**Table S1. Subgroup analyses: Associations of cardiovascular drugs use with gastric cancer incidence and mortality, stratified by sex \***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric cancer incidence** | | | | **Gastric cancer mortality** | | | |
| Men | | Women | | Men | | Women | |
| HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Duration of aspirin use, day** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.97 (0.90–1.04) | 0.38 | 0.90 (0.81–1.01) | 0.07 | 1.16 (1.06–1.27) | <0.01 | 0.98 (0.86–1.11) | 0.74 |
| 182.5 – 365.0 | 0.85 (0.76–0.95) | <0.01 | 0.80 (0.68–0.96) | 0.01 | 1.04 (0.90–1.20) | 0.62 | 0.85 (0.69–1.05) | 0.13 |
| 365.0 – 547.5 | 0.83 (0.73–0.93) | <0.01 | 0.75 (0.63–0.91) | <0.01 | 1.00 (0.86–1.17) | 0.97 | 0.91 (0.73–1.13) | 0.39 |
| ≥ 547.5 | 0.91 (0.85–0.97) | <0.01 | 0.83 (0.74–0.93) | <0.01 | 0.64 (0.57–0.72) | <0.01 | 0.78 (0.67–0.90) | <0.01 |
| *P* for trend | <0.01 |  | <0.01 |  | <0.01 |  | <0.01 |  |
| **cDDD of metformin use** |  |  |  |  |  |  |  |  |
| Non-DM | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| DM, never use | 1.20 (1.10–1.31) | <0.01 | 1.19 (1.03–1.36) | 0.02 | 1.73 (1.56–1.92) | <0.01 | 1.99 (1.72–2.30) | <0.01 |
| < 182.5 | 1.17 (1.08–1.27) | <0.01 | 1.33 (1.18–1.51) | <0.01 | 1.33 (1.19–1.49) | <0.01 | 1.69 (1.46–1.95) | <0.01 |
| 182.5 – 365.0 | 1.29 (1.16–1.44) | <0.01 | 1.24 (1.05–1.48) | 0.01 | 1.36 (1.16–1.59) | <0.01 | 1.31 (1.03–1.65) | 0.03 |
| 365.0 – 547.5 | 1.15 (0.95–1.40) | 0.14 | 1.33 (0.99–1.77) | 0.05 | 1.15 (0.86–1.53) | 0.35 | 1.09 (0.69–1.71) | 0.72 |
| ≥ 547.5 | 1.23 (0.96–1.58) | 0.11 | 1.38 (0.92–2.08) | 0.12 | 0.88 (0.56–1.38) | 0.57 | 1.13 (0.58–2.18) | 0.72 |
| *P* for trend ‡ | 0.32 |  | 0.62 |  | <0.01 |  | <0.01 |  |
| **cDDD of statin use** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.99 (0.92–1.07) | 0.82 | 1.03 (0.93–1.14) | 0.05 | 0.72 (0.64–0.82) | <0.01 | 0.59 (0.50–0.69) | <0.01 |
| 182.5 – 365.0 | 1.05 (0.94–1.17) | 0.39 | 1.15 (1.00–1.32) | 0.04 | 0.75 (0.63–0.90) | <0.01 | 0.69 (0.57–0.85) | <0.01 |
| 365.0 – 547.5 | 1.17 (1.01–1.35) | 0.04 | 1.07 (0.87–1.31) | 0.53 | 0.80 (0.63–1.01) | 0.06 | 0.78 (0.60–1.03) | 0.08 |
| ≥ 547.5 | 1.05 (0.88–1.25) | 0.62 | 1.15 (0.90–1.48) | 0.27 | 0.81 (0.61–1.08) | 0.15 | 0.61 (0.41–0.91) | 0.02 |
| *P* for trend | 0.11 |  | 0.05 |  | <0.01 |  | <0.01 |  |
| HR, hazard ratio; CI, confidence interval; cDDD, cumulative defined daily dose; DM, diabetes mellitus  \* Adjusted for age (5-year group), income, Charlson comorbidity index (continuous), and concomitant use of other CVD drugs.  † P for trend was calculated among diabetic patients only. | | | | | | | | |

