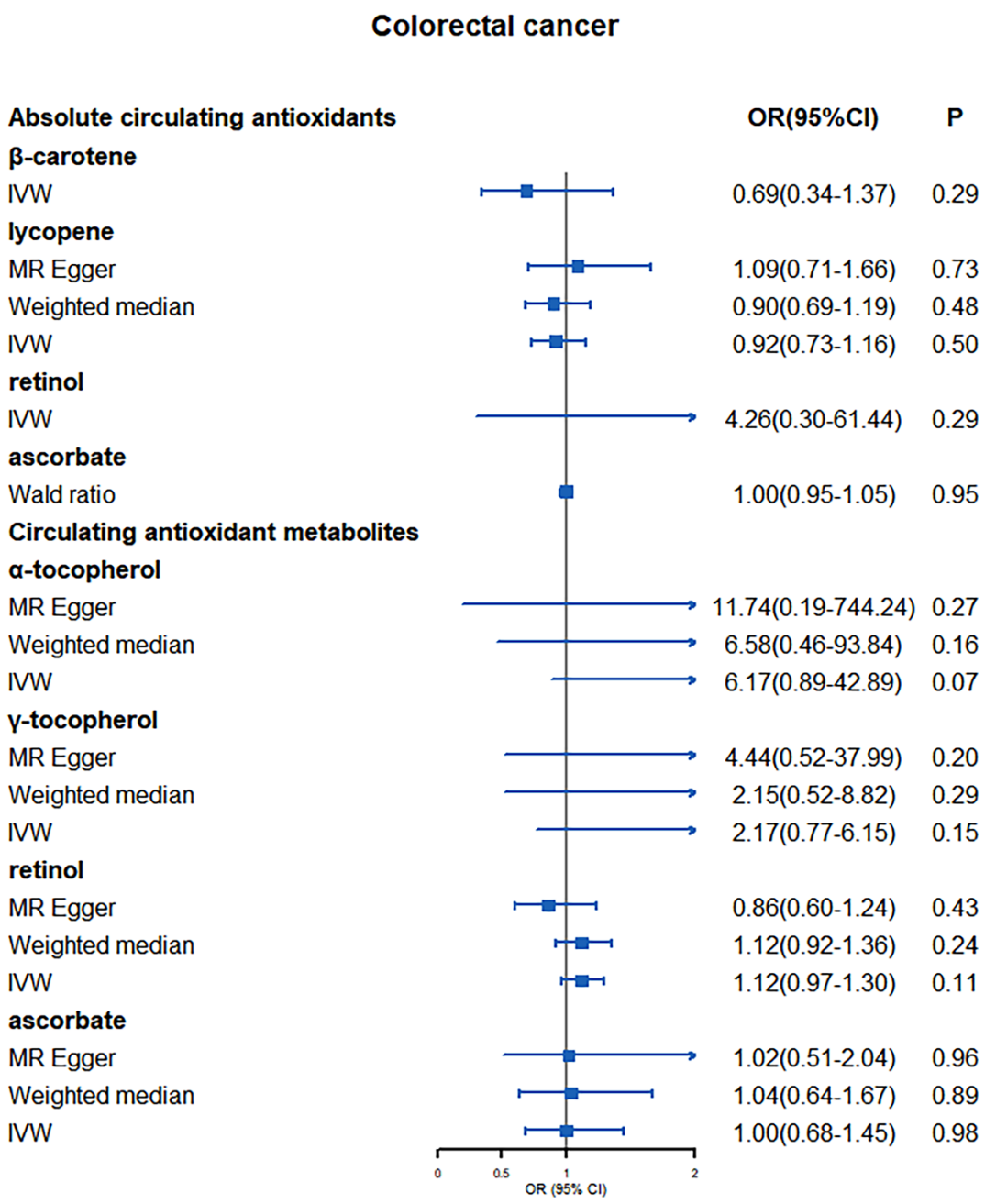
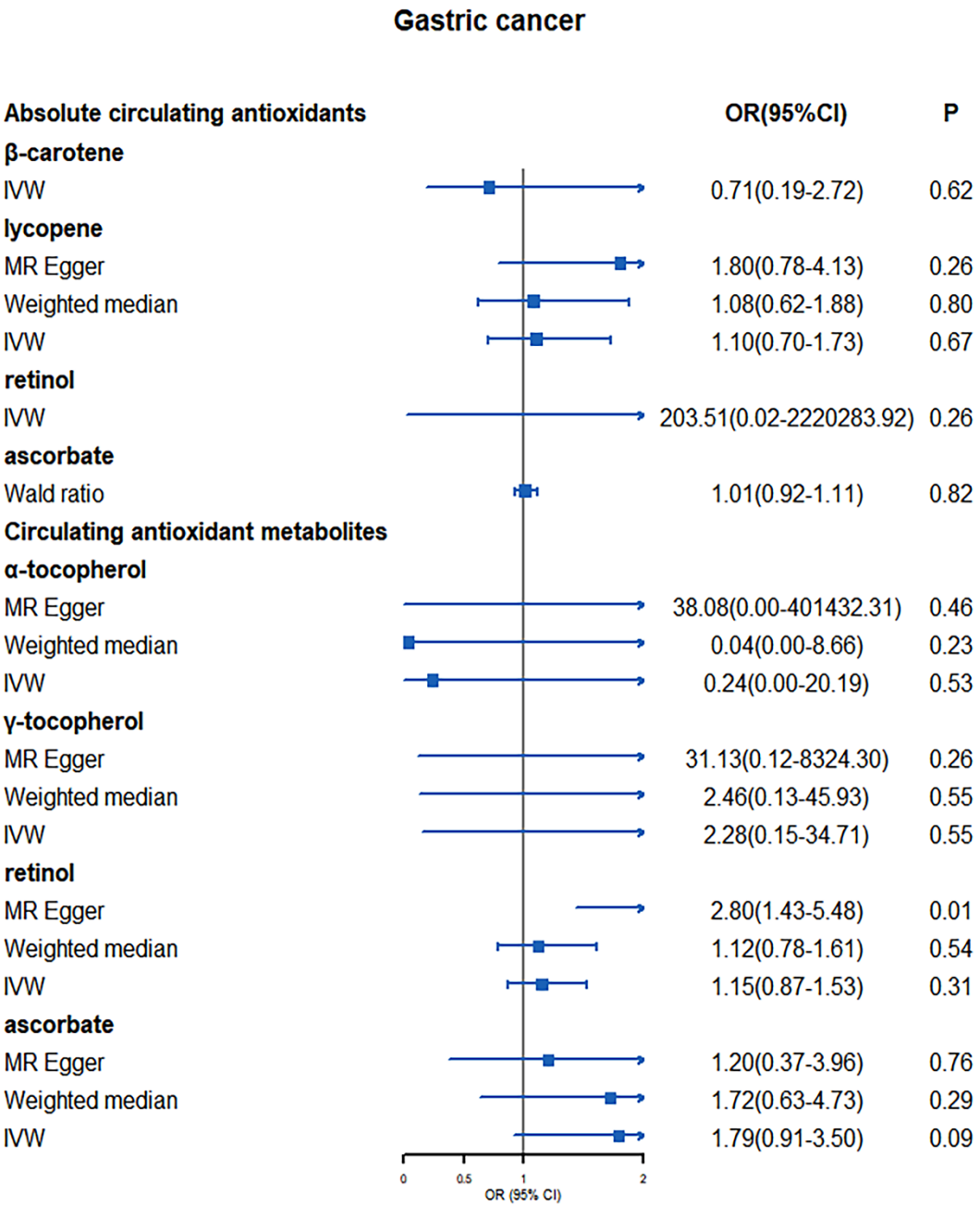
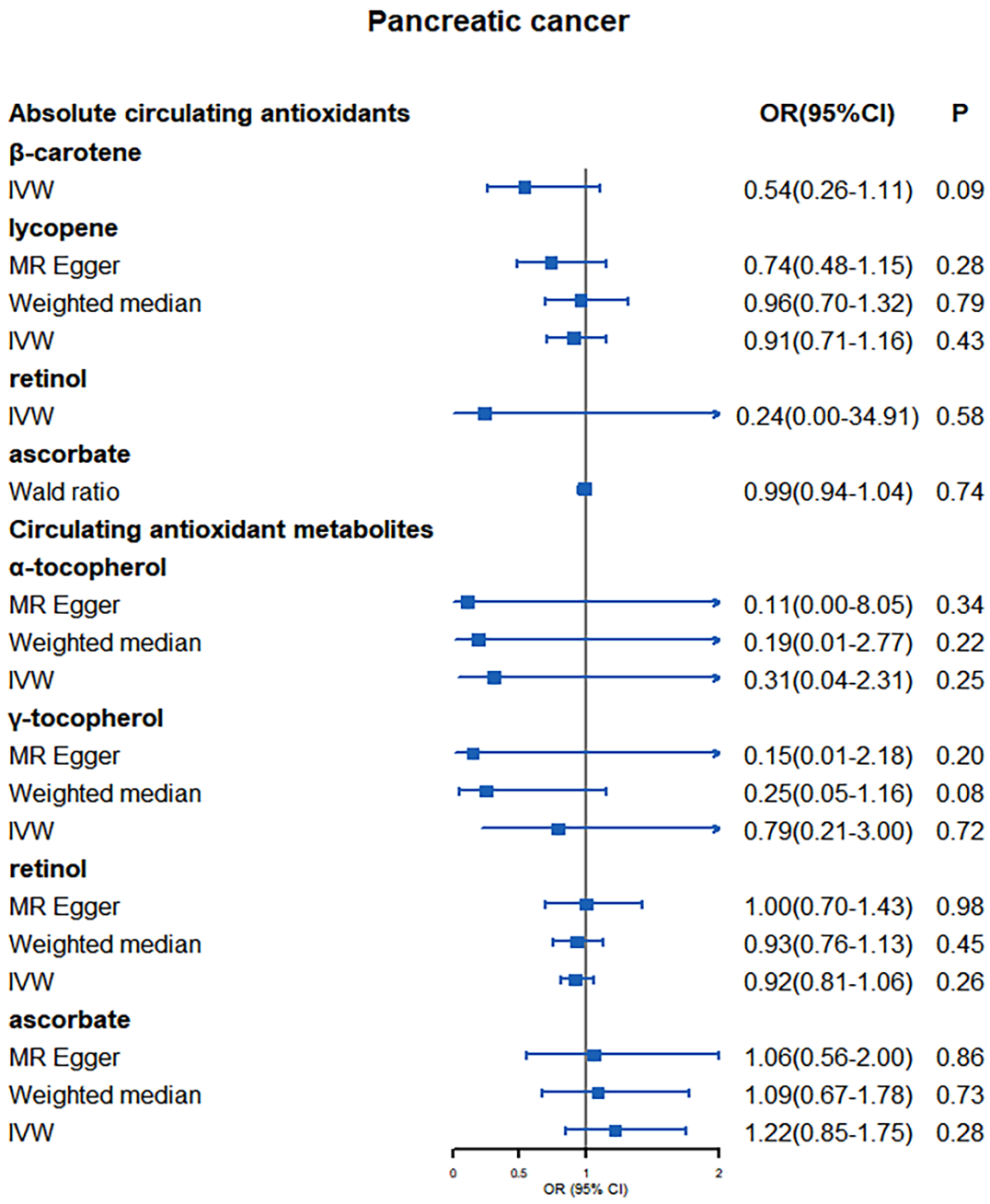
**Supplementary Figure S1. Causal association between circulating antioxidants with colorectal cancer.**



