**Supplemental table 1**. List of morphological codes in ICD-O-3 used to differentiate the histological types of esophageal and gastric cancer

|  |  |
| --- | --- |
| **Adenocarcinoma** | |
| 8140/3 | Adenocarcinoma, NOS |
| 8141/3 | Scirrhous adenocarcinoma |
| 8144/3 | Adenocarcinoma, intestinal type (C16.\_) |
| 8145/3 | cardinoma, diffuse type (adenocarcinoma, diffuse type) (C16.\_) |
| 8147/3 | basal cell adenocarcinoma |
| 8150/3 | Islet cell carcinoma (C25.\_) |
| 8154/3 | Mixed islet cell and exocrine adenocarcinoma (C25.\_) |
| 8190/3 | Trabecular adenocarcinoma |
| 8210/3 | adenocarcinoma in adenomatous polyp |
| 8211/3 | tubular adenocarcinoma |
| 8214/3 | parietal cell carcinoma (parietal cell adenocarcinoma) (C16.\_) |
| 8215/3 | Adenocarcinoma of anal glands (C21.1) |
| 8220/3 | Adenomatous polyposis coli (C18.\_) |
| 8221/3 | adenocarcinoma in multiple adenomatous polys |
| 8250/3 | Bronchiolo-alveolar adenocarcinoma, NOS (C34.\_) |
| 8251/3 | Alveolar adenocarcinoma (C34.\_) |
| 8255/3 | adenocarcinoma with mixed subtypes |
| 8260/3 | Papillary adenocarcinoma, NOS |
| 8261/3 | adenocarcinoma in villous adenoma |
| 8262/3 | villous adenocarcinoma |
| 8263/3 | adenocarcinoma in tubolovillous adenoma |
| 8270/3 | Chromophobe carcinoma (C75.1) (Chromophobe adenocarcinoma (C75.1) |
| 8290/3 | Oxyphilic adenocarcinoma |
| 8300/3 | Basophil carcinoma (C75.1) (Basophil adenocarcinoma (C75.1); Mucoid cell adenocarcinoma (C75.1)) |
| 8310/3 | clear cell adenocarcinoma |
| 8320/3 | Granular cell carcinoma (Granular cell adenocarcinoma) |
| 8322/3 | Water-clear cell adenocarcinoma (C75.0) |
| 8323/3 | mix cell adenocarcinoma |
| 8330/3 | Follicular adenocarcinoma, NOS (C73.9) |
| 8331/3 | Follicular adenocarcinoma, well differentiated (C73.9) |
| 8332/3 | Follicular adenocarcinoma, trabecular (C73.9) |
| 8333/3 | Fetal adenocarcinoma |
| 8380/3 | Endometrioid adenocarcinoma, NOS |
| 8382/3 | Endometrioid adenocarcinoma, secretory variant |
| 8383/3 | Endometrioid adenocarcinoma, ciliated cell variant |
| 8384/3 | Adenocarcinoma, endocervical type |
| 8400/3 | Sweat gland adenocarcinoma (C44.\_) |
| 8401/3 | Apocrine adenocarcinoma |
| 8408/3 | Eccrine papillary adenocarcinoma (C44.\_) SKIN |
| 8410/3 | Sebaceous adenocarcinoma (C44.\_) SKIN |
| 8413/3 | Eccrine adenocarcinoma (C44.\_) |
| 8420/3 | Ceruminous adenocarcinoma (C44.2) |
| 8480/3 | mucinous adenocarcinoma |
| 8481/3 | mucin-producing adenocarcinoma |
| 8482/3 | Mucinous adenocarcinoma, endocervical type |
| 8490/3 | signet ring cell carcinoma |
| 8503/2 | Noninfiltrating intraductal papillary adenocarcinoma (C50.\_) |
| 8503/3 | Intraductal papillary adenocarcinoma (C50.\_) |
| 8504/3 | Intracystic carcinoma, NOS (Intracystic pallilary adenocarcinoma) |
| 8510/3 | Medullary carcinoma, NOS (Medullary adenocarcinoma) |
| 8525/3 | Polymorphous low grade adenocarcinoma |
| 8530/3 | Inflammatory carcinoma (C50.\_) (Inflammatory adenocarcinoma (C50.\_)) |
| 8571/3 | adenocarcinoma with cartilaginous and osseous metaplasisa |
| 8572/3 | adenocarcinoma with spindle cell metaplasia |
| 8573/3 | adenocarcinoma with apocrine metaplasia |
| 8574/3 | Adenocarcinoma with neuroendocrine differentiation |
| 8576/3 | Hepatoid adenocarcinoma |
|  |  |
| **Esophageal squamous-cell carcinoma** | |
| 8052/3 | Papillary squamous cell carcinoma |
| 8070/3 | squamous-cell carcinoma, NOS |
| 8071/3 | squamous-cell carcinoma, keratinizing |
| 8072/3 | squamous cell carcinoma, large cell, nonkeratinizing, NOS |
| 8073/3 | Squamous cell carcinoma, small cell, nonkeratinizing |
| 8074/3 | squamous cell carcinoma, spindle cell |
| 8075/3 | Squamous cell carcinoma, microinvasive |
| 8076/3 | Squamous cell carcinoma, microinvasive |
| 8078/3 | squamous cell carcinoma with horn formation |

