

Can we prevent pancreatic cancer? EUS chemo-ablation of high-risk cysts.



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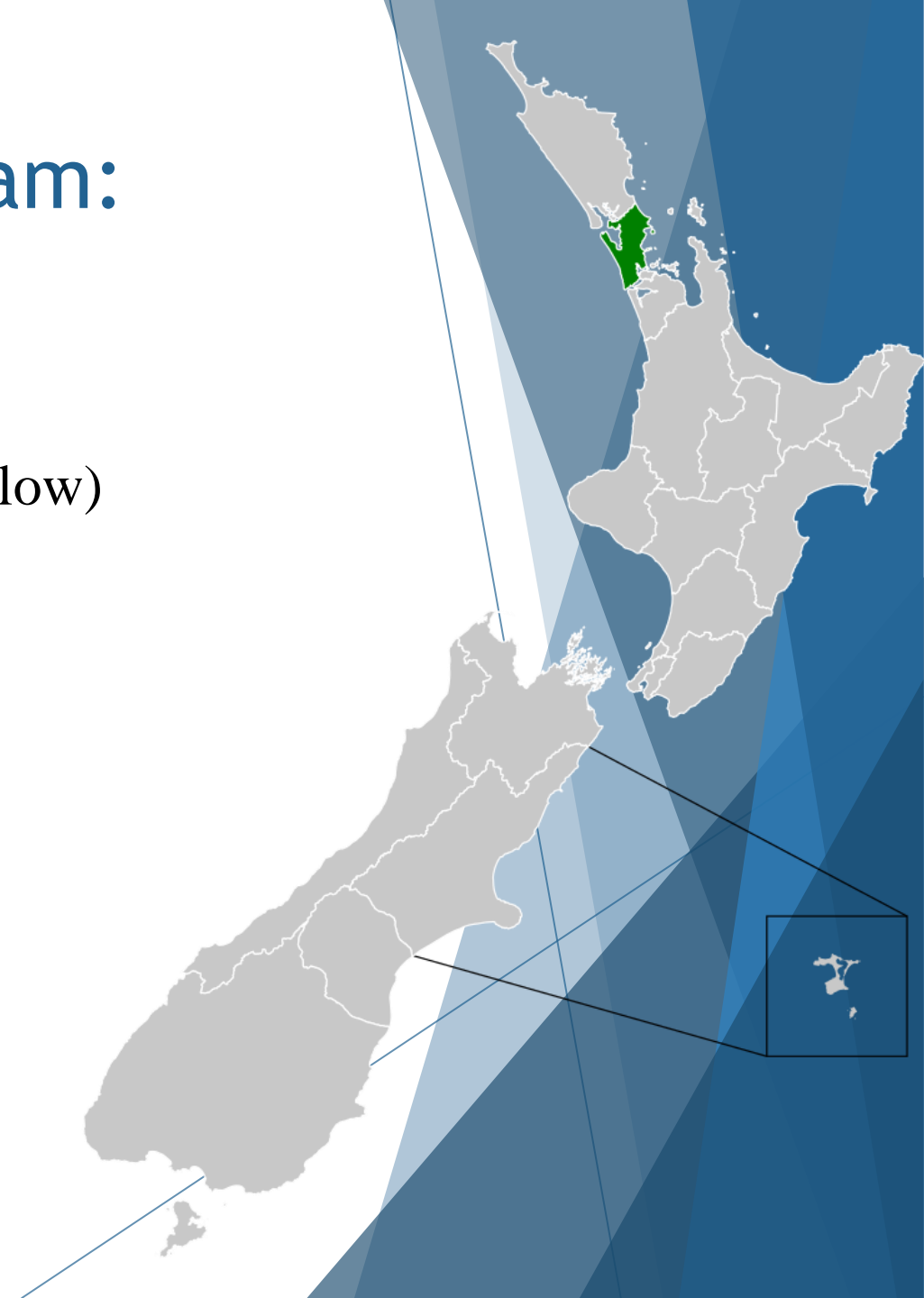


Waitemata
District Health Board

Best Care for Everyone

The pancreatic cyst ablation team:

