**Supplemental Table 1. List of Topographical and Morphological Codes Used for the Case Definition**

|  |  |  |
| --- | --- | --- |
|  | **Topographical Codes** | **Morphological Codes** |
| **Gastric Cancer** | C16.0 – Cardia, NOS  C16.1 – Fundus of stomach  C16.2 – Body of stomach  C16.3 – Gastric antrum  C16.4 – Pylorus  C16.5 – Lesser curvature of stomach, NOS  C16.6 – Greater curvature of stomach, NOS  C16.8 – Overlapping lesion of stomach  C16.9 – Stomach, NOS | 8140 – Adenocarcinoma  8260 – Papillary adenocarcinoma  8211 – Tubular adenocarcinoma  8480 – Mucinous adenocarcinoma  8255 – Adenocarcinoma with mixed subtypes  8560 – Adenosquamous carcinoma  8512 – Medullary carcinoma with lymphoid stroma  8576 – Hepatoid adenocarcinoma  8020 – Carcinoma, undifferentiated, NOS  8244 – Mixed adenoneuroendocrine carcinoma |
| **Colorectal Cancer** | C18.0 – Cecum  C18.2 – Ascending colon  C18.3 – Hepatic flexure of colon  C18.4 – Transverse colon  C18.5 – Splenic flexure of colon  C18.6 – Descending colon  C18.7 – Sigmoid colon  C18.8 – Overlapping lesion of colon  C18.9 – Colon, NOS  C19.9 – Rectosigmoid junction  C20.9 – Rectum, NOS | 8000 – Malignant neoplasm, NOS  8010 – Carcinoma, NOS  8020 – Undifferentiated carcinoma  8021 – Anaplastic carcinoma  8140 – Adenocarcinoma, NOS  8141 – Scirrhous adenocarcinoma  8143 – Superficial spreading adenocarcinoma  8144 – Adenocarcinoma, intestinal type  8147 – Basal cell adenocarcinoma  8200 – Adenoid cystic carcinoma  8210 – Adenocarcinoma in adenomatous polyp  8211 – Tubular adenocarcinoma  8215 – Adenocarcinoma of anal glands  8220 – Adenocarcinoma in adenomatous polyposis coli  8221 – Adenocarcinoma in multiple adenomatous polyps (<100)  8230 – Solid carcinoma, NOS  8255 – Adenocarcinoma with mixed sub-types  8260 – Papillary adenocarcinoma, NOS  8261 – Adenocarcinoma in villous adenoma  8262 – Villous adenocarcinoma  8263 – Adenocarcinoma in tubulovillous adenoma  8323 – Mixed cell adenocarcinoma  8410 – Sebaceous adenocarcinoma  8430 – Mucoepidermoid carcinoma  8440 – Cystadenocarcinoma, NOS  8470 – Mucinous cystadenocarcinoma  8480 – Mucinous adenocarcinoma  8481 – Mucin-producing adenocarcinoma  8490 – Signet ring cell carcinoma  8510 – Medullary carcinoma, NOS  8560 – Adenosquamous carcinoma  8570 – Adenocarcinoma with squamous metaplasia  8571 – Adenocarcinoma with cartilaginous and osseous metaplasia  8572 – Adenocarcinoma with spindle cell metaplasia  8573 – Adenocarcinoma with apocrine metaplasia  8574 – Adenocarcinoma with neuroendocrine differentiation  8576- Hepatoid adenocarcinoma |
| **Liver Cancer** | C22.0 – Liver  C22.1 – Intrahepatic bile duct | 8170 – Hepatocellular carcinoma, NOS  8171 – Hepatocellular carcinoma, fibrolamellar  8970 – Hepatoblastoma  8020 – Carcinoma, undifferentiated, NOS |
| **Pancreatic Cancer** | C25.0 – Head of pancreas  C25.1 – Body of pancreas  C25.2 – Tail of pancreas  C25.3 – Pancreatic duct  C25.4 – Islet of Langerhans  C25.7 – Other specified parts of pancreas  C25.8 – Overlapping lesion of pancreas  C25.9 – Pancreas, NOS | 8500 – Infiltrating duct carcinoma  8560 – Adenosquamous carcinoma  8480 – Mucinous adenocarcinoma  8576 – Hepatoid adenocarcinoma  8510 – Medullary carcinoma, NOS  8490 – Signet ring cell carcinoma  8020 – Carcinoma, undifferentiated, NOS  8035 – Carcinoma with osteoclast-like giant cells  8550 – Acinar cell carcinoma  8551 – Acinar cell cystadenocarcinoma  8453 – Intraductal papillary-mucinous carcinoma, invasive  8470 – Mucinous cystadenocarcinoma  8441 – Serous cystadenocarcinoma  8452 – Solid pseudopapillary carcinoma |

