

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, **Table S1.** pancreatic cancer subtypes specific ICD-O-3 histology and behavior codes. **Table S2.** United States CSS in months between 2001 and 2017 for MANEC-P patients compared to other pancreatic cancer histological subtypes. **Table S3.** MANEC-P CSS by Historical Staging. **Figure S1.** MANEC-P incidence rate distribution by sex and age groups. **Figure S2.** MANEC-P incidence rate by grade and sex. **Figure S3.** United States Annual Percentage Change (APC) of the age-adjusted incidence rate per 100,000 before and after 2010 for each year of patients diagnosed with mixed pancreatic endocrine and exocrine tumor, malignant. The (*) indicates that the APC is significantly different from zero at the $\alpha = 0.05$ level. The overall APC is -0.71 . **Figure S4.** United States Temporal Trend over the time between 2001 and 2017 shows the age-adjusted incidence rate per 100,000 for each year of patients diagnosed with pancreatic cancer histological subtypes compared to the mixed pancreatic endocrine and exocrine tumor, malignant (MANEC-P)[light blue line]. The Y-axis is not proportionate to show the pancreatic cancer histological subtypes with an age-adjusted incidence rate below 0.1. **Figure S5.** United States temporal trends between 2001 and 2017 shows the age-adjusted incidence rate per 100,000 for each year of patients diagnosed with pancreatic cancer with neuroendocrine components including the functional PNET histological subtypes in comparison to MANEC-P [light blue line]. The Y-axis is not proportionate to show the pancreatic cancer histological subtypes, with an age-adjusted incidence rate below 0.1. **Figure S6.** MANEC-P age-adjusted incidence rate by the United States of America regional map between 2001 and 2017. **Figure S7.** United States CSS over the time between 2001 and 2017 for MANEC-P patients compared with pancreatic neuroendocrine tumors subtypes.

Table S1. Pancreatic cancer subtypes specific ICD-O-3 histology and behavior codes.

| ICD-O-3 Code | Diagnosis | Solid Tumor Main Site |
|-----------------|---|---|
| 8453/3 | Intraductal papillary-mucinous neoplasm (IPMN) | |
| 8470/3 | Mucinous cystadenocarcinoma, NOS | |
| 8471/3 | Papillary mucinous cystadenocarcinoma | |
| 8140/3 | Adenocarcinoma, NOS (PDAC) | |
| 8147/3 | Basal cell adenocarcinoma | |
| 8070/3 | Squamous cell carcinoma, NOS | |
| 8560/3 | Adenosquamous carcinoma | |
| 8244/3 | Mixed Adenocarcinoma with neuroendocrine carcinoma (Composite carcinoid) | Colon and then others |
| 8574/3 | Adenocarcinoma with neuroendocrine differentiation | Colon and then others |
| 8255/3 | Adenocarcinoma with mixed subtypes (3 tumors: adenocarcinoma with two or more of the following: papillary, clear cell, mucinous, or signet) | Breast, Colon, Lung, and then others |
| 8150/3 | Pancreatic endocrine tumor, malignant (PNET) | |
| 8151/3 | Insulinoma, malignant | |
| 8152/3 | Glucagonoma, malignant | |
| 8153/3 | Gastrinoma, malignant | |
| 8154/3 | Mixed pancreatic endocrine and exocrine tumor, malignant | |
| 8155/3 | Vipoma, malignant | |
| 8156/3 | Somatostatinoma, malignant | |
| 8240/3 | Carcinoid tumor, NOS | We combined it with 8150/3 (PNET) as it probably has been |

| | | |
|--------|--------------------------------------|---------------------------|
| | | used interchangeably |
| 8013/3 | Large cell neuroendocrine carcinoma | Esophagus and then others |
| 8041/3 | Small cell carcinoma, NOS | Esophagus and then others |
| 8246/3 | Neuroendocrine carcinoma, NOS (PNEC) | |
| 8550/3 | Acinar cell carcinoma | |
| 8551/3 | Acinar cell cystadenocarcinoma | |

Table S2. United States CSS in months between 2001 and 2017 for MANEC-P patients compared to other pancreatic cancer histological subtypes.

