Pancreatic cancer update

natpernickshealthblog.wordpress.com/2021/09/08/pancreatic-cancer-update/

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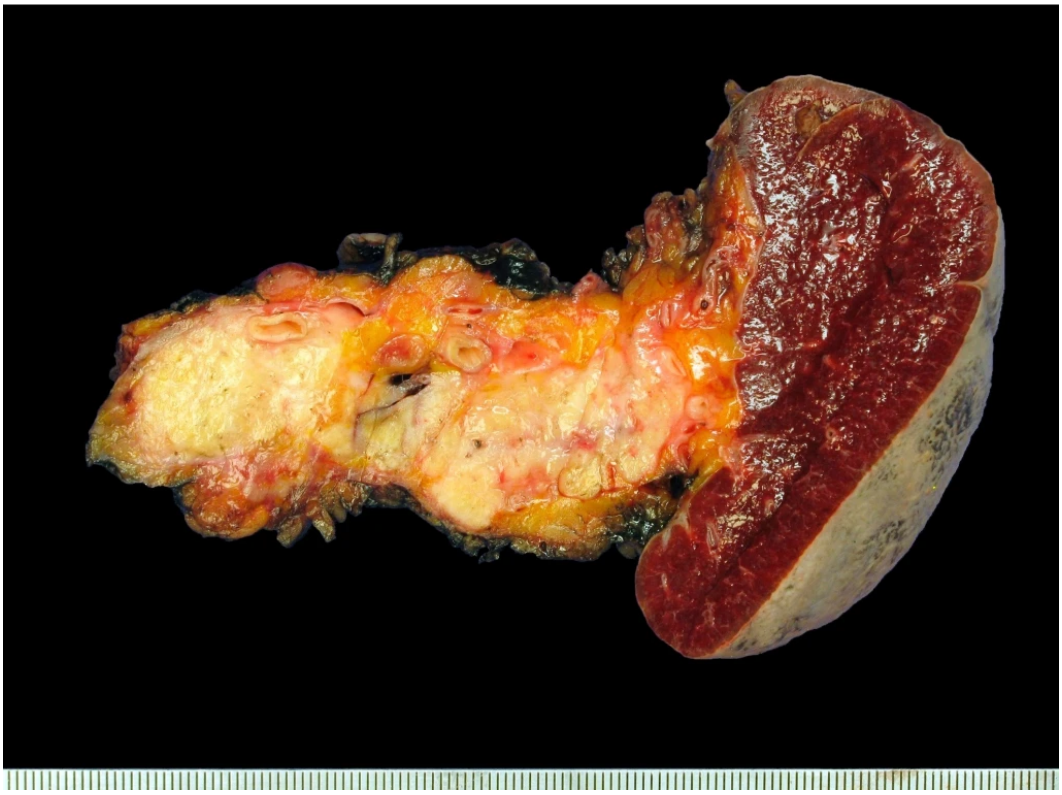
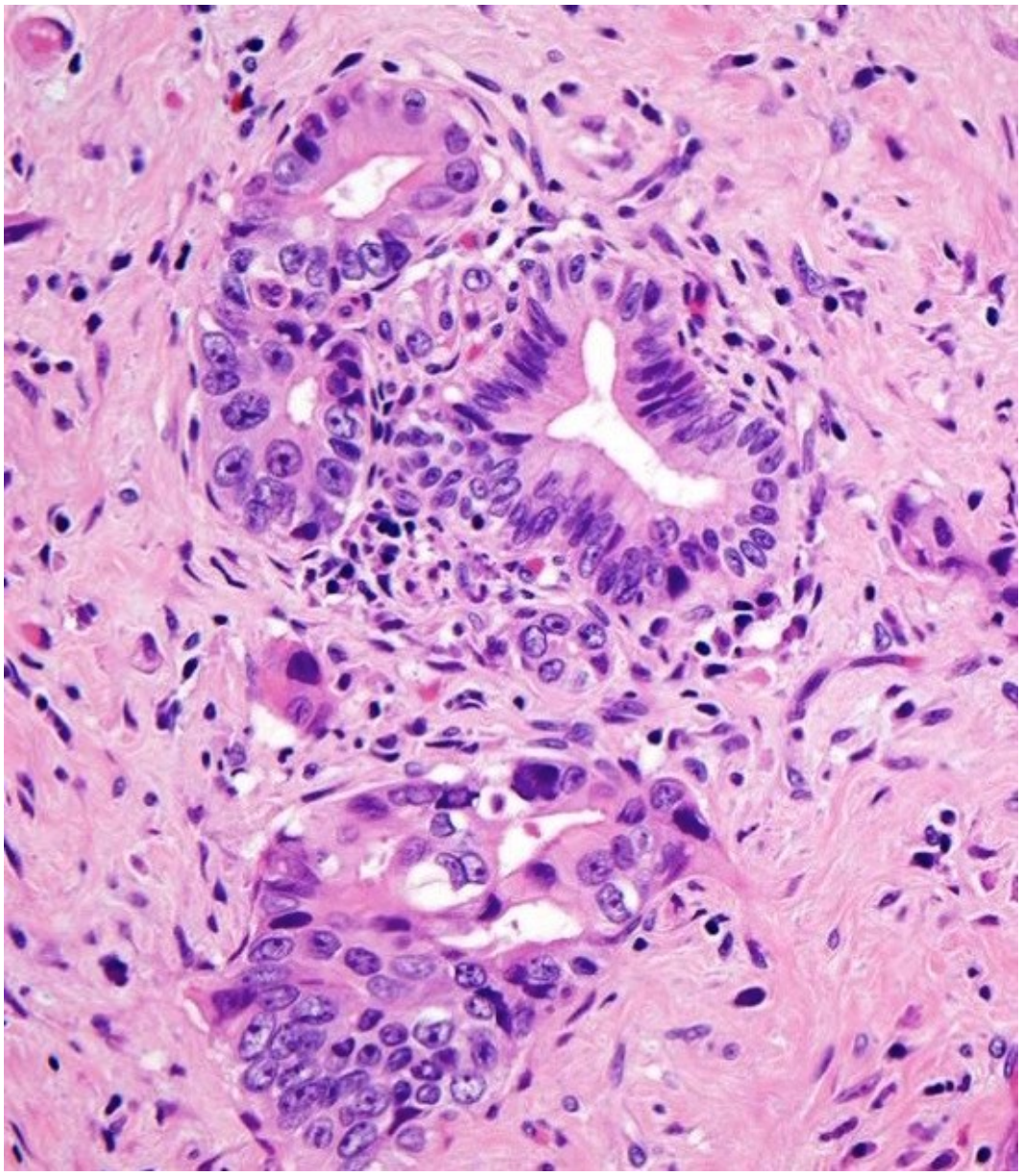
8 September 2021

