Recommendations for a More Organized and Effective Approach to the Early Detection of Pancreatic Cancer From the PRECEDE (Pancreatic Cancer Early Detection) Consortium

Pancreatic cancer is an aggressive, difficult-to-treat disease that is on track to become the second most deadly malignancy in adults by 2030.[1] Although significant advances in treatment are being made, screening and early detection hold the greatest promise in affecting mortality. Effective screening for pancreatic cancer, per National Cancer Institute recommendations, should: (1) demonstrate ability to detect early cancer; (2) show that screening reduces cancer mortality, and (3) prove that benefits of screening outweigh harms.[2] Pancreatic cancer presents several challenges in meeting these screening criteria, including its relatively low incidence in the general population, the small independent effect sizes of known environmental and nutritional risk factors, limited ability to detect the highest-risk premalignant lesions (ie, pancreatic intraepithelial neoplasia), early metastasis, and resistance to standard treatments that can be curative in other cancer types. Here we discuss the current state of pancreatic cancer screening and recommend strategic steps needed to overcome these challenges and allow proper studies to be performed to ultimately demonstrate efficacy, decreased mortality, and favorable balance of benefit over harm.

Current State of Pancreatic Cancer Screening

Implementation of an effective screening test requires identification of a target population. Because of its relatively low incidence, sensitivity and specificity levels of existing techniques are inadequate for pancreatic cancer screening in the general population.[3] Individuals meeting specific criteria based on family history of pancreatic cancer and/or presence of pathogenic germline variants (PGV) in relevant cancer risk genes, referred to as high-risk individuals (HRIs), are currently the only cohort with published guidelines recommending pancreatic cancer screening at regular intervals.[4–6] In Table 1, we summarized the current genetic and family history inclusion criteria for pancreatic cancer screening. These recommendations have been made based on expert consensus opinion, and the collection of supporting evidence is ongoing.

Published screening studies in HRIs have shown promise in the ability to detect early cancer (T1N0M0) and precursor lesions with high-grade dysplasia, another important criteria for effective screening programs. However, these studies have been limited by relatively small sample sizes, short follow-up, heterogeneity of inclusion criteria, and variability in screening techniques.[7] A meta-analysis of 16 studies published between 2004 and 2016, which included 1550 participants, found nearly 2% of HRIs had pancreatic cancer or a high-grade precursor lesion identified.[8] A 2018 study of 350 HRIs found that 9 of 10 incident pancreatic cancers discovered during a median follow-up time of 5.6 years were surgically resectable,[9] with a resulting 5-year survival rate of 60% in the surgically treated group.[10] The study cohort included 97% of patients meeting criteria based on family history of pancreatic cancer alone, and gene status was unknown for the majority. This is relevant in light of a 2021 study that found a cumulative incidence of pancreatic cancer of 3.1% at 5 years and 4.7% at 10 years, with all cases occurring in PGV carriers.[7] This study also found that 4 of 8 incident pancreatic cancers were resectable. This shift toward detection of earlier stage, resectable disease is encouraging, but larger studies with longer follow-up will be needed to exclude the possibility of lead-time bias. Two large-scale studies of ovarian cancer and prostate cancer both found that increased detection of early-stage disease did not result in a corresponding decrease in cancer mortality after long-term follow-up of 16 years and 10 years, respectively.[11,12] In addition, it is important to note that several of the published pancreatic cancer screening series have reported cancers diagnosed between screening examinations and advanced cancers apparently missed with current screening techniques.[13] Understanding the possible explanations for these interval or missed cancers and the strategies to reduce them will require consistency in intervals and methods for screening across centers and more clearly defined study populations.

