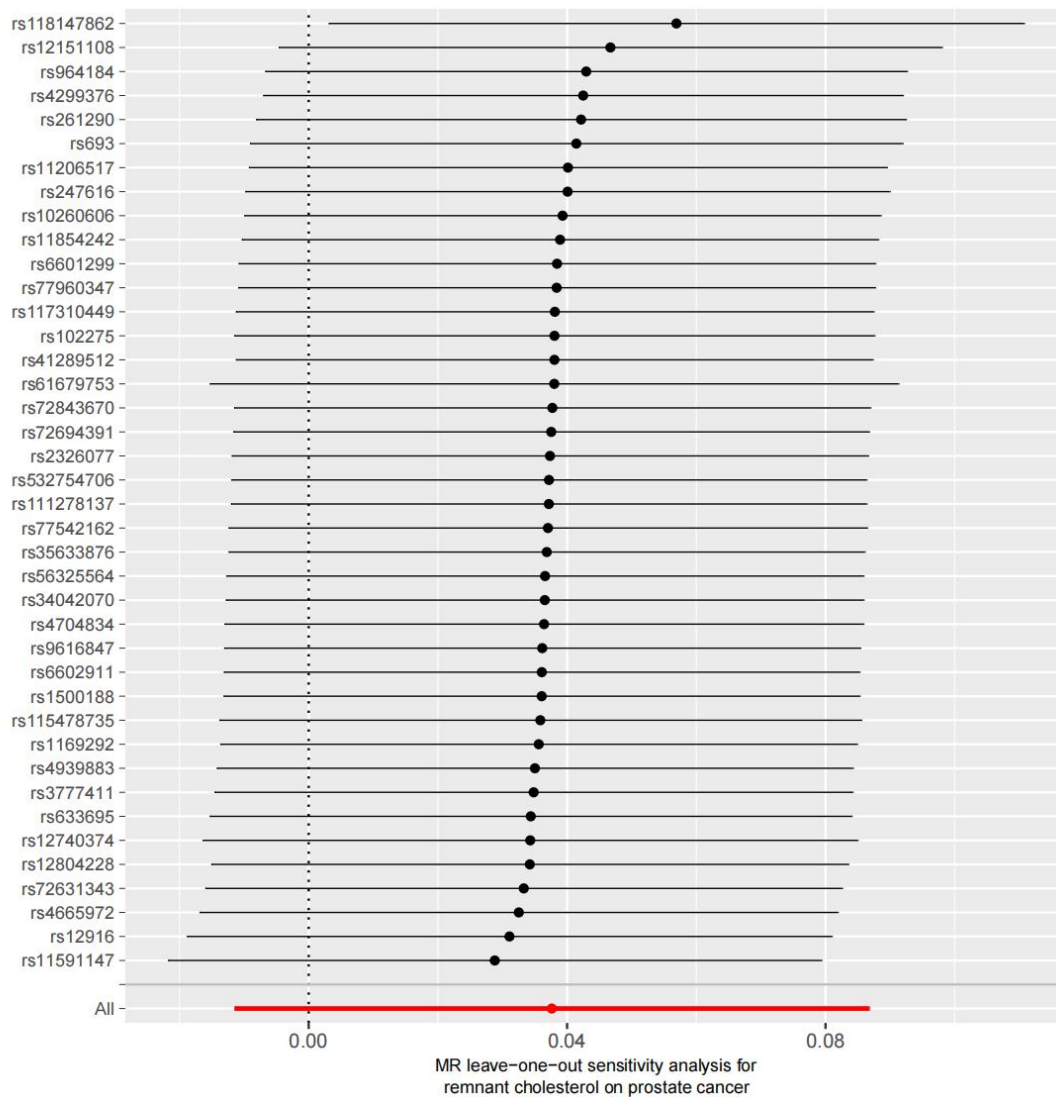


Fig.S9 Leave-one-out sensitivity analysis for remnant cholesterol on prostate cancer.