This essay summarizes current knowledge about pancreatic cancer and recent updates to our pancreatic cancer treatment targets (1).

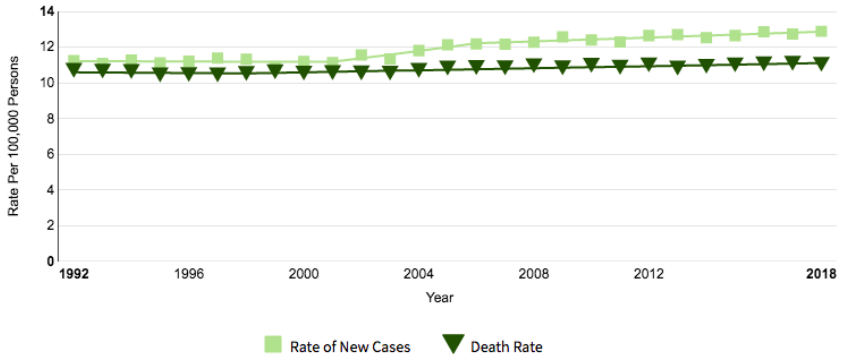


Pancreatic adenocarcinoma (yellow) within normal pancreas (orange) and spleen (red-purple).



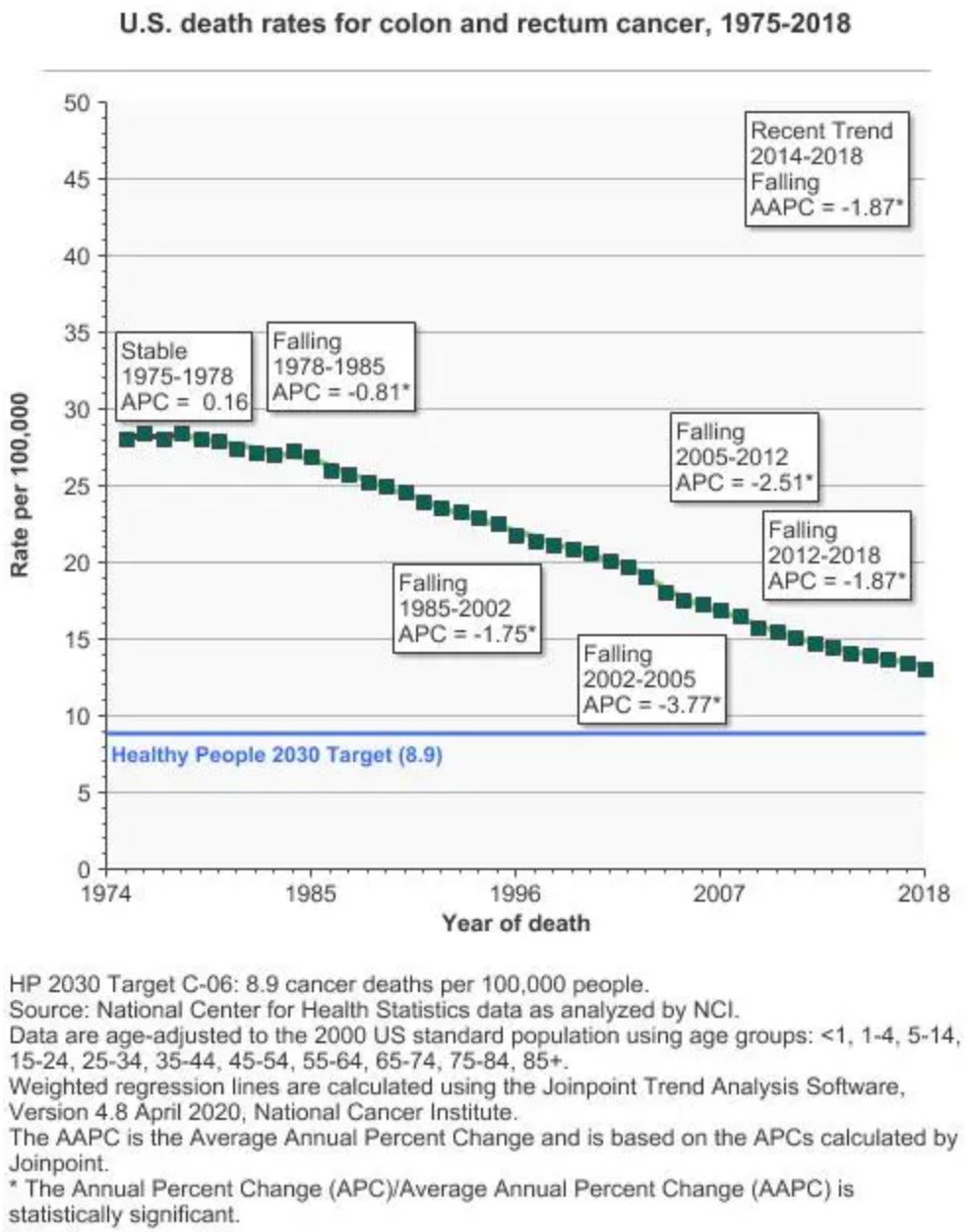
Pancreatic cancer tumor cells show marked nuclear pleomorphism (variation in size and shape) within the tumor gland at the bottom.

Pancreatic cancer is currently the #3 cause of US cancer deaths, after lung and colorectal cancer, with a projected 48,220 deaths in 2021 (2). However, it is projected to become #2 by 2030 (3), because pancreatic cancer deaths are slowly increasing and colorectal cancer deaths are markedly decreasing (4).



New cases come from SEER 13. Deaths come from U.S. Mortality.
All Races, Both Sexes. Rates are Age-Adjusted.
Modeled trend lines were calculated from the underlying rates using the Joinpoint Trend Analysis Software.