National Cancer Institute and World Health Organization[14] recommendations for effective screening also involve the weighing of benefits vs harms, both at the individual and societal level. Pancreatic cancer screening techniques have relatively low procedural risks, but published studies have reported a substantial number of noncancerous findings, including branch duct intrapapillary mucinous neoplasms, chronic pancreatitis, and extrapancreatic findings. This raises the possibility of overdiagnosis or overtreatment, issues that have complicated screening efforts for lung and prostate cancers.[15,16] A 2019 meta-analysis found that pancreatic cancer screening in 1660 patients led to 473 abnormal imaging examinations and 257 surgical procedures, with 43 pancreatic cancers and 25 findings of high-grade dysplasia in intrapapillary mucinous neoplasms or pancreatic intraepithelial neoplasia 3 lesions.[13] Although perioperative mortality is $<2\%$ in high-volume centers, consideration of risk for postoperative complications, including diabetes after surgery, for what might ultimately prove to be a benign lesion is a necessary part of individual risk–benefit analysis in current screening programs. Other unintended individual-level harms can include

Table 1. Definitions of High-Risk Individuals, Estimated Risk, and Initiation of Screening Recommendations

Inclusion criteria	Published risk estimates	Initiation of screening recommendations
Peutz-Jeghers syndrome *STK11* PGV or meeting clinical diagnostic criteria	Cumulative risk by age 70 y, 32%–36%	Age 30 y or older
Familial atypical multiple mole and melanoma *CDKN2A* PGV	Cumulative risk by 75 y, 17% SIR, 21.8	Age 35 y or older
FPC 2 or more relatives with PDA First- or second-degree relative with PDA	Overall SIR in FPC kindreds: 9.0 1 FDR SIR, 4.5 2 FDR SIR, 6.4 3 FDR SIR, 32	Age 50 y or older or 10 y younger than youngest diagnosis of PDA in family
Hereditary pancreatitis *PRSS1* PGV or confirmed family history of pancreatitis Symptomatic pancreatitis	SIR, 53 Cumulative risk to 70 y, 33%–44%	Age 40 y or older
Confirmed PGV in below listed genes First- or second-degree relative with PDA		Age 50 y or older or 10 y younger than youngest diagnosis of PDA in family
ATM	OR, 4.2–5.7	—
BRCA1	RR, 2.6	—
BRCA2	RR, 3.5–5.9	—
MLH1, MSH2, MSH6, PMS2, EPCAM	Cumulative risk to 70 y, 3.68% 6.8% *MLH1* 0.5% *MSH2* 1.4% *MSH6*	—
PALB2	Not known	—

FDR, first-degree relative; FPC, familial pancreatic cancer; OR, odds ratio; PDA, pancreatic ductal adenocarcinoma; RR, risk ratio; SIR, standardized incidence ratio.

anxiety associated with screening procedures or abnormal findings that require additional follow-up. Small studies in HRIs have suggested no significant psychological impact with screening, but additional studies in this area are needed.

Currently available imaging modalities have a reasonable ability to detect lesions >1 cm, but not precursor lesions. These modalities are also expensive and, in the case of endoscopic ultrasound (EUS), invasive. Even with consensus recommendations for HRIs, insurance coverage is variable and can impact access to care. The cost and highly specialized nature of these modalities also creates disparities in access both economically and geographically. Cost–benefit analyses will be an important part of the necessary steps toward meeting National Institutes of Health and World Health Organization standards for screening, and will be critical to developing guidelines for medical necessity and consistent insurance coverage. Significant evolution in the recognition and treatment of precursor lesions will be required before the aims of screening can ultimately shift from proving reduction in mortality due to detection of early-stage pancreatic cancers to reduction of cancer incidence.

Implementing strategies to address screening challenges in pancreatic cancer is a critical and timely issue. Expanded use of germline genetic testing in patients with pancreatic cancer has led to increased recognition of genes linked to pancreatic cancer risk. Germline testing identifies a clinically relevant PGV in approximately 10% of patients with pancreatic cancer,[17–21] and at least another 2%–5% of pancreatic cancers occur in individuals with a family history of pancreatic cancer but without an identifiable PGV. For all individuals with a newly diagnosed pancreatic cancer, germline genetic testing is now part of routine care recommended by National Comprehensive Cancer Network[6] and American Society of Clinical Oncology[22] guidelines, regardless of family history. The National Comprehensive Cancer Network guidelines also now recommend germline genetic testing for individuals who have a first-degree relative with pancreatic cancer.[6]

These expanded criteria for genetic testing will identify new HRIs eligible for pancreatic surveillance based on the consensus guidelines. With more than 60,000 new cases of pancreatic cancer per year in the United States, and known rates of PGV identification and positive family history of pancreatic cancer, in combination with increased awareness of pancreatic cancer detection, at least 120,000 individuals will be eligible for surveillance annually in the United States alone. At this volume, it is

likely that both genetic testing and imaging or procedures will be performed by an increasing number of centers and providers.