| Group | Median Time | Lower 95% | Upper 95% |
|---|-------------|-----------|-----------|
| 8154/3: Mixed pancreatic endocrine and exocrine tumor, malignant | 29 | 21 | 51 |
| 8151/3: Insulinoma, malignant | . | . | . |
| 8156/3: Somatostatinoma, malignant | . | . | . |
| 8153/3: Gastrinoma, malignant | 150 | 82 | . |
| 8150/3: Pancreatic endocrine tumor, malignant | 135 | 111 | . |
| 8152/3: Glucagonoma, malignant | 126 | 64 | . |
| 8453/3: Intraductal papillary-mucinous neoplasm (IPMN) | 69 | 54 | 128 |
| 8246/3: Neuroendocrine carcinoma, NOS | 66 | 60 | 71 |
| 8155/3: Vipoma, malignant | 46 | 16 | 193 |
| 8244/3: Mixed adenoneuroendocrine carcinoma (ICD-O-3 update) | 32 | 6 | 32 |
| 8470/3: Mucinous cystadenocarcinoma, NOS | 28 | 20 | 39 |
| 8550/3: Acinar cell carcinoma | 16 | 13 | 20 |
| 8255/3: Adenocarcinoma with mixed subtypes | 14 | 10 | 19 |
| 8574/3: Adenocarcinoma with neuroendocrine differentiation | 10 | 5 | 15 |
| 8013/3: Large cell neuroendocrine carcinoma | 9 | 8 | 13 |
| 8560/3: Adenosquamous carcinoma | 6 | 5 | 6 |
| 8041/3: Small cell carcinoma, NOS | 5 | 3 | 6 |
| 8140/3: Adenocarcinoma, NOS | 5 | . | . |
| 8070/3: Squamous cell carcinoma, NOS | 3 | 2 | 4 |
| Combined | 6 | . | . |

Table S3. MANEC-P Cancer-Specific Survival by Historical Staging.

| MANEC-P Characteristics (n) | Tumor | Median months | survival, | Survival Rate, % | | | |
|--------------------------------|-------|------------------|-----------|------------------|--------|--------|---------|
| | | | | 1-year | 3-year | 5-year | 10-year |
| All (145) | | 29.22 | | 70 | 45.5 | 37.9 | 26.8 |
| Localized only (17) | | 15 | | 94.1 | 87.8 | 87.8 | 58.2 |
| Regional (56) | | 33.89 | | 78.1 | 51.7 | 41.9 | 36.3 |
| Distant (49) | | 12.24 | | 52.3 | 22.4 | 18.7 | 12.5 |
| Unknown (23) | | 32.13 | | 68.3 | 45.5 | 30.3 | 20.2 |

