

### Severn Hepato-Pancreaticobiliary Centre

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**Our Upper GI Specialist Nurses are the keyworkers for Upper GI cancer patients only. They are there to help coordinate their care, promote continuity and to be a point of contact to access information and advice.**

***VOICEMAIL AVAILABLE ON ALL UPPER GI AND APPOINTMENTS TELEPHONE NUMBERS***

**Guidance for the care of patients with increased risk of pancreatic cancer informed by NICE Pancreatic Cancer Guidance [1], CAPS consortium recommendations[2], American College of Gastroenterology Guidance [3] and the Insight Group guidelines [4]. Produced in collaboration with University Hospitals Bristol Regional Clinical Genetics Service.**

This document is guidance and specific follow up plans may vary and be patient specific dependent on local or patient factors. Optimally patients should be enrolled in research studies as part of their follow up. Please also note the commentary in appendix 1.

#### **1. General**

At the diagnosis of pancreatic adenocarcinoma clinicians are advised:

To ask people if any of their first-degree relatives has had it and address any concerns the person has about inherited risk, if they have relatives with pancreatic cancer then advice from a local genetics service may be helpful to determine if follow up of other family members is required.

#### **2. Specific groups to undertake surveillance**

Clinicians should offer surveillance for pancreatic cancer to people with:

- hereditary pancreatitis and a PRSS1 mutation

- BRCA1, BRCA2, PALB2 or CDKN2A (p16) mutations, and one or more first-degree relatives with pancreatic cancer\*
- Peutz–Jeghers syndrome (STK11 mutation).

\*Locally – presence of a CDK4 mutation is also considered in this group

### *2.1 Start of surveillance*

- The current guidance suggests starting at age 50 in all but those with PRSS1 mutations and hereditary pancreatitis when screening should start at 40 [2].

### *2.2 Surveillance mode*

- We would routinely suggest referral to the EUROPAC study and this can be undertaken by the clinician or the patient  
[https://www.lctu.org.uk/LCTU\\_NET/Frontend/?Data=W1tiRzlgWVd4bF1dW09RPT1d](https://www.lctu.org.uk/LCTU_NET/Frontend/?Data=W1tiRzlgWVd4bF1dW09RPT1d)  
They will then advise on a follow up protocol.

If a patient doesn't wish to be part of the EUROPAC study

- Data suggests that EUS and MRI Pancreas / MRCP are the most accurate investigations [2]. CT may be an alternative in patients with hereditary pancreatitis and a PRSS1 mutation where chronic pancreatitis where calcification may occur.
- Because of the invasive nature of EUS, MRI is typically suggested but clinicians need to be aware that it is slightly less sensitive.
- Abnormalities should trigger Hepatobiliary review (+/- HpB MDT review)

### *2.3 Surveillance frequency*

- If referred to the EUROPAC study then follow guidance provided by the study team

If not part of the study then

- The frequency is not fully clear but CAPS guidance [2] suggests a one yearly imaging recommendation
- Pragmatically we have selected once yearly MRI pancreas if no contraindications to MRI

### **3. Specific groups to consider surveillance**

- 2 or more first-degree relatives with pancreatic cancer, across 2 or more generations. \*\*
- Lynch syndrome (mismatch repair gene [MLH1, MSH2, MSH6 or PMS2] mutations) and any first-degree relatives with pancreatic cancer. \*\*\*

\*\* EUROPAC inclusion criteria are wider as they don't restrict themselves to first degree relatives and our regional genetics service also take a broader view and include families with three or more relatives with pancreatic cancer.

([https://www.lctu.org.uk/LCTU\\_NET/Frontend/Default.aspx?Data=W1tRMjl1ZEdWdWRFbEVdXVtNakE0XVtbYkc5allXeGxdXVtPUT09XQ%3d%3d](https://www.lctu.org.uk/LCTU_NET/Frontend/Default.aspx?Data=W1tRMjl1ZEdWdWRFbEVdXVtNakE0XVtbYkc5allXeGxdXVtPUT09XQ%3d%3d))

\*\*\* The latest NICE guidance suggest that clinicians consider screening Lynch syndrome patients although this isn't currently part of the recommendations highlighted by the Insight Group [4] which refer to the American College of Gastroenterology [3] and Mallorca Consensus Guidance[5]. In contrast ASCO due suggest possible surveillance may be useful (See below)

#### *3.1 Surveillance mode*

NICE suggests that clinicians consider:-

A MRI/MRCP or EUS for pancreatic cancer surveillance in people without hereditary pancreatitis.