Our main goal was to address an important step in the World Health Organization screening program pathway: to conduct and report testing using agreed on and standardized methods. This step is critical to move toward eventual reporting of outcomes on a scale large enough to demonstrate screening efficacy. There is a need to optimize screening algorithms and collection of longitudinal demographic, genetic, imaging, and biomarker data over an extended period of time. Although consortia and multicenter collaborations are ideal for data collection, it is likely that a significant proportion of screening will be performed outside of these efforts, further emphasizing the need for standardization. Here, we outline important elements that can be incorporated into current practice to improve and standardize data collection for HRIs and pave the road for future research to establish the efficacy of screening and to recognize novel risk factors, markers, or imaging characteristics of early-stage cancer or precursor lesions. The type of data we collect today, and how we collect those data, will determine our ability to ultimately reduce the mortality of pancreatic cancer with a favorable ratio of benefit to harm at an acceptable societal cost.

Standardization of Family History Collection and Documentation

The collection and documentation of cancer family history is a key component of risk stratification and clinical management for families at risk for pancreatic cancer. In a general clinic setting, pertinent positive family history, including primary site of cancer and age at diagnosis in first- and second-degree relatives, is sufficient for determining surveillance eligibility.[5] The gold standard for cancer genetic counseling and the best practice approach for the high-risk clinic setting is a 3-generation pedigree, including information about primary cancer sites and ages at diagnosis for all relatives with cancer history. Confirmation of pancreatic cancer diagnoses via medical records is preferred when possible, particularly for second- or third-degree relatives, as accuracy of reporting decreases beyond first-degree relationships.[23] Pedigree documentation should also include results of genetic testing and the specific genes analyzed for any family member completing it. Discovery of new genes or new associations with known genes over time might mean that updated testing is indicated for HRIs or their tested family members.[24] With the evolving use of multigene panel testing, there has been considerable variation in the content of genetic testing offered to HRIs. Current testing in this setting should include a minimum list of the following genes from published surveillance guidelines[4,5]: *APC*, *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *MLH1*, *MSH2*, *MSH6*, *PALB2*, *PMS2*, *STK11*, and *TP*53. Among families who present meeting criteria for familial pancreatic cancer, about 15%–20% have an identifiable pathogenic germline variant, leaving 80%–85% of the heritable component of familial pancreatic cancer unknown. Standard collection of full pedigrees in this setting will power studies to identify new genetic associations. Documentation of full pedigree information in high-risk families will also allow improvements in penetrance estimation and risk modeling to provide accurate risk information to patients and families that will refine surveillance guidelines over time. We therefore include standardized reporting of pedigrees in HRIs (Table 2).

Standardized Documentation of Risk Factor Variables

Improving identification of individuals at risk for pancreatic cancer will also require a deeper understanding of all significant contributing risk factors. Both modifiable and nonmodifiable risk factors beyond the known high-/moderate-penetrance genes contribute to pancreatic cancer risk, but understanding the impact of, and interactions among, individual risk factors in HRIs remains elusive. Standard documentation of known pancreatic cancer risk factors should be part of high-risk care, and will help to drive discovery, risk stratification, and risk modeling in this population. Key risk factor variables to document include history of diabetes, along with current fasting blood glucose or hemoglobin A1C and time of onset and course of pre-existing diabetes; current weight and BMI; blood type; current and past smoking; and current and past alcohol use, including binge drinking. Few studies have comprehensively investigated the effects of modifiable factors including dietary habits, nutrition, or physical activity on pancreatic cancer risk, and future efforts to document these variables in HRIs may be warranted.

