

Supplementary table 1. 95% CIs for risk (RR) to detect multiplicative interaction and the interaction contrast ratio (ICR) together with the risk difference (RD) to detect additive interaction.

| Interaction | Multiplicative ¹ | Multiplicative ² | Additive ¹ | Additive ² |
|--|---|---|---|---|
| Age × No family history (0) Family history (1) | $p = 0.640$ RR0: 1.56–2.60 RR1: 1.15–1.69 | $p = 0.228$ RR0: 1.63–2.51 RR1: 1.21–1.64 | ICR: -1.27–0.85 RD0: 0.13–0.24 RD1: 0.06–0.20 | ICR: -1.23–1.91 RD0: 0.16–0.27 RD1: 0.09–0.21 |
| Diabetes × No family history (0) Family history (1) | $p = 0.969$ RR0: 1.16–1.92 RR1: 1.14–1.74 | $p = 0.671$ RR0: 1.26–1.81 RR1: 1.15–1.53 | ICR: -1.02–2.43 RD0: 0.05–0.26 RD1: 0.05–0.28 | ICR: -1.29–3.43 RD0: 0.09–0.27 RD1: 0.07–0.24 |
| Smoking × No family history (0) Family history (1) | $p = 0.127$ RR0: 0.79–1.16 RR1: 0.98–1.35 | $p = 0.131$ RR0: 0.83–1.12 RR1: 0.99–1.25 | ICR: -1.28–0.05 RD0: -0.07–0.05 RD1: -0.01–0.13 | ICR: -0.12–2.34 RD0: -0.07–0.04 RD1: 0.00–0.11 |
| Obesity × No family history (0) Family history (1) | $p = 0.594$ RR0: 0.97–1.49 RR1: 1.06–1.51 | $p = 0.825$ RR0: 0.94–1.34 RR1: 1.01–1.31 | ICR: -0.39–1.41 RD0: -0.01–0.14 RD1: 0.02–0.19 | ICR: -0.95–1.68 RD0: -0.02–0.11 RD1: 0.00–0.14 |
| High S-LDL-C × No family history (0) Family history (1) | $p = 0.665$ RR0: 1.20–1.70 RR1: 1.22–1.66 | $p = 0.809$ RR0: 1.20–1.58 RR1: 1.19–1.48 | ICR: -0.16–1.31 RD0: 0.06–0.17 RD1: 0.08–0.22 | ICR: -0.24–2.32 RD0: 0.07–0.17 RD1: 0.09–0.19 |
| Hypertension × No family history (0) Family history (1) | $p = 0.291$ RR0: 1.23–1.78 RR1: 1.05–1.46 | $p = 0.351$ RR0: 1.40–1.92 RR1: 1.19–1.52 | ICR: -0.78–0.62 RD0: 0.07–0.18 RD1: 0.02–0.15 | ICR: -0.84–1.69 RD0: 0.12–0.22 RD1: 0.08–0.19 |
| Diabetes × Age <50 (0) Age >50 (1) | $p = 0.563$ RR0: 1.14–2.60 RR1: 1.13–1.61 | $p = 0.813$ RR0: 1.01–2.08 RR1: 1.20–1.51 | ICR: -2.08–2.33 RD0: 0.02–0.34 RD1: 0.05–0.23 | ICR: -0.50–2.83 RD0: 0.00–0.27 RD1: 0.09–0.23 |
| Smoking × Age <50 (0) Age >50 (1) | $p = 0.767$ RR0: 0.76–1.38 RR1: 0.93–1.22 | $p = 0.898$ RR0: 0.83–1.35 RR1: 0.96–1.16 | ICR: -0.55–0.81 RD0: -0.07–0.08 RD1: -0.03–0.08 | ICR: -0.49–0.71 RD0: -0.05–0.09 RD1: -0.02–0.07 |
| Obesity × Age <50 (0) Age >50 (1) | $p = 0.032$ RR0: 1.27–2.33 RR1: 0.95–1.30 | $p = 0.174$ RR0: 1.05–1.82 RR1: 0.96–1.20 | ICR: -2.22–0.42 RD0: 0.06–0.27 RD1: -0.02–0.11 | ICR: -1.30–0.59 RD0: 0.01–0.21 RD1: -0.02–0.09 |
| High S-LDL-C × Age <50 (0) Age >50 (1) | $p = 0.002$ RR0: 1.59–2.79 RR1: 1.07–1.38 | $p = 0.005$ RR0: 1.48–2.34 RR1: 1.10–1.32 | ICR: -2.24–0.29 RD0: 0.12–0.28 RD1: 0.03–0.13 | ICR: -1.45–0.52 RD0: 0.12–0.27 RD1: 0.04–0.13 |
| Hypertension × Age <50 (0) Age >50 (1) | $p = 0.932$ RR0: 1.04–1.84 RR1: 1.14–1.50 | $p = 0.194$ RR0: 1.07–1.73 RR1: 1.31–1.62 | ICR: -0.27–1.27 RD0: 0.01–0.15 RD1: 0.06–0.16 | ICR: 0.60–1.92 RD0: 0.02–0.16 RD1: 0.12–0.21 |
| Smoking × No diabetes (0) Diabetes (1) | $p = 0.956$ RR0: 0.92–1.20 RR1: 0.74–1.43 | $p = 0.194$ RR0: 0.97–1.18 RR1: 0.72–1.16 | ICR: -1.26–1.75 RD0: -0.03–0.06 RD1: -0.15–0.18 | ICR: -1.55–0.61 RD0: -0.01–0.07 RD1: -0.18–0.08 |
| Obesity × No diabetes (0) Diabetes (1) | $p = 0.923$ RR0: 1.01–1.38 RR1: 0.82–1.51 | $p = 0.980$ RR0: 0.96–1.23 RR1: 0.86–1.30 | ICR: -1.22–1.92 RD0: 0.00–0.13 RD1: -0.10–0.21 | ICR: -0.95–1.35 RD0: -0.02–0.09 RD1: -0.09–0.15 |