A pancreatic protocol CT scan for pancreatic cancer surveillance in people with hereditary pancreatitis and a PRSS1 mutation.

It advised not to offer EUS to detect pancreatic cancer in people with hereditary pancreatitis but without PRSS1 mutation.

### **4. When to stop screening**

It is unclear when to stop and there is no international guidance or consensus[2] , however if a patient becomes too unwell for pancreatic surgery because of associated comorbidities then surveillance may be less useful as curative treatment would never be available to that individual. In addition patients may choose not to have ongoing follow up and their wishes would be respected.

### **5. Other information on risk group assessment from the American Association of Clinical Oncology (ACSO)**

ASCO also includes additional advice for the assessment of groups at risk of malignancy including some where pancreatic cancer risk is potentially increased. See

<https://www.asco.org/practice-guidelines/cancer-care-initiatives/genetics-toolkit/assessing-your-patient%E2%80%99s-hereditary>

With specific suggestions:-

*In addition to the above, testing should be done for the following common adult cancers, even in the absence of family history:*

- Breast Cancer dx < age 30-35 (TP53)
- Breast Cancer dx < age 45 (BRCA1/2)
- Any man with breast cancer (BRCA1/2)
- Ashkenazi Jewish individuals with breast cancer (any age) or pancreatic cancer (any age) (BRCA1/2)
- Colorectal cancer or endometrial cancer dx < age 50 (Lynch genes)
- the same individual with >2 of the following cancers diagnosed any age (Lynch genes): colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain tumours, sebaceous gland adenomas, keratoacanthomas and carcinoma of the small bowel

## References

1. Excellence, N.I.f.H.a.C., *Pancreatic cancer in adults: diagnosis and management*. 2018: London.
2. Canto, M.I., et al., *International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer*. *Gut*, 2013. **62**(3): p. 339-47.
3. Syngal, S., et al., *ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes*. *Am J Gastroenterol*, 2015. **110**(2): p. 223-62; quiz 263.
4. (InSiGHT), I.S.f.G.H.T. *Lynch syndrome*. 2018 18.10.2016 [cited 2018 16.06.2018]; Available from: <https://www.insight-group.org/syndromes/lynch-syndrome/>.
5. Vasen, H.F., et al., *Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts*. *Gut*, 2013. **62**(6): p. 812-23.

## Appendix 1

Comments from Alan Donaldson Consultant in Clinical Genetics,

- ‘2 or more first-degree relatives with pancreatic cancer, across 2 or more generations’. I went back to the NICE guidance & also the evidence and I’m not entirely sure what they mean by this. You could interpret as meaning both affected

family members have to be first degree relatives of your patient or the affected individuals have to be first degree relatives, but only one of whom would have to be a first degree relative of your patient e.g father & paternal grandfather. The risks in the 2<sup>nd</sup> case would be slightly lower. It is the '2 or more generations' which makes me think the latter, as I can't imagine if you are talking about first degree relatives why you would say 'or more generations'. The Europac guidance is more specific it does say 2 affected first degree relatives, then specifies who they are e.g brother, sister, mother, father, child.

- 'BRCA1, BRCA2, PALB2 or CDKN2A (p16) mutations, and one or more first-degree relatives with pancreatic cancer'. Once again I'm not sure from looking at the guidance & the evidence why it specifies you need to have a first degree relative with pancreatic cancer. It does seem unnecessarily restrictive. I would presume that the argument is that there are other contributory factors and that as first degree relatives they share the most genes with the affected individual they therefore have the highest risk. But using a hypothetical example of BRCA2, 2 males, cousins with a BRCA2 mutation, one of the cousins has inherited the BRCA2 from his father who had pancreatic cancer in his 60's, the other inheriting the BRCA2 mutation from the father's sister who died of ovarian cancer aged 45, I would have thought that the pancreatic cancer risk would be similar. Yet one would be eligible for surveillance & one wouldn't. Whereas Europac is more flexible.

From our point of view, when seeing patients in clinic, we will have to keep both NICE guidance & Europac in mind, as some patients will be eligible for Eurpoac but not under NICE.