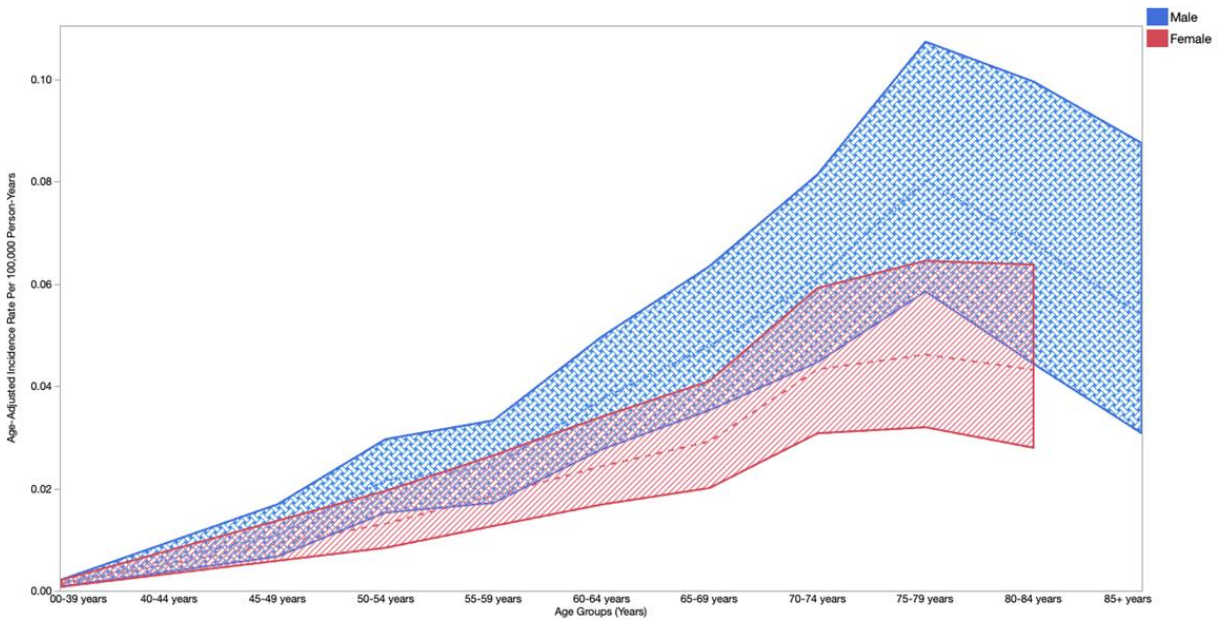


Figure S1. MANEC-P incidence rate distribution by sex and age groups.

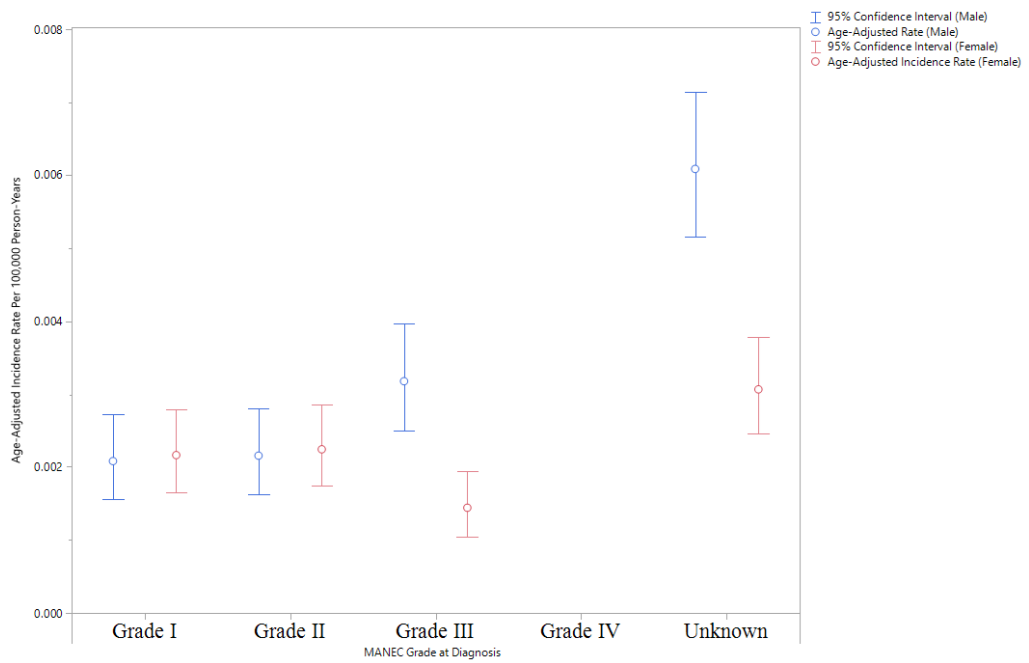


Figure S2. MANEC-P incidence rate by grade and sex.

