

Defining Sensitivity and Specificity Targets for Pancreatic Cancer Surveillance

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Faces of Pancreatic Cancer in 2020



Pancreatic Cancer: Background

- Incidence
 - In the US in 2020: 57,600 new diagnoses
47,050 deaths
 - ~1.6% life-time risk of developing PC
 - ~ 10% felt to be hereditary
- Third leading cause of cancer related mortality in US
- Five-year survival rate of 10%
 - Local disease(10%) with 5-yr survival rate of 37%
- > 90% of tumors are adenocarcinomas
- Precursor lesions for Pancreatic Adenocarcinomas
 - Pancreatic Intraepithelial Neoplasias (PanINs) 85% of PC
 - Intraductal Papillary Mucinous Neoplasms (IPMNs)
 - Mucinous cystic neoplasms

A PESSIMIST SEE THE DIFFICULTY IN
EVERY OPPORTUNITY.

AN OPTIMIST SEES THE OPPORTUNITY IN
EVERY DIFFICULTY

SIR WINSTON CHURCHILL



Why should we be optimistic?

Adapted from NCI's SEER Cancer Statistics Review 2020

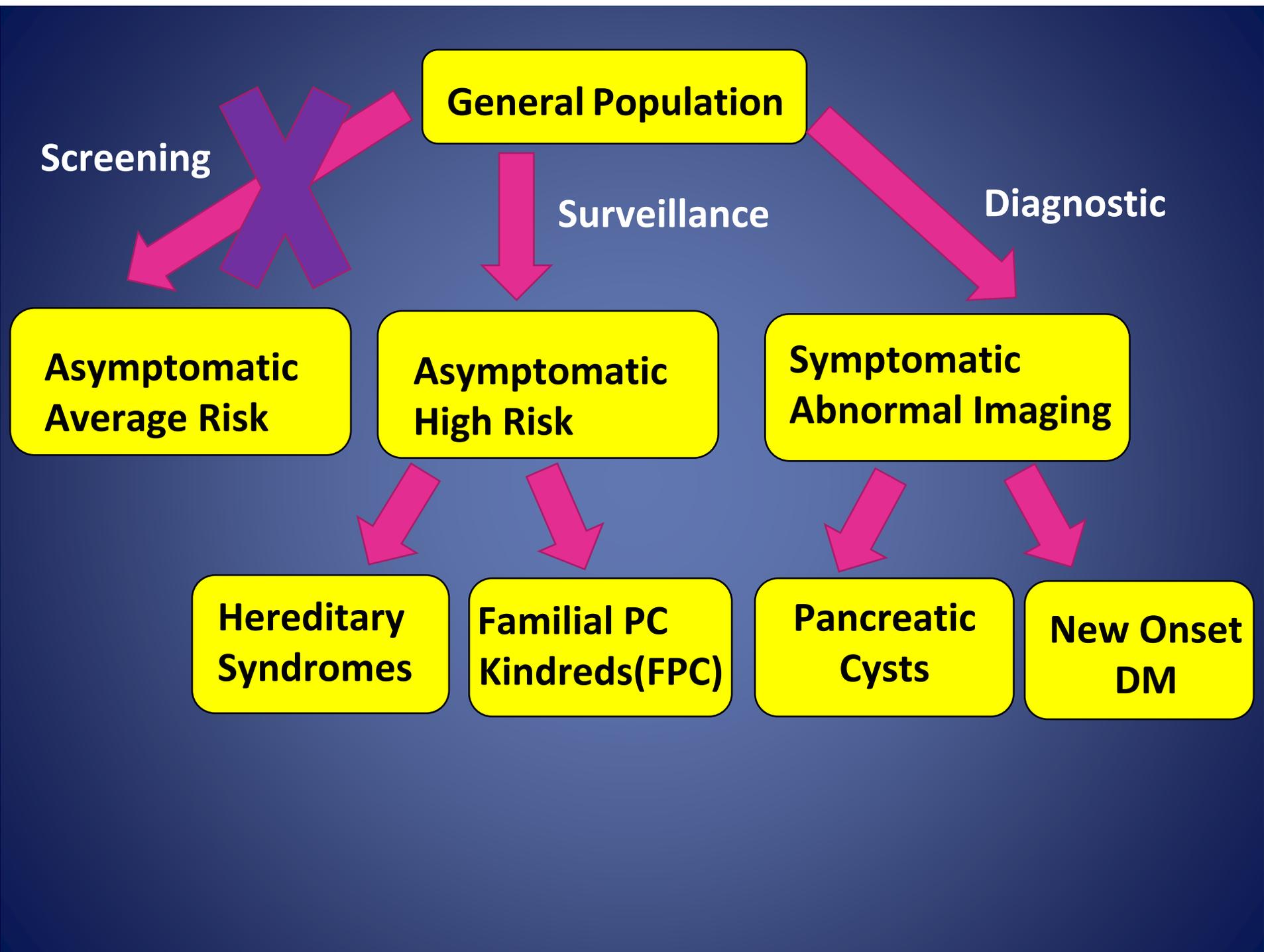
Pancreatic Cancer 5-year Relative Survival by Stage at Diagnosis for 2009-2015, All Races, Both Sexes