**Table S2. Subgroup analyses: associations of cardiovascular drugs use with gastric cancer incidence and mortality, stratified by age \***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric cancer incidence** | | | | **Gastric cancer mortality** | | | |
| Age < 65 | | Age ≥ 65 | | Age < 65 | | Age ≥ 65 | |
| HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Duration of aspirin use, day** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.93 (0.85–1.01) | 0.08 | 0.95 (0.87–1.04) | 0.29 | 1.17 (1.01–1.34) | 0.03 | 1.05 (0.96–1.14) | 0.33 |
| 182.5 – 365.0 | 0.79 (0.69–0.90) | <0.01 | 0.84 (0.73–0.96) | 0.01 | 0.83 (0.66–1.05) | 0.12 | 1.00 (0.87–1.15) | 0.98 |
| 365.0 – 547.5 | 0.75 (0.65–0.86) | <0.01 | 0.82 (0.71–0.95) | 0.01 | 0.92 (0.73–1.16) | 0.48 | 0.96 (0.83–1.11) | 0.59 |
| ≥ 547.5 | 0.83 (0.76–0.90) | <0.01 | 0.88 (0.81–0.96) | 0.01 | 0.60 (0.51–0.71) | <0.01 | 0.69 (0.63–0.77) | <0.01 |
| *P* for trend | <0.01 |  | <0.01 |  | <0.01 |  | <0.01 |  |
| **cDDD of metformin use** |  |  |  |  |  |  |  |  |
| Non-DM | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| DM, never use | 1.16 (1.05–1.29) | <0.01 | 1.12 (1.01–1.25) | 0.03 | 2.59 (2.25–2.98) | <0.01 | 1.46 (1.31–1.63) | <0.01 |
| < 182.5 | 1.15 (1.05–1.26) | <0.01 | 1.13 (1.02–1.26) | 0.02 | 1.66 (1.43–1.93) | <0.01 | 1.29 (1.16–1.45) | <0.01 |
| 182.5 – 365.0 | 1.32 (1.17–1.48) | <0.01 | 1.01 (0.87–1.18) | 0.88 | 1.63 (1.32–2.01) | <0.01 | 1.16 (0.98–1.37) | 0.09 |
| 365.0 – 547.5 | 1.20 (0.98–1.46) | 0.07 | 0.97 (0.74–1.27) | 0.82 | 1.37 (0.94–1.99) | 0.11 | 0.97 (0.71–1.33) | 0.86 |
| ≥ 547.5 | 1.06 (0.80–1.40) | 0.67 | 1.31 (0.94–1.82) | 0.11 | 1.17 (0.68–2.03) | 0.58 | 0.79 (0.48–1.32) | 0.37 |
| *P* for trend ‡ | 0.41 |  | 0.91 |  | <0.01 |  | <0.01 |  |
| **cDDD of statin use** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.90 (0.83–0.98) | 0.01 | 0.95 (0.86–1.05) | 0.31 | 0.61 (0.52–0.72) | <0.01 | 0.68 (0.60–0.77) | <0.01 |
| 182.5 – 365.0 | 0.96 (0.86–1.07) | 0.46 | 1.04 (0.91–1.19) | 0.54 | 0.67 (0.54–0.84) | <0.01 | 0.74 (0.63–0.88) | <0.01 |
| 365.0 – 547.5 | 1.05 (0.90–1.22) | 0.52 | 1.01 (0.84–1.23) | 0.88 | 0.67 (0.49–0.93) | 0.02 | 0.84 (0.67–1.04) | 0.11 |
| ≥ 547.5 | 0.95 (0.79–1.14) | 0.58 | 1.08 (0.86–1.35) | 0.51 | 0.65 (0.44–0.96) | 0.03 | 0.76 (0.57–1.01) | 0.06 |
| *P* for trend | 0.32 |  | 0.65 |  | <0.01 |  | <0.01 |  |
| HR = hazard ratio; CI = confidence interval; cDDD = cumulative defined daily dose; DM = diabetes mellitus  \* Adjusted for age (5-year group), sex, income, Charlson comorbidity index (continuous), and concomitant use of other CVD drugs.  † P for trend was calculated among diabetic patients only. | | | | | | | | |