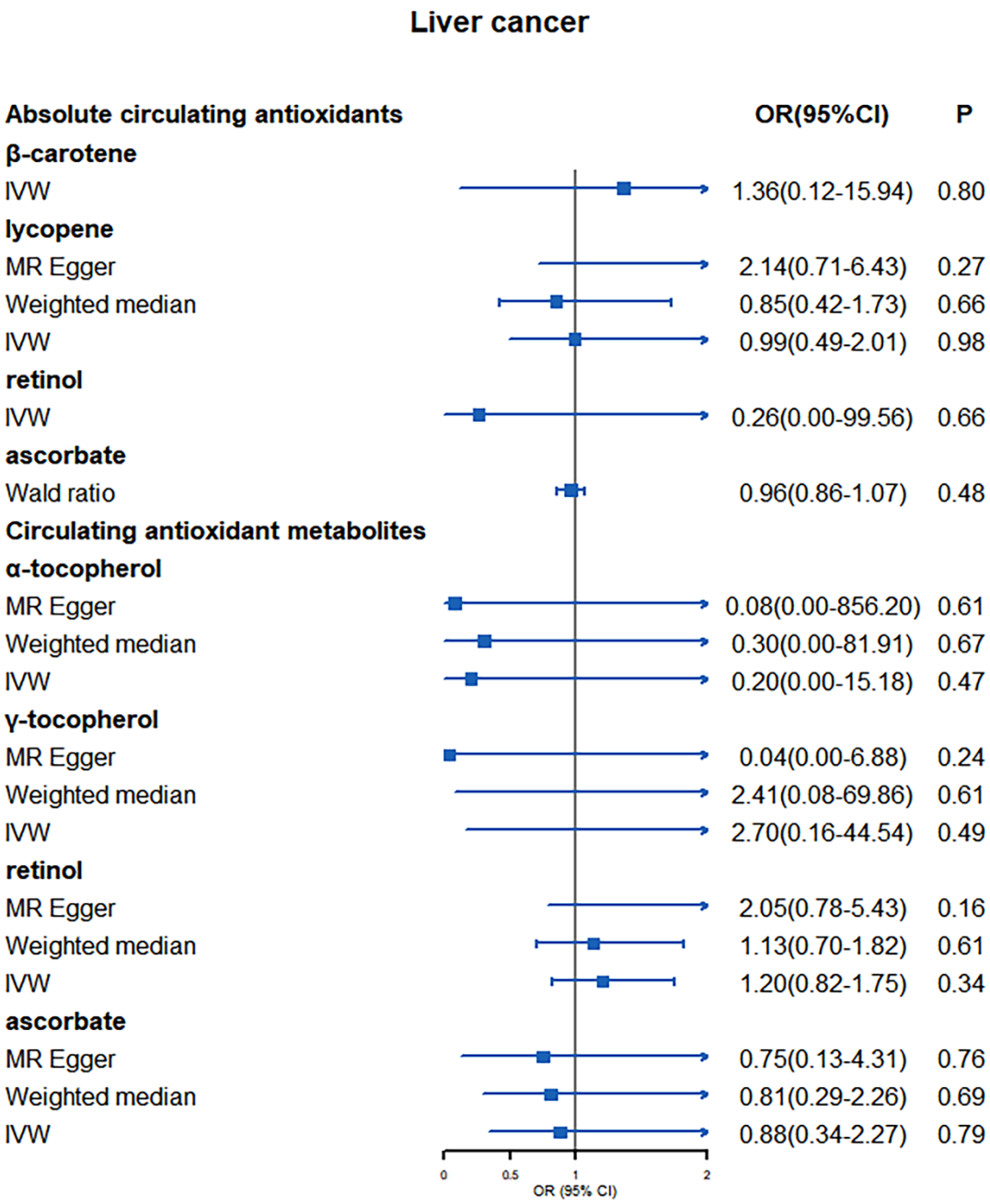
**Supplementary Figure S2. Causal association between circulating antioxidants with gastric cancer.**



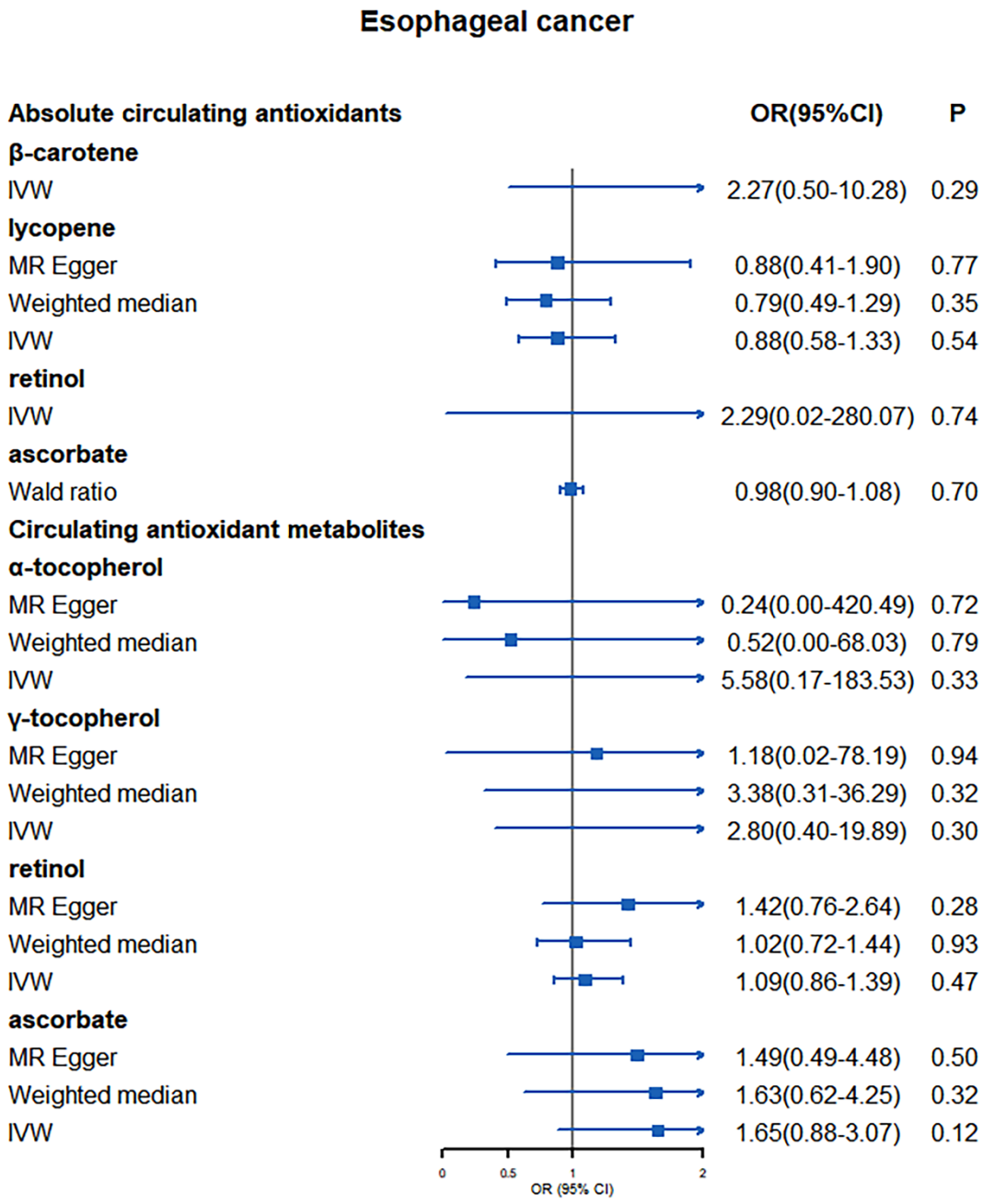
**Supplementary Figure S3. Causal association between circulating antioxidants with pancreatic cancer.**



**Supplementary Figure S4. Causal association between circulating antioxidants with liver cancer.**



**Supplementary Figure S5. Causal association between circulating antioxidants with esophageal cancer.**



**Supplementary Table S1. Instrumental variables of circulating dietary-derived antioxidants.**

| IVs | PMID | No. of SNPs | Study type | N | P | LD | Unit | $R^2$ |
|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | | | |
| β-carotene | 23134893 | 5 | GWAS | 2,344 | 5.00E-08 | 0.2 | μg/L in log-transformed | 9.00% |
| lycopene | 26861389 | 3 | GWAS | 441 | 5.00E-06 | 0.001 | μg/dL | 30.10% |
| Retinol | 21878437 | 2 | GWAS | 5006 | 5.00E-08 | 0.001 | μg/L in log-transformed | 2.30% |
| Ascorbate | 20519558 | 1 | Meta-analysis | 15,087 | 2.00E-07 | 0.001 | μmol/L | 0.90% |
| **Circulating antioxidants metabolites** | | | | | | | | |
| α-tocopherol | 24816252 | 11 | GWAS | 7,276 | 1.00E-05 | 0.001 | log10-transfomed | 3.30% |
| γ-tocopherol | 24816252 | 13 | GWAS | 5,822 | 1.00E-05 | 0.001 | log10-transfomed | 15.00% |
| Retinol | 28263315 | 24 | GWAS | 1,957 | 1.00E-05 | 0.001 | log10-transfomed | 4.80% |
| Ascorbate | 24816252 | 14 | GWAS | 2,063 | 1.00E-05 | 0.001 | log10-transfomed | 18.60% |

IVs, instrumental variables. LD, linkage disequilibrium.