Stage at Diagnosis	% of Cases	5-year Relative Survival (%)
Localized	10	37
Regional	29	12
Distant	53	3
Unknown	8	6

Colorectal Cancer 5-year Relative Survival by Stage at Diagnosis for 2009-2015, All Races, Both Sexes

Stage at Diagnosis	% of Cases	5-year Relative Survival (%)
Localized	39	89.9
Regional	35	71.3
Distant	22	14.2
Unknown	4	35.4

- Identifying the tumor at an earlier stage
- Better treatments



High Risk Individuals as Defined in 2020

Table 1. Risk for Pancreatic Cancer Related to Genetic Mutation

Genes	Common name	Risk of pancreatic cancer
STK11/LKB1	Peutz–Jeghers syndrome	RR, 132 (95% CI, 44–261)
PRSS1	Hereditary pancreatitis	SIR, 53 (95% CI, 23–105)
CDKN2A	Familial atypical multiple mole/melanoma syndrome	RR, 13–39
MLH1, MSH2, MSH6	Lynch syndrome	RR, 8.6–11
TP53	Li-Fraumeni syndrome	RR, 7.3 (95% CI, 2–19)
ATM	NA	RR, 3.92 (95% CI, 0.44–14.2)
BRCA1	Hereditary breast and ovarian cancer	RR, 2.26 (95% CI, 1.26–4.06)
BRCA2, PALB2		RR, 3.5–6.2 (95% CI 1.87–6.58)
Familial pancreas cancer in 1 or 2 first-degree relatives	Familial pancreas cancer	RR, 4–9.3

From Davee et al,⁹ adapted with permission.

NA, not applicable; RR, relative risk; SIR, standardized incidence ratio.

