

# Familial Pancreatic Cancer

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# Syndromes with Pancreatic Cancer

- HNPCC unknown
- Familial Adenomatous Polyposis (FAP) 5x
- Peutz-Jeghers lifetime risk 36%

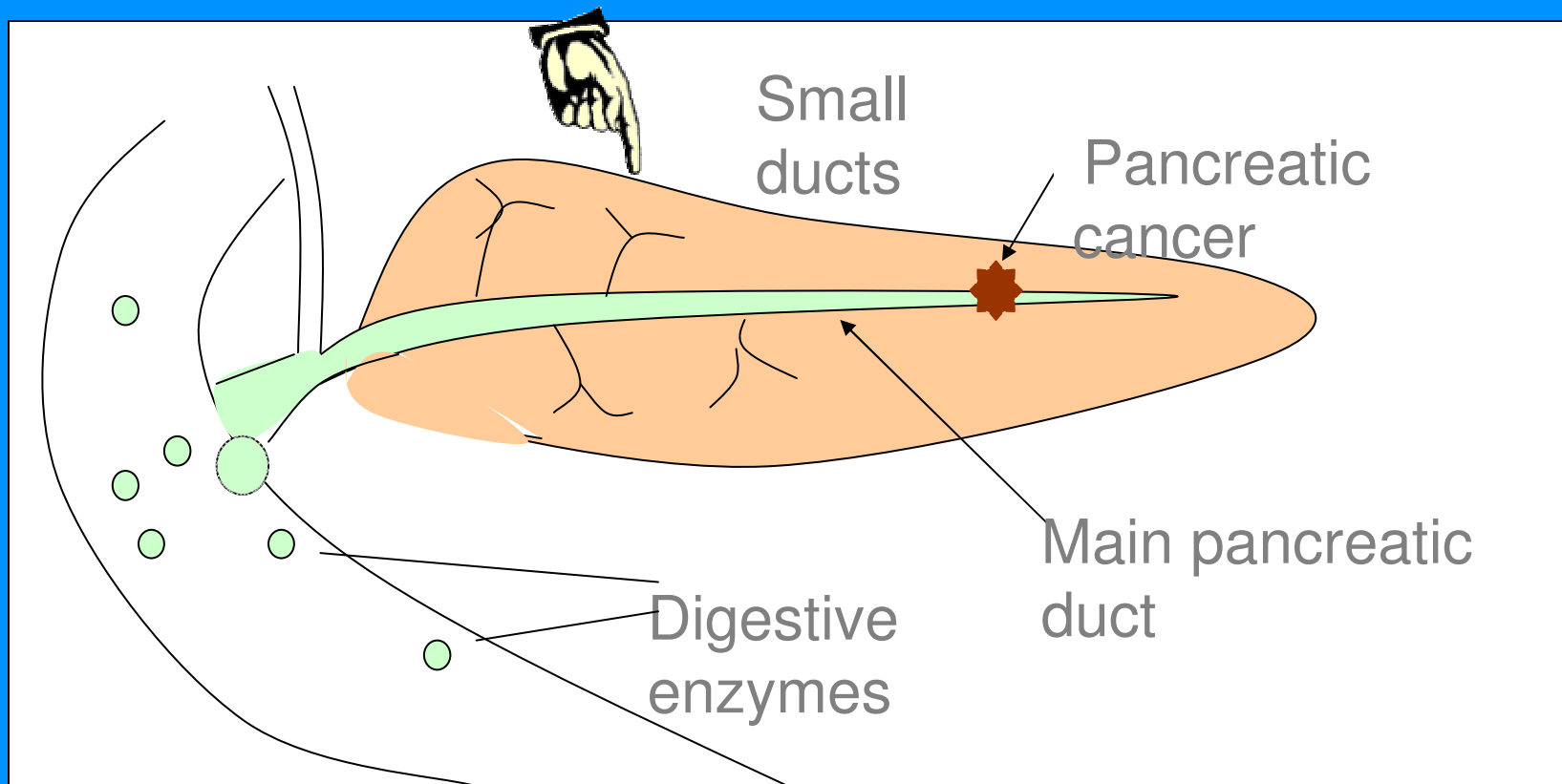
# Syndromes with Pancreatic Cancer

- Familial Atypical Mole Melanoma (FAMM) 13-20x (19%)
- Familial Breast Cancer 10x (5%)
- Hereditary pancreatitis 53x (40%)
- Cystic Fibrosis 32x (25%)