- ▶ Assoc Prof Michael Jameson (medical oncologist)
- ▶ Dr Siti Aisyah Haji Ibrahim (oncology research fellow)
- ▶ Dr Sanjeev Deva (medical oncologist)
- ▶ Prof Cristin Print (biomedical scientist)
- ▶ Assoc Prof Jonathan Koea (hepatobiliary surgeon)
- ▶ Dr Frank Weilert (gastroenterologist)
- ▶ Dr Marius van Rijnsoever (gastroenterologist)



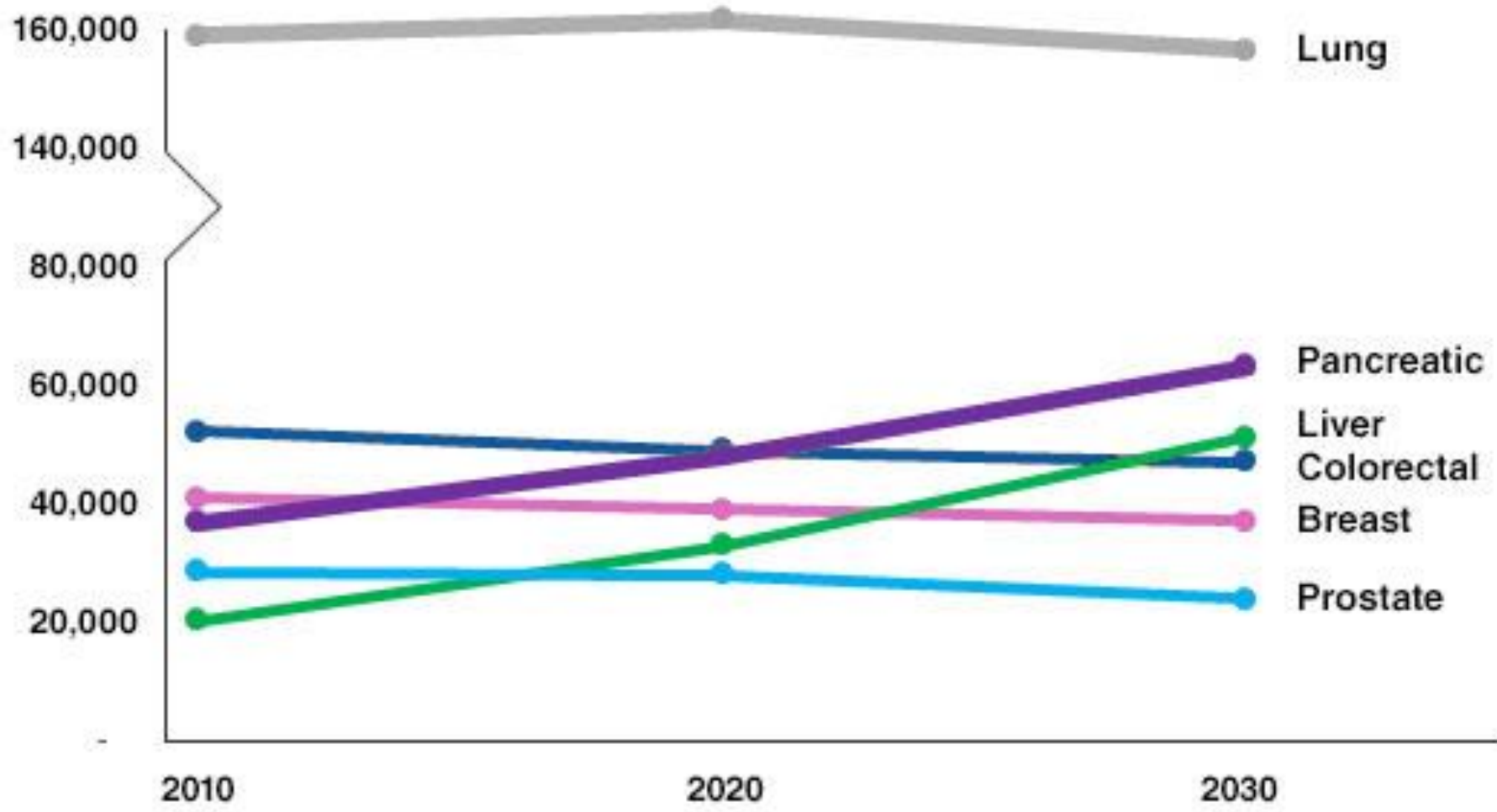
Cancer death rate down 33%

- ▶ Recent US report shows 33% drop in cancer deaths.
- ▶ 251 deaths/100,000 in 1991
- ▶ 143 deaths/100,000 in 2020