**Supplementary Table S2. SNPs of circulating antioxidants in the Mendelian randomization analysis.**

| SNP | Chr | Position | EA | OA | EAF | BEAT | SE | P | F-statistic | $R^2$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | | | | | |
| **β-carotene** | | | | | | | | | | |
| rs12934922* | 16 | 81301694 | T | A | 0.44 | 0.139 | 0.02 | 5.90E-10 | 60.21 | / |
| rs6564851 | 16 | 81264597 | G | T | 0.36 | 0.149 | 0.02 | 1.60E-24 | 98.67 | / |
| rs7501331 | 16 | 81314496 | T | C | 0.24 | -0.067 | 0.02 | 1.60E-05 | 17.69 | / |
| **lycopene** | | | | | | | | | | |
| rs2232315 | 2 | 169757432 | A | G | 0.03 | 0.74 | 0.15 | 1.00E-06 | 25.01 | / |
| rs341075 | 11 | 72257963 | A | G | 0.02 | -0.87 | 0.17 | 6.00E-07 | 24.91 | / |
| rs4635297 | 15 | 38327408 | A | C | 0.08 | 0.26 | 0.05 | 6.00E-07 | 25.97 | / |
| rs7680948 | 4 | 140447105 | A | C | 0.2 | -0.19 | 0.03 | 5.00E-09 | 38.52 | / |
| rs6108801 | 20 | 10989519 | C | T | 0.04 | -0.48 | 0.09 | 4.00E-07 | 27.32 | / |
| **lycopene** | | | | | | | | | | |
| rs10882272 | 10 | 95348182 | C | T | 0.35 | -0.03 | 0.01 | 7.00E-15 | 34.57 | / |
| rs1667255 | 18 | 29187279 | C | A | 0.31 | 0.03 | 0.01 | 6.00E-14 | 34.57 | / |
| **Ascorbate** | | | | | | | | | | |
| rs33972313 | 5 | 138715502 | C | T | 0.96 | 5.98 | 1.15 | 2.00E-07 | 27.14 | / |
| **Circulating antioxidants metabolites** | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | |
| rs10163969 | 18 | 9067439 | T | G | 0.04 | -0.04 | 0.01 | 9.39E-06 | 19.36 | 0.0027 |
| rs10245705 | 7 | 26129672 | T | C | 0.02 | -0.07 | 0.01 | 1.95E-07 | 27.25 | 0.0037 |
| rs10935814 | 3 | 150352873 | A | G | 0.1 | -0.04 | 0.01 | 9.44E-06 | 19.87 | 0.0027 |
| rs11145330 | 9 | 71733603 | A | C | 0.89 | 0.03 | 0.01 | 1.95E-06 | 22.7 | 0.0031 |
| rs11992435 | 8 | 81526083 | A | G | 0.95 | 0.03 | 0.01 | 6.38E-06 | 20.63 | 0.0028 |
| rs1404410 | 7 | 124248950 | C | G | 0.79 | -0.02 | 0.01 | 4.57E-06 | 20.6 | 0.0028 |
| rs1532701 | 16 | 55698027 | A | G | 0.55 | 0.01 | 0 | 5.07E-06 | 20.85 | 0.0029 |
| rs2074731 | 22 | 30733914 | A | C | 0.17 | -0.02 | 0 | 2.31E-06 | 22.26 | 0.003 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| rs261342 | 15 | 58731153 | C | G | 0.79 | -0.02 | 0 | 5.41E-06 | 20.86 | 0.0029 |
| rs7238006 | 18 | 31927898 | T | C | 0.93 | 0.03 | 0.01 | 6.77E-07 | 24.3 | 0.0033 |
| rs7930821 | 11 | 19142695 | T | C | 0.02 | 0.07 | 0.01 | 7.53E-06 | 19.98 | 0.0027 |
| **γ-tocopherol** | | | | | | | | | | |
| rs10077932 | 5 | 2450679 | T | C | 0.14 | -0.04 | 0.01 | 4.08E-06 | 21.35 | 0.0037 |
| rs1013104 | 17 | 12187236 | T | C | 0.44 | -0.02 | 0 | 3.83E-06 | 21.16 | 0.0036 |
| rs10466757 | 12 | 24984990 | A | T | 0.16 | 0.06 | 0.01 | 9.56E-06 | 19.66 | 0.0034 |
| rs10492212 | 12 | 107296945 | T | C | 0.16 | -0.03 | 0.01 | 8.66E-06 | 19.53 | 0.0033 |
| rs10520845 | 5 | 16879933 | A | C | 0.02 | 0.19 | 0.04 | 5.27E-06 | 20.78 | 0.0036 |
| rs1060467 | 19 | 16024538 | A | G | 0.59 | 0.02 | 0 | 2.61E-07 | 26.81 | 0.0046 |
| rs13336771 | 16 | 48318728 | A | C | 0.17 | 0.06 | 0.01 | 7.39E-06 | 20.15 | 0.0034 |
| rs261301 | 15 | 58686939 | T | C | 0.13 | 0.03 | 0.01 | 2.06E-06 | 22.56 | 0.0039 |
| rs2794327* | 1 | 3512341 | T | C | 0.67 | -0.04 | 0.01 | 8.78E-06 | 19.69 | 0.0034 |
| rs5994305 | 22 | 30820707 | A | G | 0.83 | 0.03 | 0.01 | 7.15E-07 | 24.52 | 0.0042 |
| rs6821770 | 4 | 7732805 | A | G | 0.14 | 0.04 | 0.01 | 8.92E-06 | 19.52 | 0.0033 |
| rs7038957 | 9 | 106539439 | T | C | 0.83 | -0.03 | 0.01 | 3.86E-06 | 21.43 | 0.0037 |
| rs7350776 | 15 | 33689075 | C | G | 0.7 | 0.02 | 0.01 | 3.86E-06 | 21.12 | 0.0036 |
| **Retinol** | | | | | | | | | | |
| rs10019071 | 4 | 181442264 | A | G | 0.01 | 0.66 | 0.16 | 3.64E-06 | 16.72 | 0.0085 |
| rs112293959 | 15 | 80358561 | G | A | 0.99 | -0.43 | 0.13 | 5.70E-06 | 10.88 | 0.0055 |
| rs114515641 | 3 | 118837344 | G | T | 0.03 | 0.41 | 0.13 | 7.12E-06 | 10.32 | 0.0052 |
| rs1153379 | 21 | 16678993 | A | G | 0.95 | -0.32 | 0.08 | 6.10E-06 | 14.97 | 0.0076 |
| rs1176744 | 11 | 113803028 | C | A | 0.31 | -0.21 | 0.05 | 3.52E-07 | 20.97 | 0.0106 |
| rs118025446 | 6 | 84904002 | A | G | 0.04 | -0.48 | 0.12 | 9.84E-06 | 17.38 | 0.0088 |
| rs12955464 | 18 | 10141045 | G | C | 0.87 | -0.23 | 0.06 | 3.71E-06 | 14.79 | 0.0075 |
| rs139726207 | 2 | 223878661 | G | A | 0.91 | 0.37 | 0.11 | 4.46E-06 | 11.21 | 0.0057 |
| rs149113848 | 2 | 81021743 | G | C | 0.99 | -0.96 | 0.27 | 3.47E-06 | 13.21 | 0.0067 |
| rs149478645 | 7 | 117400313 | G | A | 0.97 | -0.51 | 0.14 | 1.30E-06 | 12.79 | 0.0065 |
| rs17005512 | 4 | 83113756 | C | G | 0.17 | -0.22 | 0.06 | 2.77E-06 | 13.33 | 0.0068 |
| rs1842947 | 17 | 3316976 | G | A | 0.49 | -0.19 | 0.04 | 8.34E-07 | 20.06 | 0.0101 |
| rs2147337 | 20 | 1612282 | G | T | 0.66 | 0.16 | 0.04 | 9.00E-06 | 12.68 | 0.0064 |
| rs2367816 | 2 | 33873296 | G | A | 0.26 | 0.23 | 0.05 | 9.46E-06 | 19.64 | 0.0099 |
| rs2417325 | 12 | 14171015 | T | C | 0.09 | 0.33 | 0.08 | 1.29E-06 | 15.49 | 0.0079 |
| rs3890033 | 3 | 195591527 | C | T | 0.5 | 0.14 | 0.04 | 8.56E-06 | 11.76 | 0.006 |
| rs3898702 | 3 | 8011098 | T | C | 0.21 | -0.22 | 0.05 | 3.02E-06 | 16.35 | 0.0083 |
| rs4135385 | 3 | 41279440 | G | A | 0.76 | 0.21 | 0.05 | 9.80E-06 | 18.75 | 0.0095 |
| rs58411567 | 12 | 124387574 | A | G | 0.25 | -0.21 | 0.05 | 3.02E-07 | 15.92 | 0.0081 |
| rs6550239 | 3 | 20001318 | A | G | 0.73 | -0.18 | 0.05 | 4.40E-06 | 14.51 | 0.0074 |
| rs75308833 | 5 | 34602282 | T | C | 0.97 | -0.49 | 0.15 | 3.51E-06 | 11.27 | 0.0057 |
| rs7926028 | 11 | 50213631 | T | G | 0.47 | -0.13 | 0.04 | 2.75E-06 | 10.39 | 0.0053 |
| rs945817 | 6 | 75454012 | A | G | 0.83 | -0.28 | 0.05 | 6.46E-07 | 25.32 | 0.0128 |
| rs9586119 | 13 | 88613487 | C | T | 0.11 | 0.35 | 0.08 | 3.34E-06 | 18.24 | 0.0092 |
| **Ascorbate** | | | | | | | | | | |
| rs11167905 | 5 | 144906846 | C | T | 0.14 | -0.08 | 0.02 | 9.83E-07 | 24.03 | 0.0115 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| rs13069990 | 3 | 115620801 | T | C | 0.62 | -0.05 | 0.01 | 4.44E-06 | 21.16 | 0.0102 |
| rs13103690 | 4 | 9972778 | G | T | 0.47 | 0.05 | 0.01 | 5.20E-06 | 20.77 | 0.01 |
| rs2070006 | 4 | 155513866 | C | T | 0.37 | -0.05 | 0.01 | 4.76E-06 | 20.9 | 0.01 |
| rs577596 | 22 | 25931606 | A | G | 0.38 | -0.06 | 0.01 | 6.68E-07 | 24.74 | 0.0118 |
| rs6713914 | 2 | 59523041 | C | T | 0.44 | -0.06 | 0.01 | 3.22E-07 | 26.13 | 0.0125 |
| rs6826474 | 4 | 96650120 | T | C | 0.96 | -0.14 | 0.03 | 1.56E-06 | 23.06 | 0.0111 |
| rs6834631 | 4 | 122315665 | G | T | 0.04 | -0.13 | 0.03 | 1.03E-06 | 23.93 | 0.0115 |
| rs7112460 | 11 | 125751859 | T | C | 0.93 | 0.11 | 0.02 | 1.14E-06 | 23.63 | 0.0113 |
| rs8057559 | 16 | 73317172 | T | C | 0.96 | 0.14 | 0.03 | 9.10E-06 | 19.74 | 0.0095 |
| rs808686 | 20 | 19717135 | A | G | 0.49 | 0.06 | 0.01 | 3.01E-06 | 21.83 | 0.0105 |
| rs8105491 | 19 | 20403988 | T | G | 0.85 | -0.07 | 0.01 | 2.30E-06 | 22.24 | 0.0107 |
| rs9419004 | 10 | 134914522 | C | G | 0.28 | -0.25 | 0.06 | 6.53E-06 | 20.35 | 0.0098 |
| rs9606290 | 22 | 20218237 | A | G | 0.26 | 0.16 | 0.04 | 6.32E-06 | 20.4 | 0.0098 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error. Chr, Chromsome.