# Familial Risk

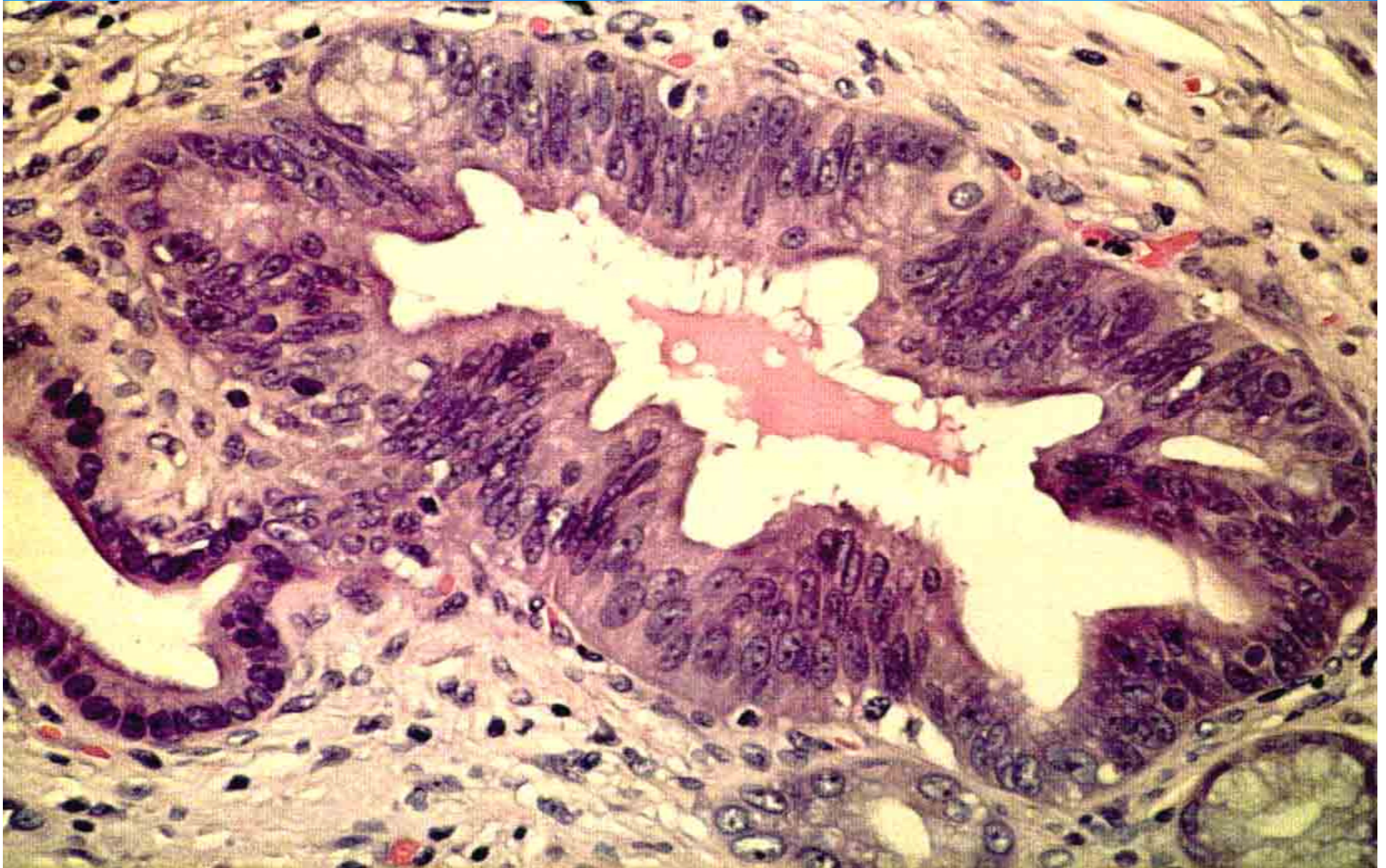
- Dependent on the gene involved
- Not all gene carriers get cancer
- Penetrance of the gene

