Digestive Diseases of the Caribbean ‘22

Pancreatic Cancer Screening and Surveillance in 2022: Are we there yet?

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Women In Endoscopy

Disclosures

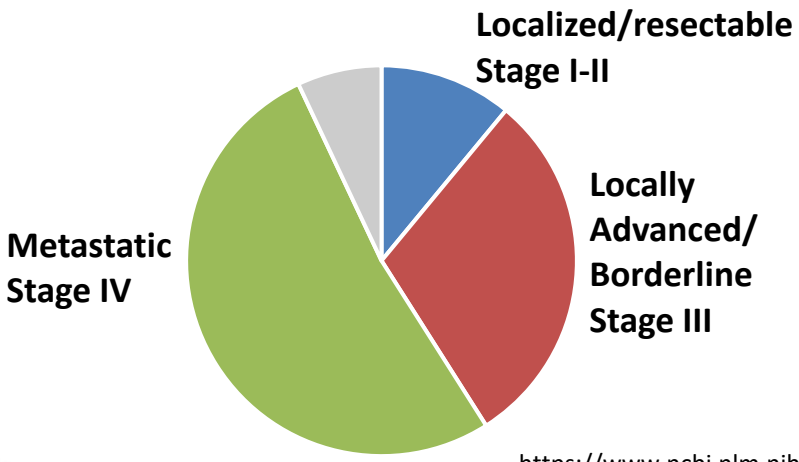
- Boston Scientific- consultant, research
- Olympus- consultant
- Fujifilm- consultant
- Medtronic- consultant
- Interscope- consultant

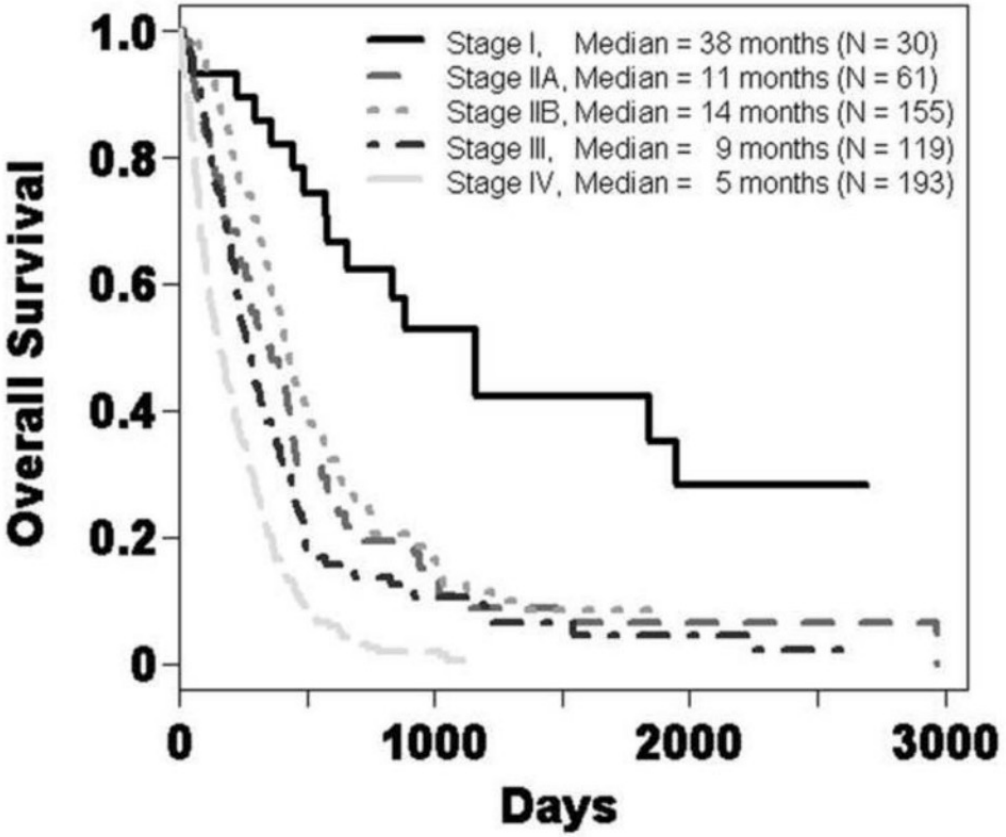
Outline

- Prevalence and survival of pancreas cancer: why do we need to screen?
- Who are high risk individuals who should be screened?
- Germline variants associated with pancreatic ca
- Pancreas diseases and risk for pancreatic ca
- Guidelines for screening and surveillance
- Challenges and future advances

Pancreatic Cancer: Epidemiology and Outcomes

- 3rd leading cause of cancer death in the United States and rising → 2nd by 2030
- Incidence only 12/100,000, but death rate as high 11/100,000
- <10% eligible for potentially curative surgery
- 5-year survival across all stages ~ 9%



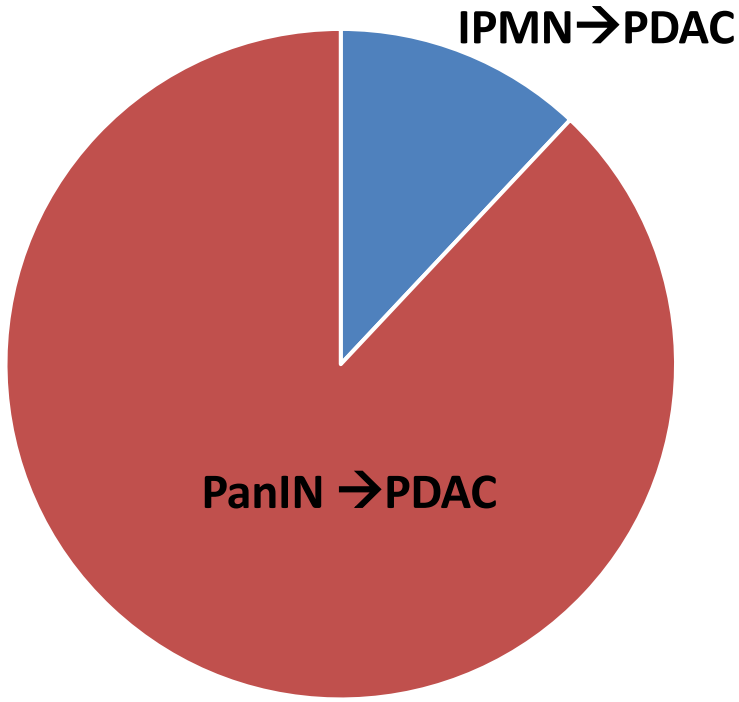


Rahib L et al. Cancer Res 2014;74:2913-2921;ACS Statistics;SEER13

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5490219/
Henrikson NB, et al. JAMA 2019

PDAC: genetic/histologic phenotypes

- 80-90% have no familial risk or genetic syndromes
- 5 – 10% have familial risk
  - At least 1 first-degree relative and 1 second-degree relative
- 3 – 5% have inherited genetic cancer syndromes
- 15% arise from mucinous cystic lesions (IPMN)



Singhi A Gastro2018; Witkiewicz AK Nat Comm 2015; Waddel et al Nature 2015; Henrikson NB, et al. JAMA 2019 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5490219/

Screening

- Goals: prevention, detection, improve survival

- Successful screening:
  - Demonstrate ability to detect early cancer
  - Demonstrate reduction in cancer-related mortality
  - Benefit > harm

- Good screening test dependent on prevalence→ PPV

Gonda, T et al, Gastro 2021

Challenges to screening for PDAC

- Low prevalence → low PPV 1.2%
- Few modifiable risk factors
- Few visible risk factors (ex IPMN)
- Non-visible risk factors (PanIN)
- Early metastasis

Current guidelines for general population: USPTF

- Recommends ***against*** screening for pancreatic cancer in ***asymptomatic,*** **average-risk** adults
  - Accuracy of detection
  - Lack of data on improvement in disease-specific morbidity, mortality or all-cause mortality**
  - Potential harm of false-positive results and treatment

**studies reviewed did not include known hereditary syndromes

Henrikson NB, et al. JAMA 2019

Who should be screened?

- Select populations with an increased prevalence and increased risk of pancreatic cancer:
  - Family history of pancreatic cancer (FPC)
  - Genetic predisposition
  - Hereditary Cancer Syndromes
  - Precursor lesions of the pancreas
  - Pancreatitis (certain etiologies)
  - New Onset Diabetes

CAPS = Cancer of the Pancreas Consortium

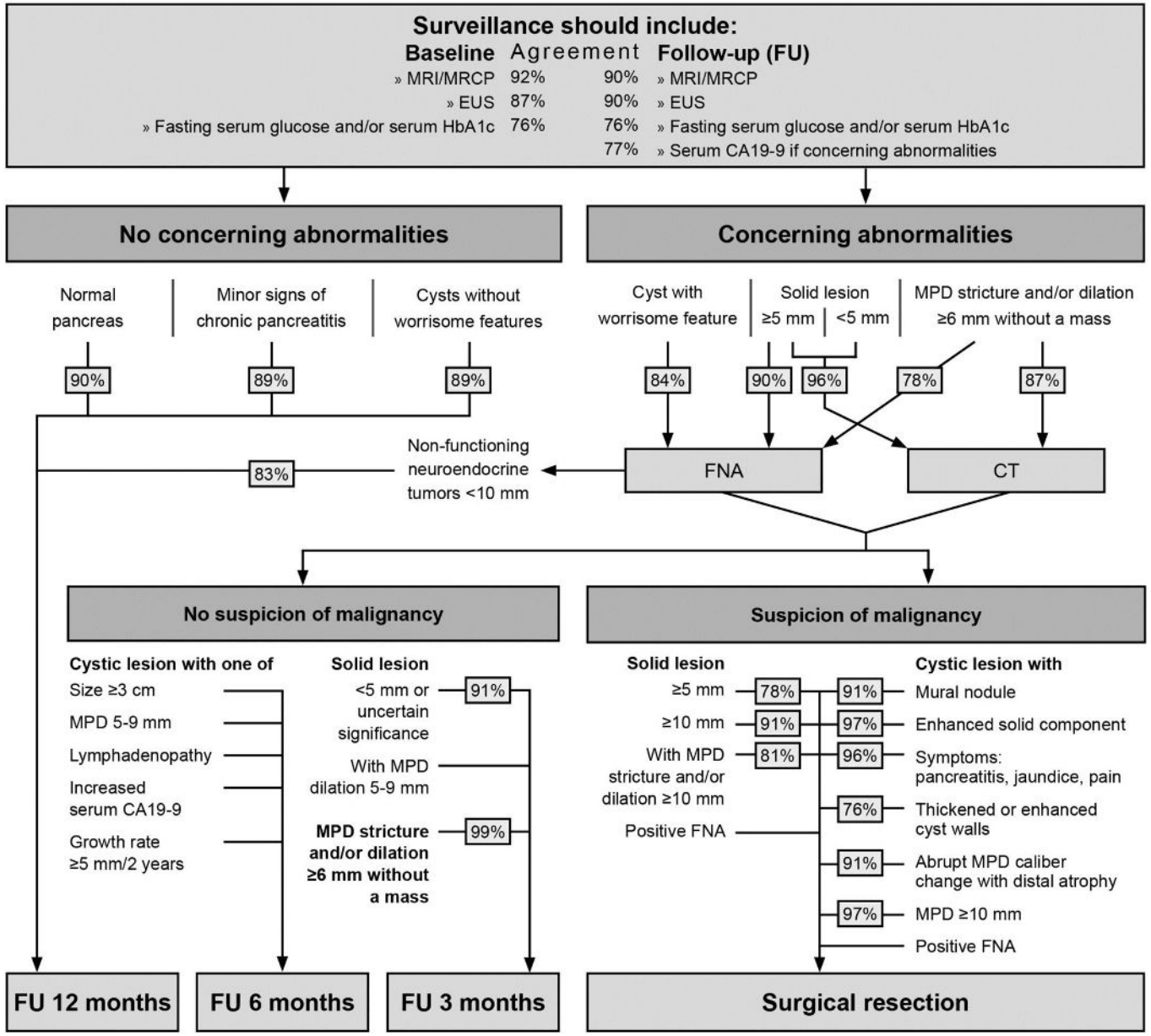
- To establish consensus guidelines for screening and surveillance
- Main goals of surveillance
  - Identify high-grade dysplastic precursor lesions
  - Identify T1N0M0 disease
- Genetic mutations that confer high risk and thus rendered eligible for surveillance
- EUS and MRCP considered adequate surveillance tools