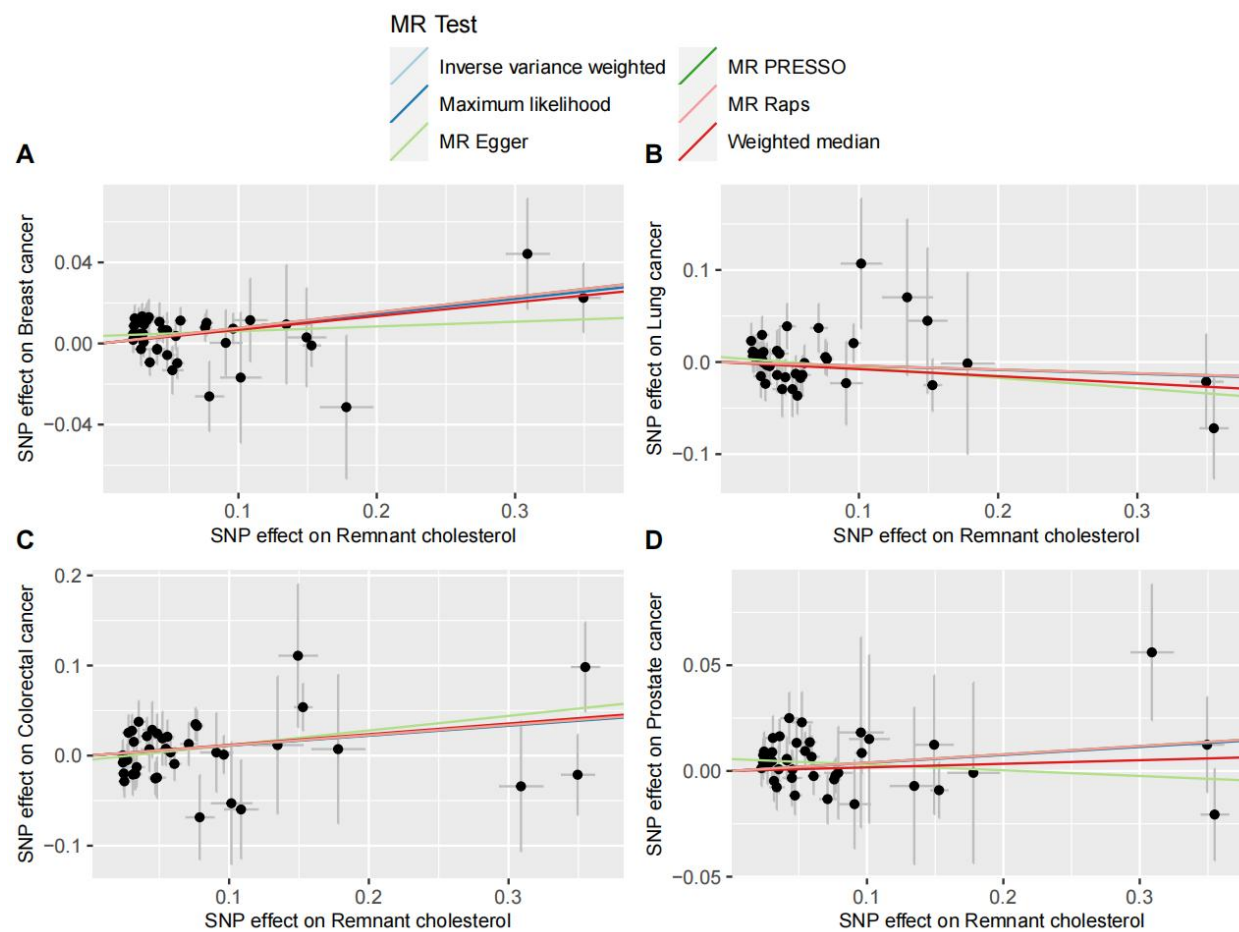


Fig.S10 Scatter plots of RC on 4 site-specific cancers in primary analysis. **A.** breast cancer. **B.** lung cancer. **C.** colorectal cancer. **D.** prostate cancer.