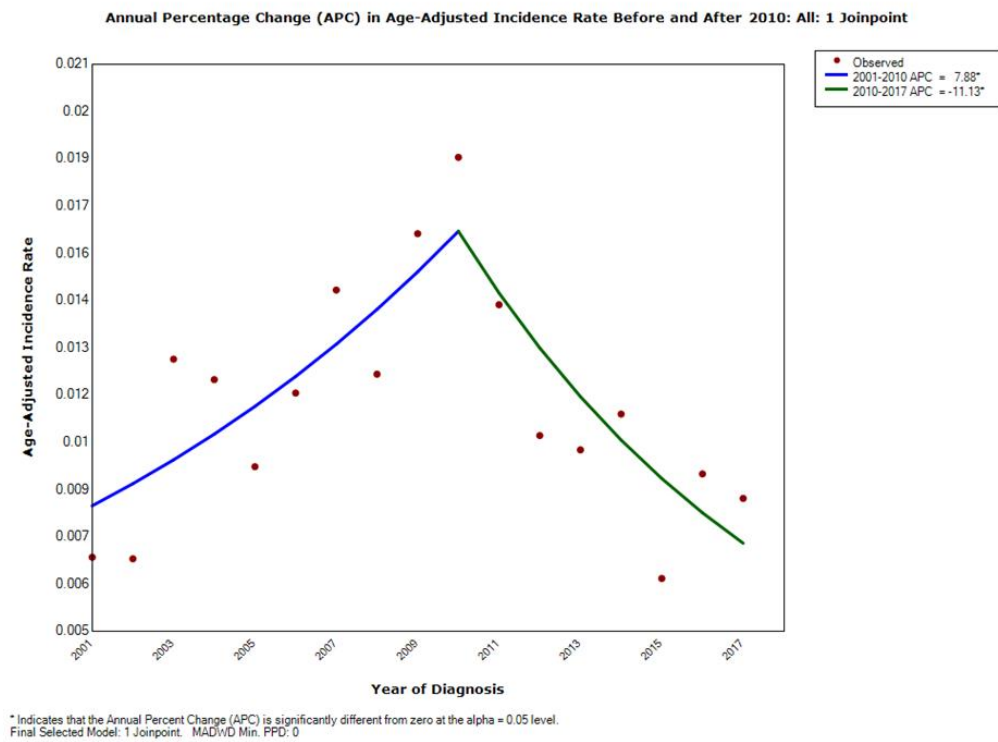


Figure S3. United States Annual Percentage Change (APC) of the age-adjusted incidence rate per 100,000 before and after 2010 for each year of patients diagnosed with mixed pancreatic endocrine and exocrine tumor, malignant. The (*) indicates that the APC is significantly different from zero at the alpha = 0.05 level. The overall APC is –0.71.

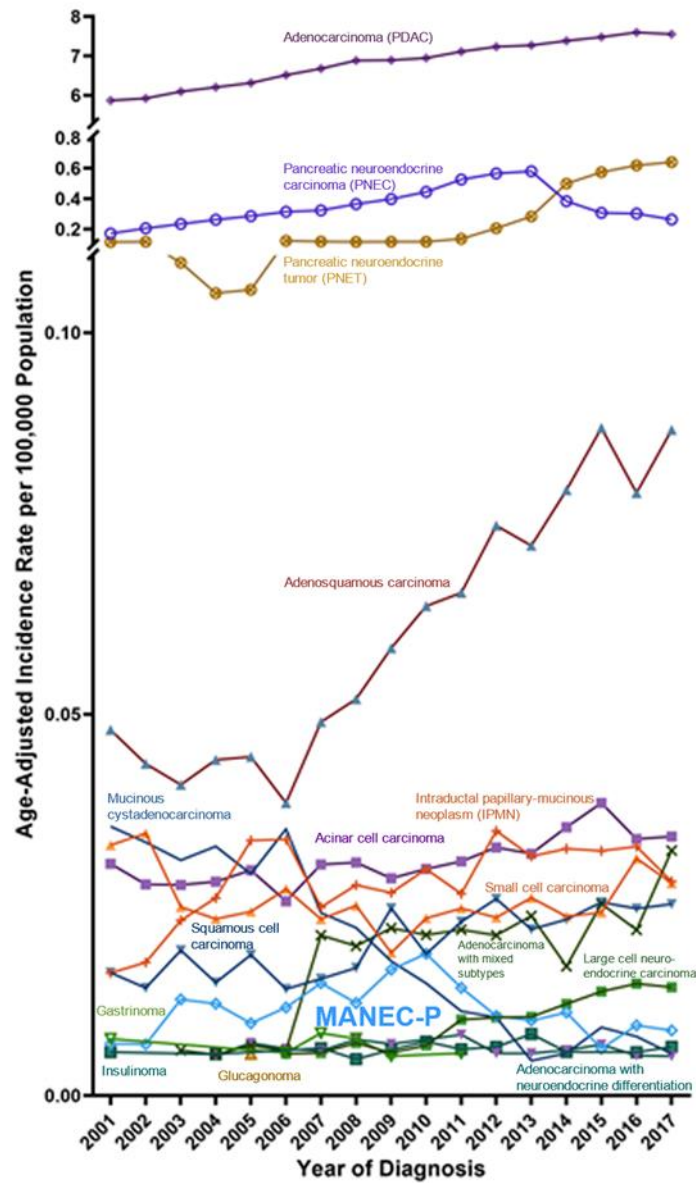


Figure S4. United States Temporal Trend over the time between 2001 and 2017 shows the age-adjusted incidence rate per 100,000 for each year of patients diagnosed with pancreatic cancer histological subtypes compared to the mixed pancreatic endocrine and exocrine tumor, malignant (MANEC-P)[light blue line]. The Y-axis is not proportionate to show the pancreatic cancer histological subtypes with an age-adjusted incidence rate below 0.1.