Table 1 Definition of high-risk individuals eligible for pancreatic cancer surveillance.

Gene mutation	PDAC family history criteria	Agreement	Grade
LKB1/STK11 (Peutz-Jeghers syndrome)	Regardless of family history	99%	1
CDKN2A p16* (FAMMM)	With at least one affected FDR	99%	1
CDKN2A p16* (FAMMM)	Regardless of family history	77%	1
BRCA2	If at least one affected FDR, or at least two affected relatives† of any degree	93%	2
PALB2	If at least one affected FDR	83%	2
MLH1/MSH2/MSH6 (Lynch)	If at least one affected FDR	84%	2
ATM	If at least one affected FDR	88%	2
BRCA1	If at least one affected FDR	69.6%‡	3
Regardless of gene mutation status	If at least three affected relatives† on the same side of the family, of whom at least one is an FDR to the individual considered for surveillance	97%	2
Regardless of gene mutation status	If at least two affected relatives† who are FDR to each other, of whom at least one is an FDR to the individual considered for surveillance	93%	2
Regardless of gene mutation status	If at least two affected relatives† on the same side of the family, of whom at least one is an FDR to the individual considered for surveillance	88%	2

Canto MI et al. Gut 2013;62:339-47.
Goggins M et al. Gut 2020;69:7-17.

Surveillance in High-Risk Patients



Goggins et al, Gut 2020

Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

ASGE guideline on screening for pancreatic cancer in individuals with genetic susceptibility: summary and recommendations

TABLE 1. Summary of recommendations

Question	Recommendation and quality of evidence
1	In individuals at increased risk of pancreatic cancer because of genetic susceptibility, we suggest screening for pancreatic cancer compared with no screening (*conditional, low quality*)
2	In individuals at increased risk of pancreatic cancer because of genetic susceptibility, we suggest screening with EUS, EUS alternating with MRI, or MRI based on patient preference and available expertise (*conditional, very low quality*) • EUS may be preferred: as the initial screening test; for patients at very high risk for pancreatic cancer like Peutz-Jeghers syndrome and FAMMM; when EUS can be combined with screening upper endoscopy or colonoscopy (eg, Lynch and Peutz-Jeghers syndrome); when there is a contraindication to MRI (eg, claustrophobia, contrast allergy, implanted metal, and renal failure) • MRI may be preferred: for patients at increased risk of adverse events from anesthesia or invasive procedures; for patients who place a high value on avoiding invasive testing; when MRI may be combined with other imaging (eg, enterography for Peutz-Jeghers syndrome).
3a	In individuals with *BRCA2* pathogenic variant, we suggest screening for pancreatic cancer compared with no screening (*conditional, very low quality*)
3b	In individuals with *BRCA1* pathogenic variant, we suggest screening for pancreatic cancer compared with no screening (*conditional, very low quality*)

Sawhney MS et al, Standards of Practice Committee, ASGE, GIE 2022

Family History of Pancreas Cancer

- ~10% of pancreatic cancer cases have a family history of cancer
- Family Cancer Kindred: family where ≥2 individuals have a history of pancreatic cancer
  - Two of the individuals have a first-degree relationship to each other (parent-child, parent-sibling)

# of First-degree relatives	Standardized Incidence Ratio	Incidence (per 100,000)
General US population	-	9
1	4.5x	41
2	6.4x	58
≥3	32.0x	288

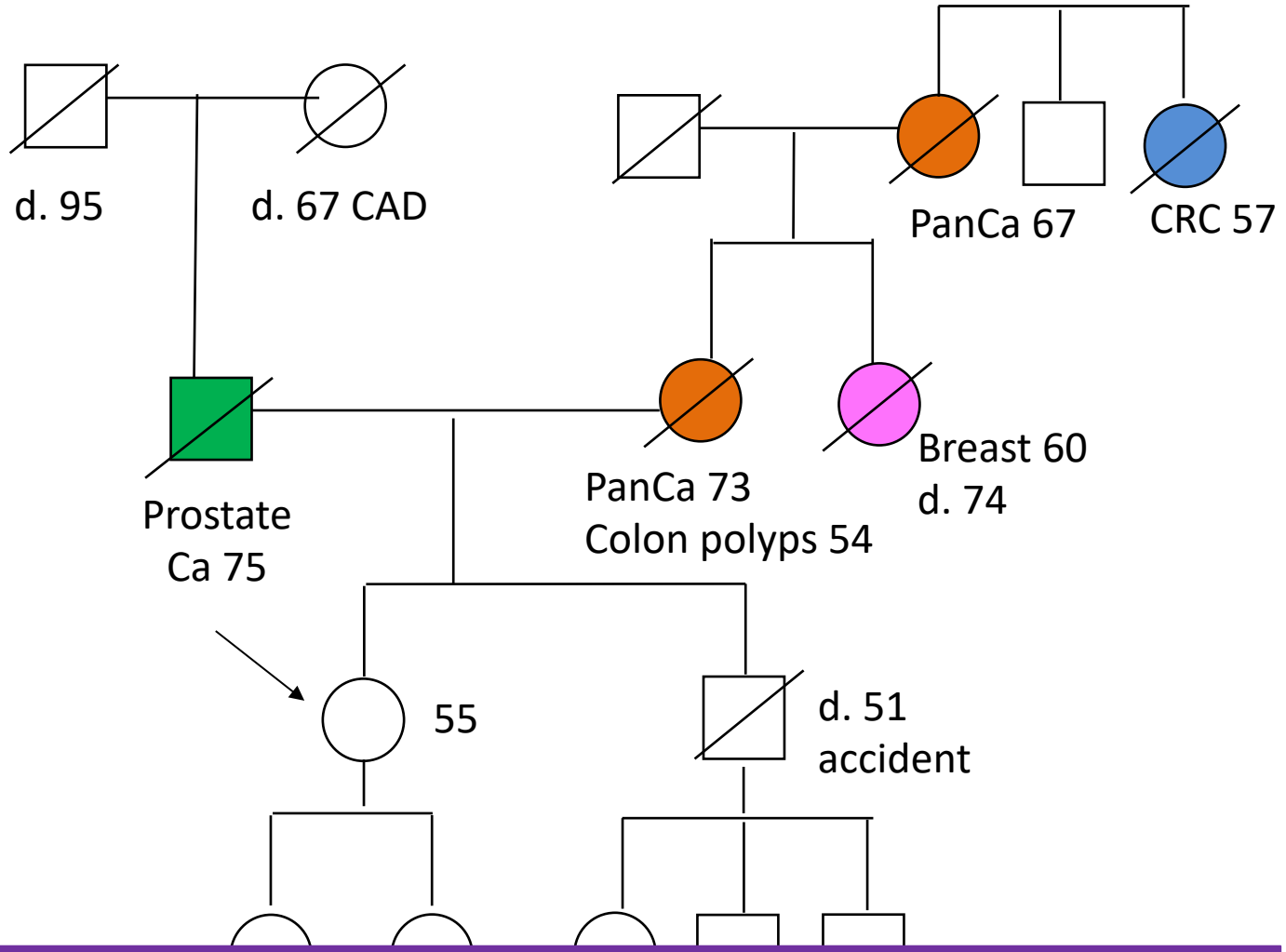
Klein A. Cancer Research 2004

Data for Screening in FPC: USPTF

- Cohort of 13 screening studies individuals (n=1317)
- CT, MRI or EUS
- Diagnostic yield:
  - In TOTAL:
    - 18 cases of pancreatic cancer were found in 1156 at increased familial risk
    - 0 cases of pancreatic cancer were found in 161 average risk individuals
    - In 8 studies (n=675) that assessed procedural harm
- There was no serious harm reported

Henrikson NB, et al. JAMA 2019
Owens DK, et al. JAMA 2019

Familial Pancreatic Cancer Kindred



Strategy for screening: Genetic testing

Courtesy of Fay Kastrinos, MD

Frequency of Germline Mutations in Familial Pancreatic Cancer

- 185 pancreatic cancer patients from FPC kindreds
- DNA sequencing of 25 cancer susceptibility genes

Results:

- 14% (25/185) carried a pathogenic mutation
- Deleterious mutations:
  - *BRCA2* (11), *ATM* (8), *CHEK2* (4), *BRCA1* (2), *PALB2* (1)
  - *CDKN2A* (4)
  - *MSH2*, *PMS2*
  - Other: *BARD1*, *NBN*, monoallelic *MUYH*

Chaffee KJ. Genet Med 2018

Association Between Inherited Germline Mutations and Risk of Pancreatic Cancer

- Methods
  - 3,030 PDAC cases at Mayo Clinic:2000-2016
  - Controls: the Genome Aggregation Database (n=123,136) and Exome Aggregation Consortium (n=53,105)
  - 21 candidate genes
- Results
  - Prevalence of mutations in unselected PDAC cases: 8.2%
  - 6 genes significantly associated with PDAC
  - Prevalence of mutations in the 6 genes: 5.5% in unselected cases; 7.9% with family history of PDAC

