Appendix – Web Only Publication

Statements for the Management of High Risk Individuals

Without Consensus Agreement or Disagreement

Who should be screened?

% Agree	% Neutral	% Disagree	Statement
25.0	12.5	62.5	Individuals with 2 relatives on the same side of the family (no FDR) with PC should be screened once they reach a certain age.
57.2	22.4	20.4	All p16 carriers should be screened, regardless of family history.
53.0	26.5	20.4	HNPCC carriers with 2 affected relatives, no FDR, should be screened.
43.9	34.7	22.4	HNPCC carriers with 1 affected relative, no FDR, should be screened.
37.5	12.5	37.5	Individuals with 2 blood relatives (no FDR) with PC one <50 years at diagnosis should be screened once they reach a certain age.
			In general, for the defined high-risk groups, screening should begin at age ___, or 10 years younger than earliest PC in the family (except PJ**S**). 40 yr 18.4% 45 yr 28.6% 50 yr 51%
			Peutz-Jegher syndrome patients should have screening beginning at age ___.

			30 yr 36.7% 35 yr 14.3% 40 yr 36.7%
71.5	12.2	16.3	New-onset diabetes in a high risk individual should lead to initiation of screening, regardless of age.
55.1	28.6	16.4	Current smokers should start screening at 5 years earlier than nonsmokers.
			Screening should stop at age ___ for an individual in a surveillance program with no evidence of a lesion. Never 16.3% 85 18.4% 80 36.7% 75 26.5% 70 2.0% ***Stop at age 75: 81.6%***

How should high risk individuals be screened?

% Agree	% Neutral	% Disagree	Statement
26.5	40.8	32.6	When performing MRI, one should always use secretin.
34.7	32.7	32.7	In the presence of severe chronic pancreatitis, EUS-screening should be discontinued

30.6	8.2	61.3	In case of detection of a cystic lesion, EUS-FNA should always be performed.
			In case of detection of a cystic lesion, EUS-FNA should be performed only when the size is larger than: 5 mm 8.2% 10mm 30.6% 20mm 32.7% 30mm 6.1% EUS-FNA should never be performed. 22.4% ***Do EUS-FNA for cyst ≥ 10 mm: 69.4%***
32.6	18.4	49.0	Whenever a cystic lesion is detected, CT should be performed.
			After a cystic lesion is detected at baseline screening and the morphological characteristics do not meet criteria for surgical resection (Sendai International Consensus Guidelines, Tanaka et al, 2006), an imaging test should be repeated after ___ months. 3 months 16.3%, 6 months 53.1%, 12 months 30.6%, 24 months 0, 36 months 0 ***Repeat imaging at 6-12 months: 83.7%***
			After a cystic lesion is newly detected at follow-up screening and the morphological characteristics do not meet criteria for surgical resection, an imaging test should be repeated after ___ months. 3 months 30.6%, 6 months 53.1%, 12 months 16.3%, 24 months 0, 36 months 0 ***Follow-up screening at 3-6 months: 83.7%***
67.4	12.2	20.4	In case of the detection of a solid lesion, EUS-FNA should always be performed.

			In case of the detection of a solid lesion, EUS-FNA should only be performed when the size is larger than: 5 mm 53.1%, 10 mm 24.5% 15 mm 0, 20 mm 0 EUS-FNA should never be performed 22.4% ***Do EUS-FNA for solid lesions (regardless of size): 77.6%***
51.0	14.3	34.7	In case of a MPD-stricture, EUS-FNA should always be performed.
38.8	18.4	42.8	In case of an indeterminate MPD-stricture, without a mass by EUS, EUS-FNA should be performed.
67.3	14.3	18.4	In case of a MPD-stricture, CT should also be performed
44.9	34.7	20.4	In case of a MPD-stricture, ERCP should also be performed

When should surgery be performed?

% Agree	% Neutral	% Disagree	Statement
59.2	20.4	20.5	Enucleation of pancreatic lesions is not indicated.
61.2	6.1	32.7	Prophylactic resection is performed for a patient with no pancreatic lesion but strong family history or genetic syndrome.
69.4		30.6	Any detectable solid lesion by EUS (and not biopsy proven or highly suspicious to be neuroendocrine, autoimmune, and other known benign conditions) should be resected.
			In making a decision to resect a solid lesion, size should be

			considered. The size should be at least: Any size 34.7%, 5 mm 34.7%, 7 mm 8.2%, 10 mm 22.4% 15 mm 0% ***Resect any solid lesion ≥ 5 mm: 65.3%***
67.4	16.3	16.4	Each of the following criteria are indications for resection of IPMN[1] when detected in a high-risk individual: cyst > 2 cm (different from sporadic); mural nodule in cyst (= to sporadic); symptoms including pancreatitis, jaundice, pain (= to sporadic); main duct diameter > 5 mm (= to sporadic)
			Each of the following are criteria for resection of IPMN[1] when detected in a high-risk individual: cyst size > ___ cm. 1 cm 10.2%, 2 cm 36.7%, 3 cm 38.8%, 4 cm 2%,disregard size 12.2% ***IPMN size ≥ 2 cm:77.5%***
Intra-operatively, further pancreatectomy (up to a possible total) should be performed in patients with otherwise reasonable life expectancy in the following situations:			
49.0	16.3	34.7	patient with R0 resection of an invasive N0 cancer BUT with the presence of PanIN-3 at margin
24.5	20.4	55.1	patient with R0 resection of an invasive N0 cancer BUT with the presence of PanIN-2 at margin
49.0	20.4	30.6	patient without cancer BUT with PanIN-3 at the margin
12.2	22.4	65.3	patient without cancer BUT with PanIN-2 at the margin
32.7	22.4	44.9	patient with R0 resection of cancer and multifocal high grade