**Table S3. Subgroup analyses: associations of cardiovascular drugs use with gastric cancer incidence and mortality, stratified by body mass index \***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric cancer incidence** | | | | **Gastric cancer mortality** | | | |
| BMI < 25 kg/m2 | | BMI ≥ 25 kg/m2 | | BMI < 25 kg/m2 | | BMI ≥ 25 kg/m2 | |
| HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Duration of aspirin use, day** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.97 (0.88–1.08) | 0.62 | 0.92 (0.80–1.05) | 0.21 | 1.25 (1.09–1.43) | <0.01 | 1.08 (0.86–1.35) | 0.50 |
| 182.5 – 365.0 | 0.94 (0.80–1.10) | 0.42 | 0.68 (0.55–0.85) | <0.01 | 0.95 (0.75–1.20) | 0.66 | 0.82 (0.57–1.16) | 0.26 |
| 365.0 – 547.5 | 0.77 (0.64–0.93) | 0.01 | 0.73 (0.59–0.91) | 0.01 | 0.96 (0.75–1.23) | 0.76 | 1.04 (0.75–1.43) | 0.83 |
| ≥ 547.5 | 0.82 (0.73–0.92) | <0.01 | 0.88 (0.78–0.99) | 0.04 | 0.68 (0.57–0.81) | <0.01 | 0.52 (0.40–0.67) | <0.01 |
| *P* for trend | <0.01 |  | <0.01 |  | <0.01 |  | <0.01 |  |
| **cDDD of metformin use** |  |  |  |  |  |  |  |  |
| Non-DM | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| DM, never use | 1.26 (1.11–1.44) | <0.01 | 1.23 (1.06–1.44) | 0.01 | 2.32 (1.97–2.72) | <0.01 | 2.23 (1.77–2.79) | <0.01 |
| < 182.5 | 1.11 (0.97–1.26) | 0.13 | 1.18 (1.02–1.35) | 0.02 | 1.49 (1.24–1.80) | <0.01 | 1.57 (1.24–1.99) | <0.01 |
| 182.5 – 365.0 | 1.46 (1.24–1.71) | <0.01 | 1.13 (0.93–1.37) | 0.24 | 1.69 (1.32–2.16) | <0.01 | 1.44 (1.03–2.01) | 0.03 |
| 365.0 – 547.5 | 1.19 (0.88–1.61) | 0.26 | 1.36 (1.00–1.84) | 0.05 | 1.55 (1.01–2.40) | 0.05 | 0.82 (0.39–1.74) | 0.61 |
| ≥ 547.5 | 1.26 (0.85–1.88) | 0.25 | 1.00 (0.63–1.60) | 0.99 | 0.83 (0.37–1.86) | 0.66 | 0.68 (0.22–2.11) | 0.50 |
| *P* for trend ‡ | 0.53 |  | 0.74 |  | <0.01 |  | <0.01 |  |
| **cDDD of statin use** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.98 (0.88–1.10) | 0.77 | 0.86 (0.75–0.98) | 0.02 | 0.71 (0.59–0.86) | <0.01 | 0.56 (0.42–0.73) | <0.01 |
| 182.5 – 365.0 | 1.11 (0.95–1.29) | 0.18 | 0.96 (0.81–1.14) | 0.63 | 0.99 (0.78–1.25) | 0.91 | 0.56 (0.39–0.81) | <0.01 |
| 365.0 – 547.5 | 1.30 (1.05–1.60) | 0.01 | 0.87 (0.68–1.12) | 0.29 | 0.88 (0.61–1.26) | 0.48 | 0.46 (0.26–0.82) | 0.01 |
| ≥ 547.5 | 1.07 (0.81–1.40) | 0.64 | 1.05 (0.80–1.40) | 0.71 | 0.66 (0.40–1.09) | 0.11 | 0.55 (0.28–1.07) | 0.08 |
| *P* for trend | 0.05 |  | 0.28 |  | 0.02 |  | <0.01 |  |
| BMI, body mass index; HR, hazard ratio; CI, confidence interval; cDDD, cumulative defined daily dose; DM, diabetes mellitus  \* Adjusted for age (5-year group), sex, income, Charlson comorbidity index (continuous), body mass index (continuous), smoking status, alcohol consumption, hypertension, and concomitant use of other CVD drugs.  † P for trend was calculated among diabetic patients only. | | | | | | | | |