*These SNPs were excluded, as they are not available in digestive system tumors risk.

**Supplementary Table S3. Association of genome-wide SNPs for circulating antioxidants with colorectal cancer.**

| SNP | EA | OA | EAF | BETA | SE | P |
|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | |
| **β-carotene** | | | | | | |
| rs6564851 | T | G | 0.47 | 0.04 | 0.06 | 0.51 |
| rs7501331 | T | C | 0.24 | 0.08 | 0.07 | 0.21 |
| **lycopene** | | | | | | |
| rs2232315 | A | G | 0.02 | -0.12 | 0.21 | 0.55 |
| rs341075 | G | A | 0.03 | 0.01 | 0.17 | 0.96 |
| rs4635297 | A | C | 0.19 | -0.07 | 0.07 | 0.33 |
| rs7680948 | C | A | 0.27 | -0.05 | 0.06 | 0.43 |
| rs6108801 | T | C | 0.03 | 0.11 | 0.16 | 0.50 |
| **retinol** | | | | | | |
| rs10882272 | C | T | 0.38 | -0.05 | 0.06 | 0.43 |
| rs1667255 | C | A | 0.39 | 0.04 | 0.06 | 0.48 |
| **ascorbate** | | | | | | |
| rs33972313 | T | C | 0.03 | -0.01 | 0.15 | 0.95 |
| **Circulating antioxidant metabolites** | | | | | | |
| **α-tocopherol** | | | | | | |
| rs10163969 | T | G | 0.04 | 0.07 | 0.15 | 0.63 |
| rs10245705 | T | C | 0.02 | -0.43 | 0.21 | 0.05 |
| rs10935814 | A | G | 0.12 | -0.15 | 0.09 | 0.09 |
| rs11145330 | C | A | 0.11 | -0.04 | 0.09 | 0.66 |
| rs11992435 | G | A | 0.06 | 0.12 | 0.12 | 0.32 |
| rs1404410 | G | C | 0.20 | 0.10 | 0.07 | 0.16 |
| rs1532701 | G | A | 0.46 | 0.02 | 0.06 | 0.69 |
| rs2074731 | A | C | 0.16 | -0.08 | 0.08 | 0.30 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs261342 | G | C | 0.22 | 0.01 | 0.07 | 0.85 |
| rs7238006 | C | T | 0.07 | -0.07 | 0.11 | 0.55 |
| rs7930821 | T | C | 0.02 | -0.10 | 0.21 | 0.63 |
| **γ-tocopherol** | | | | | | |
| rs10077932 | T | C | 0.18 | 0.08 | 0.07 | 0.25 |
| rs1013104 | T | C | 0.44 | 0.04 | 0.06 | 0.47 |
| rs10466757 | A | T | 0.25 | 0.07 | 0.06 | 0.31 |
| rs10492212 | T | C | 0.16 | -0.01 | 0.08 | 0.88 |
| rs10520845 | A | C | 0.01 | 0.12 | 0.26 | 0.64 |
| rs1060467 | G | A | 0.42 | 0.02 | 0.06 | 0.74 |
| rs13336771 | A | C | 0.15 | 0.11 | 0.08 | 0.17 |
| rs261301 | T | C | 0.14 | 0.18 | 0.08 | 0.03 |
| rs5994305 | G | A | 0.17 | -0.12 | 0.08 | 0.12 |
| rs6821770 | A | G | 0.18 | 0.02 | 0.07 | 0.84 |
| rs7038957 | C | T | 0.17 | -0.01 | 0.08 | 0.90 |
| rs7350776 | G | C | 0.30 | 0.03 | 0.06 | 0.65 |
| **retinol** | | | | | | |
| rs10019071 | A | G | 0.02 | 0.18 | 0.20 | 0.38 |
| rs112293959 | G | A | 0.03 | 0.15 | 0.16 | 0.34 |
| rs114515641 | G | T | 0.03 | -0.22 | 0.17 | 0.19 |
| rs1153379 | G | A | 0.06 | 0.09 | 0.13 | 0.46 |
| rs1176744 | C | A | 0.31 | -0.15 | 0.06 | 0.01 |
| rs118025446 | A | G | 0.04 | 0.10 | 0.14 | 0.49 |
| rs12955464 | G | C | 0.15 | -0.03 | 0.08 | 0.72 |
| rs139726207 | G | A | 0.06 | -0.14 | 0.12 | 0.22 |
| rs149113848 | G | C | 0.01 | -0.21 | 0.34 | 0.54 |
| rs149478645 | G | A | 0.02 | 0.22 | 0.19 | 0.24 |
| rs17005512 | C | G | 0.15 | 0.06 | 0.08 | 0.41 |
| rs1842947 | A | G | 0.47 | 0.04 | 0.06 | 0.53 |
| rs2147337 | T | G | 0.36 | 0.02 | 0.06 | 0.79 |
| rs2367816 | A | G | 0.24 | -0.16 | 0.07 | 0.01 |
| rs2417325 | C | T | 0.07 | -0.06 | 0.11 | 0.60 |
| rs3890033 | C | T | 0.50 | 0.03 | 0.06 | 0.65 |
| rs3898702 | T | C | 0.20 | -0.03 | 0.07 | 0.71 |
| rs4135385 | G | A | 0.23 | 0.09 | 0.07 | 0.19 |
| rs58411567 | A | G | 0.23 | -0.11 | 0.07 | 0.11 |
| rs6550239 | G | A | 0.23 | 0.05 | 0.07 | 0.48 |
| rs75308833 | T | C | 0.03 | -0.05 | 0.18 | 0.79 |
| rs7926028 | G | T | 0.48 | -0.01 | 0.06 | 0.79 |
| rs945817 | A | G | 0.19 | -0.02 | 0.07 | 0.76 |
| rs9586119 | C | T | 0.09 | 0.17 | 0.10 | 0.09 |
| **ascorbate** | | | | | | |
| rs11167905 | C | T | 0.15 | 0.08 | 0.08 | 0.30 |
| rs13069990 | T | C | 0.39 | 0.03 | 0.06 | 0.64 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs13103690 | G | T | 0.46 | -0.01 | 0.06 | 0.88 |
| rs2070006 | T | C | 0.38 | -0.05 | 0.06 | 0.38 |
| rs577596 | A | G | 0.35 | -0.12 | 0.06 | 0.05 |
| rs6713914 | C | T | 0.46 | 0.00 | 0.06 | 0.95 |
| rs6826474 | T | C | 0.03 | -0.24 | 0.17 | 0.17 |
| rs6834631 | G | T | 0.04 | 0.11 | 0.14 | 0.41 |
| rs7112460 | T | C | 0.06 | -0.06 | 0.12 | 0.60 |
| rs8057559 | T | C | 0.03 | 0.13 | 0.17 | 0.46 |
| rs808686 | G | A | 0.49 | -0.09 | 0.06 | 0.12 |
| rs8105491 | T | G | 0.15 | 0.10 | 0.08 | 0.18 |
| rs9419004 | C | G | 0.27 | -0.04 | 0.06 | 0.55 |
| rs9606290 | A | G | 0.26 | -0.08 | 0.07 | 0.22 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error.