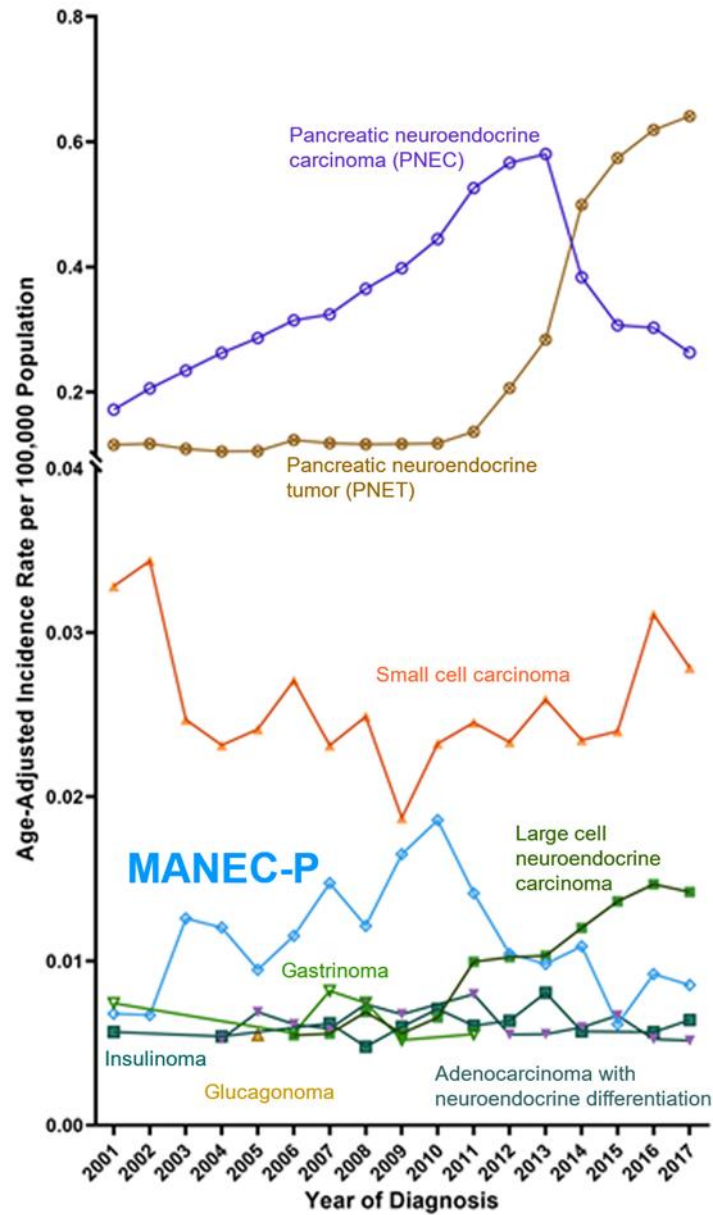


Figure S5. United States temporal trends between 2001 and 2017 shows the age-adjusted incidence rate per 100,000 for each year of patients diagnosed with pancreatic cancer with neuroendocrine components including the functional PNET histological subtypes in comparison to MANEC-P [light blue line]. The Y-axis is not proportionate to show the pancreatic cancer histological subtypes, with an age-adjusted incidence rate below 0.1.