**Table S4. Subgroup analyses: associations of cardiovascular drugs use with gastric cancer incidence and mortality, stratified by smoking status \***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric cancer incidence** | | | | **Gastric cancer mortality** | | | |
| Non-current smoker | | Current smoker | | Non-current smoker | | Current smoker | |
| HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Duration of aspirin use, day** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.95 (0.86–1.05) | 0.32 | 0.96 (0.82–1.12) | 0.59 | 1.15 (1.00–1.32) | 0.05 | 1.33 (1.08–1.64) | 0.01 |
| 182.5 – 365.0 | 0.83 (0.71–0.96) | 0.02 | 0.83 (0.64–1.07) | 0.16 | 0.89 (0.71–1.12) | 0.32 | 0.94 (0.65–1.38) | 0.77 |
| 365.0 – 547.5 | 0.76 (0.65–0.90) | <0.01 | 0.75 (0.57–0.99) | 0.04 | 1.07 (0.86–1.33) | 0.56 | 0.78 (0.51–1.19) | 0.25 |
| ≥ 547.5 | 0.83 (0.76–0.92) | <0.01 | 0.92 (0.78–1.08) | 0.31 | 0.61 (0.51–0.72) | <0.01 | 0.66 (0.49–0.88) | <0.01 |
| *P* for trend | <0.01 |  | 0.07 |  | <0.01 |  | 0.01 |  |
| **cDDD of metformin use** |  |  |  |  |  |  |  |  |
| Non-DM | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| DM, never use | 1.25 (1.11–1.41) | <0.01 | 1.26 (1.05–1.53) | 0.02 | 2.36 (2.03–2.75) | <0.01 | 2.10 (1.63–2.71) | <0.01 |
| < 182.5 | 1.18 (1.05–1.32) | 0.01 | 1.07 (0.89–1.28) | 0.46 | 1.53 (1.29–1.82) | <0.01 | 1.52 (1.16–1.99) | <0.01 |
| 182.5 – 365.0 | 1.43 (1.24–1.65) | <0.01 | 1.03 (0.80–1.33) | 0.80 | 1.71 (1.36–2.15) | <0.01 | 1.35 (0.91–2.00) | 0.14 |
| 365.0 – 547.5 | 1.29 (1.00–1.66) | 0.05 | 1.25 (0.85–1.84) | 0.25 | 1.60 (1.06–2.40) | 0.02 | 0.58 (0.22–1.55) | 0.28 |
| ≥ 547.5 | 1.35 (0.96–1.90) | 0.08 | 0.73 (0.38–1.42) | 0.36 | 1.04 (0.52–2.08) | 0.92 | 0.26 (0.04–1.84) | 0.18 |
| *P* for trend ‡ | 0.27 |  | 0.24 |  | <0.01 |  | <0.01 |  |
| **cDDD of statin use** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.94 (0.85–1.03) | 0.20 | 0.92 (0.78–1.08) | 0.29 | 0.67 (0.56–0.80) | <0.01 | 0.63 (0.46–0.85) | <0.01 |
| 182.5 – 365.0 | 1.07 (0.94–1.22) | 0.29 | 0.98 (0.77–1.23) | 0.84 | 0.77 (0.61–0.98) | 0.03 | 0.96 (0.66–1.40) | 0.83 |
| 365.0 – 547.5 | 1.05 (0.87–1.27) | 0.58 | 1.22 (0.90–1.66) | 0.19 | 0.60 (0.41–0.87) | 0.01 | 1.08 (0.64–1.82) | 0.78 |
| ≥ 547.5 | 1.13 (0.91–1.42) | 0.27 | 0.92 (0.62–1.36) | 0.67 | 0.53 (0.32–0.87) | 0.01 | 0.88 (0.45–1.71) | 0.70 |
| *P* for trend | 0.32 |  | 0.98 |  | <0.01 |  | 0.28 |  |
| HR, hazard ratio; CI, confidence interval; cDDD, cumulative defined daily dose; DM, diabetes mellitus  \* Adjusted for age (5-year group), sex, income, Charlson comorbidity index (continuous), body mass index (continuous), alcohol consumption, hypertension, and concomitant use of other CVD drugs.  † P for trend was calculated among diabetic patients only. | | | | | | | | |