# SURVEILLANCE

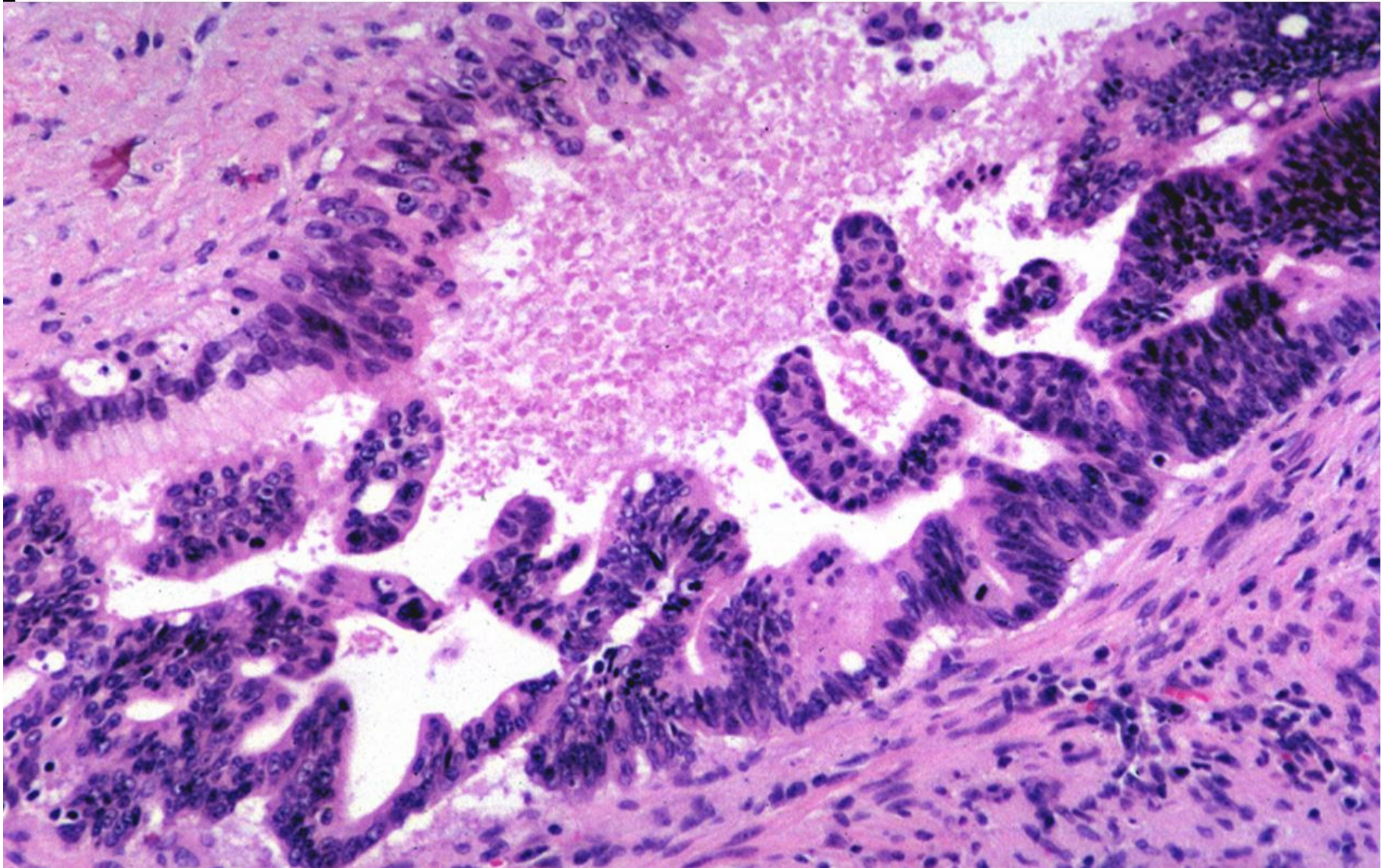


**Pancreatic cancer forms in the small and mid-size ducts first.**

# Pancreatic Dysplasia: PanIN II



# PanIN III: Carcinoma in-situ



# The task at hand

Identify patients