- ▶ Only 12% 5-survival rate pancreas cancer
- ▶ Incidence of pancreas cancer increasing 1% per year
- ▶ Currently no screening or early intervention program.

<https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21763>

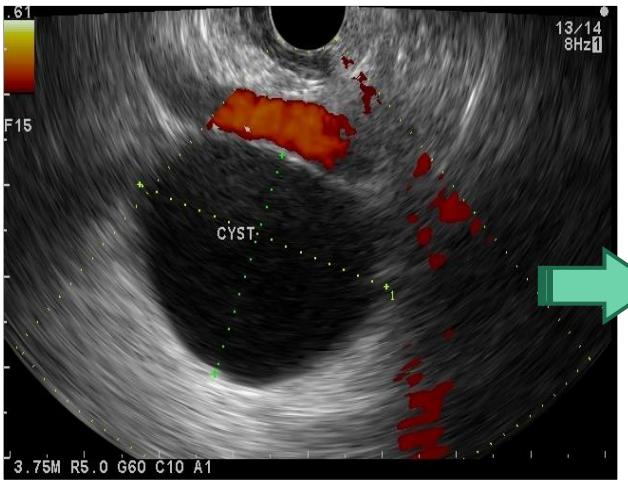
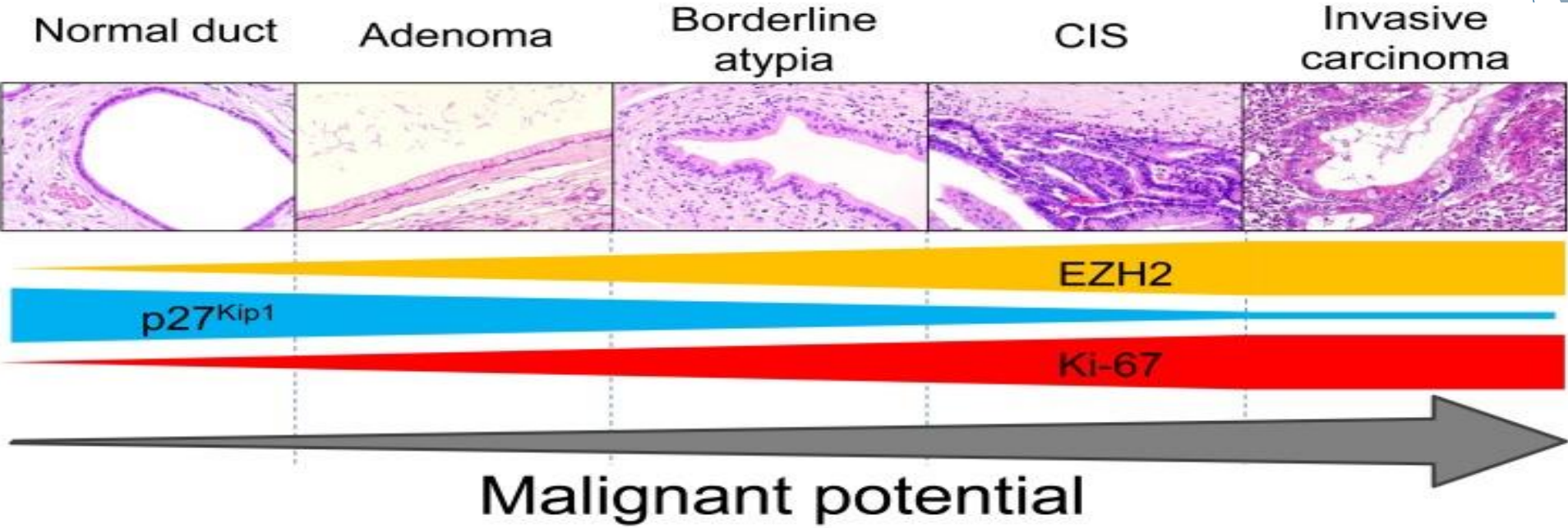
Projected Cancer-Related Deaths



