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

|  |  |  |
| --- | --- | --- |
|  | **Topographical Codes** | **Morphological Codes** |
| **Gastric Cancer** | C16.0 – Cardia, NOSC16.1 – Fundus of stomachC16.2 – Body of stomachC16.3 – Gastric antrumC16.4 – PylorusC16.5 – Lesser curvature of stomach, NOSC16.6 – Greater curvature of stomach, NOSC16.8 – Overlapping lesion of stomachC16.9 – Stomach, NOS | 8140 – Adenocarcinoma8260 – Papillary adenocarcinoma8211 – Tubular adenocarcinoma8480 – Mucinous adenocarcinoma8255 – Adenocarcinoma with mixed subtypes8560 – Adenosquamous carcinoma8512 – Medullary carcinoma with lymphoid stroma8576 – Hepatoid adenocarcinoma8020 – Carcinoma, undifferentiated, NOS8244 – Mixed adenoneuroendocrine carcinoma |
| **Colorectal Cancer** | C18.0 – CecumC18.2 – Ascending colonC18.3 – Hepatic flexure of colonC18.4 – Transverse colonC18.5 – Splenic flexure of colonC18.6 – Descending colonC18.7 – Sigmoid colonC18.8 – Overlapping lesion of colonC18.9 – Colon, NOSC19.9 – Rectosigmoid junctionC20.9 – Rectum, NOS | 8000 – Malignant neoplasm, NOS8010 – Carcinoma, NOS8020 – Undifferentiated carcinoma8021 – Anaplastic carcinoma8140 – Adenocarcinoma, NOS8141 – Scirrhous adenocarcinoma8143 – Superficial spreading adenocarcinoma8144 – Adenocarcinoma, intestinal type8147 – Basal cell adenocarcinoma8200 – Adenoid cystic carcinoma8210 – Adenocarcinoma in adenomatous polyp8211 – Tubular adenocarcinoma8215 – Adenocarcinoma of anal glands8220 – Adenocarcinoma in adenomatous polyposis coli8221 – Adenocarcinoma in multiple adenomatous polyps (<100)8230 – Solid carcinoma, NOS8255 – Adenocarcinoma with mixed sub-types8260 – Papillary adenocarcinoma, NOS8261 – Adenocarcinoma in villous adenoma8262 – Villous adenocarcinoma 8263 – Adenocarcinoma in tubulovillous adenoma8323 – Mixed cell adenocarcinoma8410 – Sebaceous adenocarcinoma8430 – Mucoepidermoid carcinoma8440 – Cystadenocarcinoma, NOS8470 – Mucinous cystadenocarcinoma8480 – Mucinous adenocarcinoma8481 – Mucin-producing adenocarcinoma8490 – Signet ring cell carcinoma8510 – Medullary carcinoma, NOS8560 – Adenosquamous carcinoma8570 – Adenocarcinoma with squamous metaplasia8571 – Adenocarcinoma with cartilaginous and osseous metaplasia8572 – Adenocarcinoma with spindle cell metaplasia8573 – Adenocarcinoma with apocrine metaplasia8574 – Adenocarcinoma with neuroendocrine differentiation8576- Hepatoid adenocarcinoma |
| **Liver Cancer** | C22.0 – LiverC22.1 – Intrahepatic bile duct | 8170 – Hepatocellular carcinoma, NOS8171 – Hepatocellular carcinoma, fibrolamellar8970 – Hepatoblastoma8020 – Carcinoma, undifferentiated, NOS |
| **Pancreatic Cancer** | C25.0 – Head of pancreasC25.1 – Body of pancreasC25.2 – Tail of pancreasC25.3 – Pancreatic ductC25.4 – Islet of LangerhansC25.7 – Other specified parts of pancreasC25.8 – Overlapping lesion of pancreasC25.9 – Pancreas, NOS | 8500 – Infiltrating duct carcinoma8560 – Adenosquamous carcinoma8480 – Mucinous adenocarcinoma8576 – Hepatoid adenocarcinoma8510 – Medullary carcinoma, NOS8490 – Signet ring cell carcinoma8020 – Carcinoma, undifferentiated, NOS8035 – Carcinoma with osteoclast-like giant cells8550 – Acinar cell carcinoma8551 – Acinar cell cystadenocarcinoma8453 – Intraductal papillary-mucinous carcinoma, invasive8470 – Mucinous cystadenocarcinoma8441 – Serous cystadenocarcinoma8452 – 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**