Hu et al, JAMA. 2018

Association Between Inherited Germline Mutations and Risk of Pancreatic Cancer

Table 3. Comparisons of Mutation Carriers by Panel Gene Between Pancreatic Cancer Cases and gnomAD Controls

Genes	Cases			gnomAD Controls			Cancer Risk[a]	
	Cases With Mutations, No.	Individuals Tested, No.[b]	Carrier Frequency, %	Controls With Mutations, No.	Individuals Tested, No.	Carrier Frequency, %	Odds Ratio (95% CI)	Adjusted *P* Value[c]
Genes Significantly Associated With Pancreatic Cancer								
CDKN2A	9	2999	0.30	15	99 493	0.02	12.33 (5.43-25.61)	<.001
TP53	6	2999	0.20	25	104 162	0.02	6.70 (2.52-14.95)	<.001
MLH1	4	2999	0.13	25	103 526	0.02	6.66 (1.94-17.53)	.01
BRCA2	57	2999	1.90	313	102 739	0.30	6.20 (4.62-8.17)	<.001
ATM	69	2999	2.30	386	104 016	0.37	5.71 (4.38-7.33)	<.001
BRCA1	18	2999	0.60	208	104 122	0.20	2.58 (1.54-4.05)	.002

Inherited Cancer Syndromes Associated with Pancreatic Cancer

Inherited Cancer Syndrome	Affected Genes	Relative Risk
Hereditary Breast and Ovarian Cancer (HBOC)*	*BRCA1, BRCA2*	**2-10**
Non-HBOC	*PALB2*	**increased**
Lynch Syndrome	*MLH1, MSH2, MSH6, PMS2*	**8**
Familial Atypical Mole Melanoma (FAMMM)	*CDKN2A (p16)*	**13-22**
Peutz-Jeghers Syndrome (PJS)	*STK11/LKB1*	**132**
Ataxia Telangiectasia	*ATM*	**2.7-5**
Hereditary Pancreatitis	*PRSS1, SPINK, CTRC*	**26-60**

Guidelines for **Genetic Testing** in PC

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2021
Hereditary Cancer Testing Criteria

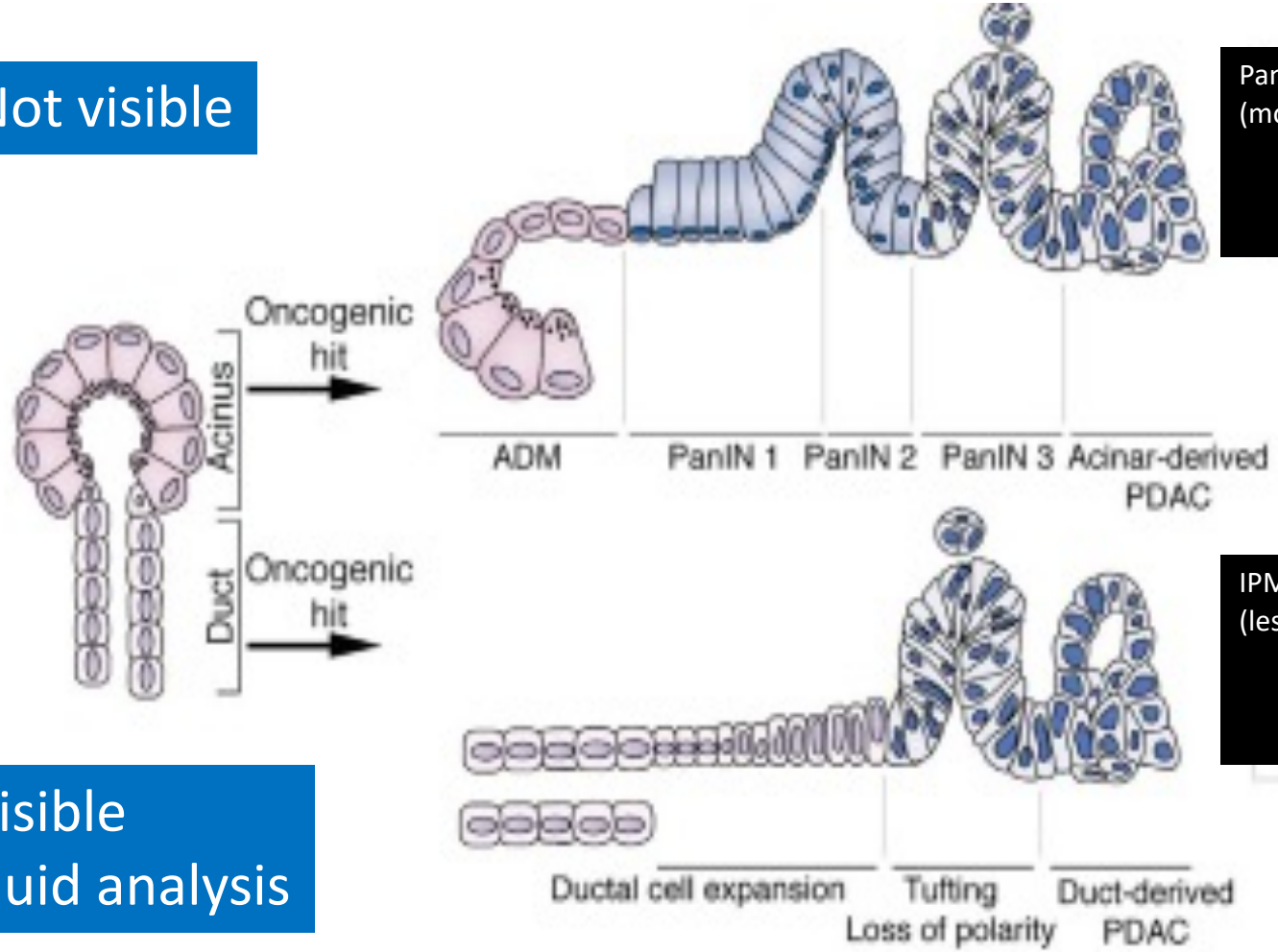
TESTING CRITERIA FOR PANCREATIC CANCER SUSCEPTIBILITY GENES[a]

DIAGNOSIS	TESTING CRITERIA
Exocrine pancreatic cancers →	Recommend genetic counseling and germline testing[m] for • All individuals diagnosed with exocrine pancreatic cancer[n] • First-degree relatives of individuals diagnosed with exocrine pancreatic cancer[o]

- Multi-gene panel testing: Genes that are typically tested for include *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, Lynch syndrome genes, *PALB2*, *STK11*, and *TP53*

Precursor Lesions: Targets for Early Detection of Pancreatic Cancer

PanIN- Not visible



Pancreatic Ductal Adenocarcinoma (more common)

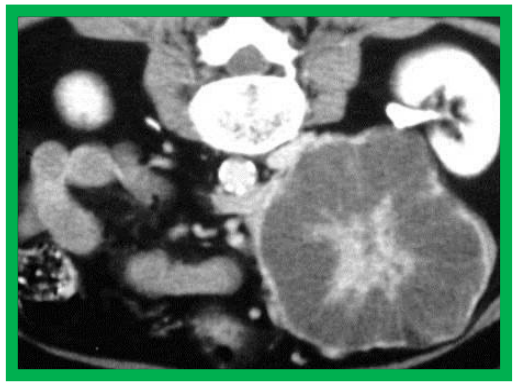
IPMN associated Adenocarcinoma (less common)

IPMN- Visible
- Fluid analysis

Courtesy of Tamas Gonda, MD

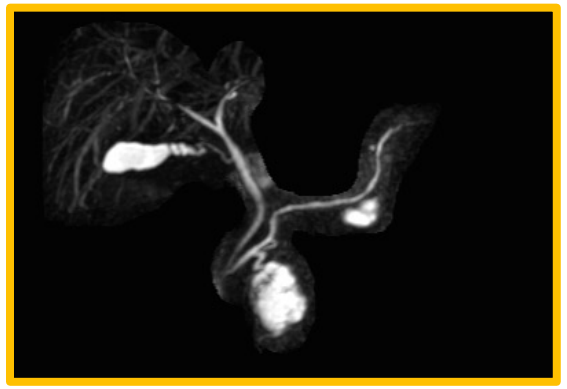
Pancreatic Cystic Neoplasms: Risk of Cancer

Serous Cyst (SCA)