Standardization of Imaging and Reporting

Most studies have found imaging by magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography, and EUS to be superior to other modalities, similar to each other in accuracy and complementary for early lesion detection.[13] At present, there is no other surveillance test, including serum-based or endoscopically obtained biomarkers, that compares in accuracy or yield. Both EUS and MRI have excellent accuracy for the detection of pancreatic masses or cystic lesions >1 cm and changes in pancreatic duct caliber. EUS, however, currently has a higher sensitivity in the identification of small lesions (<1 cm) and in the identification of parenchymal abnormalities. Although MRI images are stored and accessible, EUS images are rarely, if ever, recorded in a high-resolution manner. This significantly limits both the clinical ability to compare studies between multiple time points and the potential for image analysis-based research. Although radiology reporting is increasingly standardized, there are no specific templates developed for patients undergoing screening procedures. EUS

Table 2. Proposed Areas of Standardization of Template Use in High-Risk Individuals

Areas of standardization	Proposed template elements	Examples
Family history	Pedigree templates (ie, commercially available templates [Prodigy])	3- to 4-generation pedigree with PGV information Confirmation of reported pancreatic cancers with records
Genetic testing	Minimum gene list and plan for updating	Panels including all known genes linked to pancreatic cancer risk Updated testing for families with outdated results
Indication for screening	Pathogenic germline variants in specific genes or family history	Familial pancreatic cancer Pathogenic germline variants Family history of pancreatic cancer
Acquisition of specific EUS views	Confirmation of capture of 8 key views of the pancreas and peripancreatic structures from the duodenal and gastric position	Duodenal views: Distal CBD/proximal PD/ampulla view Porta hepatis HOP with PD Pancreas parenchyma, portal confluence Gastric views: Celiac axis, SMA, aorta Tail of pancreas view with splenorenal angle Body of pancreas view at level of SA and SV Right lateral pancreas margin (PD toward HOP)
EUS procedural details	Templated acquisition of procedural data points	Type of EUS performed (radial vs linear); length of procedure; sedation used
EUS parenchymal descriptors	Use of templated drop-down menu for specific predefined parenchymal changes	Hyperechoic foci or strands; lobularity; microcysts; atrophy; calcifications; heterogeneous pancreas; fatty pancreas
EUS pancreatic duct descriptors	Use of drop-down menu for specific measurements and characteristics of MPD	Record diameter in head, body, and tail of pancreas Stricture, wall irregularities, filling defects and ampullary examination
Solid and cystic lesion descriptors	Use of drop-down menu for characteristics and biopsy/aspiration techniques and details	Size in 2 dimensions; location; echogenicity; communication with MPD; cystic component; vascular invasion; upstream dilation or atrophy; EUS impression
Tissue acquisition	Use of template for procedural details and tissue or fluid obtained	Technical details (needle size, approach, number of passes); biopsy details (amount of fluid or number of cores obtained) Testing performed (cytology, tumor sequencing, fluid analysis, other cyst fluid–based biomarkers)
Assessment of EUS adequacy and overall impression	Template for assessment of procedural adequacy, recommendations for future imaging	Provide scale of adequacy (adequate, partially adequate or limited/inadequate) and ability to make recommendations based on examination (recommend continued use of EUS vs other modalities for screening)
Assessment of overall impression	Template for overall impression and changes (if applicable) to prior EUS examination	Provide description of overall impression (normal/abnormal of uncertain significance/worrisome or significant abnormalities and provide comparison to prior examination

CBD, common bile duct; HOP, head of pancreas; MPD, main pancreatic duct; PC, pancreatic cancer; PD, pancreatic duct; SA, splenic artery; SMA, superior mesenteric artery; SV, splenic vein.

reporting is less frequently templated and most current reporting templates have been developed for different contexts, which leads to further gaps in both clinical care and research. With an expected increase in demand for these studies, it is imperative that we enhance our ability to acquire and report EUS abnormalities in a standardized manner.