US death rates for pancreatic cancer, 1992-2018 (5)



US death rates for colorectal cancer, 1975-2018 (14)

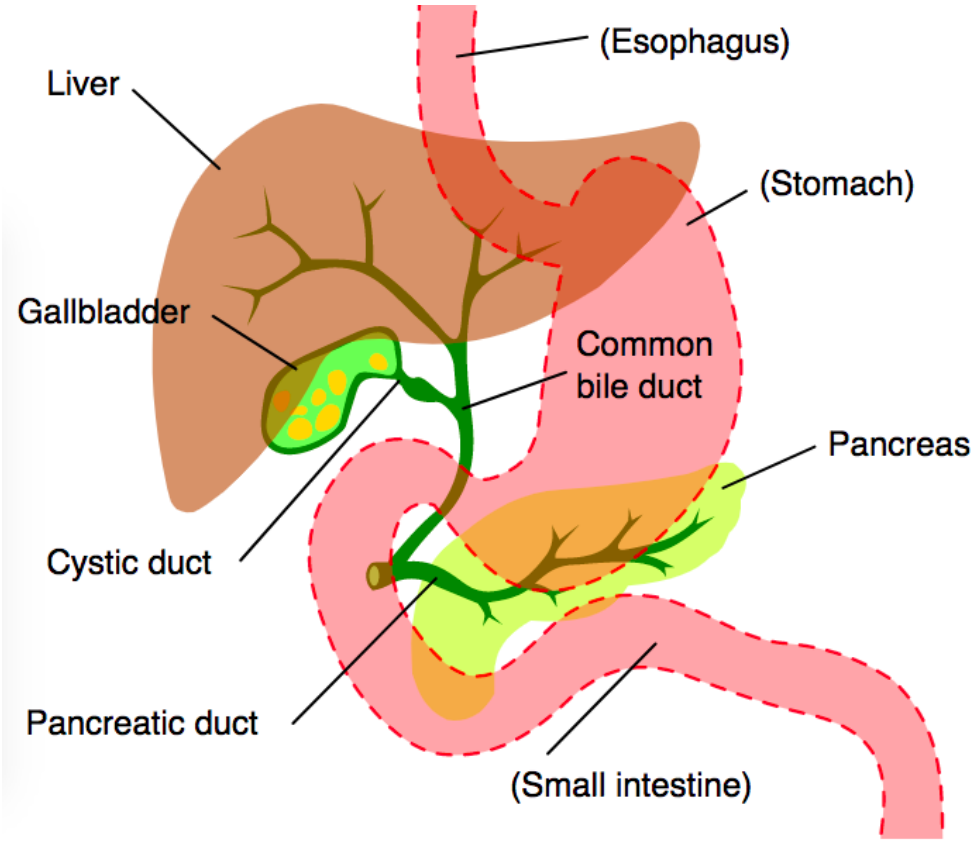
Overall, Americans have a 1.7% lifetime risk of pancreatic cancer (5).

Pancreatic cancer has a 5 year relative survival rate of only 10% (2) with minimal improvements since the mid-1970s, unlike other cancers. Most patients (52%) are diagnosed with metastatic disease and have a 5 year relative survival of only 3% (2). For the 11% of patients with locally confined disease, the 5 year survival is still only 39%. This is likely due to the early dissemination of premalignant cells, typically before malignancy can even be detected (6).

We recently reviewed attributable risk factors for pancreatic cancer to determine what percentage of cases are due to each risk factor (4). These risk factors often overlap and add up to more than 100%:

Random chronic stress / bad luck – 25-35%
Non O blood group – 17%
Excess weight – 15%
Cigarette smoking (tobacco) – 15%
Type 2 diabetes – 9%
Excessive alcohol use – 5%
Diet – 5%
Family history / germline – 2%
Chronic pancreatitis – 1%

A newly described risk factor that may account for many of the “random chronic stress” cases is variant anatomy of the biliary ductal system (7). The variant anatomy may distort the usual pressures in this ductal system, causing reflux of bile into the pancreas or reflux of pancreatic juices into the biliary system. This may cause inflammation and ultimately cancer (8), analogous to how gastric reflux can cause esophageal cancer (9, 10).