**Asymptomatic
High Risk**

**Hereditary
Syndrome**

**Familial PC
Kindred (FPC)**

Imaging Study

Advanced Neoplasia

**No Advanced
Neoplasia**

Surgery

Surveillance

Summary of Recommendations of the 2019 International CAPS Consortium: How

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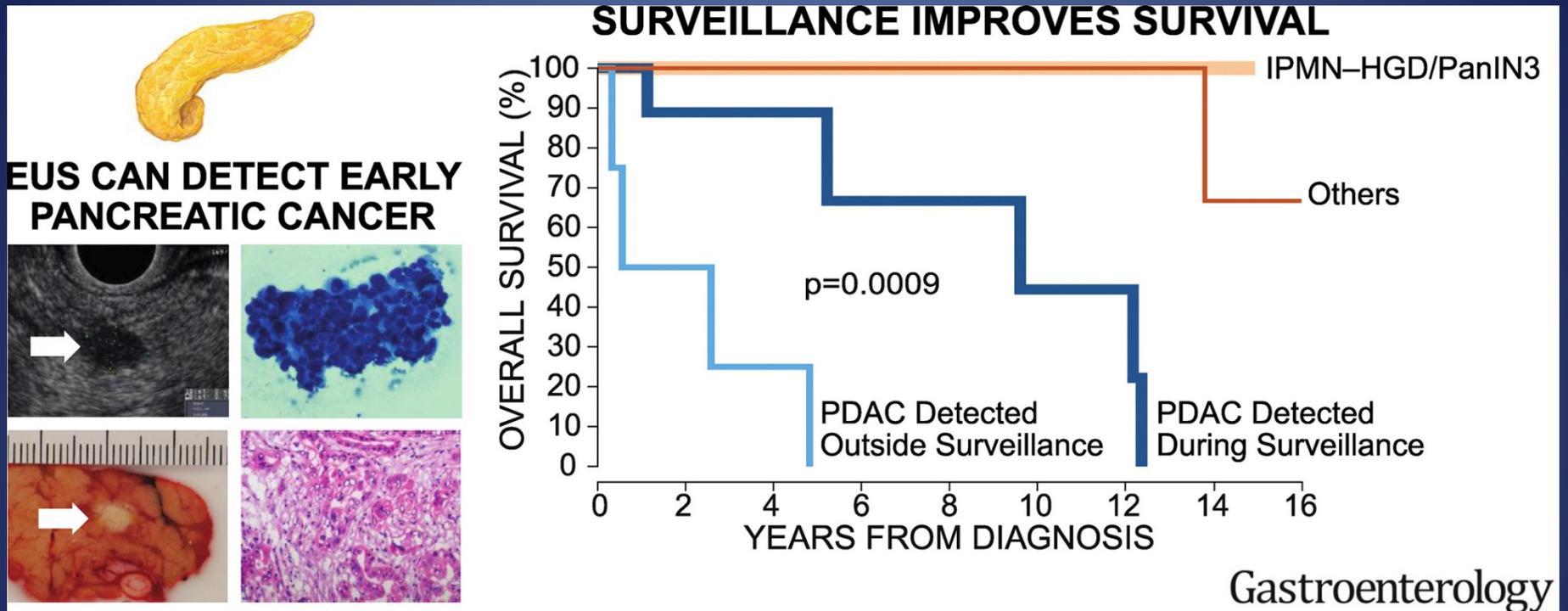
Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium

[Michael Goggins](#),¹ [Kasper Alexander Overbeek](#),² [Randall Brand](#),³ [Sapna Syngal](#),⁴ [Marco Del Chiaro](#),⁵ [Detlef K Bartsch](#),⁶ [Claudio Bassi](#),⁷ [Alfredo Carrato](#),⁸ [James Farrell](#),⁹ [Elliot K Fishman](#),¹⁰ [Paul Fockens](#),¹¹ [Thomas M Gress](#),¹² [Jeanin E van Hooft](#),¹³ [R H Hruban](#),¹⁴ [Fay Kastrinos](#),^{15,16} [Allison Klein](#),¹⁷ [Anne Marie Lennon](#),¹⁸ [Aimee Lucas](#),¹⁹ [Walter Park](#),¹⁵ [Anil Rustgi](#),¹⁶ [Diane Simeone](#),²⁰ [Elena Stoffel](#),²¹ [Hans F A Vasen](#),²² [Djuna L Cahen](#),² [Marcia Irene Canto](#),¹⁸ [Marco Bruno](#),² and International Cancer of the Pancreas Screening (CAPS) consortium

- At Baseline
 - MRI/MRCP + EUS + fasting blood glucose and/or HbA1c
- During follow-up
 - Alternate MRI/MRCP and EUS
(no consensus if and how to alternate)
 - Routinely test fasting blood glucose and/or HbA1c
- Intervals
 - 12 months if no abnormalities, or only non-concerning abnormalities
 - 3 or 6 months if concerning abnormalities for which immediate surgery is not indicated
 - Surgery if positive FNA and/or a high suspicion of malignancy on imaging

Long-term outcomes of Pancreatic Surveillance in Individuals at High Risk for PDAC

354 individuals at high risk based on FH or genetic factors
 Surveillance with combination of EUS, MRI or CT as part of CAPS4



Summary of pertinent findings after initial screening:

1. Cumulative incidence of invasive PDAC was 3.4% (12/354 HRI)
2. PDAC and high-grade precursor lesions develop in 7% of HRI at a rate of progression of 1.6% per year
3. Nine of 10 PDACs were resectable (stage I or II)
4. Three-year survival rate of 90%