Standardization of Endoscopic Ultrasound

The goal of EUS imaging in HRIs is to provide complete and reproducible examination of the pancreas and generate a uniform format report that can allow for both image and description comparison between time points and across different providers. A first step in standardization is to create a definition of a complete examination defined by imaging landmarks to

assess imaging adequacy. Reporting of landmarks should be analogous to now-established colonoscopy standards,[25] and recording of these landmarks should be mandatory. A list of proposed EUS landmarks is provided in Table 2. Adequacy of a pancreatic EUS examination can be analogous to colonoscopy quality assessment,[26] and will depend on procedural-, anatomic-, and sedation-related factors. However, this assessment will likely be impactful, as it will guide further recommendations and use of EUS in surveillance.

Standardized reporting exists for pancreatic mass[27] or cystic neoplasia assessment, and these can generally be adopted for screening of HRIs. However, in only a minority of patients are these findings identified, and our current understanding of evolution of pancreatic precursors suggests that more subtle findings, such as parenchymal changes, can be important to recognize precursors.[28,29] Most of these parenchymal changes were initially described in relation to chronic pancreatitis-associated changes, but have since been associated with changes observed in neoplastic progression.[28,30] Improved resolution of B-mode EUS imaging and enhanced imaging modalities (ie, elastography and contrast enhancement) will likely further improve our ability to characterize parenchymal changes associated with early neoplastic development. An obvious parallel to draw on is the unequivocal benefit of high-resolution white light and virtual chromoendoscopy in detection of gastric and colonic neoplasia in luminal imaging. Substantial efforts have been made to define and characterize mucosal changes and patterns, and only through these efforts was the significance of these findings validated.[31] A similar effort might be required to understand the parenchymal changes seen in pancreatic EUS, to understand the temporal evolution of these changes in HRIs, and perhaps to identify the phenotype of pancreatic parenchymal changes associated with specific germline mutational status. This can only be accomplished if we define specific terminology and use predetermined image-capture areas to document these changes.

An achievable immediate goal for the EUS field will be to standardize image capture and template reporting. This will result in higher-quality care in surveillance of HRIs and allow comparison of data between time points and providers. We would even propose the creation of a training module to aid in uniform image capture and terminology use by providers who care for HRIs. These objectives can likely be fulfilled with currently available technologies and resources. However, the evolving role of enhanced image analysis and artificial intelligence–based evaluation will require higher quality and resolution image capture and the ability to store these images or video segments for future analysis. This is a much more resource-intensive proposition, which will likely require greater integration of EUS images in standard image repositories, such as picture archiving and communication systems. This is an area where multicenter collaborative consortiums will play a critical role.

Conclusions

We are at an inflection point in the history of pancreatic cancer screening. There is an increasing opportunity to decrease mortality of pancreatic cancer through early detection, and the growing number of patients who will be eligible for screening highlights the importance of well-organized, large-scale, long-term, longitudinal follow-up studies of a population with sufficiently high risk for cancer that screening impact can be assessed adequately. Undoubtedly, progress toward more effective early-detection biomarkers and less invasive (and less expensive) screening approaches will become available in the future. However, for patients with familial pancreatic cancer and those with pathogenic germline variants that increase risk for pancreatic cancer, cross-sectional and endoscopic imaging will likely remain the cornerstone of surveillance for a period of time. Consortiums like PRECEDE (Pancreatic Cancer Early Detection),[32] CAPS (Cancer of the Pancreas Screening),[33] the Dutch Familial Pancreatic Cancer Surveillance study,[7] and EUROPAC (European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer)[34] are well positioned to collect these data and, given the relatively low event rate in surveillance cohorts, these large, multi-institutional studies will be critical in defining the natural history and predictors of progression. However, given the expected volume of screening procedures, it is essential that standardization is broadly practiced even outside of these registries and that we define and develop resources to achieve a common standard irrespective of the practice setting.

We would emphasize that urgent steps to assure future success include:

- Adherence to guidelines to perform germline testing in all pancreatic cancer patients and individuals with a family history of pancreatic cancer using a minimum set of genes that are part of consensus pancreas screening guidelines
- Standardization of data collection for pancreatic cancer patients and HRIs across relevant domains, with use of uniform templates and instruments when possible, including:
  - Cancer family history (3-generation pedigree)
  - Modifiable risk factors
  - MRI and EUS variables
- Creation of centralized or broadly accessible data and image repositories

Failure to meet these benchmarks will exponentially increase the difficulty of assessing the efficacy of existing and future pancreatic cancer screening techniques for both HRIs and other at-risk populations.