**Supplemental table 2**. Hazard ratio (HR) with 95% confidence interval for incident esophageal adenocarcinoma and esophageal squamous-cell carcinoma related to metabolic syndrome with first two years follow-up excluded.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Esophageal adenocarcinoma** | | | **Esophageal squamous-cell carcinoma** | | |
| **Exposure** | **No.** | **HR†** | **HR‡** | **No.** | **HR†** | **HR§** |
|  |  |  |  |  |  |  |
| **Metabolic syndrome**# | |  |  |  |  |  |
| No | 21 | 1.0 | 1.0 | 24 | 1.0 | 1.0 |
| Yes | 31 | 1.53 (0.88-2.68) | 1.07 (0.52-2.21) | 19 | 0.83 (0.45-1.53) | 2.52 (0.94-6.74) |
|  |  |  |  |  |  |  |
| **Waist circumference** |  |  |  |  |  |  |
| Women<80 cm, men<94 cm | 10 | 1.0 | 1.0 | 15 | 1.0 | 1.0 |
| Women≥80 cm, men≥94 cm | 42 | 3.08 (1.54-6.17) | 1.79 (0.76-4.18) | 28 | 1.23 (0.65-2.32) | 2.03 (0.79-5.20) |
|  |  |  |  |  |  |  |
| **HDL** |  |  |  |  |  |  |
| Women≥1.3 mmol/L, men≥1.0 mmol/L | 45 | 1.0 | 1.0 | 36 | 1.0 | 1.0 |
| Women<1.3 mmol/L, men<1.0 mmol/L | 7 | 0.70 (0.32-1.57) | 0.46 (0.16-1.33) | 6 | 0.63 (0.26-1.51) | 0.65 (0.19-2.24) |
|  |  |  |  |  |  |  |
| **Triglycerides** |  |  |  |  |  |  |
| <1.7 mmol/L | 24 | 1.0 | 1.0 | 27 | 1.0 | 1.0 |
| ≥1.7 mmol/L | 28 | 1.38 (0.80-2.38) | 0.86 (0.43-1.71) | 16 | 0.78 (0.42-1.45) | 1.31 (0.57-3.00) |
|  |  |  |  |  |  |  |
| **Hypertension**¤ |  |  |  |  |  |  |
| No | 15 | 1.0 | 1.0 | 11 | 1.0 | 1.0 |
| Yes | 37 | 0.84 (0.45-1.57) | 0.66 (0.31-1.44) | 32 | 1.11 (0.54-2.29) | 3.39 (0.96-11.95) |
|  |  |  |  |  |  |  |
| **Non-fasting glucose^** |  |  |  |  |  |  |
| <5.6 mmol/L | 27 | 1.0 | 1.0 | 17 | 1.0 | 1.0 |
| ≥5.6 mmol/L | 25 | 1.00 (0.58-1.73) | 0.86 (0.43-1.72) | 26 | 1.82 (0.98-3.36) | 3.00 (1.07-8.46) |

† Adjusted for age (<60, ≥60 years), sex (women, men).

‡ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30, ≥ 30 kg/m2), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

§ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30, ≥ 30 kg/m2), education (primary/secondary school, high school, university), smoking status (no, yes), alcohol intake (>4, 4, 2-3, 1 times per week, and none), family cancer history (no, yes).

# Metabolic syndrome was defined by the presence of ≥3 of following 5 factors: increased waist circumference (men≥94 cm, women≥80 cm), elevated triglycerides (≥1.7 mmol/L), low HDL (men<1.0 mmol/L, women<1.3 mmol/L), hypertension (systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg), and high non-fasting glucose (≥5.6 mmol/L).

^ Additionally adjusted for time since last meal (<3, 3-5, ≥5 hours).