**Table S5. Subgroup analyses: associations of cardiovascular drugs use with gastric cancer incidence and mortality, stratified by alcohol consumption \***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric cancer incidence** | | | | **Gastric cancer mortality** | | | |
| Alcohol < 20g/day | | Alcohol ≥ 20g/day | | Alcohol < 20g/day | | Alcohol ≥ 20g/day | |
| HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Duration of aspirin use, day** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.91 (0.83–1.00) | 0.04 | 1.26 (1.02–1.54) | 0.03 | 1.17 (1.04–1.33) | 0.01 | 1.40 (1.00–1.95) | 0.05 |
| 182.5 – 365.0 | 0.84 (0.73–0.97) | 0.01 | 0.73 (0.49–1.08) | 0.12 | 0.88 (0.71–1.08) | 0.22 | 1.17 (0.68–2.02) | 0.57 |
| 365.0 – 547.5 | 0.75 (0.64–0.87) | <0.01 | 0.84 (0.57–1.24) | 0.37 | 0.99 (0.80–1.21) | 0.91 | 1.06 (0.58–1.97) | 0.84 |
| ≥ 547.5 | 0.83 (0.76–0.91) | <0.01 | 0.96 (0.76–1.20) | 0.72 | 0.61 (0.52–0.71) | <0.01 | 0.74 (0.48–1.14) | 0.18 |
| *P* for trend | <0.01 |  | 0.48 |  | <0.01 |  | 0.40 |  |
| **cDDD of metformin use** |  |  |  |  |  |  |  |  |
| Non-DM | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| DM, never use | 1.23 (1.11–1.38) | <0.01 | 1.36 (1.05–1.77) | 0.02 | 2.28 (1.98–2.62) | <0.01 | 2.37 (1.62–3.45) | <0.01 |
| < 182.5 | 1.13 (1.02–1.26) | 0.02 | 1.19 (0.93–1.53) | 0.17 | 1.55 (1.33–1.81) | <0.01 | 1.30 (0.83–2.05) | 0.25 |
| 182.5 – 365.0 | 1.27 (1.11–1.46) | <0.01 | 1.50 (1.08–2.07) | 0.02 | 1.50 (1.21–1.86) | <0.01 | 2.40 (1.45–3.97) | <0.01 |
| 365.0 – 547.5 | 1.24 (0.99–1.56) | 0.01 | 1.47 (0.84–2.56) | 0.17 | 1.27 (0.85–1.89) | 0.24 | 1.36 (0.43–4.28) | 0.60 |
| ≥ 547.5 | 1.22 (0.89–1.67) | 0.22 | 0.64 (0.20–1.98) | 0.44 | 0.87 (0.45–1.67) | 0.67 | - | - |
| *P* for trend ‡ | 0.72 |  | 0.80 |  | <0.01 |  | 0.11 |  |
| **cDDD of statin use** |  |  |  |  |  |  |  |  |
| Never use | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  | 1.00 (Reference) |  |
| < 182.5 | 0.95 (0.87–1.03) | 0.22 | 0.82 (0.64–1.04) | 0.10 | 0.65 (0.55–0.76) | <0.01 | 0.73 (0.47–1.14) | 0.16 |
| 182.5 – 365.0 | 1.05 (0.93–1.18) | 0.45 | 1.01 (0.72–1.42) | 0.94 | 0.85 (0.70–1.04) | 0.12 | 0.47 (0.21–1.07) | 0.07 |
| 365.0 – 547.5 | 1.12 (0.95–1.33) | 0.19 | 0.88 (0.52–1.48) | 0.63 | 0.70 (0.51–0.97) | 0.03 | 0.70 (0.26–1.91) | 0.49 |
| ≥ 547.5 | 1.13 (0.92–1.39) | 0.24 | 0.64 (0.32–1.30) | 0.22 | 0.66 (0.44–0.99) | 0.04 | 0.24 (0.03–1.76) | 0.16 |
| *P* for trend | 0.19 |  | 0.16 |  | <0.01 |  | 0.01 |  |
| HR, hazard ratio; CI, confidence interval; cDDD, cumulative defined daily dose; DM, diabetes mellitus  \* Adjusted for age (5-year group), sex, income, Charlson comorbidity index (continuous), body mass index (continuous), smoking status, hypertension, and concomitant use of other CVD drugs.  † P for trend was calculated among diabetic patients only. | | | | | | | | |