TAMAS A. GONDA
JESSICA N. EVERETT
Department of Medicine
Perlmutter Cancer Center
NYU Langone Health
New York, New York

MICHAEL WALLACE
Mayo Clinic
Jacksonville, Florida
Sheikh Shakbout Medical City
Abu Dhabi, United Arab Emirates

DIANE M. SIMEONE
Perlmutter Cancer Center
Departments of Surgery and Pathology
NYU Langone Health
New York, New York

On behalf of the PRECEDE Consortium

References

1. Rahib L, Smith BD, Aizenberg R, et al. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res 2014;74:2913–2921.
2. Screening tests. National Cancer Institute. Updated March 12, 2021. Available at: https://www.cancer.gov/about-cancer/screening/screening-tests. Accessed September 16, 2021.
3. US Preventive Services Task ForceOwens DK, Davidson KW, et al. Screening for pancreatic cancer: US Preventive Services Task Force reaffirmation recommendation statement. JAMA 2019;322:438–444.
4. Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. Gut 2020;69:7–17.
5. Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol 2015;110:223–262; quiz 263.
6. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 1.2021. National Comprehensive Cancer Network, 2020.
7. Overbeek KA, Levink IJM, Koopmann BDM, et al. Long-term yield of pancreatic cancer surveillance in high-risk individuals [published online ahead of print April 5, 2021]. Gut https://doi.org/10.1136/gutjnl-2020-323611.
8. Paiella S, Salvia R, De Pastena M, et al. Screening/surveillance programs for pancreatic cancer in familial high-risk individuals: a systematic review and proportion meta-analysis of screening results. Pancreatology 2018;18:420–428.
9. Canto MI, Almario JA, Schulick RD, et al. Risk of neoplastic progression in individuals at high risk for pancreatic cancer undergoing long-term surveillance. Gastroenterology 2018;155:740–751.e2.
10. Canto MI, Kerdsirichairat T, Yeo CJ, et al. Surgical outcomes after pancreatic resection of screening-detected lesions in individuals at high risk for developing pancreatic cancer. J Gastrointest Surg 2020;24:1101–1110.
11. Menon U, Gentry-Maharaj A, Burnell M, et al. Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet 2021;397:2182–2193.
12. Martin RM, Donovan JL, Turner EL, et al. Effect of a low-intensity PSA-based screening intervention on prostate cancer mortality: the CAP randomized clinical trial. JAMA 2018;319:883–895.
13. Corral JE, Mareth KF, Riegert-Johnson DL, et al. Diagnostic yield from screening asymptomatic individuals at high risk for pancreatic cancer: a meta-analysis of cohort studies. Clin Gastroenterol Hepatol 2019;17:41–53.
14. World Health Organization Screening Programmes. A Short Guide. Increase Effectiveness, Maximize Benefits and Minimize Harm. World Health Organization, 2020.
15. Callister MEJ, Sasieni P, Robbins HA. Overdiagnosis in lung cancer screening. Lancet Respir Med 2021;9:7–9.
16. Loeb S, Bjurlin MA, Nicholson J, et al. Overdiagnosis and overtreatment of prostate cancer. Eur Urol 2014;65:1046–1055.
17. Brand R, Borazanci E, Speare V, et al. Prospective study of germline genetic testing in incident cases of pancreatic adenocarcinoma. Cancer 2018;124:3520–3527.
18. Yurgelun MB, Chittenden AB, Morales-Oyarvide V, et al. Germline cancer susceptibility gene variants, somatic second hits, and survival outcomes in patients with resected pancreatic cancer. Genet Med 2019;21:213–223.
19. Shindo K, Yu J, Suenaga M, et al. Deleterious germline mutations in patients with apparently sporadic pancreatic adenocarcinoma. J Clin Oncol 2017;35:3382–3390.
20. Grant RC, Selander I, Connor AA, et al. Prevalence of germline mutations in cancer predisposition genes in patients with pancreatic cancer. Gastroenterology 2015;148:556–564.
21. Hu C, Hart SN, Bamlet WR, et al. Prevalence of pathogenic mutations in cancer predisposition genes among pancreatic cancer patients. Cancer Epidemiol Biomarkers Prev 2016;25:207–211.
22. Stoffel EM, McKernin SE, Brand R, et al. Evaluating susceptibility to pancreatic cancer: ASCO Provisional Clinical Opinion. J Clin Oncol 2019;37:153–164.
23. Ziogas A, Anton-Culver H. Validation of family history data in cancer family registries. Am J Prev Med 2003;24:190–198.
24. Riley BD, Culver JO, Skrzynia C, et al. Essential elements of genetic cancer risk assessment, counseling, and testing: updated recommendations of the National Society of Genetic Counselors. J Genet Couns 2012;21:151–161.
25. Lieberman D, Nadel M, Smith RA, et al. Standardized colonoscopy reporting and data system: report of the Quality Assurance Task Group of the National Colorectal Cancer Roundtable. Gastrointest Endosc 2007;65:757–766.
26. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Gastrointest Endosc 2015;81:31–53.
27. Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the american Pancreatic Association. Gastroenterology 2014;146:291–304.e1.
28. Konings I, Cahen DL, Harinck F, et al. Evolution of features of chronic pancreatitis during endoscopic ultrasound-based