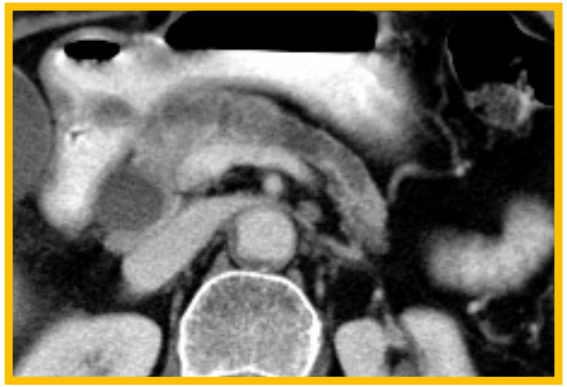
~0%

Branch Duct IPMN



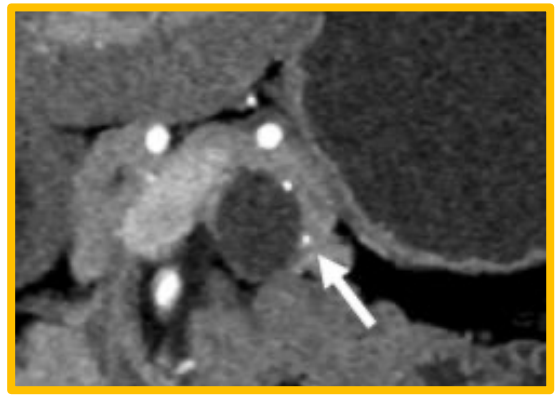
1(0)-36%

Main Duct IPMN



11-80%

Mucinous Cystic Neoplasm



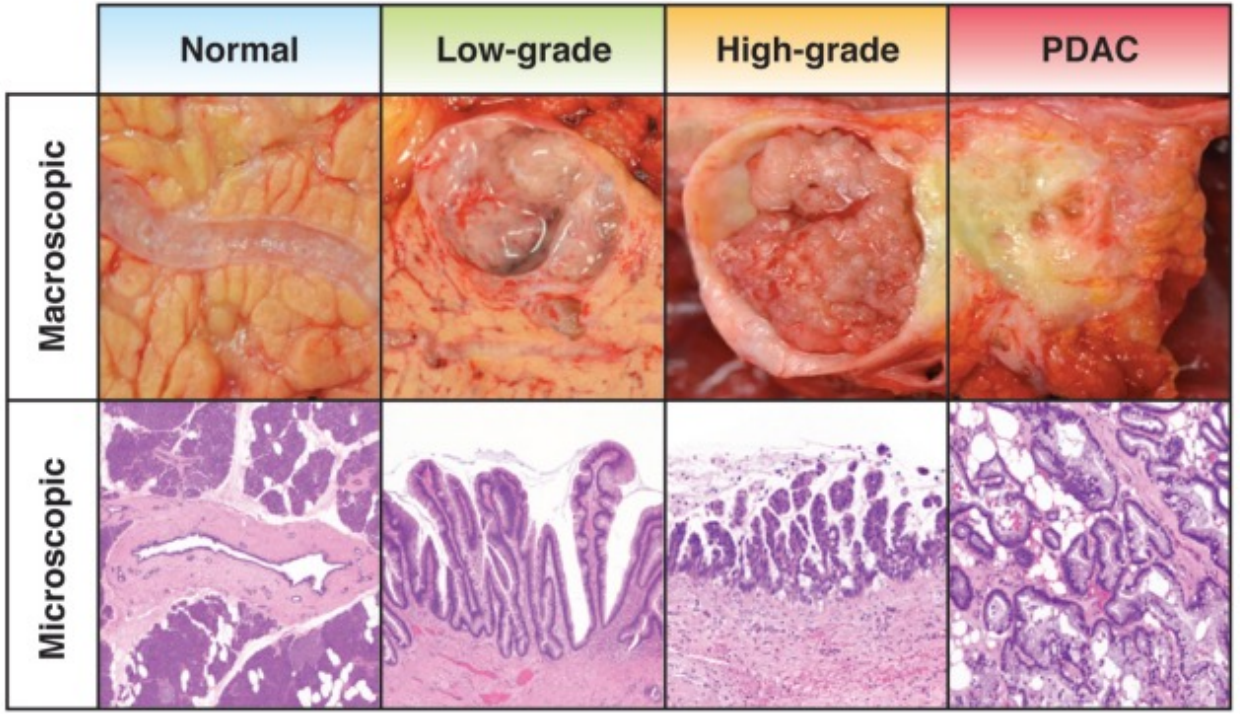
5-20%

Concomitant (not IPMN derived) Carcinoma:
2-11.2%

Singhi AD Gastro 2019; Tanaka M Pancreas 2018

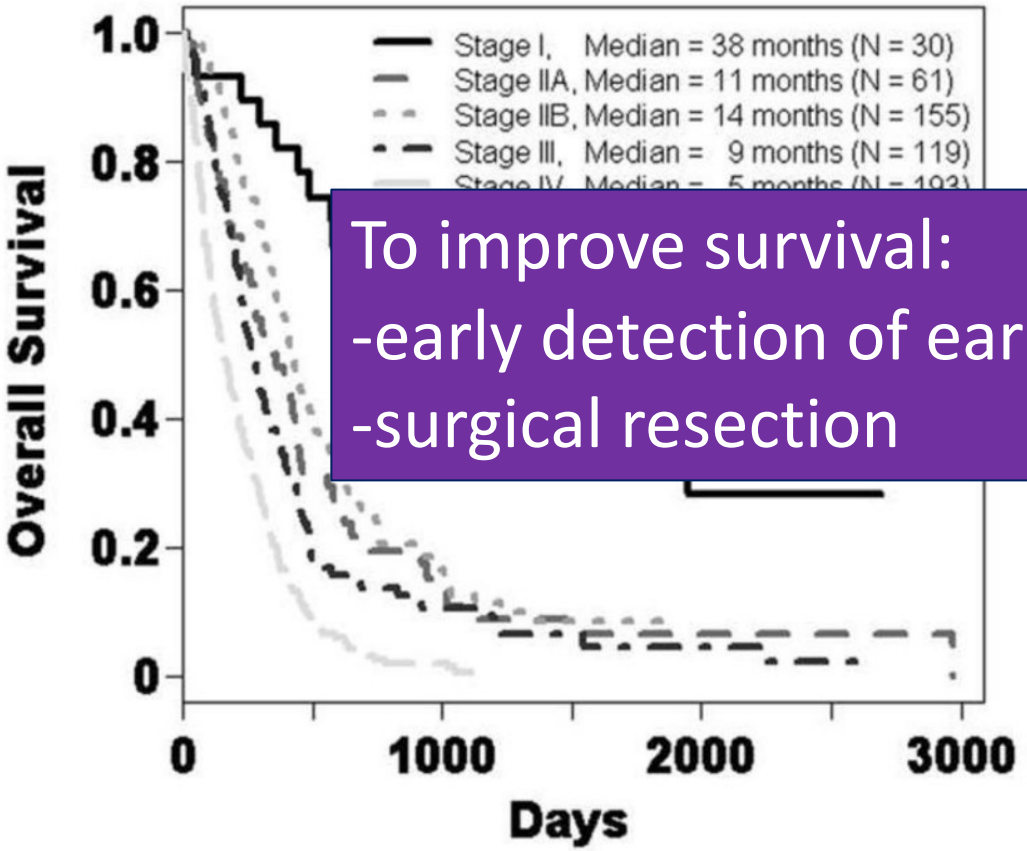
Intraductal Papillary Mucinous Neoplasia (IPMN)

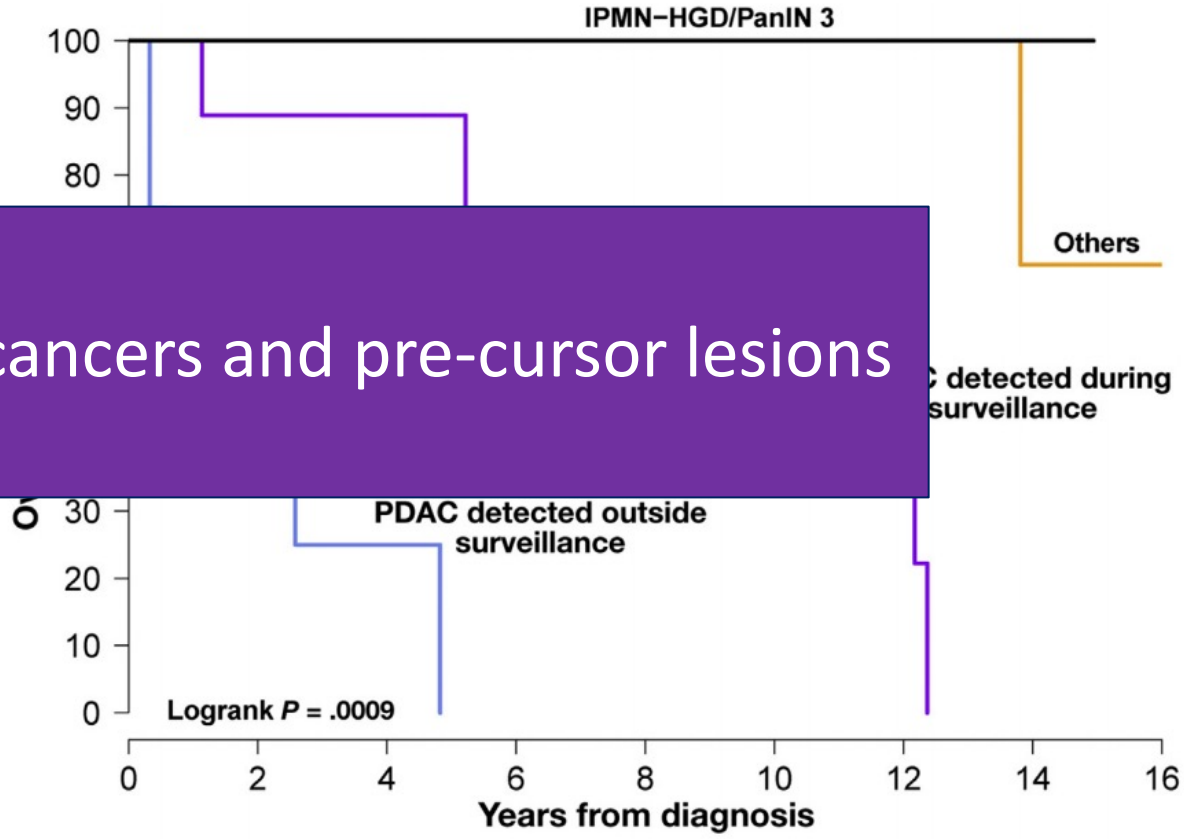
- Detected in ~15% of asymptomatic individuals with abdominal MRI
- 3 types:
  - Main pancreatic duct (MD; 10-35%)
  - Branch duct (BD; 40-65%)
  - Mixed (15-40%)
- Among resected IPMNs:
  - HGD: 62% MD, 58% mixed type, 24% BD
  - Panc ca: 44% MD, 45% mixed type, 17% BD



Singhi AD. Gastroenterology 2019

Early detection of pancreatic cancer: impact on survival



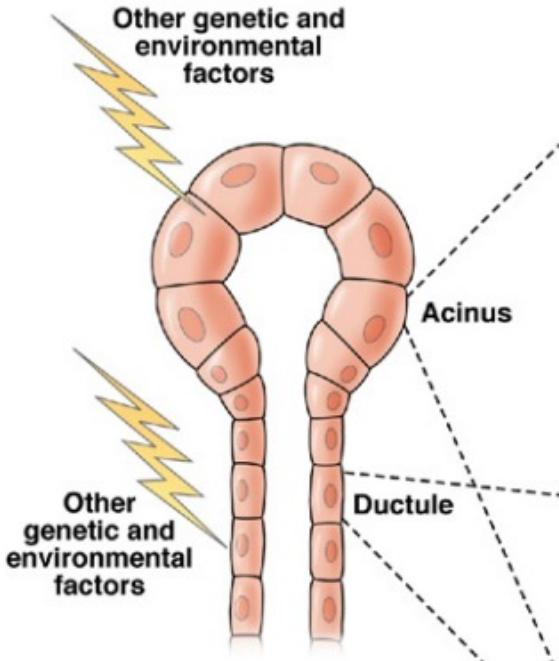


To improve survival:
-early detection of early cancers and pre-cursor lesions
-surgical resection