**Supplemental table 3**. Hazard ratio (HR) with 95% confidence interval for incident gastric adenocarcinoma related to metabolic syndrome with first two year follow up excluded.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total** | | | **Women** | | | **Men** | | |
| **Exposure** | **No.** | **HR†** | **HR‡** | **No.** | **HR†** | **HR§** | **No.** | **HR†** | **HR§** |
|  |  |  |  |  |  |  |  |  |  |
| **Metabolic syndrome**# | | |  |  |  |  |  |  |  |
| No | 127 | 1.0 | 1.0 | 53 | 1.0 | 1.0 | 74 | 1.0 | 1.0 |
| Yes | 156 | 1.23 (0.94-1.62) | 1.73 (1.17-2.56) | 60 | 1.17 (0.80-1.73) | 1.41 (0.86-2.32) | 96 | 1.35 (0.99-1.83) | 1.28 (0.91-1.80) |
|  |  |  |  |  |  |  |  |  |  |
| **Waist circumference** | |  |  |  |  |  |  |  |  |
| Men<94 cm, women<80 cm | 86 | 1.0 | 1.0 | 30 | 1.0 | 1.0 | 56 | 1.0 | 1.0 |
| Men≥94 cm, women≥80 cm | 197 | 1.40 (1.04-1.88) | 2.14 (1.36-3.36) | 83 | 1.29 (0.85-1.98) | 1.86 (1.03-3.38) | 114 | 1.55 (1.19-2.13) | 1.31 (0.91-1.90) |
|  |  |  |  |  |  |  |  |  |  |
| **HDL** |  |  |  |  |  |  |  |  |  |
| Men≥1.0 mmol/L, women≥1.3 mmol/L | 217 | 1.0 | 1.0 | 89 | 1.0 | 1.0 | 128 | 1.0 | 1.0 |
| Men<1.0 mmol/L, women<1.3 mmol/L | 62 | 1.08 (0.78-1.50) | 1.06 (0.70-1.60) | 24 | 0.72 (0.46-1.27) | 0.68 (0.39-1.63) | 38 | 1.46 (1.01-2.10) | 1.36 (0.93-1.97) |
|  |  |  |  |  |  |  |  |  |  |
| **Triglycerides** | |  |  |  |  |  |  |  |  |
| <1.7 mmol/L | 170 | 1.0 | 1.0 | 80 | 1.0 | 1.0 | 90 | 1.0 | 1.0 |
| ≥1.7 mmol/L | 111 | 0.86 (0.65-1.14) | 0.96 (0.67-1.37) | 33 | 0.70 (0.46-1.06) | 0.61 (0.37-1.00) | 78 | 0.98 (0.73-1.33) | 0.90 (0.66-1.24) |
|  |  |  |  |  |  |  |  |  |  |
| **Hypertension**¤ | |  |  |  |  |  |  |  |  |
| No | 57 | 1.0 | 1.0 | 23 | 1.0 | 1.0 | 34 | 1.0 | 1.0 |
| Yes | 226 | 1.74 (1.21-2.50) | 1.65 (1.04-2.64) | 90 | 2.19 (1.32-3.64) | 2.77 (1.49-5.15) | 136 | 1.39 (0.95-2.04) | 1.36 (0.92-2.02) |
|  |  |  |  |  |  |  |  |  |  |
| **Non-fasting glucose^** | |  |  |  |  |  |  |  |  |
| <5.6 mmol/L | 131 | 1.0 | 1.0 | 50 | 1.0 | 1.0 | 81 | 1.0 | 1.0 |
| ≥5.6 mmol/L | 152 | 1.43 (1.09-1.88) | 1.96 (1.35-2.84) | 63 | 1.58 (1.08-2.30) | 1.85 (1.17-2.92) | 89 | 1.16 (0.86-1.58) | 1.21 (0.88-1.66) |

† Adjusted for age (<60, ≥60 years).

‡ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30,≥ 30 kg/m2 ), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

§ Adjusted to age (<60, ≥60 years), BMI (<25, 25-30,≥ 30 kg/m2 ), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

# Metabolic syndrome was defined by the presence of ≥3 of following 5 factors: increased waist circumference (men≥94 cm, women≥80 cm), elevated triglycerides (≥1.7 mmol/L), low HDL (men<1.0 mmol/L, women<1.3 mmol/L), hypertension (systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg), and high non-fasting glucose (≥5.6 mmol/L).

^ Additionally adjusted for time since last meal (<3, 3-5, ≥5 hours).