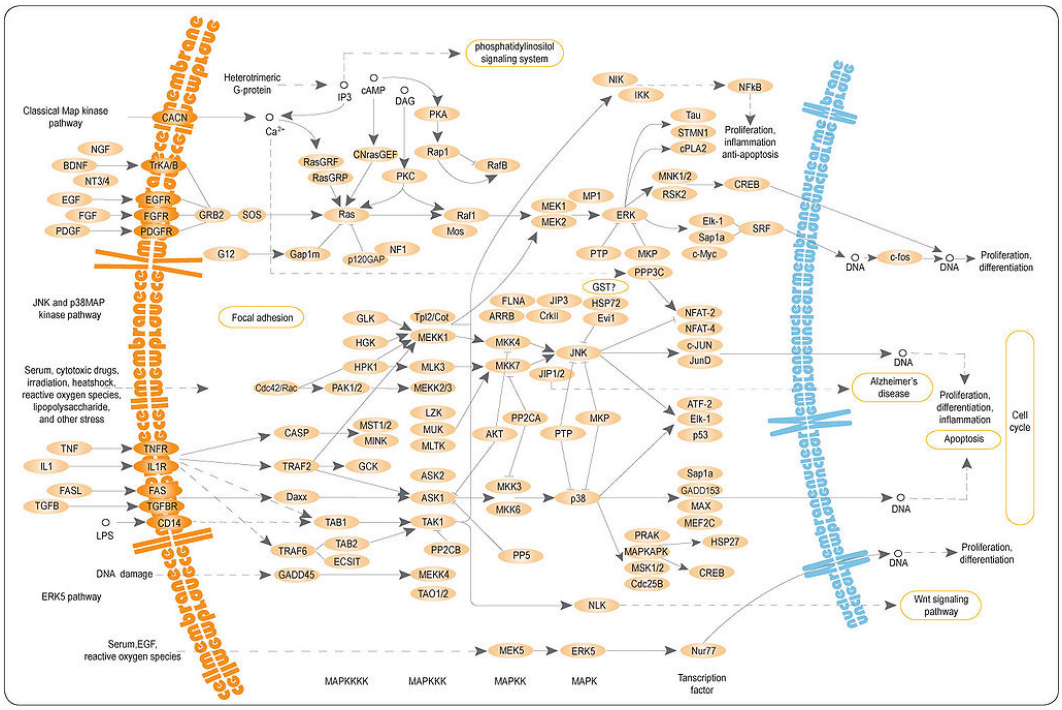


Typically the bile ducts from the liver and gallbladder merge to form the common bile duct (CBD) above the pancreas and the CBD merges with the pancreatic duct in the small intestine (ampulla). Variations have been associated with pancreatic cancer (15).

What would a successful treatment strategy look like for pancreatic cancer? We recently speculated that there exists a large combination of partially effective treatments against pancreatic cancer (perhaps 8-10) that will produce high rates of long term survival even though the individual treatments will not (11, 12). This is similar to childhood leukemia, in

which 4-5 drugs produce curative treatment, but only when given together. We suggest using therapies based not just on targeting the cancer cells themselves but also targeting the cancer microenvironment, systemic chronic inflammation, hormones, immune system dysfunction, relevant germline variations and risk factors, both behavioral and non behavioral.

Cancer can be viewed as a multidimensional web of biological pathways. To sufficiently reduce its malignant properties, therapy needs to successfully damage multiple strands on the web, not just the strands dealing with cell growth.



Weblike pattern of a single pathway important in normal and malignant cell growth.

These challenges remain:

- We must prove that a large combination of partially effective treatments against pancreatic cancer will produce high rates of long term survival, even though the individual treatments will not. Currently, this is just a theory.
- Even if our theory about large combinations of therapy is correct, more effective therapies need to be developed against the different aspects of the malignant process discussed above other than cell growth.
- Receiving large combinations of therapies is difficult for patients and often seems cruel, although our experience with childhood leukemia suggests that it can be made more tolerable (13).

- We may need to develop 30 or more partially effective therapies to choose from to get the 8-10 therapies that are substantially effective in combination. But even so, it will be difficult to determine which combination of drugs will be most effective and how to optimally administer them. If there are 30 partially effective drugs against pancreatic cancer, then there are 6 million combinations of 8 drugs (11). Using machine learning, cell lines and animal models may be helpful to determine which combinations should be tested using clinical trials (1).
- Our framework for thinking and talking about cancer must change. Adult cancers are due to marked changes in systemic networks, not to a single local problem, and so cannot be "fixed" with a single therapy. Thus, we should stop talking about cures due to "silver bullets". In addition, particularly for adult cancers, we should focus on managing cancer to reduce related deaths and symptoms, not on removing all cancer cells from the body.

How you can help:

- Follow our Curing Cancer Blog at **https://natpernickshealthblog.wordpress.com** .
- Sign up for our Curing Cancer Network monthly newsletter by clicking at **https://lp.constantcontactpages.com/su/onz6IND** .
- Become an example to others of anti-cancer behavior. Read our American Code Against Cancer at **http://www.natpernick.com/AmericanCodeAgainstCancer.html**, decide what steps you can take to reduce your cancer risk and spread the word through your social networks.
- Contact me at **Nat@PathologyOutlines.com** with your suggestions or thoughts.

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