**Supplementary Table S4. Association of genome-wide SNPs for circulating antioxidants with gastric cancer.**

| SNP | EA | OA | EAF | BETA | SE | P |
|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | |
| **β-carotene** | | | | | | |
| rs6564851 | T | G | 0.47 | 0.03 | 0.11 | 0.81 |
| rs7501331 | T | C | 0.24 | 0.10 | 0.13 | 0.44 |
| **lycopene** | | | | | | |
| rs2232315 | A | G | 0.02 | -0.06 | 0.40 | 0.88 |
| rs341075 | G | A | 0.03 | 0.42 | 0.32 | 0.19 |
| rs4635297 | A | C | 0.19 | -0.02 | 0.14 | 0.89 |
| rs7680948 | C | A | 0.27 | -0.13 | 0.12 | 0.31 |
| rs6108801 | T | C | 0.03 | 0.08 | 0.31 | 0.79 |
| **retinol** | | | | | | |
| rs10882272 | C | T | 0.38 | -0.30 | 0.11 | 0.01 |
| rs1667255 | C | A | 0.39 | 0.02 | 0.11 | 0.87 |
| **ascorbate** | | | | | | |
| rs33972313 | T | C | 0.03 | -0.07 | 0.30 | 0.82 |
| **Circulating antioxidant metabolites** | | | | | | |
| **α-tocopherol** | | | | | | |
| rs10163969 | T | G | 0.04 | -0.32 | 0.28 | 0.26 |
| rs10245705 | T | C | 0.02 | -0.31 | 0.42 | 0.46 |
| rs10935814 | A | G | 0.12 | 0.14 | 0.17 | 0.42 |
| rs11145330 | C | A | 0.11 | -0.17 | 0.17 | 0.32 |
| rs11992435 | G | A | 0.06 | 0.25 | 0.24 | 0.29 |
| rs1404410 | G | C | 0.20 | -0.12 | 0.14 | 0.40 |
| rs1532701 | G | A | 0.46 | 0.17 | 0.11 | 0.11 |
| rs2074731 | A | C | 0.16 | -0.25 | 0.15 | 0.10 |
| rs261342 | G | C | 0.22 | -0.22 | 0.13 | 0.10 |
| rs7238006 | C | T | 0.07 | 0.19 | 0.22 | 0.38 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs7930821 | T | C | 0.02 | -0.23 | 0.40 | 0.57 |
| **γ-tocopherol** | | | | | | |
| rs10077932 | T | C | 0.18 | -0.22 | 0.14 | 0.12 |
| rs1013104 | T | C | 0.44 | 0.07 | 0.11 | 0.55 |
| rs10466757 | A | T | 0.25 | -0.01 | 0.13 | 0.91 |
| rs10492212 | T | C | 0.16 | 0.21 | 0.15 | 0.16 |
| rs10520845 | A | C | 0.01 | 0.26 | 0.51 | 0.60 |
| rs1060467 | G | A | 0.42 | -0.03 | 0.11 | 0.76 |
| rs13336771 | A | C | 0.15 | 0.21 | 0.15 | 0.18 |
| rs261301 | T | C | 0.14 | 0.25 | 0.16 | 0.11 |
| rs5994305 | G | A | 0.17 | -0.23 | 0.15 | 0.12 |
| rs6821770 | A | G | 0.18 | -0.05 | 0.14 | 0.72 |
| rs7038957 | C | T | 0.17 | -0.03 | 0.15 | 0.83 |
| rs7350776 | G | C | 0.30 | 0.35 | 0.12 | 0.00 |
| **retinol** | | | | | | |
| rs10019071 | A | G | 0.02 | -0.09 | 0.39 | 0.82 |
| rs112293959 | G | A | 0.03 | 0.12 | 0.31 | 0.70 |
| rs114515641 | G | T | 0.03 | 0.82 | 0.32 | 0.01 |
| rs1153379 | G | A | 0.06 | -0.18 | 0.24 | 0.47 |
| rs1176744 | C | A | 0.31 | 0.05 | 0.12 | 0.70 |
| rs118025446 | A | G | 0.04 | -0.06 | 0.28 | 0.84 |
| rs12955464 | G | C | 0.15 | 0.04 | 0.16 | 0.81 |
| rs139726207 | G | A | 0.06 | 0.20 | 0.23 | 0.37 |
| rs149113848 | G | C | 0.01 | 1.55 | 0.66 | 0.02 |
| rs149478645 | G | A | 0.02 | -0.75 | 0.37 | 0.04 |
| rs17005512 | C | G | 0.15 | -0.02 | 0.15 | 0.87 |
| rs1842947 | A | G | 0.47 | -0.09 | 0.11 | 0.40 |
| rs2147337 | T | G | 0.36 | 0.11 | 0.11 | 0.32 |
| rs2367816 | A | G | 0.24 | -0.11 | 0.13 | 0.39 |
| rs2417325 | C | T | 0.07 | -0.16 | 0.21 | 0.46 |
| rs3890033 | C | T | 0.50 | -0.16 | 0.11 | 0.16 |
| rs3898702 | T | C | 0.20 | 0.06 | 0.14 | 0.66 |
| rs4135385 | G | A | 0.23 | 0.14 | 0.13 | 0.28 |
| rs58411567 | A | G | 0.23 | 0.20 | 0.13 | 0.13 |
| rs6550239 | G | A | 0.23 | 0.02 | 0.13 | 0.86 |
| rs75308833 | T | C | 0.03 | -0.44 | 0.34 | 0.20 |
| rs7926028 | G | T | 0.48 | 0.03 | 0.11 | 0.80 |
| rs945817 | A | G | 0.19 | 0.04 | 0.14 | 0.78 |
| rs9586119 | C | T | 0.09 | 0.07 | 0.19 | 0.73 |
| **ascorbate** | | | | | | |
| rs11167905 | C | T | 0.15 | 0.08 | 0.15 | 0.61 |
| rs13069990 | T | C | 0.39 | -0.15 | 0.11 | 0.17 |
| rs13103690 | G | T | 0.46 | 0.09 | 0.11 | 0.43 |
| rs2070006 | T | C | 0.38 | 0.02 | 0.11 | 0.87 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs577596 | A | G | 0.35 | -0.19 | 0.11 | 0.09 |
| rs6713914 | C | T | 0.46 | -0.01 | 0.11 | 0.94 |
| rs6826474 | T | C | 0.03 | 0.23 | 0.34 | 0.49 |
| rs6834631 | G | T | 0.04 | -0.12 | 0.27 | 0.66 |
| rs7112460 | T | C | 0.06 | -0.16 | 0.22 | 0.48 |
| rs8057559 | T | C | 0.03 | -0.14 | 0.33 | 0.68 |
| rs808686 | G | A | 0.49 | -0.11 | 0.11 | 0.33 |
| rs8105491 | T | G | 0.15 | 0.01 | 0.15 | 0.96 |
| rs9419004 | C | G | 0.27 | -0.18 | 0.12 | 0.14 |
| rs9606290 | A | G | 0.26 | 0.04 | 0.13 | 0.78 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error.

**Supplementary Table S5. Association of genome-wide SNPs for circulating antioxidants with pancreatic cancer.**

| SNP | EA | OA | EAF | BETA | SE | P |
|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | |
| **β-carotene** | | | | | | |
| rs6564851 | T | G | 0.47 | 0.07 | 0.06 | 0.22 |
| rs7501331 | T | C | 0.24 | 0.11 | 0.07 | 0.12 |
| **lycopene** | | | | | | |
| rs2232315 | A | G | 0.02 | -0.39 | 0.21 | 0.07 |
| rs341075 | G | A | 0.03 | 0.00 | 0.17 | 0.98 |
| rs4635297 | A | C | 0.19 | -0.02 | 0.07 | 0.82 |
| rs7680948 | C | A | 0.27 | 0.06 | 0.07 | 0.37 |
| rs6108801 | T | C | 0.03 | -0.10 | 0.16 | 0.55 |
| **retinol** | | | | | | |
| rs10882272 | C | T | 0.38 | 0.12 | 0.06 | 0.05 |
| rs1667255 | C | A | 0.39 | 0.03 | 0.06 | 0.58 |
| **ascorbate** | | | | | | |
| rs33972313 | T | C | 0.03 | 0.05 | 0.16 | 0.74 |
| **Circulating antioxidant metabolites** | | | | | | |
| **α-tocopherol** | | | | | | |
| rs10163969 | T | G | 0.04 | 0.07 | 0.15 | 0.66 |
| rs10245705 | T | C | 0.02 | 0.03 | 0.22 | 0.91 |
| rs10935814 | A | G | 0.12 | 0.15 | 0.09 | 0.10 |
| rs11145330 | C | A | 0.11 | -0.03 | 0.09 | 0.78 |
| rs11992435 | G | A | 0.06 | 0.02 | 0.13 | 0.86 |
| rs1404410 | G | C | 0.20 | 0.00 | 0.07 | 0.96 |
| rs1532701 | G | A | 0.46 | -0.02 | 0.06 | 0.69 |
| rs2074731 | A | C | 0.16 | 0.08 | 0.08 | 0.33 |
| rs261342 | G | C | 0.22 | -0.04 | 0.07 | 0.54 |
| rs7238006 | C | T | 0.07 | -0.15 | 0.12 | 0.21 |
| rs7930821 | T | C | 0.02 | -0.16 | 0.21 | 0.46 |
| **γ-tocopherol** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs10077932 | T | C | 0.18 | -0.09 | 0.08 | 0.23 |
| rs1013104 | T | C | 0.44 | -0.12 | 0.06 | 0.04 |
| rs10466757 | A | T | 0.25 | -0.10 | 0.07 | 0.14 |
| rs10492212 | T | C | 0.16 | 0.04 | 0.08 | 0.61 |
| rs10520845 | A | C | 0.01 | 0.01 | 0.27 | 0.98 |
| rs1060467 | G | A | 0.42 | -0.03 | 0.06 | 0.56 |
| rs13336771 | A | C | 0.15 | -0.09 | 0.08 | 0.25 |
| rs261301 | T | C | 0.14 | -0.18 | 0.08 | 0.03 |
| rs5994305 | G | A | 0.17 | 0.05 | 0.08 | 0.50 |
| rs6821770 | A | G | 0.18 | 0.05 | 0.08 | 0.49 |
| rs7038957 | C | T | 0.17 | 0.10 | 0.08 | 0.22 |
| rs7350776 | G | C | 0.30 | -0.04 | 0.06 | 0.50 |
| **retinol** | | | | | | |
| rs10019071 | A | G | 0.02 | -0.17 | 0.21 | 0.43 |
| rs112293959 | G | A | 0.03 | 0.09 | 0.17 | 0.57 |
| rs114515641 | G | T | 0.03 | -0.30 | 0.17 | 0.08 |
| rs1153379 | G | A | 0.06 | -0.10 | 0.13 | 0.45 |
| rs1176744 | C | A | 0.31 | 0.08 | 0.06 | 0.19 |
| rs118025446 | A | G | 0.04 | 0.04 | 0.15 | 0.77 |
| rs12955464 | G | C | 0.15 | 0.00 | 0.08 | 0.99 |
| rs139726207 | G | A | 0.06 | 0.01 | 0.12 | 0.94 |
| rs149113848 | G | C | 0.01 | 0.44 | 0.35 | 0.21 |
| rs149478645 | G | A | 0.02 | -0.08 | 0.20 | 0.67 |
| rs17005512 | C | G | 0.15 | -0.04 | 0.08 | 0.58 |
| rs1842947 | A | G | 0.47 | 0.02 | 0.06 | 0.72 |
| rs2147337 | T | G | 0.36 | -0.06 | 0.06 | 0.32 |
| rs2367816 | A | G | 0.24 | -0.09 | 0.07 | 0.22 |
| rs2417325 | C | T | 0.07 | 0.01 | 0.11 | 0.92 |
| rs3890033 | C | T | 0.50 | -0.08 | 0.06 | 0.21 |
| rs3898702 | T | C | 0.20 | 0.04 | 0.07 | 0.56 |
| rs4135385 | G | A | 0.23 | -0.06 | 0.07 | 0.41 |
| rs58411567 | A | G | 0.23 | 0.05 | 0.07 | 0.49 |
| rs6550239 | G | A | 0.23 | -0.03 | 0.07 | 0.62 |
| rs75308833 | T | C | 0.03 | -0.04 | 0.18 | 0.82 |
| rs7926028 | G | T | 0.48 | -0.04 | 0.06 | 0.50 |
| rs945817 | A | G | 0.19 | -0.01 | 0.07 | 0.93 |
| rs9586119 | C | T | 0.09 | -0.11 | 0.10 | 0.30 |
| **ascorbate** | | | | | | |
| rs11167905 | C | T | 0.15 | -0.13 | 0.08 | 0.12 |
| rs13069990 | T | C | 0.39 | 0.04 | 0.06 | 0.48 |
| rs13103690 | G | T | 0.46 | -0.01 | 0.06 | 0.86 |
| rs2070006 | T | C | 0.38 | 0.03 | 0.06 | 0.65 |
| rs577596 | A | G | 0.35 | -0.04 | 0.06 | 0.52 |
| rs6713914 | C | T | 0.46 | -0.08 | 0.06 | 0.18 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs6826474 | T | C | 0.03 | 0.03 | 0.18 | 0.87 |
| rs6834631 | G | T | 0.04 | -0.02 | 0.14 | 0.88 |
| rs7112460 | T | C | 0.06 | -0.06 | 0.12 | 0.61 |
| rs8057559 | T | C | 0.03 | 0.13 | 0.18 | 0.47 |
| rs808686 | G | A | 0.49 | 0.03 | 0.06 | 0.56 |
| rs8105491 | T | G | 0.15 | -0.07 | 0.08 | 0.37 |
| rs9419004 | C | G | 0.27 | 0.00 | 0.07 | 0.94 |
| rs9606290 | A | G | 0.26 | 0.06 | 0.07 | 0.35 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error.