.....**after** they have started down the neoplastic pathway

.....***before*** *the neoplasia becomes invasive*

# Endoscopic Surveillance

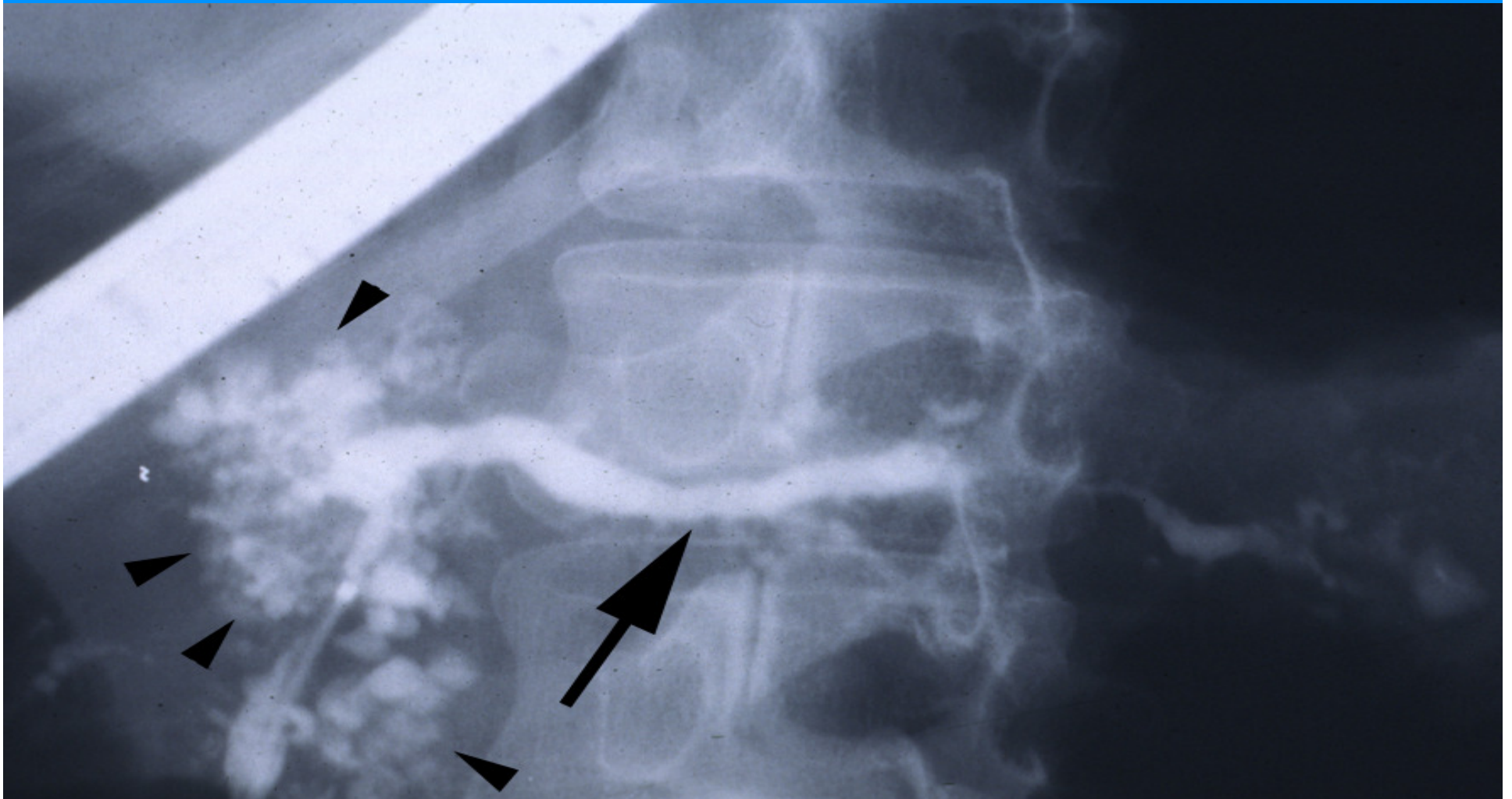
- Endoscopic Ultrasound
- ERCP
- Centers with experience

