Toward Precision Pancreatic Cancer Care
Robert Goldberg, PhD

Unlike in many other tumor types, in pancreatic cancer, patients and physicians lack reliable and accessible tools for early detection in the primary care setting. In the absence of blood- or saliva-based tests, researchers and patient advocacy organizations have partnered to validate algorithms that build on the statistical association between the onset of diabetes and pancreatic cancer found in the literature.

In this regard, the Enriching New-Onset Diabetes for Pancreatic Cancer (END-PAC) model for early pancreatic cancer screening is a welcome development indeed. As stated in the article by Schwartz et al, elsewhere in this issue, END-PAC is a "statistical framework that uses age, change in blood glucose, and change in weight to predict [pancreatic cancer] risk in patients with [new-onset diabetes]." END-PAC algorithms are not conceived as a general population screening test. Instead, the model stratifies based on an abnormal glycemic measure and age and weight. Based on its accuracy compared with CT imaging, the model is a reliable method of detection.

The Pancreatic Cancer Action Network (PanCAN), a patient advocacy group that has played an indispensable role in advancing clinical trials for pancreatic cancer, developed the model and is currently conducting a prospective trial (Early Detection Initiative) to evaluate the outcomes of a screening strategy using the END-PAC model.

To avoid the usual delay patients can face in gaining access to and coverage for new diagnostics, PanCAN has used the data from its initial END-PAC validation to establish the value of the test to insurance companies and other payers. The study examined whether finding more pancreatic cancer, even if detected earlier, exceeded a cost per quality-adjusted life-years (QALY) gained of $100,000 with screening. Schwartz et al bluntly stated the “money or life” equation: the more people who are accurately screened for early pancreatic cancer, the more money that will be spent on treating the disease. This fact is because “patients with resectable [pancreatic cancer] live longer and thus accrue higher treatment and monitoring costs.”

This article is the “first pass” on cost-effectiveness. The diagnostic value is still being evaluated. More granular data from the clinical trial will help determine which subpopulations are most likely to benefit from early screening without crossing the $100,000 per QALY threshold.

Use of the $100,000 per QALY threshold—the maximum that would be paid for an additional year of worthwhile life—is similarly a placeholder. Contrary to what has been asserted in other publications, using QALY is highly subjective. As Nobel laureate Daniel Kahneman has pointed out, comparing pain or preference for life between people is impossible, and it is equally impossible to compare different stages and circumstances surrounding the individual. Hence, Kahneman regards QALY as a useless measure of value. More troubling, one could argue that testing for the early presence of pancreatic cancer, a condition with poor life expectancy and few effective treatment options, costs more than it is worth. From that perspective, the most cost-effective strategy for a payer would be not to find more pancreatic cancer cases, primarily if they are discovered when the cancer is resectable.

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Such pessimism can be popular, even profitable, but I believe it is unwarranted. The END-PAC algorithm is one of the first noninvasive computational methods to precisely predict pancreatic cancer at an earlier stage. The time and cost required to produce more refined versions are declining thanks to the firepower of machine learning and the use of analytic tools such as causal inference.

Groups such as PanCAN show that it is possible to rapidly collect dense, dynamic data (multiomics) on behalf of every patient to capture changes in clinical phenotype and disease states. The organization has sequenced the tumors of thousands of patients with pancreatic cancer. Once those data are integrated with longitudinal patient-level data and causally focused computational methods, earlier detection will guide optimizing treatment.

Some tantalizing assumptions await exploration. Although retrospective studies have shown that statin use after cancer diagnosis was not significantly associated with survival, it was linked to a 21% reduced hazard of death in those who used a statin and were diagnosed with grade I or II pancreatic ductal adenocarcinoma, and to a similar extent in those who had undergone a pancreatectomy, those with chronic pancreatitis, and those who had not been treated with a statin before cancer diagnosis.3

Similarly, even absent new treatments for advanced pancreatic cancer, with general use, END-PAC could likely be used to establish a causal relationship between new-onset diabetes and pancreatic cancer that can guide supportive care to extend survival without resorting to surgery. Indeed, the presence of and treatments for preexisting conditions such as diabetes, depression, and autoimmune disorders directly impact treatment effectiveness and toxicity, and possibly higher rates of complications after cancer surgery (including more extended length of stay and in-hospital mortality).

Additionally, there is evidence that existing therapies reduce the need for postacute care after surgery. Between 2006 and 2015, the percentage of patients with pancreatic cancer who died in the hospital declined from 12% to 7%. A slight shift from nursing home discharges after surgery to home healthcare was also seen during the same period. To the extent that treatment costs for cancer diagnosed early are 2 to 4 times less than for cancer diagnosed late, the END-PAC algorithm can also be a cost-saving tool.

Finally, the END-PAC approach enables a new research paradigm that allows for the early and ongoing evaluation of individuals through health states while at the same time allowing healthcare providers to measure and optimize the clinical, emotional, transparency, and economic value of both detection and treatment. Indeed, such dynamic (adaptive) strategies are necessary because randomized trials are infeasible and inadequate for advancing precision pancreatic cancer care. Instead, as the study by Schwartz et al1 shows, the intersection of large databases of electronic health records and causal methods designed to evaluate dynamic strategies can make personalized plans possible and clinical studies more efficient.

Disclosures: Dr. Goldberg has disclosed not having any financial interests, arrangements, or affiliations with the manufacturers of any products discussed in this article or their competitors.

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