Poruk et al Ann Surg 2013; Canto MI Gastro 2018

Etiologies of Chronic Pancreatitis at Highest Risk of Pancreatic Cancer

Hereditary Pancreatitis



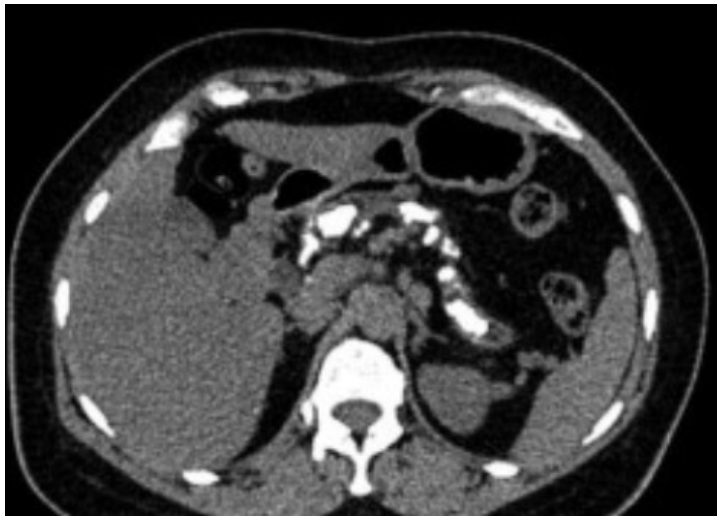
Gene	Key features
PRSS1	• Autosomal dominant • High penetrance
SPINK1	• High frequency in general population but low penetrance (N34S mutation) • Disease modifying rather than disease causing
CFTR	• May be associated with CF disease • Majority of the >1600 CFTR mutations have unknown functional and clinical significance; only a minority are disease-causing mutations

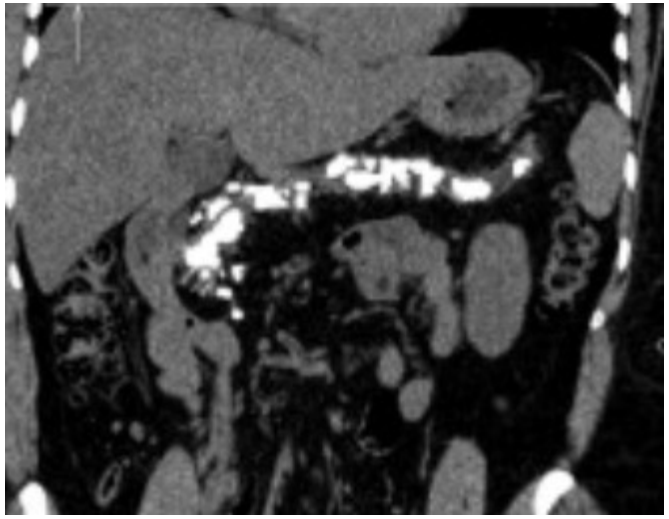
Study population	SIR (95% CI)	CI at age 70 (95% CI)	% with a *PRSS1* Mutation	No. of pancre-atic cancer cases	No. at risk at age 70
This Report[a] USA	*59 (19–138)*	*7.2% (0–15.4%)*	*100*	*5*	*29*
Lowenfels et al. (1997) International	53 (23–105)	40% (9–71%)	Unknown	8	10
Howes et al. (2004) EUROPAC	67 (50–82)	18.8% (8.6–29%)	78	26	31[b]
Rebours et al. (2009) France	87 (42–113)	(at age 75: 53.5% [7–76%])	68	10	11

Ooi C et al Gastro 2010; Shelton CA et al AJG 2018

Etiologies of Chronic Pancreatitis at Highest Risk of Pancreatic Cancer

- Tropical pancreatitis
  - Significantly higher risk > gen population (possibly higher than other forms of hereditary pancreatitis)
  - Younger onset then other etiologies of CP
  - 8% of patients presenting with TCP had PDAC





Chari ST Pancreas 1994; Balakrishnan V JOP 2008

Screening for Pancreatic Cancer in Chronic Pancreatitis

- Not recommended in most patients with chronic pancreatitis
  - Consider if other risk factors and in those with younger onset CP in the absence of germline mutation
- Recommended in hereditary pancreatitis (PRSS1 mutation)
- Recommended in tropical pancreatitis
- Challenging diagnosis in most cases due to non-specific imaging

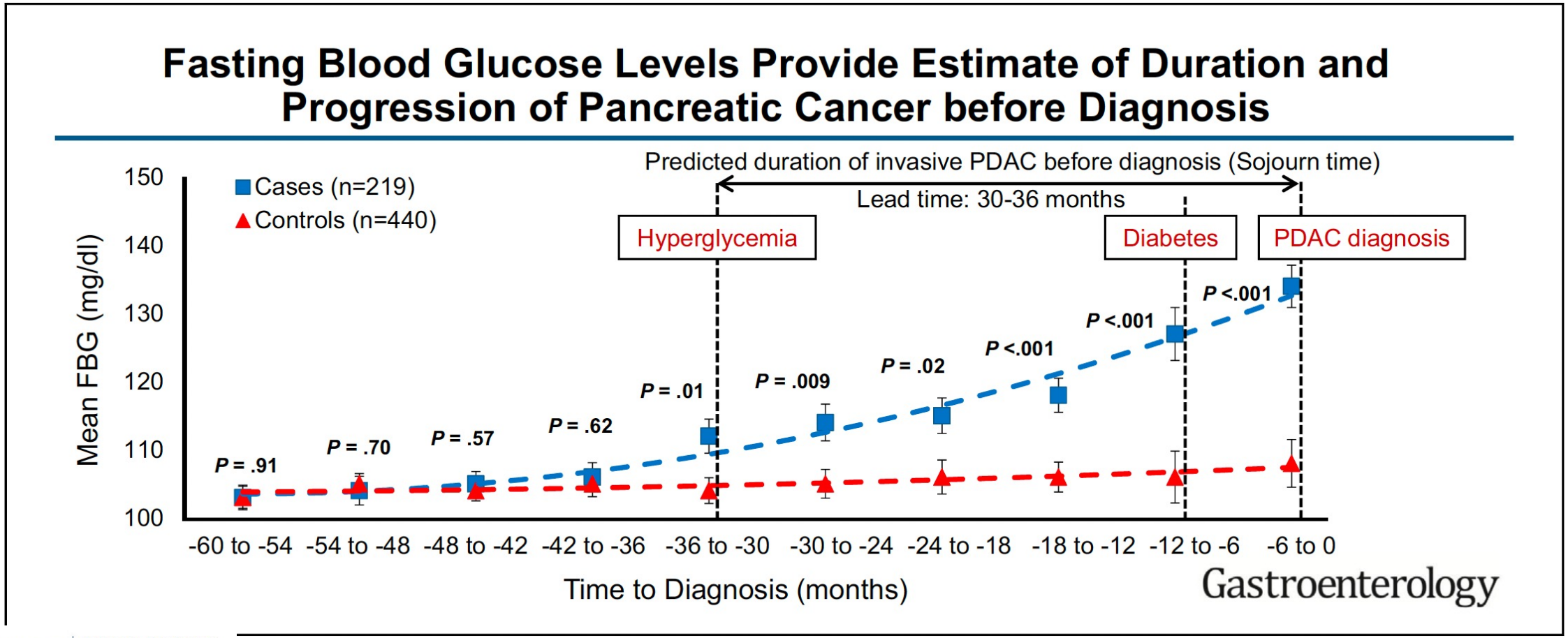
Pancreatitis: when to get **genetic** testing?

- Molecular genetic testing may be considered in any individual with **pancreatitis** and any **one** of the following:
  - Unexplained acute pancreatitis in childhood
  - Recurrent acute pancreatitis of unknown cause
  - Chronic pancreatitis of unknown cause, particularly with onset <25 years
  - At least one relative with recurrent acute pancreatitis, chronic pancreatitis of unknown cause, or childhood pancreatitis of unknown cause

Hasan A et al., Gastrointestin Endosc Clin N Am. 2018

Fasting Blood Glucose Levels Provide Estimate of Duration and Progression of Pancreatic Cancer Before Diagnosis

Ayush Sharma,[1] Thomas C. Smyrk,[2] Michael J. Levy,[1] Mark A. Topazian,[1] and Suresh T. Chari[1]



When to start screening?

Inherited Cancer Syndrome/ Gene mutations	Screening initiation	+ Family History	Risk
Peutz-Jeghers Syndrome (PJS) STK11 gene carrier	At least 30 years old		
Familial Atypical Mole Melanoma (FAMMM) (CDKN2A)	At 50 years or 10 years younger than the youngest relative with pancreatic cancer; *CDKN2A* begin at 40 years*	≥1 pancreatic cancer cases in the family* who is a FDR or SDR of the eligible subject	10%
Hereditary Breast and Ovarian Cancer (HBOC)* BRCA2, PALB2	At 50 years or 10 years younger than the youngest relative with pancreatic cancer; *CDKN2A* begin at 40 years*	≥1 pancreatic cancer cases in the family* who is a FDR or SDR of the eligible subject	10%
Lynch Syndrome (*MLH1, MSH2, MSH6, PMS2, EPCAM) BRCA1, ATM*	At 55* years or 10 years younger than the youngest relative with pancreatic cancer	≥1 pancreatic cancer cases in the family who is a FDR or SDR of the eligible subject	5%
Hereditary pancreatitis *PRSS1, SPINK, CFTR, CTRC*	At 40 years or 20 years since first attack of pancreatitis		

ASGE guidelines: when to start

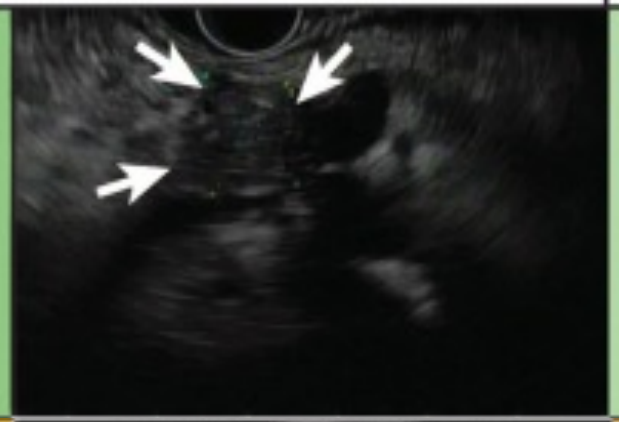
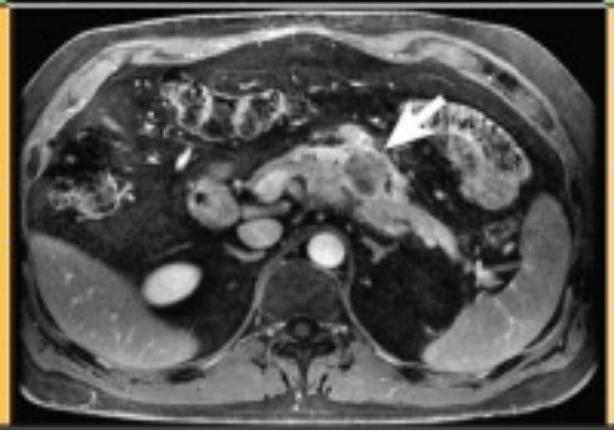
6	For each of the following conditions, we recommend the following starting ages:
	(a) *BRCA2* pathogenic variant: age 50 or 10 years earlier than the youngest relative with pancreatic cancer.
	(b) *BRCA1* pathogenic variant: age 50 or 10 years earlier than the youngest relative with pancreatic cancer.
	(c) *PALB2* pathogenic variant: age 50 or 10 years earlier than the youngest relative with pancreatic cancer.
	(d) FPC syndrome: age 50 or 10 years earlier than the youngest relative with pancreatic cancer (screening is recommended for all first-degree relatives of affected family members).
	(e) FAMMM syndrome: age 40 or 10 years earlier than the youngest relative with pancreatic cancer.
	(f) Peutz-Jeghers syndrome: age 35 or 10 years earlier than the youngest relative with pancreatic cancer.
	(g) Heterozygotes for *ATM* pathogenic variant with first- or second-degree relative with pancreatic cancer: age 50 or 10 years earlier than the youngest relative with pancreatic cancer.
	(h) Lynch syndrome with first- or second-degree relative with pancreatic cancer: age 50 or 10 years earlier than the youngest relative with pancreatic cancer.
	(i) Autosomal-dominant hereditary pancreatitis: age 40.