**Supplemental Table 2. Additional Factors Associated with Gastrointestinal Cancers**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Gastric Cancer, N (%)** | | | **Colorectal Cancer, N (%)** | | |
|  | **Cases**  **(N=1,233)** | **Controls**  **(N=10,543)** | **OR [95% CI]**a | **Cases**  **(N=18,595)** | **Controls**  **(N=160,122)** | **OR [95% CI]**b |
| **Body Mass Index** |  |  |  |  |  |  |
| <18.5 | 16 (1.3) | 99 (0.9) | 1.19 [0.63-2.25] | 2,915 (15.7) | 24,237 (15.1) | 1.13 [0.98-1.29] |
| 18.5-24.9 | 203 (16.5) | 1,564 (14.8) | 1.00 [reference] | 271 (1.5) | 1,931 (1.2) | 1.00 [reference] |
| 25-29.9 | 245 (19.9) | 2,142 (20.3) | 0.87 [0.69-1.10] | 3,637 (19.6) | 30,047 (18.8) | 1.03 [0.97-1.09] |
| 30-39.9 | 229 (18.6) | 1,551 (14.7) | 1.19 [0.92-1.53] | 3,617 (19.5) | 26,147 (16.3) | **1.18 [1.11-1.25]** |
| 40+ | 53 (4.3) | 389 (3.7) | 0.98 [0.65-1.48] | 954 (5.1) | 7,041 (4.4) | **1.19 [1.09-1.30]** |
| Unknown | 487 (39.5) | 4,798 (45.5) | - | 7,201 (38.7) | 70,719 (44.2) | - |
| **Family history of cancer** |  |  |  |  |  |  |
| No | 1,226 (99.4) | 10,513 (99.7) | 1.00 [reference] | 17,275 (92.9) | 149,208 (93.2) | 1.00 [reference] |
| Yes | 7 (0.6) | 30 (0.3) | 1.86 [0.75-4.62] | 1,320 (7.1) | 10,914 (6.8) | 0.99 [0.92-1.05] |
| **Prior chronic alcohol consumption** |  |  |  |  |  |  |
| No | 1,038 (84.2) | 8,937 (84.8) | 1.00 [reference] | 15,610 (83.9) | 137,553 (85.9) | 1.00 [reference] |
| Yes | 195 (15.8) | 1,606 (15.2) | **0.78 [0.62-0.98]** | 2,985 (16.1) | 22,569 (14.1) | **1.11 [1.05-1.17]** |
| **Prior tobacco use** |  |  |  |  |  |  |
| No | 675 (54.7) | 6,960 (66.0) | 1.00 [reference] | 11,850 (63.7) | 110,390 (68.9) | 1.00 [reference] |
| Yes | 558 (45.3) | 3,583 (34.0) | **1.70 [1.40-2.06]** | 6,745 (36.3) | 49,732 (31.1) | **1.18 [1.14-1.24]** |
| **Prior Barrett’s esophagus** |  |  |  |  |  |  |
| No | 1,131 (91.7) | 10,480 (99.4) | 1.00 [reference] | - | - | - |
| Yes | 102 (8.3) | 63 (0.6) | **13.28 [8.50-20.74]** | - | - | - |
| **Prior gastric intestinal metaplasia** |  |  |  |  |  |  |
| No | 1,108 (89.9) | 10,507 (99.7) | 1.00 [reference] | - | - | - |
| Yes | 125 (10.1) | 36 (0.3) | **47.50 [27.63-81.64]** | - | - | - |
| **Prior gastric dysplasia** |  |  |  |  |  |  |
| No | 1,226 (99.4) | 10,540 (100.0) | 1.00 [reference] | - | - | - |
| Yes | 7 (0.6) | 3 (0.0) | 0.46 [0.10-2.16] | - | - | - |
| **Prior atrophic gastritis** |  |  |  |  |  |  |
| No | 1,227 (99.5) | 10,536 (99.9) | 1.00 [reference] | - | - | - |
| Yes | 6 (0.5) | 7 (0.1) | **7.84 [1.21-50.70]** | - | - | - |
| **Prior peptic ulcer disease** |  |  |  |  |  |  |
| No | 1,165 (94.5) | 10,267 (97.4) | 1.00 [reference] | - | - | - |
| Yes | 68 (5.5) | 276 (2.6) | 1.17 [0.76-1.78] | - | - | - |
| **Prior Helicobacter Pylori infection** |  |  |  |  |  |  |
| No | 1,177 (95.5) | 10,263 (97.3) | 1.00 [reference] | - | - | - |
| Yes | 56 (4.5) | 280 (2.7) | 1.43 [0.94-2.16] | - | - | - |