BIOMARKER



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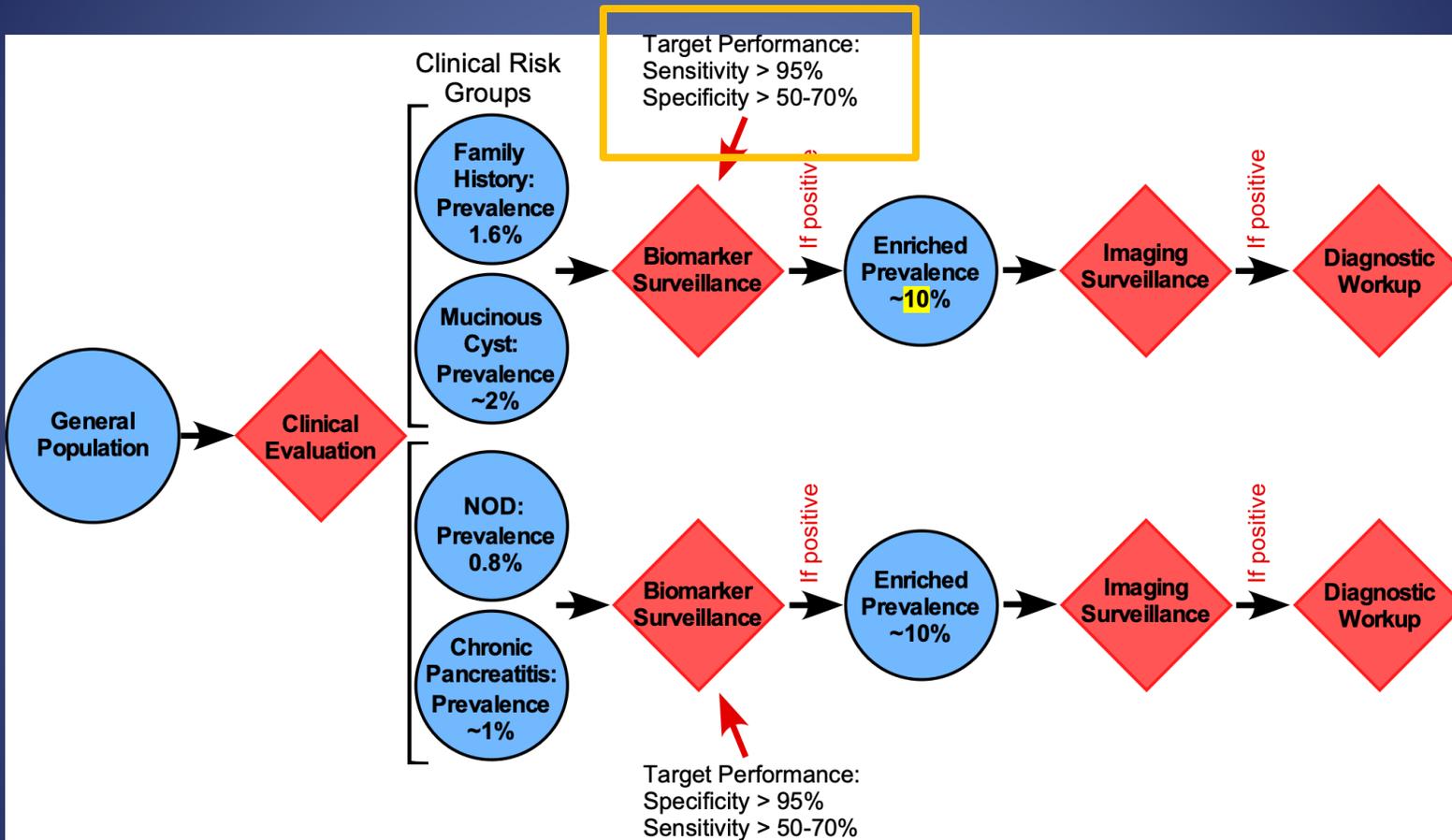
Familial PC
Kindred (FPC)