Sawhney MS et al, Standards of Practice Committee, ASGE, GIE 2022

Goals of a surveillance program

- Resectable carcinoma
  - Detection and treatment of T1N0M0
- Detection and treatment of PanIN-3
- Detection and treatment of IPMN with high grade dysplasia

Surveillance Imaging Methods: EUS and MRI

		Advantages for early detection	Disadvantages for early detection
Endoscopic ultrasound (EUS)		• Highest sensitivity and specificity • Provides excellent resolution for small lesions • Can be used with FNA for diagnosis	• Not practical for routine screening • Can be dependent on technical expertise
Magnetic resonance imaging (MRI)		• High sensitivity and specificity • Provides good soft tissue contrast • Does not expose patient to radiation	• Less standardized than CT • Can be difficult to do for patients with certain medical devices, claustrophobia, or allergies to gadolinium

Risk of Neoplastic Progression in Individuals at High Risk for Pancreatic Cancer Undergoing Long-term Surveillance

Marcia Irene Canto,[1,2,*] **Jose Alejandro Almario**,[1,3,*] Richard D. Schulick,[4] Charles J. Yeo,[5] Alison Klein,[2] Amanda Blackford,[2] Eun Ji Shin,[1] Abanti Sanyal,[6] Gayane Yenokyan,[6] Anne Marie Lennon,[1] Ihab R. Kamel,[7] Elliot K. Fishman,[7] Christopher Wolfgang,[8] Matthew Weiss,[8] Ralph H. Hruban,[3] and Michael Goggins[1,3]

- 1998-2014
- 354 eligible asymptomatic HRI
- EUS, MRI, CT (after 2015, EUS and MRI)
- Normal Pancreas or EUS of CP: annually
- Cysts or indeterminate radiographic lesions: 6-12 months
- Cysts with mural nodule, large cysts, or dilated pancreatic duct: 3-6 months

Gastroenterology, 2018

EUS findings and neoplastic progression

Table 3. Cox Proportional Hazards Regression Model for Neoplastic Progression After Adjusting for Time, Varying Radiologic Progression, and Type of Radiologic Progression

	Adjusted Model		
	HR	*P* value	95% CI
Any radiologic progression	23.9		
Type of radiologic progression			
Cyst or duct changes	41.2		
Solid mass	422.6		
Age at baseline > 60 years	1.6		
Mutation positive	0.6		
Total lesions at baseline ≥ 3	4.8		
Dilated MPD at baseline[a]	1.6		

CI, confidence interval.
[a]Dilated MPD defined by Rosemont criteria (≥3.5 mm in the head, ≥2.5 mm in the body, and/or ≥1.5 mm in the tail), but <5 mm in any area.

- Detection rate for PDAC/HGD: 7%
- Rate of progression 1.6%/yr
- Overall survival 57%
- 3 year survival rate 85% screened HRI vs 25% (outside surveillance)

Worrisome features:

- Cyst size ≥3cm
- Thickened cyst walls
- MPD dilation >5mm

n cyst or

in MPD

months or

>4mm in 1 year

Predictors of Ca in HRI and PFC

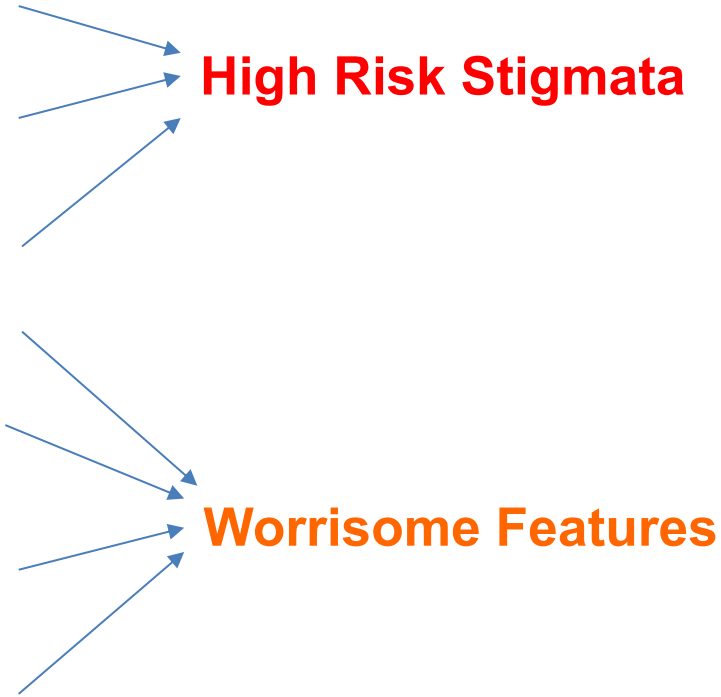
Pancreatic abnormalities on imaging			
Solid lesion, n (%)	7 (70)	14 (4)	<0.001
Indeterminate lesion*, n (%)	1 (10)	33 (9)	>0.99
Cystic lesion, n (%)	5 (50)	188 (53)	>0.99
Cystic lesion with solid component or mural nodule, n (%)	2 (20)	3 (1)	0.006
Cystic lesion with growth speed>5 mm/ year, n (%)	3 (30)	22 (6)	0.03
Main pancreatic duct 5–9 mm (with or without focal lesion), n (%)	4 (40)	17 (5)	0.001

Patient and family characteristics were assessed at baseline, pancreatic abnormalities scored if present at any visit.
*Hypoechoic or hypointense lesions of unknown significance that could not with certainty be classified as solid or cystic at diagnosis.
PDAC, pancreatic ductal adenocarcinoma.

Overbeek K Gastro 2021

Risk of Cancer Based on Cyst Findings

	OR (Meta-Analysis)	Heterogeneity between studies
Jaundice	17	Low
Dilated PD (>7 mm)	7.2	High
Mural Nodule	**9.2**	**Intermediate**
>3 cm cyst	62	High
Symptoms/Pancreatitis	1.65 2-3	High HIgh
Atrophy	1.5-2	High
Enhancing or Thickened Cyst Wall	**1.5-2**	**High**



EUS outcomes in *BRCA1/2, ATM* & *PALB2* carriers

- Retrospective analysis of BRCA1/BRCA2/ATM/PALB2 carriers who underwent EUS at a tertiary care center
- Aimed to investigate outcomes of EUS–based PDAC surveillance *without a family history* of PDAC
- 64 of 194 (33%) carriers had no family history of PDAC and had at least 1 EUS for surveillance

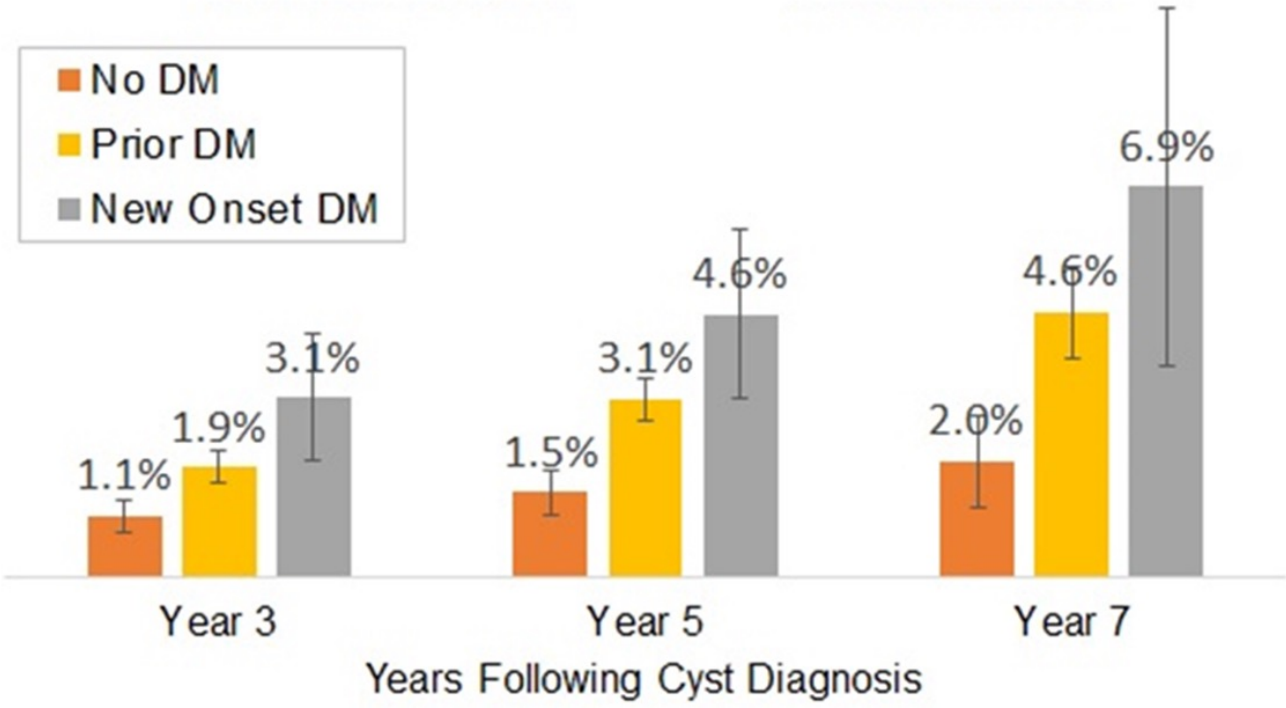
	Total (*N* = 64)	%
EUS findings		
Any abnormality	28	44%
PDAC	2	3%
Mass	3	5%
Cyst	17	27%
Mass/cyst after initial EUS	5	8%
Parenchymal abnormality	10	16%
Heterogeneity	4	6%
Hyperechoic	2	3%
Lobularity	4	6%
Fatty	6	9%