# Endoscopic Ultrasound Findings



# ERCP

- irregular ducts
- ectatic side branches
- sacculations



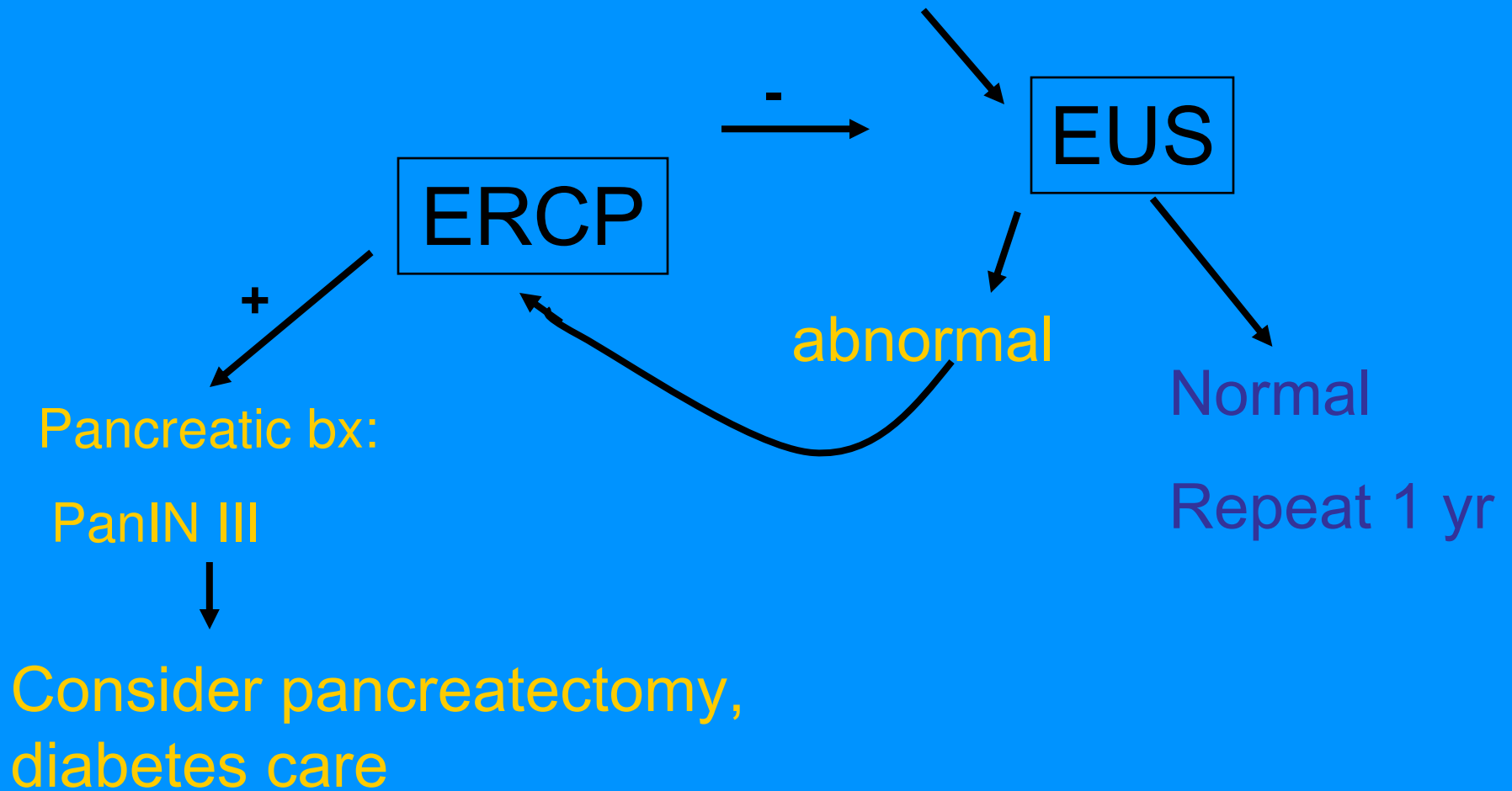
# Adjunct tests

- Ca 19.9
- CEA
- CT scan

If EUS and ERCP are abnormal  
consider lap tailectomy for  
histologic diagnosis