Imaging Study

Surgery

Surveillance

Overall Strategy for Surveillance of High-Risk Groups



Adapted from Liu et al. Cancer Epidemiol Biomarkers Prev. 2020

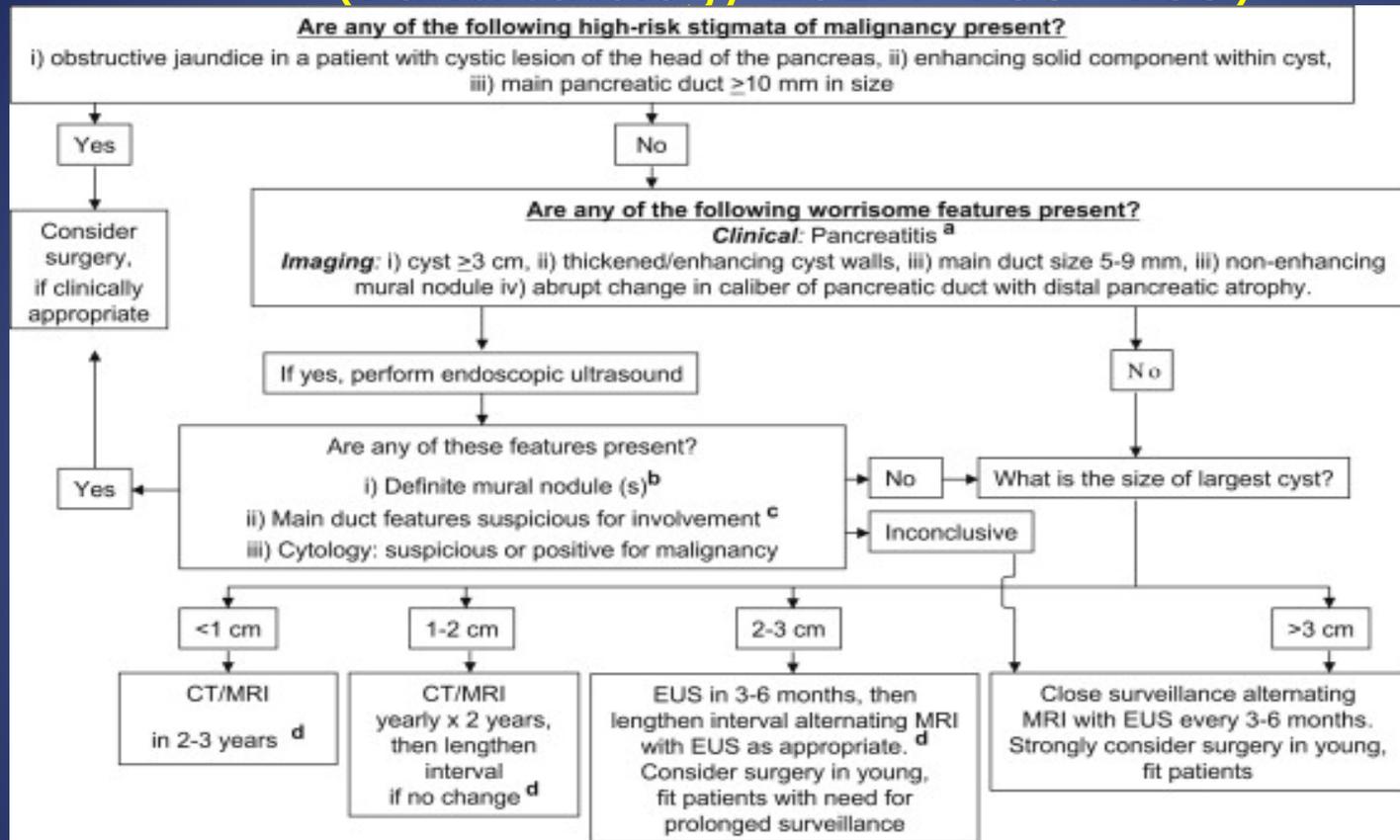
Pancreatic Cyst Management

- Who should you resect?
Treatment
- Who should you follow?
Surveillance
- Who should you forget?
No further management required