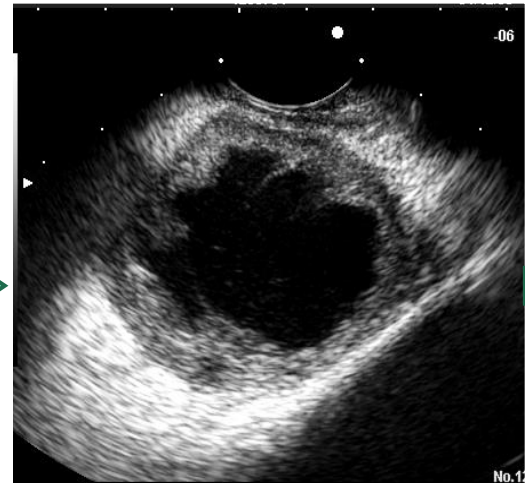
Screening and early intervention

- ▶ Skin cancer -> ablation, chemo cream, resection
- ▶ Barrett's oesophagus -> PPI, endoscopic resection /RFA
- ▶ Bowel cancer -> bowel screening, removal of adenomas
- ▶ Breast cancer -> mammogram, lumpectomy
- ▶ Prostate cancer -> PSA screening, brachytherapy
- ▶ Cervical cancer -> pap smears, laser, HPV vaccination
- ▶ Lung cancer -> low dose CT for at risk population
- ▶ Pancreas cancer -> no screening or early intervention

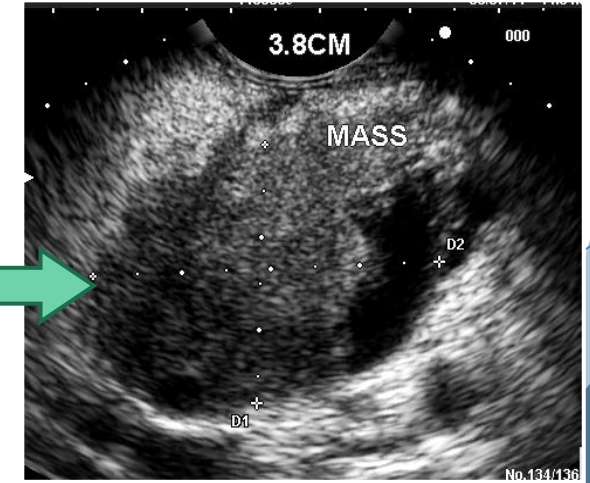
Development of pancreas cancer



Thin wall



Wall thickening



mass

Pancreatic cysts

- ▶ Prevalence of incidental pancreatic cystic 2.6 to 19.6%
- ▶ Increase of prevalence, size and numbers with age
- ▶ Intraductal papillary mucinous neoplasms (IPMN) most common
- ▶ IPMN responsible for 20-30% of pancreatic cancer cases

- ▶ Low risk IPMN -> 7% cancer risk at 10 years
- ▶ High risk IPMN - > 25% cancer risk at 10 years

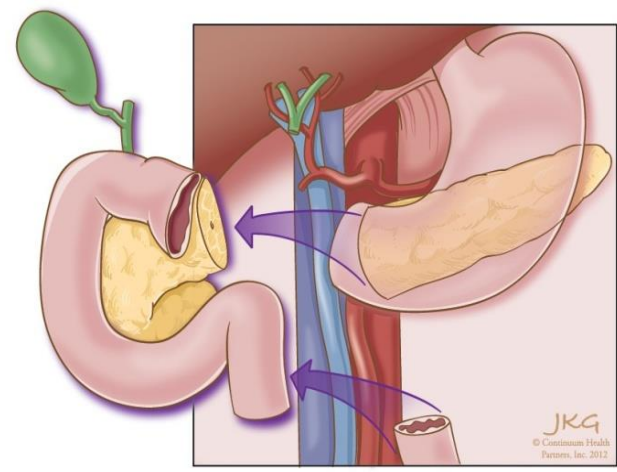
Clin Gastroenterol Hepatol. 2017;15(10):1509-20 e4.