**Supplementary Table S6. Association of genome-wide SNPs for circulating antioxidants with liver cancer.**

| SNP | EA | OA | EAF | BETA | SE | P |
|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | |
| **β-carotene** | | | | | | |
| rs6564851 | T | G | 0.47 | 0.07 | 0.06 | 0.22 |
| rs7501331 | T | C | 0.24 | 0.11 | 0.07 | 0.12 |
| **lycopene** | | | | | | |
| rs2232315 | A | G | 0.02 | -0.39 | 0.21 | 0.07 |
| rs341075 | G | A | 0.03 | 0.00 | 0.17 | 0.98 |
| rs4635297 | A | C | 0.19 | -0.02 | 0.07 | 0.82 |
| rs7680948 | C | A | 0.27 | 0.06 | 0.07 | 0.37 |
| rs6108801 | T | C | 0.03 | -0.31 | 0.35 | 0.38 |
| **retinol** | | | | | | |
| rs10882272 | C | T | 0.38 | 0.12 | 0.06 | 0.05 |
| rs1667255 | C | A | 0.39 | 0.03 | 0.06 | 0.58 |
| **ascorbate** | | | | | | |
| rs33972313 | T | C | 0.03 | 0.05 | 0.16 | 0.74 |
| **Circulating antioxidant metabolites** | | | | | | |
| **α-tocopherol** | | | | | | |
| rs10163969 | T | G | 0.04 | 0.07 | 0.15 | 0.66 |
| rs10245705 | T | C | 0.02 | 0.03 | 0.22 | 0.91 |
| rs10935814 | A | G | 0.12 | 0.15 | 0.09 | 0.10 |
| rs11145330 | C | A | 0.11 | -0.03 | 0.09 | 0.78 |
| rs11992435 | G | A | 0.06 | -0.12 | 0.27 | 0.66 |
| rs1404410 | G | C | 0.20 | 0.00 | 0.07 | 0.96 |
| rs1532701 | G | A | 0.46 | -0.02 | 0.06 | 0.69 |
| rs2074731 | A | C | 0.16 | 0.08 | 0.08 | 0.33 |
| rs261342 | G | C | 0.22 | -0.04 | 0.07 | 0.54 |
| rs7238006 | C | T | 0.07 | -0.15 | 0.12 | 0.21 |
| rs7930821 | T | C | 0.02 | -0.16 | 0.21 | 0.46 |
| **γ-tocopherol** | | | | | | |
| rs10077932 | T | C | 0.18 | -0.09 | 0.08 | 0.23 |
| rs1013104 | T | C | 0.44 | -0.12 | 0.06 | 0.04 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs10466757 | A | T | 0.25 | -0.10 | 0.07 | 0.14 |
| rs10492212 | T | C | 0.16 | 0.04 | 0.08 | 0.61 |
| rs10520845 | A | C | 0.01 | 0.01 | 0.27 | 0.98 |
| rs1060467 | G | A | 0.42 | -0.03 | 0.06 | 0.56 |
| rs13336771 | A | C | 0.15 | -0.09 | 0.08 | 0.25 |
| rs261301 | T | C | 0.14 | -0.18 | 0.08 | 0.03 |
| rs5994305 | G | A | 0.17 | 0.05 | 0.08 | 0.50 |
| rs6821770 | A | G | 0.18 | 0.05 | 0.08 | 0.49 |
| rs7038957 | C | T | 0.17 | 0.10 | 0.08 | 0.22 |
| rs7350776 | G | C | 0.30 | -0.04 | 0.06 | 0.50 |
| **retinol** | | | | | | |
| rs10019071 | A | G | 0.02 | -0.17 | 0.21 | 0.43 |
| rs112293959 | G | A | 0.03 | 0.09 | 0.17 | 0.57 |
| rs114515641 | G | T | 0.03 | -0.30 | 0.17 | 0.08 |
| rs1153379 | G | A | 0.06 | -0.10 | 0.13 | 0.45 |
| rs1176744 | C | A | 0.31 | 0.08 | 0.06 | 0.19 |
| rs118025446 | A | G | 0.04 | 0.04 | 0.15 | 0.77 |
| rs12955464 | G | C | 0.15 | 0.00 | 0.08 | 0.99 |
| rs139726207 | G | A | 0.06 | 0.01 | 0.12 | 0.94 |
| rs149113848 | G | C | 0.01 | 0.44 | 0.35 | 0.21 |
| rs149478645 | G | A | 0.02 | -0.08 | 0.20 | 0.67 |
| rs17005512 | C | G | 0.15 | -0.04 | 0.08 | 0.58 |
| rs1842947 | A | G | 0.47 | 0.02 | 0.06 | 0.72 |
| rs2147337 | T | G | 0.36 | -0.06 | 0.06 | 0.32 |
| rs2367816 | A | G | 0.24 | -0.09 | 0.07 | 0.22 |
| rs2417325 | C | T | 0.07 | 0.01 | 0.11 | 0.92 |
| rs3890033 | C | T | 0.50 | -0.08 | 0.06 | 0.21 |
| rs3898702 | T | C | 0.20 | 0.04 | 0.07 | 0.56 |
| rs4135385 | G | A | 0.23 | -0.06 | 0.07 | 0.41 |
| rs58411567 | A | G | 0.23 | 0.05 | 0.07 | 0.49 |
| rs6550239 | G | A | 0.23 | -0.03 | 0.07 | 0.62 |
| rs75308833 | T | C | 0.03 | -0.04 | 0.18 | 0.82 |
| rs7926028 | G | T | 0.48 | -0.04 | 0.06 | 0.50 |
| rs945817 | A | G | 0.19 | -0.01 | 0.07 | 0.93 |
| rs9586119 | C | T | 0.09 | -0.11 | 0.10 | 0.30 |
| **ascorbate** | | | | | | |
| rs11167905 | C | T | 0.15 | -0.13 | 0.08 | 0.12 |
| rs13069990 | T | C | 0.39 | 0.04 | 0.06 | 0.48 |
| rs13103690 | G | T | 0.46 | -0.01 | 0.06 | 0.86 |
| rs2070006 | T | C | 0.38 | 0.03 | 0.06 | 0.65 |
| rs577596 | A | G | 0.35 | -0.04 | 0.06 | 0.52 |
| rs6713914 | C | T | 0.46 | -0.08 | 0.06 | 0.18 |
| rs6826474 | T | C | 0.03 | 0.03 | 0.18 | 0.87 |
| rs6834631 | G | T | 0.04 | -0.02 | 0.14 | 0.88 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs7112460 | T | C | 0.06 | -0.06 | 0.12 | 0.61 |
| rs8057559 | T | C | 0.03 | 0.13 | 0.18 | 0.47 |
| rs808686 | G | A | 0.49 | 0.03 | 0.06 | 0.56 |
| rs8105491 | T | G | 0.15 | -0.07 | 0.08 | 0.37 |
| rs9419004 | C | G | 0.27 | 0.00 | 0.07 | 0.94 |
| rs9606290 | A | G | 0.26 | 0.06 | 0.07 | 0.35 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error.

**Supplementary Table S7. Association of genome-wide SNPs for circulating antioxidants with esophageal cancer.**

| SNP | EA | OA | EAF | BETA | SE | P |
|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | | |
| β-carotene | | | | | | |
| rs6564851 | T | G | 0.47 | -0.08 | 0.10 | 0.44 |
| rs7501331 | T | C | 0.24 | -0.19 | 0.12 | 0.11 |
| **lycopene** | | | | | | |
| rs2232315 | A | G | 0.02 | 0.22 | 0.37 | 0.55 |
| rs341075 | G | A | 0.03 | -0.33 | 0.30 | 0.27 |
| rs4635297 | A | C | 0.19 | -0.07 | 0.13 | 0.60 |
| rs7680948 | C | A | 0.27 | -0.02 | 0.11 | 0.85 |
| rs6108801 | T | C | 0.03 | 0.09 | 0.28 | 0.75 |
| **retinol** | | | | | | |
| rs10882272 | C | T | 0.38 | 0.03 | 0.10 | 0.80 |
| rs1667255 | C | A | 0.39 | 0.08 | 0.10 | 0.46 |
| **ascorbate** | | | | | | |
| rs33972313 | T | C | 0.03 | 0.11 | 0.28 | 0.70 |
| **Circulating antioxidant metabolites** | | | | | | |
| **α-tocopherol** | | | | | | |
| rs10163969 | T | G | 0.04 | -0.21 | 0.26 | 0.43 |
| rs10245705 | T | C | 0.02 | -0.26 | 0.39 | 0.50 |
| rs10935814 | A | G | 0.12 | 0.10 | 0.16 | 0.50 |
| rs11145330 | C | A | 0.11 | 0.02 | 0.16 | 0.92 |
| rs11992435 | G | A | 0.06 | 0.22 | 0.22 | 0.33 |
| rs1404410 | G | C | 0.20 | -0.07 | 0.13 | 0.60 |
| rs1532701 | G | A | 0.46 | -0.08 | 0.10 | 0.43 |
| rs2074731 | A | C | 0.16 | -0.13 | 0.14 | 0.36 |
| rs261342 | G | C | 0.22 | 0.17 | 0.12 | 0.17 |
| rs7238006 | C | T | 0.07 | -0.43 | 0.20 | 0.03 |
| rs7930821 | T | C | 0.02 | -0.08 | 0.37 | 0.82 |
| **γ-tocopherol** | | | | | | |
| rs10077932 | T | C | 0.18 | 0.14 | 0.13 | 0.29 |
| rs1013104 | T | C | 0.44 | -0.07 | 0.10 | 0.51 |
| rs10466757 | A | T | 0.25 | 0.09 | 0.12 | 0.44 |
| rs10492212 | T | C | 0.16 | 0.01 | 0.14 | 0.92 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs10520845 | A | C | 0.01 | 0.31 | 0.47 | 0.51 |
| rs1060467 | G | A | 0.42 | 0.03 | 0.10 | 0.76 |
| rs13336771 | A | C | 0.15 | 0.05 | 0.14 | 0.75 |
| rs261301 | T | C | 0.14 | 0.09 | 0.15 | 0.55 |
| rs5994305 | G | A | 0.17 | -0.15 | 0.14 | 0.26 |
| rs6821770 | A | G | 0.18 | 0.04 | 0.13 | 0.77 |
| rs7038957 | C | T | 0.17 | -0.20 | 0.14 | 0.14 |
| rs7350776 | G | C | 0.30 | -0.28 | 0.11 | 0.01 |
| **retinol** | | | | | | |
| rs10019071 | A | G | 0.02 | 0.48 | 0.37 | 0.20 |
| rs112293959 | G | A | 0.03 | -0.30 | 0.29 | 0.30 |
| rs114515641 | G | T | 0.03 | -0.16 | 0.30 | 0.60 |
| rs1153379 | G | A | 0.06 | -0.16 | 0.23 | 0.48 |
| rs1176744 | C | A | 0.31 | -0.12 | 0.11 | 0.28 |
| rs118025446 | A | G | 0.04 | -0.24 | 0.26 | 0.35 |
| rs12955464 | G | C | 0.15 | 0.05 | 0.14 | 0.75 |
| rs139726207 | G | A | 0.06 | 0.16 | 0.21 | 0.45 |
| rs149113848 | G | C | 0.01 | -0.62 | 0.61 | 0.31 |
| rs149478645 | G | A | 0.02 | -0.31 | 0.34 | 0.36 |
| rs17005512 | C | G | 0.15 | -0.29 | 0.14 | 0.04 |
| rs1842947 | A | G | 0.47 | -0.01 | 0.10 | 0.93 |
| rs2147337 | T | G | 0.36 | 0.03 | 0.11 | 0.80 |
| rs2367816 | A | G | 0.24 | -0.04 | 0.12 | 0.73 |
| rs2417325 | C | T | 0.07 | -0.01 | 0.20 | 0.97 |
| rs3890033 | C | T | 0.50 | 0.06 | 0.11 | 0.55 |
| rs3898702 | T | C | 0.20 | 0.24 | 0.13 | 0.06 |
| rs4135385 | G | A | 0.23 | -0.03 | 0.12 | 0.79 |
| rs58411567 | A | G | 0.23 | 0.03 | 0.12 | 0.79 |
| rs6550239 | G | A | 0.23 | -0.23 | 0.12 | 0.05 |
| rs75308833 | T | C | 0.03 | 0.12 | 0.32 | 0.70 |
| rs7926028 | G | T | 0.48 | 0.00 | 0.10 | 0.99 |
| rs945817 | A | G | 0.19 | 0.04 | 0.13 | 0.73 |
| rs9586119 | C | T | 0.09 | 0.24 | 0.18 | 0.19 |
| **ascorbate** | | | | | | |
| rs11167905 | C | T | 0.15 | -0.15 | 0.14 | 0.28 |
| rs13069990 | T | C | 0.39 | 0.07 | 0.10 | 0.47 |
| rs13103690 | G | T | 0.46 | 0.01 | 0.10 | 0.92 |
| rs2070006 | T | C | 0.38 | 0.04 | 0.10 | 0.72 |
| rs577596 | A | G | 0.35 | 0.06 | 0.11 | 0.60 |
| rs6713914 | C | T | 0.46 | -0.15 | 0.10 | 0.13 |
| rs6826474 | T | C | 0.03 | -0.24 | 0.31 | 0.45 |
| rs6834631 | G | T | 0.04 | 0.04 | 0.25 | 0.86 |
| rs7112460 | T | C | 0.06 | -0.28 | 0.21 | 0.17 |
| rs8057559 | T | C | 0.03 | -0.07 | 0.31 | 0.81 |