# Surveillance

$\geq 2$  family members



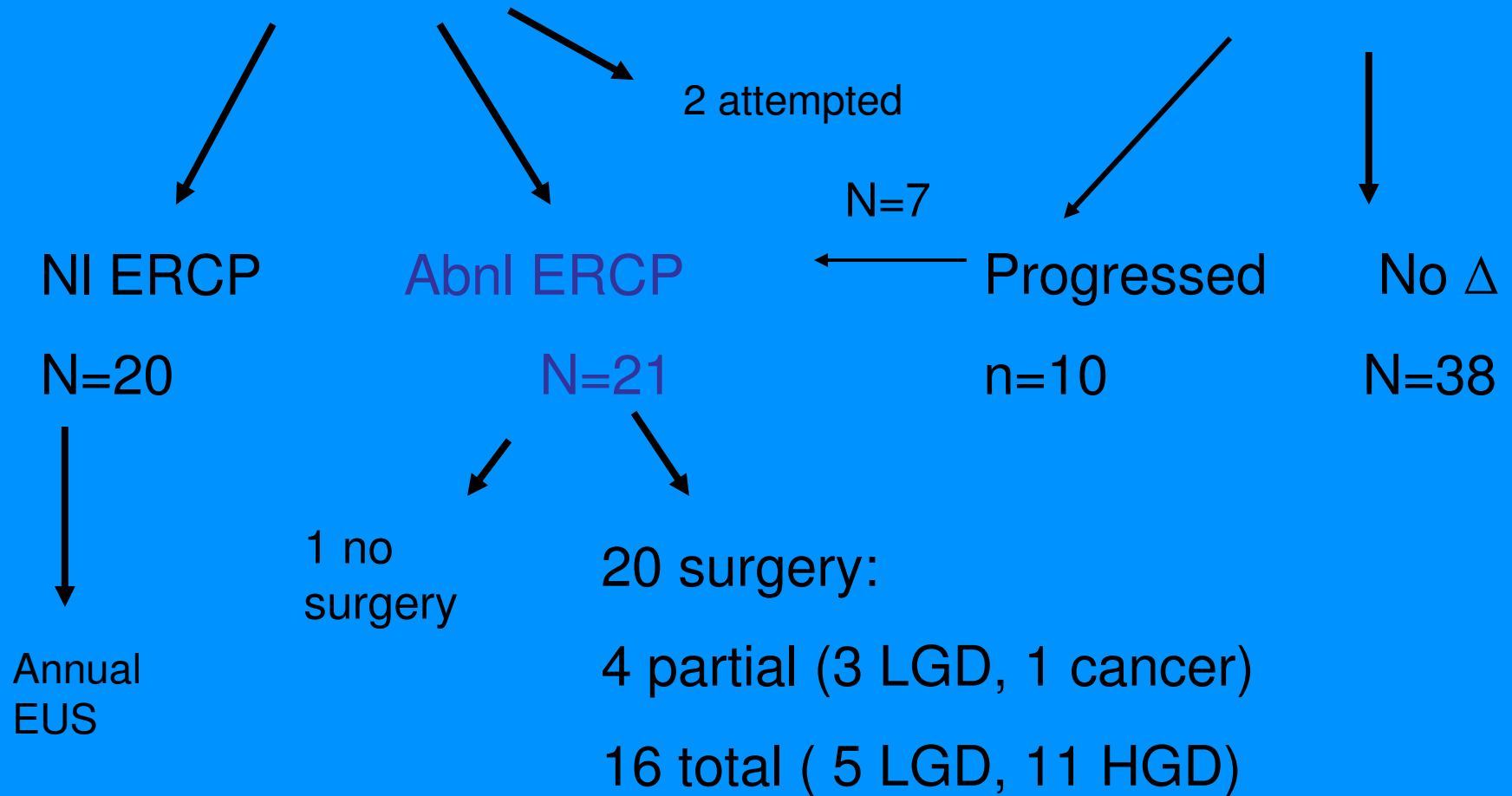
# 100 patients in surveillance

- 10 year program
- 73 different families
- Heterogeneous group of kindreds with different genetic causes
- Average years of surveillance = 5

100 patients

52 abnormal EUS

48 normal EUS

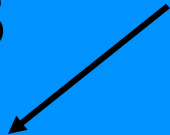


# Surgery

- Decision for pancreatectomy based on histology
- 2 step operation: laparoscopic tailectomy  
+/- second operation for completion

# F/U 20 surgical patients

N=15



Total Pancreatectomy

- No cancers
- 5 LGD
- 10 HGD

N=5



Partial Pancreatectomy

- 4 LGD and 1 Cancer

# Follow-up: surgical group

- 15 ptns S/P total pancreatectomy
- 5 partial pancreatectomy (Low grade & 1 cancer)
- No pancr. cancers developed post-op
- All with widespread pancr. precancer
- 1- 10 years of follow-up
- One lung cancer

# Follow-up: 20 ptn surgical group

- 2 patients with duodenal ulcers – need lifetime PPI
- 5 diabetics pre-surgery—all diabetics post
- 1 ptn s/p pancreatic transplant 2<sup>o</sup> to hypoglycemia
- 1 ptn *failing medical F/U* died of hypoglycemia

# 4 patients lost to F/U

- All had history of drug use or heavy alcohol
- 4 unemployed or marginally employed
- Better psychologically screening in selection criteria for screening