IPMN in New Zealand

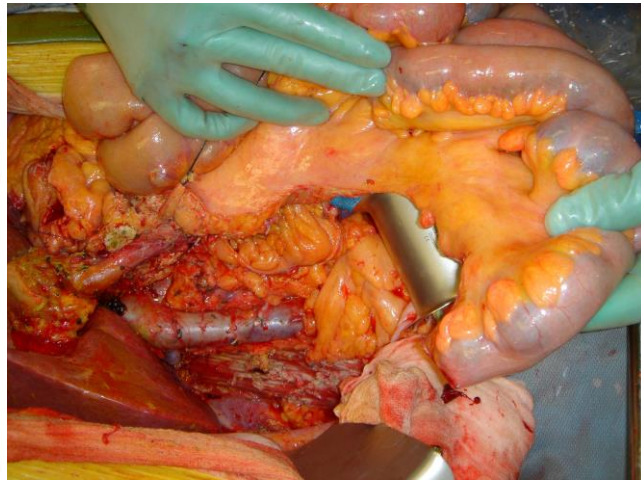
- ▶ 1450 IPMNs found on recent public MRI/CT scans in Auckland
- ▶ Large burden on MRI scanners for follow-up

- ▶ Often, we only observe the “natural history of cysts” during MDT’s
- ▶ Surgical pancreas removal (Whipple's) 2% mortality, 30% morbidity
- ▶ Multiple comorbidities and age often preclude surgery

- ▶ Māori have 50% higher incidence pancreatic cancer
- ▶ Māori have 30% higher mortality compared to non-Māori patients
- ▶ We must address this inequity and prevent progression to cancer