ASGE guidelines:
-BRCA 1/2 individual eligible for screening even if no FDR with panc ca

Katona B, et al. Pancreas 2021

Diabetes Status and Risk of Cyst Progression

Comparison	Multivariable Cox Proportional Hazard Model	
	HR (95% CI)	p-value
NODM vs No DM	15.5 (4.97-87.8)	0.0004
NODM vs Prior DM History	10.4 (2.46-44.3)	0.002
Prior History vs. No DM	1.49 (0.38-6.20)	0.281



Schweber et al Pancreatology 2020

CAPS = Cancer of the Pancreas Consortium

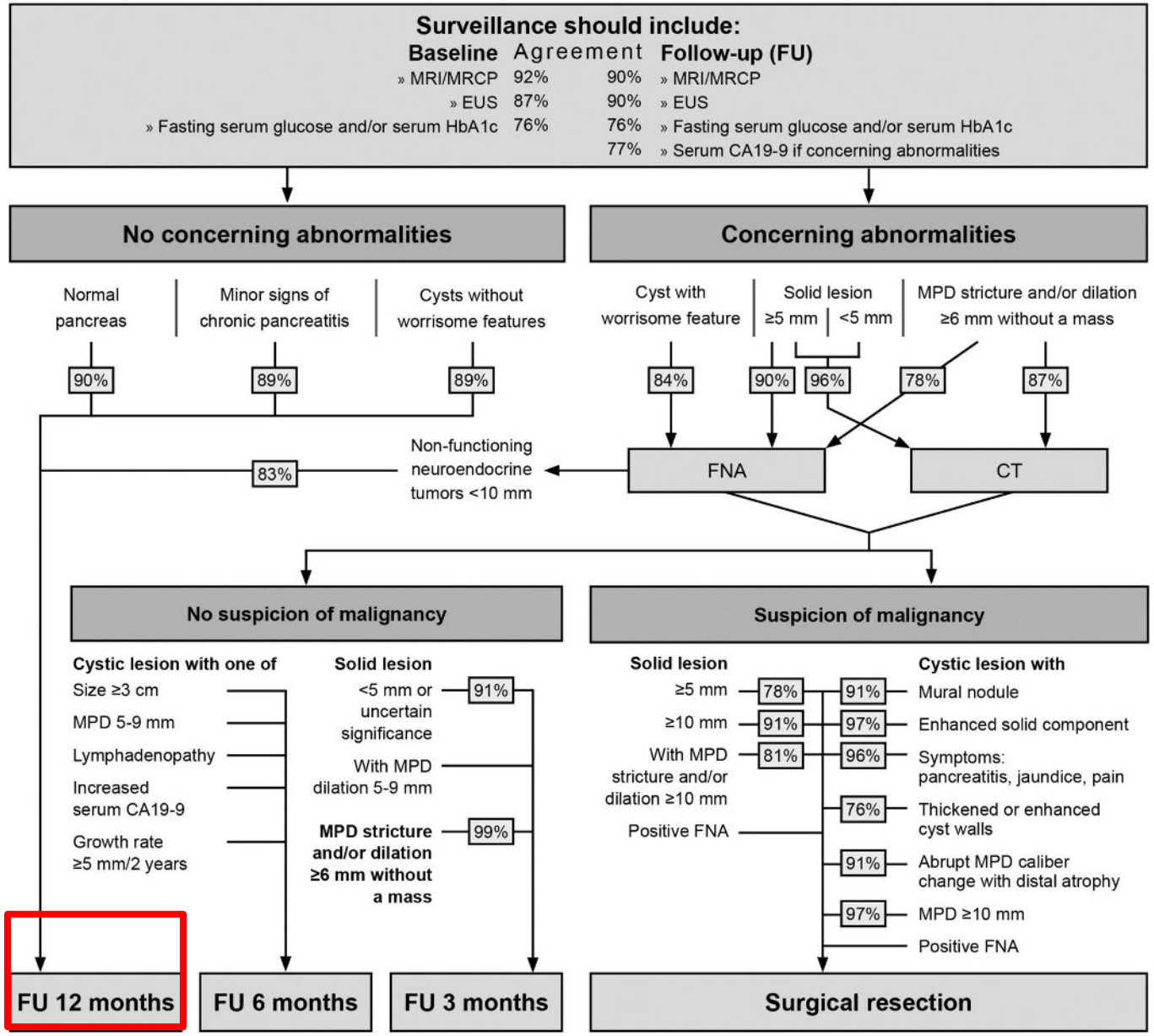
- To establish consensus guidelines for screening and surveillance
- Main goals of surveillance
  - Identify high-grade dysplastic precursor lesions
  - Identify T1N0M0 disease
- Genetic mutations that confer high risk and thus rendered eligible for surveillance
- EUS and MRCP considered adequate surveillance tools

Table 1 Definition of high-risk individuals eligible for pancreatic cancer surveillance.

Gene mutation	PDAC family history criteria	Agreement	Grade
LKB1/STK11 (Peutz-Jeghers syndrome)	Regardless of family history	99%	1
CDKN2A p16* (FAMMM)	With at least one affected FDR	99%	1
CDKN2A p16* (FAMMM)	Regardless of family history	77%	1
BRCA2	If at least one affected FDR, or at least two affected relatives† of any degree	93%	2
PALB2	If at least one affected FDR	83%	2
MLH1/MSH2/MSH6 (Lynch)	If at least one affected FDR	84%	2
ATM	If at least one affected FDR	88%	2
BRCA1	If at least one affected FDR	69.6%‡	3
Regardless of gene mutation status	If at least three affected relatives† on the same side of the family, of whom at least one is an FDR to the individual considered for surveillance	97%	2
Regardless of gene mutation status	If at least two affected relatives† who are FDR to each other, of whom at least one is an FDR to the individual considered for surveillance	93%	2
Regardless of gene mutation status	If at least two affected relatives† on the same side of the family, of whom at least one is an FDR to the individual considered for surveillance	88%	2

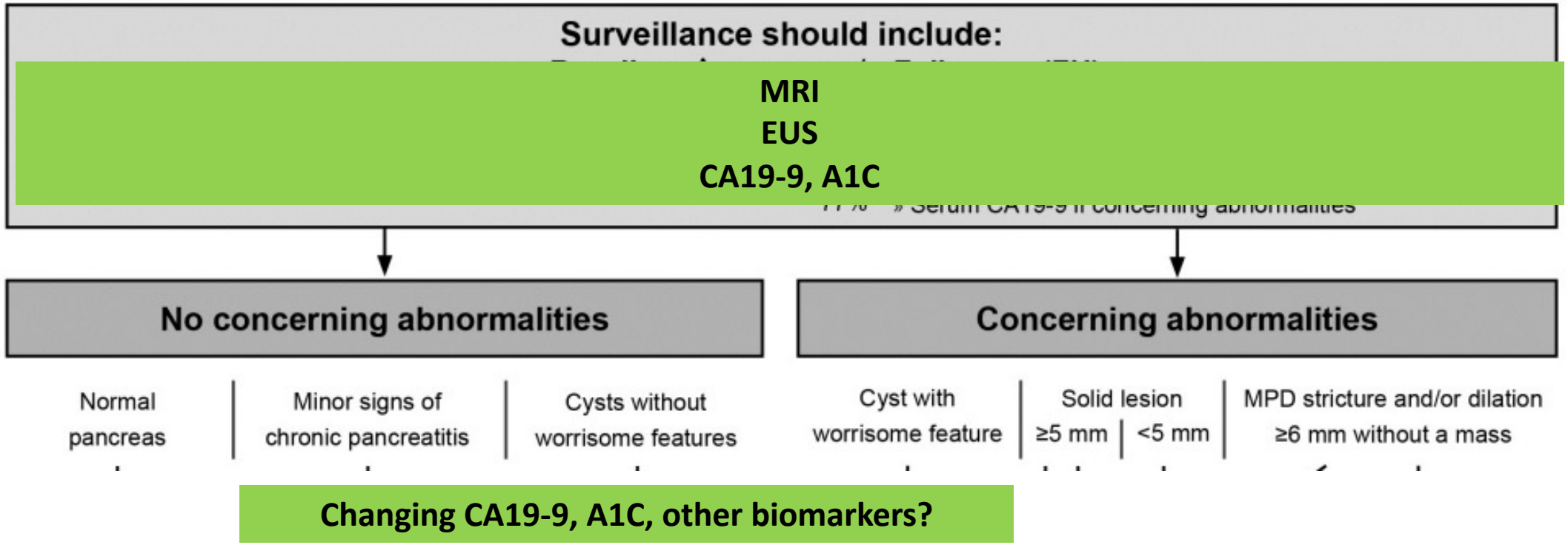
Canto MI et al. Gut 2013;62:339-47.
Goggins M et al. Gut 2020;69:7-17.

Surveillance in High-Risk Patients



Goggins et al, Gut 2020

Summarized algorithm



Annual surveillance alternating EUS/MRI

Multidisciplinary Evaluation q3-6 months EUS/MRI

Multidisciplinary Evaluation → Surgical Resection

Courtesy of Tamas Gonda, MD

Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

ASGE guideline on screening for pancreatic cancer in individuals with genetic susceptibility: summary and recommendations

TABLE 1. Summary of recommendations

Question	Recommendation and quality of evidence
1	In individuals at increased risk of pancreatic cancer because of genetic susceptibility, we suggest screening for pancreatic cancer compared with no screening (*conditional, low quality*)
2	In individuals at increased risk of pancreatic cancer because of genetic susceptibility, we suggest screening with EUS, EUS alternating with MRI, or MRI based on patient preference and available expertise (*conditional, very low quality*) • EUS may be preferred: as the initial screening test; for patients at very high risk for pancreatic cancer like Peutz-Jeghers syndrome and FAMMM; when EUS can be combined with screening upper endoscopy or colonoscopy (eg, Lynch and Peutz-Jeghers syndrome); when there is a contraindication to MRI (eg, claustrophobia, contrast allergy, implanted metal, and renal failure) • MRI may be preferred: for patients at increased risk of adverse events from anesthesia or invasive procedures; for patients who place a high value on avoiding invasive testing; when MRI may be combined with other imaging (eg, enterography for Peutz-Jeghers syndrome).
3a	In individuals with *BRCA2* pathogenic variant, we suggest screening for pancreatic cancer compared with no screening (*conditional, very low quality*)
3b	In individuals with *BRCA1* pathogenic variant, we suggest screening for pancreatic cancer compared with no screening (*conditional, very low quality*)

Sawhney MS et al, Standards of Practice Committee, ASGE, GIE 2022

Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

ASGE guideline on screening for pancreatic cancer in individuals with genetic susceptibility: summary and recommendations

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Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

2	In individuals at increased risk of pancreatic cancer because of genetic susceptibility, we suggest screening with EUS, EUS alternating with MRI, or MRI based on patient preference and available expertise (*conditional, very low quality*) • EUS may be preferred: as the initial screening test; for patients at very high risk for pancreatic cancer like Peutz-Jeghers syndrome and FAMMM; when EUS can be combined with screening upper endoscopy or colonoscopy (eg, Lynch and Peutz-Jeghers syndrome); when there is a contraindication to MRI (eg, claustrophobia, contrast allergy, implanted metal, and renal failure) • MRI may be preferred: for patients at increased risk of adverse events from anesthesia or invasive procedures; for patients who place a high value on avoiding invasive testing; when MRI may be combined with other imaging (eg, enterography for Peutz-Jeghers syndrome).