Non-Surgical Group n=80  
1 patient developed Pancr Cancer

- 1 mets PC 10 months post abnl EUS

# Environmental/Behavioral Factors

# Limitations of study

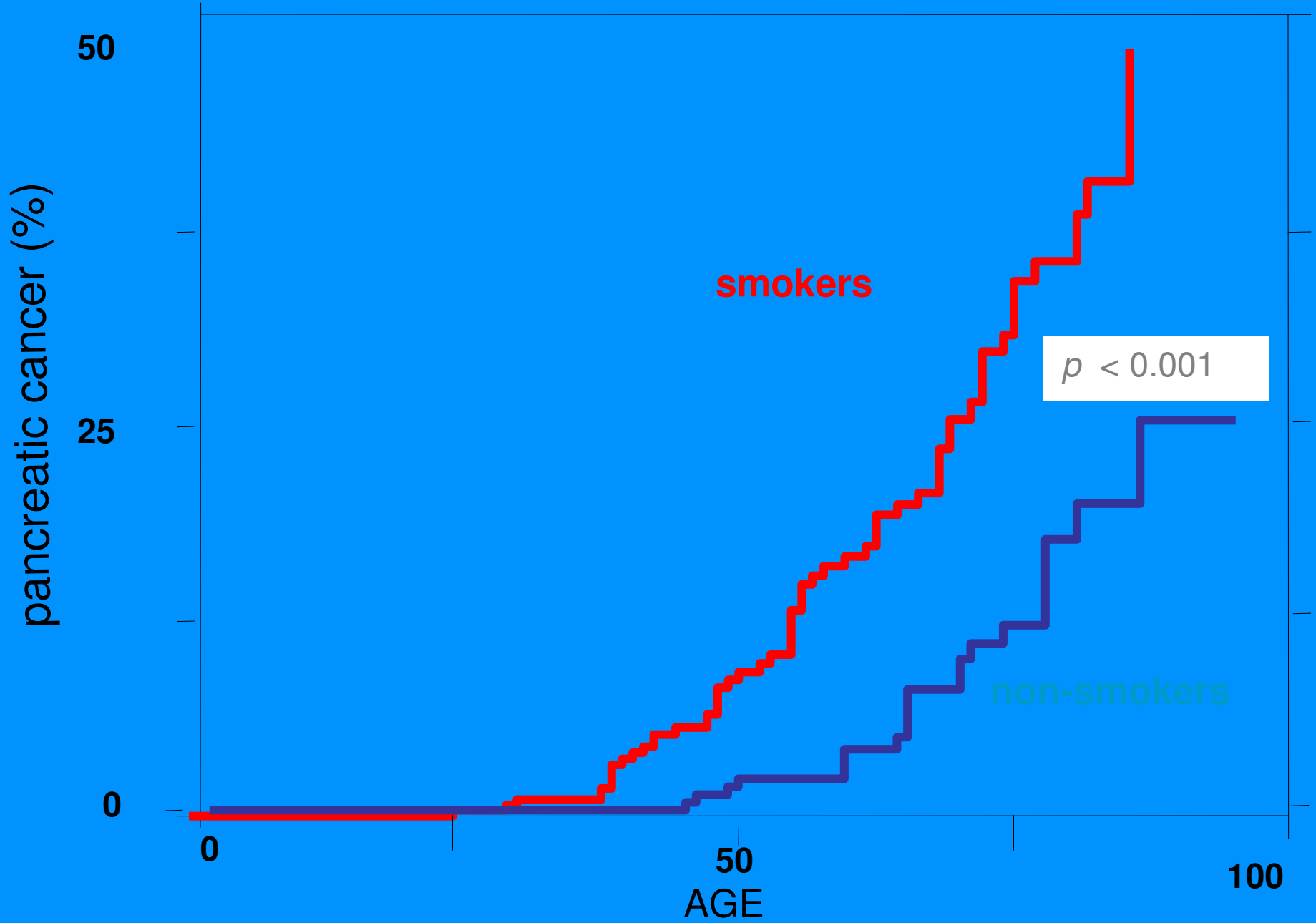
- ERCP & EUS have high pos pred value
- Sensitivity and specificity unknown
- No pathology on non-surgical patients