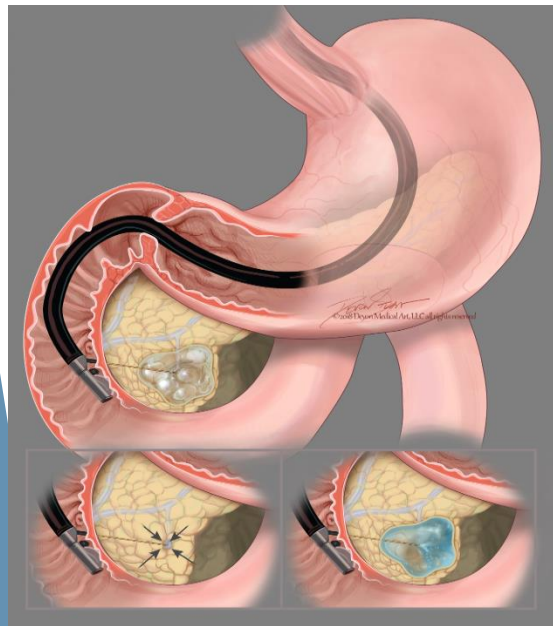
Whipple surgery



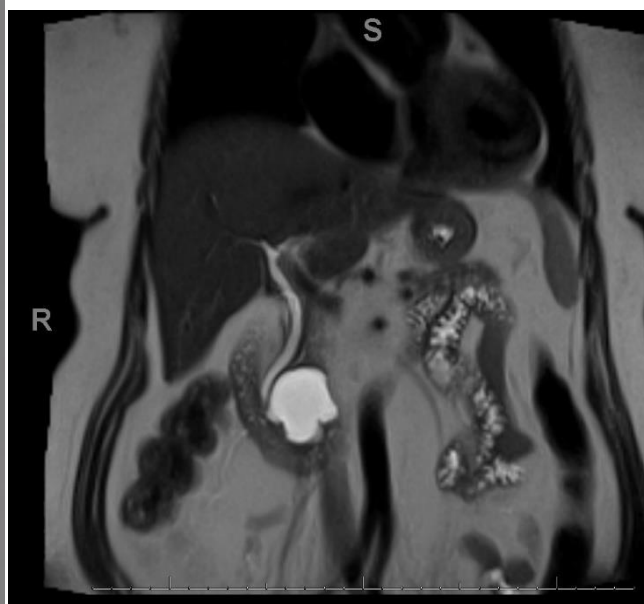
Mort 1-5%, SAE 20-40%



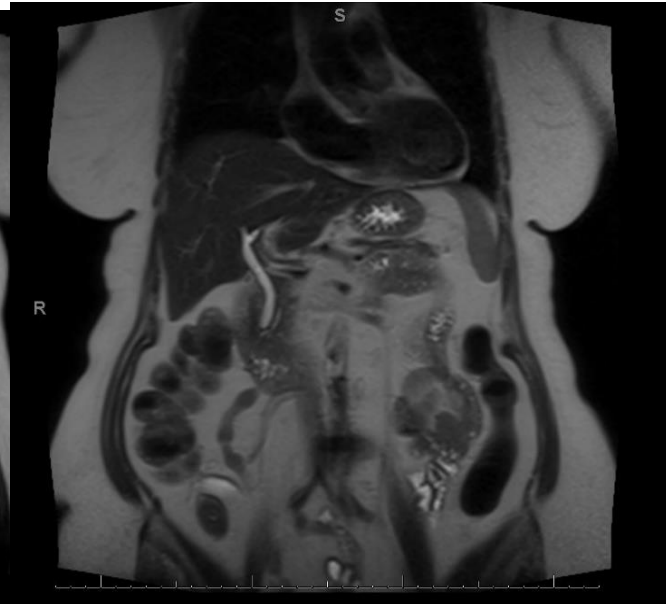
\$97,000



EUS guided ablation



Mort 0%, SAE 3-10%



\$4,100

Chemo-ablation of cysts

- ▶ First trials with low dose ethanol ablation started in 2005
- ▶ Cyst fluid is aspirated and replaced with ablation-chemical
- ▶ Then ethanol with chemotherapy additive
- ▶ Followed by ethanol free chemotherapy injection
- ▶ Mild pain was common, severe complications rare.
- ▶ This can potentially prevent cancer/surgery and regress the cyst



Current Gastroenterology Reports.
21. 10.1007/s11894-019-0686-5.