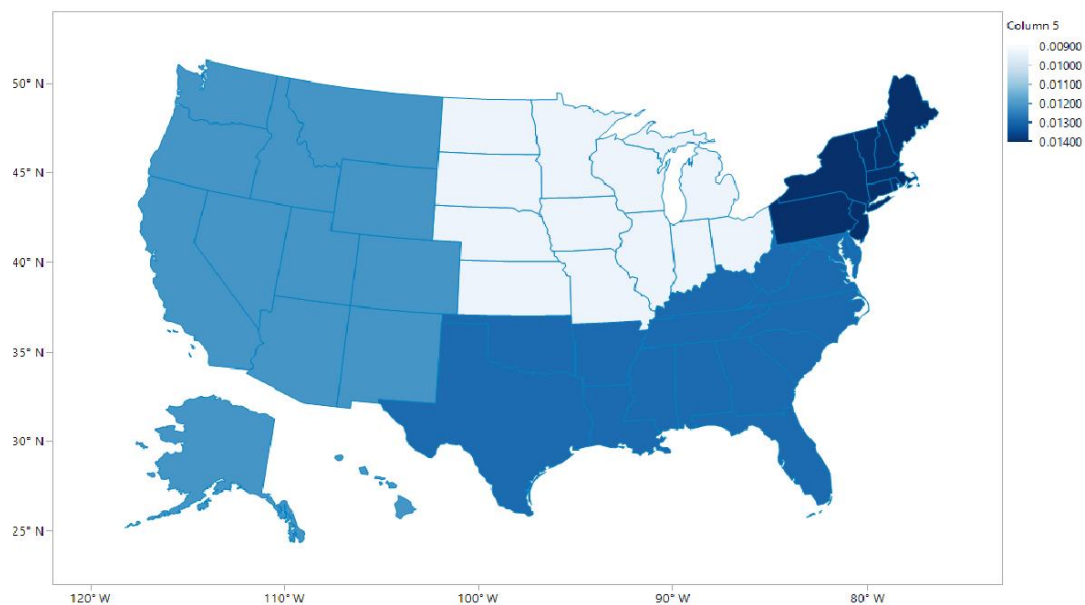


Figure S6. MANEC-P age-adjusted incidence rate by the United States of America regional map between 2001 and 2017.

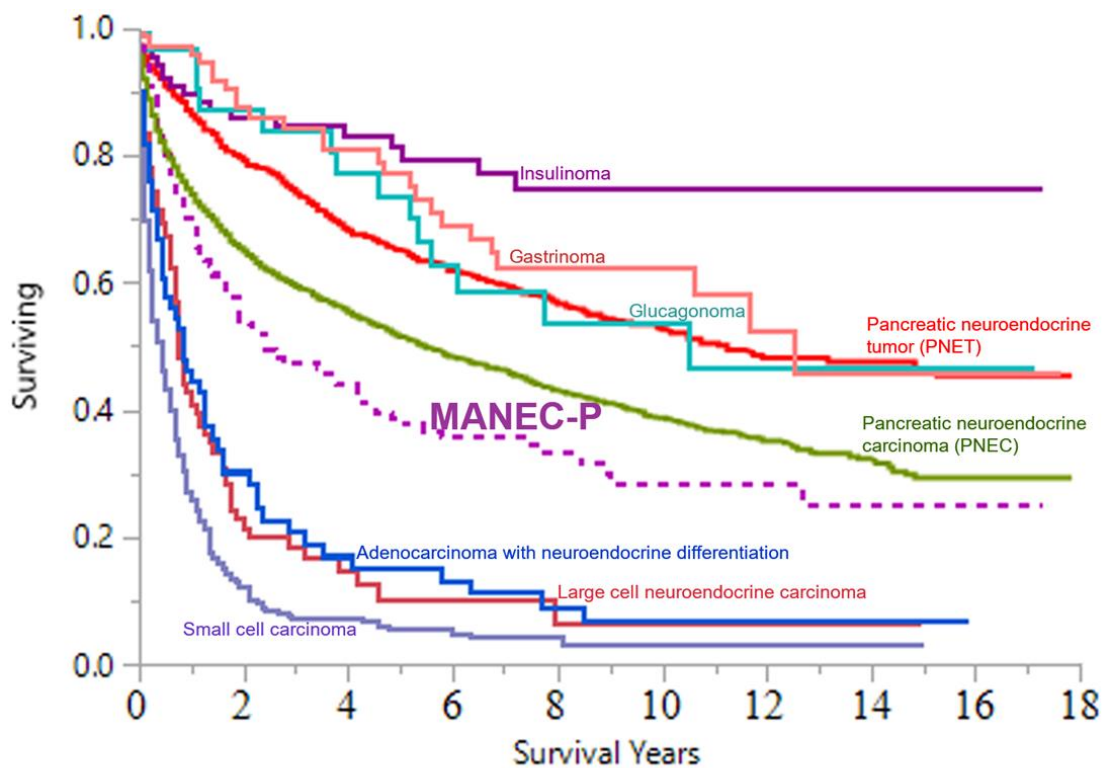


Figure S7. United States CSS over the time between 2001 and 2017 for MANEC-P patients compared with pancreatic neuroendocrine tumors subtypes.