surveillance of individuals at high risk for pancreatic cancer. Endosc Int Open 2018;6:E541–E548.
29. Catalano MF, Sahai A, Levy M, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. Gastrointest Endosc 2009;69:1251–1261.
30. LeBlanc JK, Chen JH, Al-Haddad M, et al. Can endoscopic ultrasound predict pancreatic intraepithelial neoplasia lesions in chronic pancreatitis?: a retrospective study of pathologic correlation. Pancreas 2014;43:849–854.
31. Shaukat A, Kaltenbach T, Dominitz JA, et al. Endoscopic recognition and management strategies for malignant colorectal polyps: recommendations of the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020;159:1916–1934.e2.
32. The Pancreatic Cancer Early Detection Research Consortium (PRECEDE). Available at: www.precedestudy.org. Accessed September 16, 2021.
33. Canto MI, Harinck F, Hruban RH, et al. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. Gut 2013;62:339–347.
34. The European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC). Volume 2021.

Acknowledgments
PRECEDE Consortium: Laufey Amundadottir, PhD; Georg Beyer, MD; Yan Bi, MD, PhD; Randall E. Brand, MD; Teresa Brentnall, MD; Darren Carpizo, MD, PhD; Alfredo Carrato, MD, PhD; Jennifer Chun, MPH; Daniel Chung, MD; Beth Dudley, MS; Julia Earl, PhD; James Farrell, MD; Melissa Fava, MPA; Eitan Friedman, MD, PhD; Srinivas Gaddam, MD; Steve Gallinger, MSc, MD; Talia Golan, MD; John Graff, PhD, MS; William Greenhalf, PhD; Aaron Grossberg, MD, PhD; Philip Hart, MD; Heather Hampel, MS; Spring Holter, MS; Gregory Idos, MD, MS; Priyanka Kanth, MD; Fay Kastrinos, MD; Bryson Katona, MD, PhD; Vivek Kaul, MD; Kelsey Klute, MD; Sonia Kupfer, MD; Richard S. Kwon, MD; Joy Liau, MD; James Lin, MD; James Lindberg, MD; Andrew Lowy, MD; Aimee Lucas, MD; Julia Mayerle, MD; Nipun Merchant, MD; Salvatore Paiella, MD, PhD; Jennifer Permuth, PhD, MS; Intan Schrader, MBBS, PhD; Rosalie Sears, MD; Brett Sheppard, MD; Jens Siveke, MD; Daniel Sussman, MD; and George Zogopoulos, MD, PhD.

Conflicts of interest
The authors disclose no conflicts.

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2021.08.036