# Gene-Environment Interactions

251 members of 28 families

- Smoking
- diabetes
- gender
- number of affected family members

*Rulyak et al.*



# Cost Effectiveness

- Hypothetical cohort of 100 patients

- EUS +/- ERCP at age 50

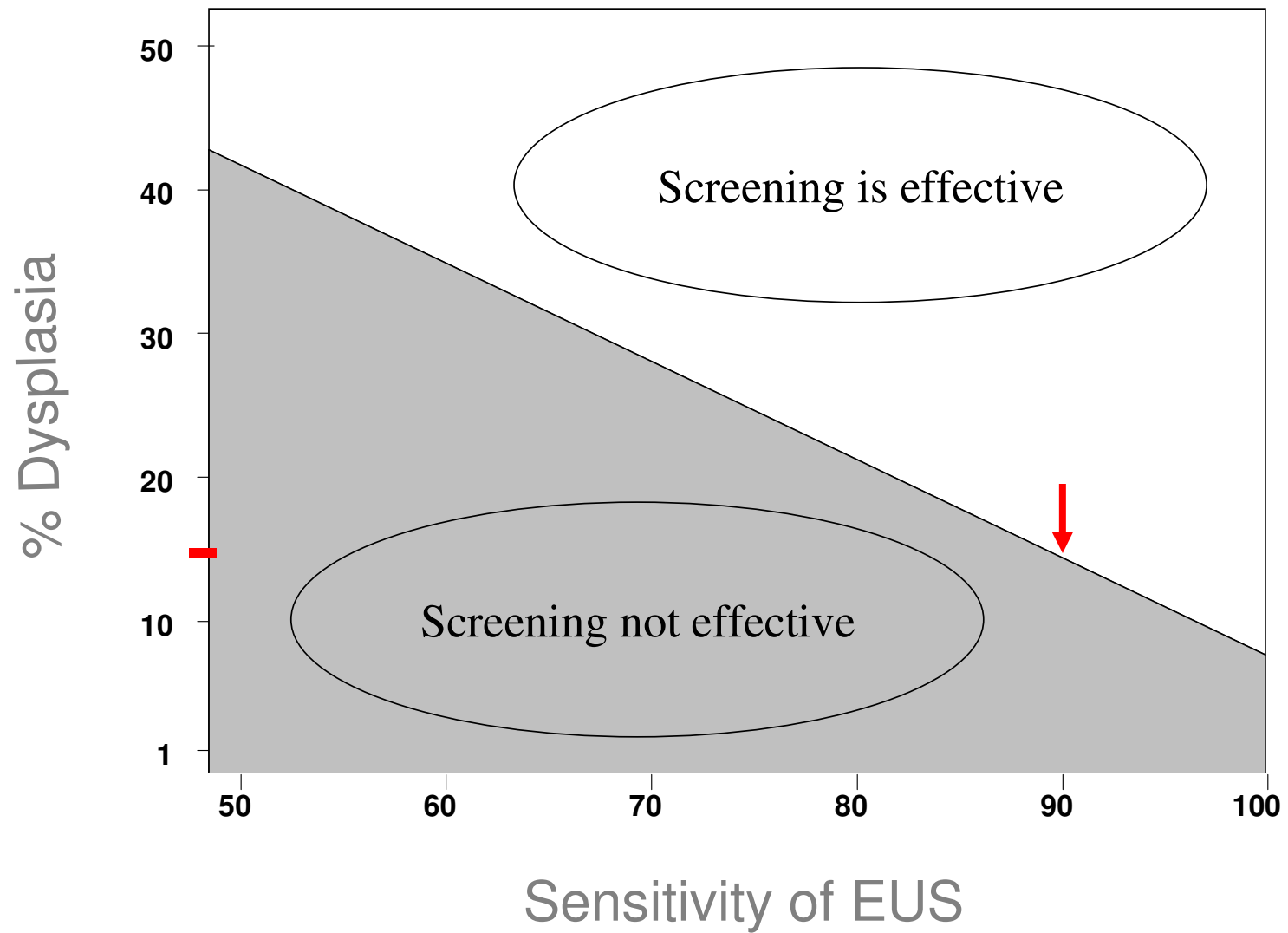
If both tests abnormal: pancreatectomy

- Lifetime medical care costs and life expectancy

Rulyak et al. Cost-Effectiveness of Pancreatic Cancer Screening in Familial Pancreatic Cancer Kindreds. *Gastrointest Endosc* 57, 23-29 (2003).

# Endoscopic Screening: Cost-Effective?

- Cost-effectiveness ratio= \$17,000  
(mammography 22K; pap smear 250K; CRC 6-92k)
- Procedure costs have limited impact
- Screening after age 70 is not cost effective



# Summary

- ~ 10-17% of PC may be due to genetics
- Most FPC is probably from unknown genes
- Penetrance plays a key role
- Gene/environment interactions influence penetrance and age at onset

# Summary

- FPC patients should be followed at specialized centers with pancreatic surveillance expertise
- Only the most highly selected patients should be given the option for pancreatectomy
- Endoscopic surveillance appears to be promising; more biomarkers are needed
- Screening is cost-effective as long as prevalence of dysplasia is 16%