			dysplasia in the resected specimen but NOT at the margin
28.6	18.4	53.0	patient with R0 resection of cancer and unifocal high grade dysplasia in the resected specimen but NOT at the margin
32.6	22.4	44.9	patient with no cancer BUT with multifocal PanIN-3 in the resected specimen but NOT at the margin
8.1	24.5	67.4	patient without cancer BUT with multifocal PanIN-2 in the resected specimen but NOT at the margin
18.4	26.5	55.1	patient without cancer BUT with the presence of unifocal PanIN-3 in the resected specimens, NOT at the margin
Postoperatively, further pancreatectomy (up to a possible total) should be performed in patients with otherwise reasonable life expectancy in the following situations:			
61.2	12.2	26.5	To achieve R0 resection of cancer.
25.0	16.3	38.8	patient who already had R0 resection of an invasive N0 cancer but has PanIN-3 at the margin
4.0	22.4	73.4	patient who already R0 resection of an invasive N0 cancer but has PanIN-2 at the margin
42.9	26.5	30.6	patient without cancer in the resected specimen BUT has PanIN-3 at the margin
22.4	18.4	59.2	patient who had R0 resection of cancer but had multifocal high grade dysplasia in the resected specimen but NOT at the margin
10.2	18.4	71.4	patient who underwent R0 resection of cancer but had unifocal high grade dysplasia in the resected specimen but NOT at the margin

22.4	26.5	51.0	patient who did not have cancer but had multifocal PanIN-3 in the resected specimen but NOT at the margin
10.2	20.4	69.4	patient who did not have cancer but had unifocal PanIN-3 in the resected specimen but NOT at the margin
0	18.4	81.6	patient who did not have cancer but had unifocal PanIN-2 in the resected specimens but NOT at the margin
			Follow-up imaging should be performed __ months after surgery with any PanIN 3 in the resected pancreas. 3 months 32.7%, 6 months 46.9%, 12 months 20.4%, 24 months, 36 months 0

What are the goals of screening? What outcome(s) would be considered a "success"?

% Agree	% Neutral	% Disagree	Statement
38.8	28.6	32.7	One of the pathologic lesions that is a potential target for early detection and treatment is extra-pancreatic neoplasm
73.5	12.2	14.3	Detection and treatment of unifocal PanIN-3 should be considered a success of a screening program.
59.1	14.3	26.6	Detection and treatment of IPMN with low or intermediate grade dysplasia should be considered a success of a screening program.
61.2	4.1	34.7	Detection and treatment of invasive cancer >T1N0M0 resectable with margins negative on follow-up, should be considered a

			success of a screening program.
			Detection and treatment of pancreatic neuroendocrine tumor (PancNet) should be considered a success of a screening program. Irrespective of size 34.7%, > 5mm 22.4%, > 10mm 36.7%, > 15mm 0, > 20 mm 6.1% ***Detection and treatment of any pancreatic neuroendocrine tumor should be considered a success: 65.2%***
16.3	32.7	51	There is evidence-based medicine that supports the contention that precursor lesions in high risk groups PROGRESS FASTER to invasive cancer than do precursor lesions in the general population.
30.6	26.5	42.9	There is evidence-based medicine that supports the contention that precursor lesions in high-risk individuals ARE MORE LIKELY TO PROGRESS to invasive cancer than precursor lesions in the general population.
16.3	32.7	51.0	I suspect that precursor lesions in high risk groups PROGRESS FASTER to invasive cancer than do precursor lesions in the general population.
30.6	26.5	42.9	I suspect that precursor lesions in high risk individuals ARE MORE LIKELY TO PROGRESS to invasive cancer than precursor lesions in the general population.

1. Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Falconi M, Shimizu M, Yamaguchi K, Yamao K, Matsuno S. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006;6:17-32.

Standard Pathology Protocols for the Handling of Pancreatic Resections and Their Reporting

The goals of the pathologic examination of pancreata removed as part of screening studies are to establish the diagnoses and to prepare well-oriented biosamples for future studies. Since the lesions removed are often small, and the pancreas is prone to autodigestion, the preparation of these biosamples in a timely manner is critical. Resected specimens should be examined fresh. Surgical margins and any other clinical frozen sections for intraoperative consultations should obviously take priority. The specimen should be carefully oriented. If invasive cancer is not seen grossly, the pathologist should start at one end and serially bread-loaf the pancreas in 1-2mm slices. Each slice should be examined grossly and any lesions can be photographed. For research purposes, consideration should be given to harvesting tissue for laser capture microdissection. To harvest this tissue, every ~4th slice and any gross lesions should then be placed in Optimal Controlled Temperature (OCT) media and sectioned for frozen section. A 5-micron hematoxylin and eosin (H & E) section should be prepared on a regular slide, and then 20 unstained frozen sections (cut at 10 microns) should be prepared on slides, to allow for laser capture microdissection, and immediately placed in deep freezer. These sections then represent well-oriented, well-preserved representative sections of the pancreas and all grossly visible lesions on appropriate slides for laser capture microdissection. If an invasive PC is grossly identified, then after the processing described above, the specimen should be prepared for research studies if appropriate institutional review board (IRB) approval is in place, such as storing the cancer fresh-frozen in a tumor bank and xenografting. One also needs to bank fresh-frozen normal tissue, including spleen, normal pancreas, and/or normal duodenum for research.