Challenges of a Surveillance Program

- Poor ability to detect PanINs
- How long to follow normal findings
- How long to follow-up of benign and stable findings
  - Ex. SB-IPMNs
- Risks associated with surveillance: overdiagnosis, false positives and negatives, diverted resources

Can we do better?

ORIGINAL ARTICLE

Standardization of EUS imaging and reporting in high-risk individuals of pancreatic adenocarcinoma: consensus statement of the Pancreatic Cancer Early Detection Consortium

Tamas A. Gonda, MD,[1] James Farrell, MD,[2] Michael Wallace, MD,[3] Lauren Khanna, MD,[1] Eileen Janec, MD,[1] Richard Kwon, MD,[4] Michael Saunders, MD,[5] Uzma D. Siddiqui, MD,[6] Randall Brand, MD,[7] Diane M. Simeone, MD[8] for the PRECEDE Consortium*

New York, New York; New Haven, Connecticut; Jacksonville, Florida; Ann Arbor, Michigan; Seattle, Washington; Chicago, Illinois; Pittsburgh, Pennsylvania, USA

TABLE 2. Pancreatic parenchyma evaluation and proposed histologic/neoplastic correlates

EUS parenchymal abnormality	Description of finding	Distribution of pancreatic changes	Possible histologic correlate in chronic pancreatitis	Possible neoplastic correlate
Hyperechoic foci	Small (<5 mm) distinct reflectors	HOP/TOP/BOP throughout gland	Fibrosis	
Hyperechoic strands	String or line-like (>5 mm) distinct reflectors	HOP/TOP/BOP throughout gland	Fibrosis	

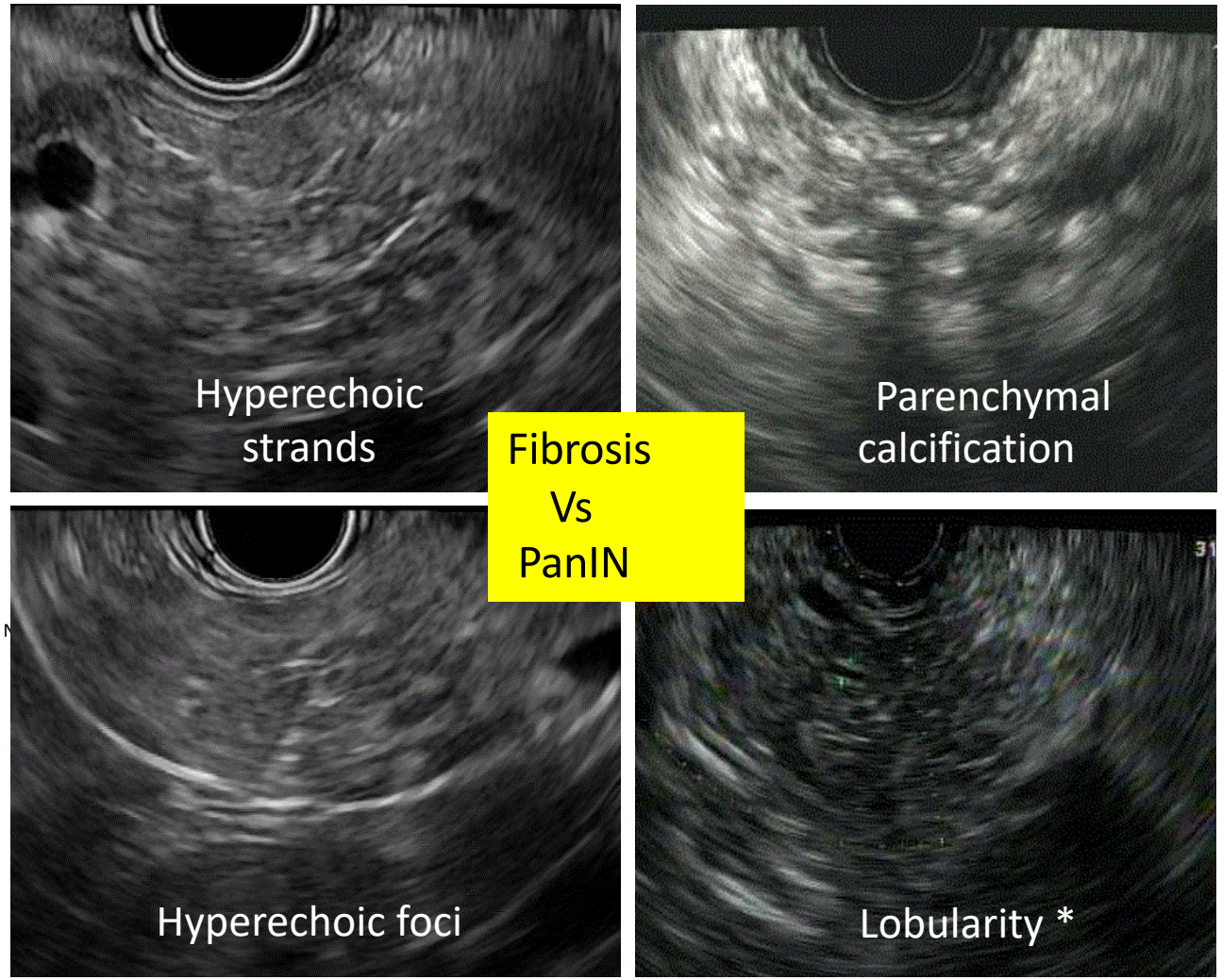
SUPPLEMENTARY TABLE 3. Recommended pancreatic EUS image capture

Endoscopic position	EUS view	Measurement
Duodenal bulb	Distal CBD, proximal PD, ampulla view (Fig. 1A)	Measurement of proximal PD, distal CBD
Duodenal bulb	Porta hepatis (hepatic artery, portal vein, CBD) (Fig. 1B)	CBD
Duodenal bulb	Pancreas parenchyma, portal confluence (Fig. 1C)	MPD
Duodenal bulb	Pancreas parenchyma (neck of pancreas/genu), region of superior mesenteric vein (Fig. 1D)	MPD
Gastric fundus	Celiac axis, superior mesenteric artery, aorta (Fig. 2A)	
Gastric fundus	Tail of pancreas view with splenorenal angle (Fig. 2B)	MPD
Gastric fundus	Body of pancreas view at level of splenic artery and vein (Fig. 2C)	MPD
Gastric fundus/body	Right lateral pancreas margin (PD toward head of pancreas) (Fig. 2D)	MPD
	dorsal split)	

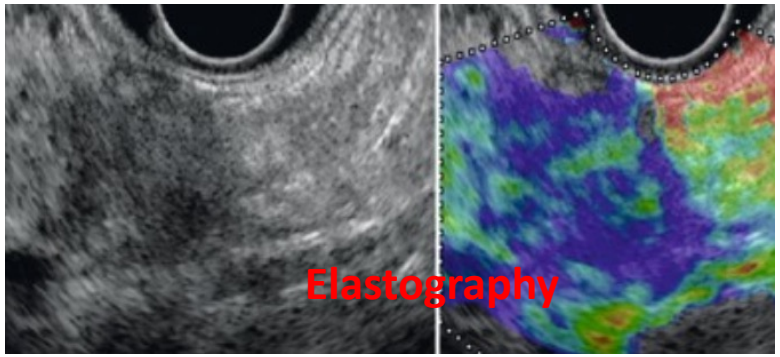
Solid lesion	Solid lesion with different echogenicity from the pancreas parenchyma	HOP/TOP/BOP throughout gland	Focal inflammation and/or necrosis	Neoplasm/splenule focal inflammation
Fatty pancreas	Bright or hyperechoic pancreas	HOP/TOP/BOP throughout gland		

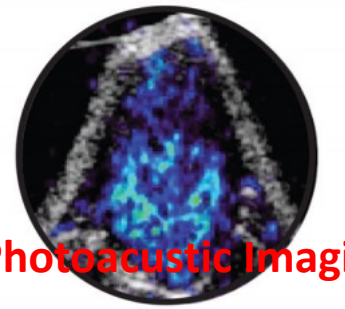
Early detection of premalignant lesions (PanIN)

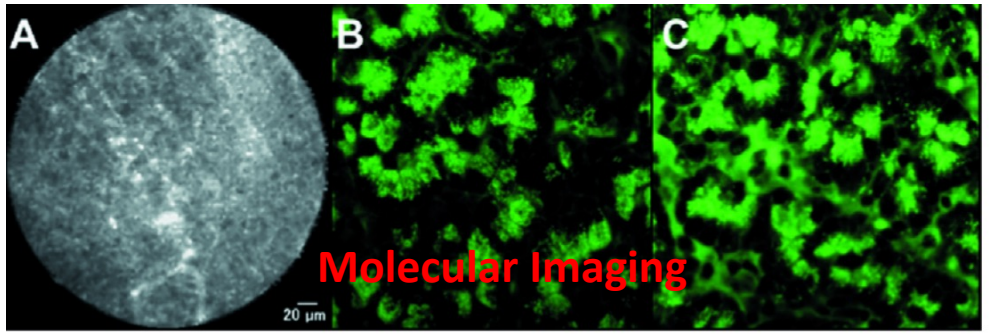
Endoscopic Ultrasound - today



Future Endoscopic Imaging







Future study

- Artificial intelligence
- Identifying additional risk factors- databases and consortiums
  - CAPS, PRECEDE, Dutch Pancreas Group
- Improved imaging diagnostics
- Circulating tumor cells
- Understanding the significance of multiple normal exams

Conclusion

- Goal of screening/surveillance: detect resectable and precursor lesions->Enriching population can improve detection
- HRI= family history of PDAC, genetic susceptibility, hereditary syndromes, precursor lesions, types of CP, NOD
- Genetic testing recommended on anyone with PDAC; Family Kindreds, Inherited syndromes, Genetic susceptibility +/- FDR
- Multiple guidelines available for initiation of screening
- EUS and MRI recommended modalities
- Need to work in multidisciplinary team and consortiums
- Further study needed to improve detectability of non-visible risks

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Thank You!

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