

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

Note: Screening is only intended for asymptomatic individuals and should be performed 10 years before age of diagnosis in closest relative affected with pancreatic cancer. Individuals undergoing pancreatic cancer screening should have a 10-year life expectancy and no co-morbidities that would limit the diagnostic evaluation or surgical treatment. The screening should be performed by a provider with experience in screening technique.

RISK PRESENTATION SCREENING Proceed to diagnostic evaluation Yes • Annual: Presence of Physical examination pancreatic cancer o Laboratory studies (CA 19-9, fasting glucose, amylase, lipase and hemoglobin A1c) symptoms¹? o Imaging studies (MRI abdomen with and without contrast/MRCP) and consider alternating with endoscopic ultrasound (EUS) Yes • Consider baseline EUS³ High risk²? No pancreatic cancer screening recommended

MRCP = magnetic resonance cholangiopancreatography

- Weight loss
- Jaundice
- Abdominal/back pain
- Nausea/vomiting

¹ Pancreatic cancer symptoms include:

² See Appendix A - Pancreatic Cancer (PC) High Risk Criteria

³ EUS will be repeated if patient develops other symptoms or if physical exam, blood markers or imaging tests show any abnormality



Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

APPENDIX A: Pancreatic Cancer (PC) High Risk Criteria

Risk Factors	High Risk Criteria ¹	Age To Begin Pancreatic Cancer Screening
Pancreatic cancer family history	Two or more relatives (from the same side of the family) who developed PC ¹	50 years or 10 years prior to earliest pancreatic cancer in the family whichever is earlier
CDKN2A/p16 mutation	With no family history	40 years or 10 years prior to earliest pancreatic cancer in the family whichever is earlier
STK11 mutation (Peutz Jeghers Syndrome)		30-35 years or 10 years prior to earliest pancreatic cancer in the family whichever is earlier
PRSS1 mutation (Hereditary pancreatitis) ²		40 years or 20 years after onset of pancreatitis whichever is earlier
ATM mutation	Only if patient has PC family history or other risk factors ³	50 year or 10 years prior to earliest pancreatic cancer in the family whichever is earlier
BRCA1 and BRCA2 mutation (hereditary breast and ovarian cancer syndrome)		
PALB2 mutation		
MMR mutation (Lynch Syndrome, MLH1, MSH2, MSH6, EPCAM)		
p53 mutation (Li-Fraumeni Syndrome)		

Note: Some patients may not fit the criteria perfectly and risk assessment will be done by discussion with genetic counselor and expert physician given this is an evolving field

Consider referral to MD Anderson Pancreatic Cancer High Risk Clinic. Referrals can be made by:
 Phone: 1-877-632-6789; Monday – Friday, 8 a.m. to 11 p.m. CST and weekends and holidays from 8 a.m. to 7 p.m. CST

[•] Email: physicianreferrals@mdanderson.org

²For individuals with pathogenic/likely pathogenic variants in *PRSS1* or other hereditary pancreatitis genes and a clinical phenotype consistent with hereditary pancreatitis

³ History of chronic/acute recurrent pancreatitis, new onset diabetes, pancreatic cysts, etc.



Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS

- Abe, T., Blackford, A. L., Tamura, K., Ford, M., McCormick, P., Chuidian, M., ... Goggins, M. (2019). Deleterious germline mutations are a risk factor for neoplastic progression among high-risk individuals undergoing pancreatic surveillance. *Journal of Clinical Oncology*, 37(13), 1070-1080. doi:10.1200/JCO.18.01512
- Birch, J. M., Alston, R. D., McNally, R. J., Evans, D. G. R., Kelsey, A. M., Harris, M., ... Varley, J. M. (2001). Relative frequency and morphology of cancers in carriers of germline TP53 mutations. *Oncogene*, 20(34), 4621-4628. doi:10.1038/sj.onc.1204621
- Brand, R. E., Lerch, M. M., Rubinstein, W. S., Neoptolemos, J. P., Whitcomb, D. C., Hruban, R. H., ... Canto, M. I. (2007). Advances in counselling and surveillance of patients at risk for pancreatic cancer. *Gut*, 56(10), 1460-1469. doi:10.1136/gut.2006.108456
- Brune, K. A., Lau, B., Palmisano, E., Canto, M., Goggins, M. G., Hruban, R. H., & Klein, A. P. (2010). Importance of age of onset in pancreatic cancer kindreds. *Journal of the National Cancer Institute*, 102(2), 119-126. doi:10.1093/jnci/djp466
- Canto, M. I., Almario, J. A., Schulick, R. D., Yeo, C. J., Klein, A., Blackford, A., ... Goggins, M. (2018). Risk of neoplastic progression in individuals at high risk for pancreatic cancer undergoing long-term surveillance. *Gastroenterology*, 155(3), 740-751.e2. doi:10.1053/j.gastro.2018.05.035
- Canto, M. I., Harinck, F., Hruban, R. H., Offerhaus, G. J., Poley, J.W., Kamel, I., ... Bruno, M. (2013). International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut*, 62(3), 339-347. doi:10.1136/gutjnl-2012-303108
- Capurso, G., Paiella, S., Carrara, S., Butturini, G., Secchettin, E., Frulloni, L., ... Falconi, M. (2020). Italian registry of families at risk of pancreatic cancer: AISP Familial Pancreatic Cancer Study Group. *Digestive and Liver Disease*, 52(10), 1126-1130. doi:10.1016/j.dld.2020.07.027
- Goggins, M., Overbeek, K. A., Brand, R., Syngal, S., Del Chiaro, M., Bartsch, D. K., ... Bruno, M. (2020). Management of patients with increased risk for familial pancreatic cancer: Updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut*, 69(1), 7-17. doi:10.1136/gutjnl-2019-319352
- Hu, C., Hart, S. N., Polley, E. C., Gnanaolivu, R., Shimelis, H., Lee, K. Y., ... Couch, F. J. (2018). Association between inherited germline mutations in cancer predisposition genes and risk of pancreatic cancer. *JAMA*, 319(23), 2401-2409. doi:10.1001/jama.2018.6228
- Iqbal, J., Ragone, A., Lubinski, J., Lynch, H. T., Moller, P., Ghadirian, P., ... the Hereditary Breast Cancer Study Group. (2012). The incidence of pancreatic cancer in BRCA1 and BRCA2 mutation carriers. *British Journal of Cancer*, 107(12), 2005-2009. doi:10.1038/bjc.2012.483
- Klein, A. P. (2012). Genetic susceptibility to pancreatic cancer. *Molecular Carcinogenesis*, 51(1), 14-24. doi:10.1002/mc.20855
- Klein, A. P., Brune, K. A., Petersen, G. M., Goggins, M., Tersmette, A. C., Offerhaus, G. J. A., ... Hruban, R. H. (2004). Prospective risk of pancreatic cancer in familial pancreatic cancer kindreds. *Cancer Research*, 64(7), 2634-2638. doi:10.1158/0008-5472.CAN-03-3823
- Klein, A. P., Hruban, R. H., Brune, K. A., Petersen, G. M., & Goggins, M. (2001). Familial pancreatic cancer. Cancer Journal (Sudbury, Mass.), 7(4), 266-273. PMID: 11561603

Continued on next page



Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS - continued

- Matsubayashi, H., Takaori, K., Morizane, C., & Kiyozumi, Y. (2019). Familial pancreatic cancer and surveillance of high-risk individuals. *Gut and Liver*, 13(5), 498-505. doi:10.5009/gnl18449
- National Comprehensive Cancer Network. (2023). *Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.* (NCCN Guideline Version 3.2023). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf
- Obazee, O., Archibugi, L., Andriulli, A., Soucek, P., Małecka-Panas, E., Ivanauskas, A., ... Canzian, F. (2019). Germline BRCA2 K3326X and CHEK2 I157T mutations increase risk for sporadic pancreatic ductal adenocarcinoma. *International Journal of Cancer*, 145(3), 686-693. doi:10.1002/ijc.32127
- Ohmoto, A., Yachida, S., & Morizane, C. (2019). Genomic features and clinical management of patients with hereditary pancreatic cancer syndromes and familial pancreatic cancer. *International Journal of Molecular Sciences*, 20(3), 561. doi:10.3390/ijms20030561
- Roch, A. M., Schneider, J., Carr, R. A., Lancaster, W. P., House, M. G., Zyromski, N. J., ... Ceppa, E. P. (2019). Are BRCA1 and BRCA2 gene mutation patients underscreened for pancreatic adenocarcinoma? *Journal of Surgical Oncology*, 119(6), 777-783. doi:10.1002/jso.25376
- Shindo, K., Yu, J., Suenaga, M., Fesharakizadeh, S., Cho, C., Macgregor-Das, A., ... Goggins, M. (2017). Deleterious germline mutations in patients with apparently sporadic pancreatic adenocarcinoma. *Journal of Clinical Oncology*, 35(30). 3382-3390. doi:3382-3390.10.1200/JCO.2017.72.3502
- Zhan, W., Shelton, C. A., Greer, P. J., Brand, R. E., & Whitcomb, D. C. (2018). Germline variants and risk for pancreatic cancer: A systematic review and emerging concepts. *Pancreas*, 47(8), 924-936. doi:10.1097/MPA.0000000000001136



Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

DEVELOPMENT CREDITS

This screening algorithm is based on majority expert opinion of the Pancreatic Cancer Screening workgroup at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Core Development Team Leads

Therese Bevers, MD (Clinical Cancer Prevention)
Manoop Bhutani, MD (Gastroenterology Hepatology & Nutrition)
Florencia McAllister, MD (Clinical Cancer Prevention)

Workgroup Members

Olga N. Fleckenstein, BS*
Ernest Hawk, MD (Clinical Cancer Prevention)
Matthew Katz, MD (Surgical Oncology)
Thoa Kazantsev, MSN, RN, OCN*
Riya Kottoor, MSN, RN (Clinical Cancer Prevention)
Maureen Mork, MS (Clinical Cancer Genetics)
Eduardo Vilar Sanchez, MD, PhD (Clinical Cancer Prevention)

^{*} Clinical Effectiveness Development Team