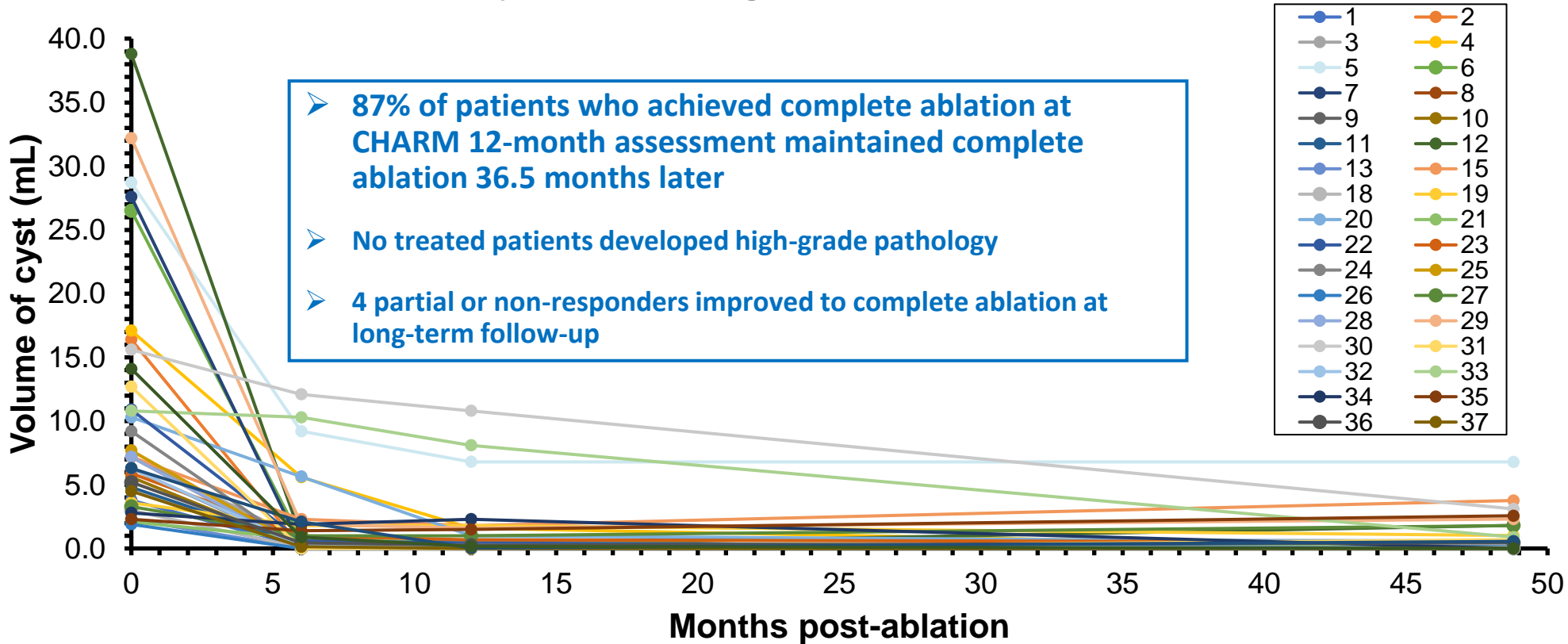
CHARM Study results

- ▶ Complete response: >95% reduction in size

	No.	Overall % reduction in cyst size after 12m	Complete response after 12m No. (%)	Major Adverse Events No. (%)	Moderate Adverse Events No. (%)
Alcohol arm	18	85	11 (61)	1 (6)	4 (22)
Alcohol-free arm	21	84	14 (67)	0 (0)	0 (0)
Total	39	84.5	25 (64)	1 (3)	4 (10)

Is EUS chemoablation durable?

Volume of Pancreatic Cysts Following Ablation in the CHARM I Trial



Chemo-ablation study

- ▶ Single arm, pilot phase 2 study
- ▶ Recruitment of 20 patients from Auckland, Northland or Waikato
- ▶ Inclusion:
 - ▶ IPMN cyst >3cm or 2cm and increasing
- ▶ Exclusion:
 - ▶ Known pancreatic cancer
 - ▶ Contraindication for FNA (bleeding, anticoagulation)
 - ▶ High grade duct communication, or main duct > 5mm

Chemo-ablation protocol

- ▶ Cyst contents will be aspirated using endoscopic ultrasound (EUS) using 19G needle.
- ▶ Cyst fluid will be stored for genetic analysis
- ▶ Cyst fluid will be replaced with gemcitabine/paclitaxel chemo
- ▶ Day-stay procedure, patient can go home same day
- ▶ Blood test day after procedure to check for pancreatitis
- ▶ Follow-up assessment at week 2 and 4.
- ▶ MRI scan at 3 months to assess response.

Outcomes

- ▶ Technical EUS chemo-ablation success rate
- ▶ Complete cysts response 95% volume decrease
- ▶ Partial cyst response 75-95% volume decrease
- ▶ Gene expression panel of ~ 70 candidate biomarker genes for gemcitabine, paclitaxel, irinotecan and oxaliplatin responsiveness and IPMN progression.
- ▶ Gene mutation analysis for 30 mutations associated with chemo response.

Conclusion

- ▶ Will be first trial in New Zealand for EUS chemoablation
- ▶ Recruitment in North Shore hospital and Waikato hospital.
- ▶ Hopefully the first step in preventing pancreatic cancer development in NZ patients with high-risk cysts.

Thank you Gut Cancer Foundation for:

- **Sponsoring innovative research in New Zealand.**
- **Facilitating access to latest pancreatic cyst treatments for NZ patients.**
- **Will hopefully prevent cancer progression for 20 NZ patients.**
- **Once cyst ablation is established with trial, this should result in cyst chemo-ablation access for other patients**