| | | | | | | |
|---|---|---|---|---|---|---|
| rs808686 | G | A | 0.49 | -0.15 | 0.10 | 0.13 |
| rs8105491 | T | G | 0.15 | -0.11 | 0.14 | 0.45 |
| rs9419004 | C | G | 0.27 | -0.17 | 0.11 | 0.14 |
| rs9606290 | A | G | 0.26 | 0.00 | 0.12 | 0.99 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error.

**Supplementary Table S8. MR analysis results of associations between circulating antioxidants and colorectal cancer.**

| | SE | β(95%CI) | OR(95%CI) | P | Heterogeneity | | | | pleiotropy | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | MR Egger | | IVW | | MR-Egger intercept | | MR-PRESO | |
| **β-carotene** | | | | | Q | P | Q | P | intercept | P | No. of outlier | P |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 0.86 | 0.35 | / | / | / | / |
| IVW | 0.35 | -0.37(-1.07-0.32) | 0.69(0.34-1.37) | 0.29 | | | | | | | | |
| **lycopene** | | | | | | | | | | | | |
| MR Egger | 0.22 | 0.08(-0.35-0.51) | 1.09(0.71-1.66) | 0.73 | | | | | | | | |
| Weighted median | 0.14 | -0.10(-0.38-0.18) | 0.90(0.69-1.19) | 0.48 | 1.17 | 0.76 | 1.95 | 0.75 | -0.07 | 0.44 | NA | 0.78 |
| IVW | 0.12 | -0.08(-0.31-0.15) | 0.92(0.73-1.16) | 0.50 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 0.00 | 0.95 | / | / | / | / |
| IVW | 1.36 | 1.45(-1.22-4.12) | 4.26(0.30-61.44) | 0.29 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| Wald ratio | 0.03 | 0.00(-0.05-0.05) | 1.00(0.95-1.05) | 0.95 | / | / | / | / | / | / | / | / |
| **Circulating antioxidant metabolites** | | | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | | | |
| MR Egger | 2.12 | 2.46(-1.69-6.61) | 11.74(0.19-744.24) | 0.27 | | | | | | | | |
| Weighted median | 1.36 | 1.88(-0.77-4.54) | 6.58(0.46-93.84) | 0.16 | 8.60 | 0.47 | 8.72 | 0.56 | -0.02 | 0.74 | NA | 0.71 |
| IVW | 0.99 | 1.82(-0.12-3.76) | 6.17(0.89-42.89) | 0.07 | | | | | | | | |
| **γ-tocopherol** | | | | | | | | | | | | |
| MR Egger | 1.10 | 1.49(-0.66-3.64) | 4.44(0.52-37.99) | 0.20 | | | | | | | | |
| Weighted median | 0.72 | 0.76(-0.65-2.18) | 2.15(0.52-8.82) | 0.29 | 9.98 | 0.44 | 10.54 | 0.48 | -0.03 | 0.47 | NA | 0.53 |
| IVW | 0.53 | 0.77(-0.27-1.82) | 2.17(0.77-6.15) | 0.15 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | 0.19 | -0.15(-0.51-0.21) | 0.86(0.60-1.24) | 0.43 | | | | | | | | |
| Weighted median | 0.10 | 0.11(-0.08-0.31) | 1.12(0.92-1.36) | 0.24 | 24.44 | 0.32 | 27.10 | 0.25 | 0.07 | 0.14 | NA | 0.27 |
| IVW | 0.07 | 0.12(-0.03-0.26) | 1.12(0.97-1.30) | 0.11 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| MR Egger | 0.35 | 0.02(-0.67-0.71) | 1.02(0.51-2.04) | 0.96 | | | | | | | | |
| Weighted median | 0.24 | 0.04(-0.44-0.52) | 1.04(0.64-1.67) | 0.89 | 15.38 | 0.22 | 15.38 | 0.28 | 0.00 | 0.94 | NA | 0.35 |
| IVW | 0.19 | 0.00(-0.38-0.37) | 1.00(0.68-1.45) | 0.98 | | | | | | | | |

SE, standard error. OR, odds ratio. IVW, Inverse variance weighted.

**Supplementary Table S9. MR analysis results of associations between circulating antioxidants and gastric cancer.**

| | SE | β(95%CI) | OR(95%CI) | P | Heterogeneity | | | | Pleiotropy | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | MR Egger | | IVW | | MR-Egger intercept | | MR-PRESO | |
| β-carotene | | | | | Q | P | Q | P | intercept | P | No. of outlier | P |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 0.40 | 0.52 | / | / | / | / |
| IVW | 0.69 | -0.34(-1.68-1.00) | 0.71(0.19-2.72) | 0.62 | | | | | | | | |
| **lycopene** | | | | | | | | | | | | |
| MR Egger | 0.42 | 0.59(-0.24-1.42) | 1.80(0.78-4.13) | 0.26 | | | | | | | | |
| Weighted median | 0.28 | 0.07(-0.48-0.63) | 1.08(0.62-1.88) | 0.80 | 0.75 | 0.86 | 2.65 | 0.62 | -0.21 | 0.26 | NA | 0.50 |
| IVW | 0.23 | 0.10(-0.35-0.55) | 1.10(0.70-1.73) | 0.67 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 3.21 | 0.07 | / | / | / | / |
| IVW | 4.74 | 5.32(-3.98-14.61) | 203.51(0.02-2220283.92) | 0.26 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| Wald ratio | 0.05 | 0.01(-0.09-0.11) | 1.01(0.92-1.11) | 0.82 | / | / | / | / | / | / | / | / |
| **Circulating antioxidant metabolites** | | | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | | | |
| MR Egger | 4.73 | 3.64(-5.62-12.9) | 38.08(0.00-401432.31) | 0.46 | | | | | | | | |
| Weighted median | 2.81 | -3.34(-8.84-2.16) | 0.04(0.00-8.66) | 0.23 | 11.85 | 0.22 | 13.78 | 0.18 | -0.15 | 0.26 | NA | 0.19 |
| IVW | 2.26 | -1.42(-5.84-3.01) | 0.24(0.00-20.19) | 0.53 | | | | | | | | |
| **γ-tocopherol** | | | | | | | | | | | | |
| MR Egger | 2.85 | 3.44(-2.15-9.03) | 31.13(0.12-8324.30) | 0.26 | | | | | | | | |
| Weighted median | 1.49 | 0.90(-2.03-3.83) | 2.46(0.13-45.93) | 0.55 | 17.81 | 0.06 | 19.76 | 0.06 | -0.12 | 0.32 | NA | 0.09 |
| IVW | 1.39 | 0.83(-1.89-3.55) | 2.28(0.15-34.71) | 0.55 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | 0.34 | 1.03(0.36-1.70) | 2.80(1.43-5.48) | 0.01 | | | | | | | | |
| Weighted median | 0.19 | 0.11(-0.25-0.48) | 1.12(0.78-1.61) | 0.54 | 19.31 | 0.63 | 27.19 | 0.25 | -0.24 | 0.01 | NA | 0.25 |
| IVW | 0.14 | 0.14(-0.14-0.42) | 1.15(0.87-1.53) | 0.31 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| MR Egger | 0.61 | 0.19(-1.00-1.38) | 1.20(0.37-3.96) | 0.76 | | | | | | | | |
| Weighted median | 0.51 | 0.54(-0.46-1.55) | 1.72(0.63-4.73) | 0.29 | 6.58 | 0.88 | 7.21 | 0.89 | 0.05 | 0.44 | NA | 0.92 |
| IVW | 0.34 | 0.58(-0.09-1.25) | 1.79(0.91-3.50) | 0.09 | | | | | | | | |

SE, standard error. OR, odds ratio. IVW, Inverse variance weighted.