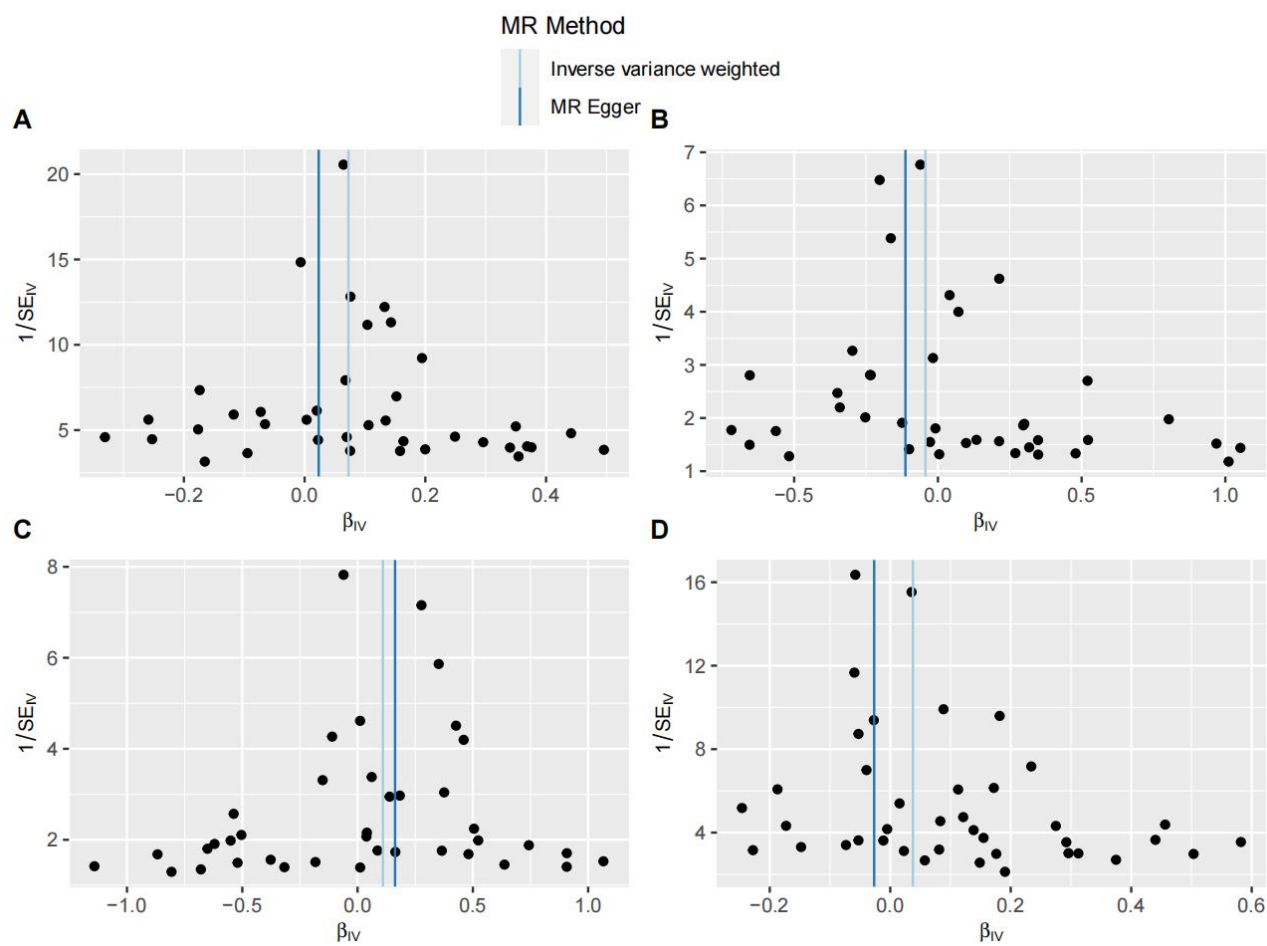


Fig.S11 Funnel plots of RC on 4 site-specific cancers in primary analysis. **A.** breast cancer. **B.** lung cancer. **C.** colorectal cancer. **D.** prostate cancer.