| **Prior Vitamin B12 deficiency** |  |  |  |  |  |  |
| No | 1,168 (94.7) | 10,321 (97.9) | 1.00 [reference] | - | - | - |
| Yes | 65 (5.3) | 222 (2.1) | **2.69 [1.86-3.89]** | - | - | - |
| **Prior Crohn’s disease** |  |  |  |  |  |  |
| No | - | - | - | 18,540 (99.7) | 159,758 (99.8) | 1.00 [reference] |
| Yes | - | - | - | 55 (0.3) | 364 (0.2) | 1.24 [0.88-1.76] |
| **Prior colonoscopy** |  |  |  |  |  |  |
| No | - | - | - | 16,835 (90.5) | 140,267 (87.6) | 1.00 [reference] |
| Yes | - | - | - | 1,760 (9.5) | 19,855 (12.4) | **0.62 [0.59-0.66]** |
| **Prior ulcerative colitis** |  |  |  |  |  |  |
| No | - | - | - | 18,469 (99.3) | 159,444 (99.6) | 1.00 [reference] |
| Yes | - | - | - | 126 (0.7) | 678 (0.4) | **1.79 [1.43-2.24]** |
|  | **Liver Cancer, N (%)** | | | **Pancreatic Cancer, N (%)** | | |
|  | **Cases**  **(N=2,329)** | **Controls**  **(N=19,987)** | **OR [95% CI]**c | **Cases**  **(N=567)** | **Controls**  **(N=4,820)** | **OR [95% CI]**d |
| **Body Mass Index** |  |  |  |  |  |  |
| <18.5 | 34 (1.5) | 204 (1.0) | 0.95 [0.54-1.67] | 7 (1.2) | 60 (1.2) | 0.82 [0.36-1.88] |
| 18.5-24.9 | 500 (21.5) | 3,586 (17.9) | 1.00 [reference] | 124 (21.9) | 946 (19.6) | 1.00 [reference] |
| 25-29.9 | 556 (23.9) | 4,955 (24.8) | 0.93 [0.77-1.13] | 143 (25.2) | 1,170 (24.3) | 0.89 [0.68-1.17] |
| 30-39.9 | 524 (22.5) | 3,559 (17.8) | **1.31 [1.06-1.63]** | 112 (19.8) | 894 (18.5) | 0.79 [0.58-1.09] |
| 40+ | 113 (4.9) | 934 (4.7) | 0.92 [0.65-1.31] | 36 (6.3) | 225 (4.7) | 1.16 [0.74-1.82] |
| Unknown | 602 (25.8) | 6,749 (33.8) | - | 145 (25.6) | 1,525 (31.6) | - |
| **Family history of cancer** |  |  |  |  |  |  |
| No | 2,296 (98.6) | 19,894 (99.5) | 1.00 [reference] | 562 (99.1) | 4,795 (99.5) | 1.00 [reference] |
| Yes | 33 (1.4) | 93 (0.5) | 1.65 [0.83-3.27] | 5 (0.9) | 25 (0.5) | 1.70 [0.64-4.54] |
| **Prior chronic alcohol consumption** |  |  |  |  |  |  |
| No | 1,594 (68.4) | 16,374 (81.9) | 1.00 [reference] | 438 (77.2) | 3,829 (79.4) | 1.00 [reference] |
| Yes | 735 (31.6) | 3,613 (18.1) | **1.30 [1.09-1.55]** | 129 (22.8) | 991 (20.6) | 1.06 [0.82-1.36] |
| **Prior tobacco use** |  |  |  |  |  |  |
| No | 968 (41.6) | 12,866 (64.4) | 1.00 [reference] | 313 (55.2) | 3,116 (64.6) | 1.00 [reference] |
| Yes | 1,361 (58.4) | 7,121 (35.6) | **1.82 [1.55-2.14]** | 254 (44.8) | 1,704 (35.4) | **1.26 [1.01-1.57]** |
| **Prior diabetes** |  |  |  |  |  |  |
| No | 1,419 (60.9) | 16,033 (80.2) | 1.00 [reference] | 398 (70.2) | 3,928 (81.5) | 1.00 [reference] |
| Yes | 910 (39.1) | 3,954 (19.8) | **2.45 [2.09-2.87]** | 169 (29.8) | 892 (18.5) | **1.83 [1.44-2.32]** |
| **Prior alpha-1 antitrypsin deficiency** |  |  |  |  |  |  |
| No | 2,325 (99.8) | 19,982 (100.0) | 1.00 [reference] | - | - | - |
| Yes | 4 (0.2) | 5 (0.0) | 2.37 [0.24-23.34] | - | - | - |
| **Prior alcoholic fatty liver disease** |  |  |  |  |  |  |
| No | 2,315 (99.4) | 19,982 (100.0) | 1.00 [reference] | - | - | - |