**Supplementary Table S10. MR analysis results of associations between circulating antioxidants and pancreatic cancer.**

| | SE | β(95%CI) | OR(95%CI) | P | Heterogeneity | | | | pleiotropy | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | MR Egger | | IVW | | MR-Egger intercept | | MR-PRESO | |
| **β-carotene** | | | | | Q | P | Q | P | intercept | P | No. of outlier | P |
| MR Egger | | / | / | / | | | | | | | | |
| Weighted median | | / | / | / | / | / | 1.03 | 0.31 | / | / | / | / |
| IVW | 0.37 | -0.62(-1.36-0.11) | 0.54(0.26-1.11) | 0.09 | | | | | | | | |
| **lycopene** | | | | | | | | | | | | |
| MR Egger | 0.23 | -0.30(-0.74-0.14) | 0.74(0.48-1.15) | 0.28 | | | | | | | | |
| Weighted median | 0.16 | -0.04(-0.36-0.27) | 0.96(0.70-1.32) | 0.79 | 2.79 | 0.43 | 3.94 | 0.41 | 0.09 | 0.46 | NA | 0.40 |
| IVW | 0.12 | -0.10(-0.34-0.14) | 0.91(0.71-1.16) | 0.43 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 3.20 | 0.07 | / | / | / | / |
| IVW | 2.53 | -1.41(-6.38-3.55) | 0.24(0.00-34.91) | 0.58 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| Wald ratio | 0.03 | -0.01(-0.06-0.04) | 0.99(0.94-1.04) | 0.74 | / | / | / | / | / | / | / | / |
| **Circulating antioxidant metabolites** | | | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | | | |
| MR Egger | 2.20 | -2.23(-6.55-2.09) | 0.11(0.00-8.05) | 0.34 | | | | | | | | |
| Weighted median | 1.37 | -1.66(-4.34-1.02) | 0.19(0.01-2.77) | 0.22 | 5.04 | 0.83 | 5.34 | 0.87 | 0.03 | 0.60 | NA | 0.79 |
| IVW | 1.03 | -1.18(-3.19-0.84) | 0.31(0.04-2.31) | 0.25 | | | | | | | | |
| **γ-tocopherol** | | | | | | | | | | | | |
| MR Egger | 1.36 | -1.88(-4.53-0.78) | 0.15(0.01-2.18) | 0.20 | | | | | | | | |
| Weighted median | 0.79 | -1.39(-2.93-0.15) | 0.25(0.05-1.16) | 0.08 | 14.09 | 0.17 | 16.77 | 0.11 | 0.07 | 0.20 | NA | 0.14 |
| IVW | 0.68 | -0.24(-1.58-1.10) | 0.79(0.21-3.00) | 0.72 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | 0.18 | 0.00(-0.36-0.35) | 1.00(0.70-1.43) | 0.98 | | | | | | | | |
| Weighted median | 0.10 | -0.08(-0.27-0.12) | 0.93(0.76-1.13) | 0.45 | 14.67 | 0.88 | 14.86 | 0.90 | -0.02 | 0.66 | NA | 0.90 |
| IVW | 0.07 | -0.08(-0.22-0.06) | 0.92(0.81-1.06) | 0.26 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| MR Egger | 0.33 | 0.06(-0.58-0.70) | 1.06(0.56-2.00) | 0.86 | | | | | | | | |
| Weighted median | 0.25 | 0.09(-0.40-0.58) | 1.09(0.67-1.78) | 0.73 | 6.81 | 0.87 | 7.09 | 0.90 | 0.02 | 0.61 | NA | 0.90 |
| IVW | 0.18 | 0.20(-0.16-0.56) | 1.22(0.85-1.75) | 0.28 | | | | | | | | |

SE, standard error. OR, odds ratio. IVW, Inverse variance weighted.

**Supplementary Table S11. MR analysis results of associations between circulating antioxidants and liver cancer.**

| | SE | β(95%CI) | OR(95%CI) | P | Heterogeneity | | | | pleiotropy | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | MR Egger | | IVW | | MR-Egger intercept | | MR-PRESO | |
| **β-carotene** | | | | | Q | P | Q | P | intercept | P | No. of outlier | P |
| MR Egger | | | | | | | | | | | | |
| Weighted median | | | | | / | / | 2.55 | 0.11 | / | / | / | / |
| IVW | 1.25 | 0.31(-2.15-2.77) | 1.36(0.12-15.94) | 0.80 | | | | | | | | |
| **lycopene** | | | | | | | | | | | | |
| MR Egger | 0.56 | 0.76(-0.34-1.86) | 2.14(0.71-6.43) | 0.27 | | | | | | | | |
| Weighted median | 0.36 | -0.16(-0.87-0.55) | 0.85(0.42-1.73) | 0.66 | 3.98 | 0.26 | 7.52 | 0.11 | -0.33 | 0.20 | NA | 0.17 |
| IVW | 0.36 | -0.01(-0.72-0.70) | 0.99(0.49-2.01) | 0.98 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | | | | | | | | | | | | |
| Weighted median | | | | | / | / | 0.03 | 0.86 | / | / | / | / |
| IVW | 3.03 | -1.34(-7.28-4.60) | 0.26(0.00-99.56) | 0.66 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| Wald ratio | 0.06 | -0.04(-0.15-0.07) | 0.96(0.86-1.07) | 0.48 | / | / | / | / | / | / | / | / |
| **Circulating antioxidant metabolites** | | | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | | | |
| MR Egger | 4.71 | -2.47(-11.7-6.75) | 0.08(0.00-856.20) | 0.61 | | | | | | | | |
| Weighted median | 2.87 | -1.22(-6.84-4.41) | 0.30(0.00-81.91) | 0.67 | 6.96 | 0.64 | 7.01 | 0.72 | 0.03 | 0.84 | NA | 0.70 |
| IVW | 2.20 | -1.59(-5.9-2.72) | 0.20(0.00-15.18) | 0.47 | | | | | | | | |
| **γ-tocopherol** | | | | | | | | | | | | |
| MR Egger | 2.69 | -3.35(-8.63-1.93) | 0.04(0.00-6.88) | 0.24 | | | | | | | | |
| Weighted median | 1.72 | 0.88(-2.49-4.25) | 2.41(0.08-69.86) | 0.61 | 11.86 | 0.29 | 15.87 | 0.15 | 0.19 | 0.10 | NA | 0.13 |
| IVW | 1.43 | 0.99(-1.81-3.80) | 2.70(0.16-44.54) | 0.49 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | 0.50 | 0.72(-0.25-1.69) | 2.05(0.78-5.43) | 0.16 | | | | | | | | |
| Weighted median | 0.24 | 0.12(-0.35-0.60) | 1.13(0.70-1.82) | 0.61 | 35.21 | 0.04 | 37.40 | 0.03 | -0.14 | 0.25 | NA | 0.19 |
| IVW | 0.19 | 0.18(-0.19-0.56) | 1.20(0.82-1.75) | 0.34 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| MR Egger | 0.89 | -0.28(-2.03-1.46) | 0.75(0.13-4.31) | 0.76 | | | | | | | | |
| Weighted median | 0.52 | -0.21(-1.24-0.82) | 0.81(0.29-2.26) | 0.69 | 19.63 | 0.07 | 19.71 | 0.10 | 0.02 | 0.84 | NA | 0.19 |
| IVW | 0.48 | -0.13(-1.07-0.82) | 0.88(0.34-2.27) | 0.79 | | | | | | | | |

SE, standard error. OR, odds ratio. IVW, Inverse variance weighted.

**Supplementary Table S12. MR analysis results of associations between circulating antioxidants and esophageal cancer.**

| | SE | β(95%CI) | OR(95%CI) | P | Heterogeneity | | | | pleiotropy | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute circulating antioxidants** | | | | | MR Egger | | IVW | | MR-Egger intercept | | MR-PRESO | |
| **β-carotene** | | | | | Q | P | Q | P | intercept | P | No. of outlier | P |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 1.47 | 0.22 | / | / | / | / |
| IVW | 0.77 | 0.82(-0.69-2.33) | 2.27(0.50-10.28) | 0.29 | | | | | | | | |
| **lycopene** | | | | | | | | | | | | |
| MR Egger | 0.39 | -0.13(-0.90-0.64) | 0.88(0.41-1.90) | 0.77 | | | | | | | | |
| Weighted median | 0.25 | -0.23(-0.72-0.26) | 0.79(0.49-1.29) | 0.35 | 1.60 | 0.66 | 1.60 | 0.81 | 0.00 | 1.00 | NA | 0.72 |
| IVW | 0.21 | -0.13(-0.55-0.29) | 0.88(0.58-1.33) | 0.54 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | / | / | / | / | | | | | | | | |
| Weighted median | / | / | / | / | / | / | 0.49 | 0.48 | / | / | / | / |
| IVW | 2.45 | 0.83(-3.98-5.64) | 2.29(0.02-280.07) | 0.74 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| Wald ratio | 0.05 | -0.02(-0.11-0.07) | 0.98(0.90-1.08) | 0.70 | / | / | / | / | / | / | / | / |
| **Circulating antioxidant metabolites** | | | | | | | | | | | | |
| **α-tocopherol** | | | | | | | | | | | | |
| MR Egger | 3.81 | -1.44(-8.91-6.04) | 0.24(0.00-420.49) | 0.72 | | | | | | | | |
| Weighted median | 2.49 | -0.66(-5.54-4.22) | 0.52(0.00-68.03) | 0.79 | 8.86 | 0.45 | 9.73 | 0.46 | 0.10 | 0.37 | NA | 0.51 |
| IVW | 1.78 | 1.72(-1.77-5.21) | 5.58(0.17-183.53) | 0.33 | | | | | | | | |
| **γ-tocopherol** | | | | | | | | | | | | |
| MR Egger | 2.14 | 0.16(-4.04-4.36) | 1.18(0.02-78.19) | 0.94 | | | | | | | | |
| Weighted median | 1.21 | 1.22(-1.16-3.59) | 3.38(0.31-36.29) | 0.32 | 11.71 | 0.30 | 11.96 | 0.37 | 0.04 | 0.65 | NA | 0.44 |
| IVW | 1.00 | 1.03(-0.93-2.99) | 2.80(0.40-19.89) | 0.30 | | | | | | | | |
| **retinol** | | | | | | | | | | | | |
| MR Egger | 0.32 | 0.35(-0.27-0.97) | 1.42(0.76-2.64) | 0.28 | | | | | | | | |
| Weighted median | 0.18 | 0.02(-0.33-0.37) | 1.02(0.72-1.44) | 0.93 | 21.15 | 0.51 | 21.93 | 0.52 | -0.07 | 0.39 | NA | 0.54 |
| IVW | 0.12 | 0.09(-0.15-0.33) | 1.09(0.86-1.39) | 0.47 | | | | | | | | |
| **ascorbate** | | | | | | | | | | | | |
| MR Egger | 0.56 | 0.40(-0.71-1.5) | 1.49(0.49-4.48) | 0.50 | | | | | | | | |
| Weighted median | 0.49 | 0.49(-0.47-1.45) | 1.63(0.62-4.25) | 0.32 | 9.28 | 0.68 | 9.33 | 0.75 | 0.01 | 0.83 | NA | 0.79 |
| IVW | 0.32 | 0.50(-0.12-1.12) | 1.65(0.88-3.07) | 0.12 | | | | | | | | |

SE, standard error. OR, odds ratio. IVW, Inverse variance weighted.