¹Study participants free of coronary heart disease at baseline ($n = 1958$). ²All study participants ($n = 2682$).

Frames highlight statistically significant interactions.

Supplementary table 1. Continues.

| Interaction | Multiplicative ¹ | Multiplicative ² | Additive ¹ | Additive ² |
|--|-------------------------------|-------------------------------|--------------------------------------|--------------------------------------|
| High S-LDL-C × No diabetes (0) | $p = 0.478$ RR0: 1.28–1.65 | $p = 0.542$ RR0: 1.26–1.52 | ICR: -1.59–2.25 RD0: 0.09–0.18 | ICR: -1.08–1.95 RD0: 0.10–0.17 |
| Diabetes (1) | RR1: 0.87–1.60 | RR1: 0.95–1.44 | RD1: -0.07–0.24 | RD1: -0.03–0.21 |
| Hypertension × No diabetes (0) | $p = 0.755$ RR0: 1.19–1.54 | $p = 0.812$ RR0: 1.32–1.62 | ICR: -1.68–1.77 RD0: -0.09–0.25 | ICR: -0.66–2.14 RD0: 0.11–0.19 |
| Diabetes (1) | RR1: 0.82–1.73 | RR1: 1.01–1.93 | RD1: 0.06–0.15 | RD1: 0.02–0.32 |
| Obesity × No smoking (0) | $p = 0.034$ RR0: 1.15–1.57 | $p = 0.007$ RR0: 1.11–1.41 | ICR: -1.50–(-0.01) RD0: 0.05–0.18 | ICR: -1.29–(-0.19) RD0: 0.04–0.16 |
| Smoking (1) | RR1: 0.66–1.28 | RR1: 0.69–1.12 | RD1: -0.04–0.09 | RD1: -0.15–0.04 |
| High S-LDL-C × No smoking (0) | $p = 0.830$ RR0: 1.22–1.62 | $p = 0.953$ RR0: 1.22–1.51 | ICR: -0.52–0.68 RD0: 0.07–0.18 | ICR: -0.49–0.50 RD0: 0.08–0.18 |
| Smoking (1) | RR1: 1.17–1.77 | RR1: 1.15–1.56 | RD1: 0.06–0.21 | RD1: 0.06–0.19 |
| Hypertension × No smoking (0) | $p = 0.649$ RR0: 1.16–1.58 | $p = 0.887$ RR0: 1.34–1.73 | ICR: -0.39–0.78 RD0: 0.05–0.16 | ICR: -0.47–0.68 RD0: 0.12–0.21 |
| Smoking (1) | RR1: 1.15–1.75 | RR1: 1.25–1.72 | RD1: 0.05–0.21 | RD1: 0.10–0.23 |
| High S-LDL-C × No obesity (0) | $p = 0.870$ RR0: 1.25–1.63 | $p = 0.895$ RR0: 1.24–1.51 | ICR: -0.53–1.67 RD0: 0.08–0.18 | ICR: -0.54–1.05 RD0: 0.09–0.17 |
| Obesity (1) | RR1: 1.09–1.76 | RR1: 1.08–1.56 | RD1: 0.04–0.26 | RD1: 0.04–0.22 |
| Hypertension × No obesity (0) | $p = 0.953$ RR0: 1.17–1.54 | $p = 0.676$ RR0: 1.33–1.64 | ICR: -0.91–0.87 RD0: 0.06–0.15 | ICR: -1.55–0.25 RD0: 0.12–0.20 |
| Obesity (1) | RR1: 0.91–1.87 | RR1: 1.13–2.18 | RD1: -0.03–0.23 | RD1: 0.07–0.29 |
| Hypertension × No high S-LDL-C (0) | $p = 0.100$ RR0: 1.31–1.91 | $p = 0.074$ RR0: 1.47–2.01 | ICR: -1.00–0.69 RD0: 0.08–0.19 | ICR: -0.65–0.88 RD0: 0.14–0.24 |
| High S-LDL-C (1) | RR1: 1.03–1.42 | RR1: 1.16–1.50 | RD1: 0.01–0.15 | RD1: 0.07–0.19 |

¹Study participants free of coronary heart disease at baseline ($n = 1958$). ²All study participants ($n = 2682$).

Frames highlight statistically significant interactions.