Common Pancreatic Cysts

No Malignant Potential	Malignant Potential
Pseudocyst	Intraductal papillary mucinous neoplasm
Serous cystadenoma	Mucinous cystic neoplasm
Retention Cyst	Cystic neuroendocrine tumor
Lymphoepithelial cyst	Solid pseudopapillary neoplasm

Revisions of International Consensus Fukuoka Guidelines: Algorithm for the management of suspected BD-IPMN (Pancreatology 2017: 738– 753)



a. Pancreatitis may be an indication for surgery for relief of symptoms.

b. Differential diagnosis includes mucin. Mucin can move with change in patient position, may be dislodged on cyst lavage and does not have Doppler flow. Features of true tumor nodule include lack of mobility, presence of Doppler flow and FNA of nodule showing tumor tissue

c. Presence of any one of thickened walls, intraductal mucin or mural nodules is suggestive of main duct involvement. In their absence main duct involvement is inconclusive.

d. Studies from Japan suggest that on follow-up of subjects with suspected BD-IPMN there is increased incidence of pancreatic ductal adenocarcinoma unrelated to malignant transformation of the BD-IPMN(s) being followed. However, it is unclear if imaging surveillance can detect early ductal adenocarcinoma, and, if so, at what interval surveillance imaging should be performed.

Performance of International Consensus Fukuoka Guidelines for the management of suspected asymptomatic BD-IPMN

(Xu et al. Medicine 2017 96:35)

- Multi-center study of 405 patients undergoing resection for an

Sensitivity for HGD/CA	73.2%
Specificity for HGD/CA	45.6%
PPV for HGD/CA	19.4%
NPV for HGD/CA	90.4%

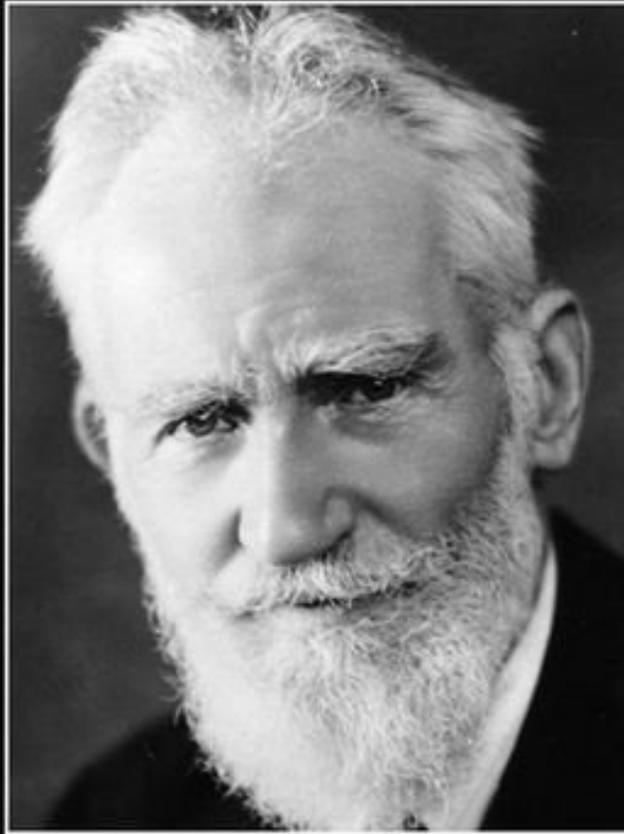
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asymptomatic
included.
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Who to Resect?

	Current Guidelines	Proposed
Sensitivity for HGD/CA	62-73%	80-85%
Specificity for HGD/CA	46-79%	90%
PPV for HGD/CA	19-52%	80%
NPV for HGD/CA	82-90%	95%

Xu et al. Medicine 2017 and Singhi et al. GIE 2015



Both optimists and pessimists
contribute to society. The optimist
invents the aeroplane, the pessimist
the parachute.

— *George Bernard Shaw* —

Questions to Address

1. Considering the topics covered in your session, **what are the most important takeaways?**

2. **What actions should be taken to implement them?**

3. **Can the topics discussed in the session be implemented by the EDRN? YES**

4. **Should the topics discussed be written up as a manuscript for the community engaged in biomarker research? ALREADY HAS THIS YEAR!!**