| Yes | 14 (0.6) | 5 (0.0) | 1.83 [0.17-19.45] | - | - | - |
| **Prior nonalcoholic fatty liver disease** |  |  |  |  |  |  |
| No | 2,188 (93.9) | 19,743 (98.8) | 1.00 [reference] | - | - | - |
| Yes | 141 (6.1) | 244 (1.2) | **1.85 [1.28-2.69]** | - | - | - |
| **Prior chronic viral hepatitis B** |  |  |  |  |  |  |
| No | 2,052 (88.1) | 19,864 (99.4) | 1.00 [reference] | - | - | - |
| Yes | 277 (11.9) | 123 (0.6) | **21.13 [14.59-30.61]** | - | - | - |
| **Prior chronic viral hepatitis C** |  |  |  |  |  |  |
| No | 1,610 (69.1) | 19,786 (99.0) | 1.00 [reference] | - | - | - |
| Yes | 719 (30.9) | 201 (1.0) | **39.22 [29.33-52.43]** | - | - | - |
| **Prior cirrhosis** |  |  |  |  |  |  |
| No | 1,661 (71.3) | 19,898 (99.6) | 1.00 [reference] | - | - | - |
| Yes | 668 (28.7) | 89 (0.4) | **29.08 [19.96-42.35]** | - | - | - |
| **Prior hemochromatosis** |  |  |  |  |  |  |
| No | 2,293 (98.5) | 19,972 (99.9) | 1.00 [reference] | - | - | - |
| Yes | 36 (1.5) | 15 (0.1) | **7.77 [2.71-22.24]** | - | - | - |
| **Prior autoimmune hepatitis** |  |  |  |  |  |  |
| No | 2,324 (99.8) | 19,983 (100.0) | 1.00 [reference] | - | - | - |
| Yes | 5 (0.2) | 4 (0.0) | 0.39 [0.07-2.21] | - | - | - |
| **Prior gastrointestinal hemorrhage** |  |  |  |  |  |  |
| No | 2,091 (89.8) | 19,448 (97.3) | 1.00 [reference] | - | - | - |
| Yes | 238 (10.2) | 539 (2.7) | 0.97 [0.70-1.35] | - | - | - |
| **Prior glycogen storage disease** |  |  |  |  |  |  |
| No | 2,329 (100.0) | 19,985 (100.0) | 1.00 [reference] | - | - | - |
| Yes | 0 (0.0) | 2 (0.0) | Not calculable | - | - | - |
| **Prior pancreatic cysts** |  |  |  |  |  |  |
| No | - | - | - | 559 (98.6) | 4,812 (99.8) | 1.00 [reference] |
| Yes | - | - | - | 8 (1.4) | 8 (0.2) | **5.75 [2.02-16.33]** |
| **Prior chronic pancreatitis** |  |  |  |  |  |  |
| No | - | - | - | 557 (98.2) | 4,809 (99.8) | 1.00 [reference] |
| Yes | - | - | - | 10 (1.8) | 11 (0.2) | **3.71 [1.35-10.23]** |

aAdjusted for long-term PPI Use, Body Mass Index (BMI), family history of gastric cancer, alcohol use, smoking, Barrett’s esophagus, gastric intestinal metaplasia, atrophic gastritis, peptic ulcer disease, Helicobacter pylori infection, vitamin B12 deficiency and gastric dysplasia

bAdjusted for long-term PPI Use, BMI, family history of colorectal cancer, alcohol use, smoking, Crohn’s disease, ulcerative colitis and colonoscopy use

cAdjusted for long-term PPI Use, BMI, family history of liver cancer, alcohol use, smoking, alpha-1 antitrypsin deficiency, AFLD, NAFLD, chronic viral hepatitis B and C, cirrhosis, hemochromatosis, autoimmune hepatitis, gastrointestinal hemorrhage, glycogen storage disease and diabetes

dAdjusted for long-term PPI Use, BMI, family history of pancreatic cancer, alcohol use, smoking, diabetes, chronic pancreatitis and cystic fibrosis

**Supplemental Figure 1. Flow Diagrams for Cases and Controls**







