Pancreatic cancer: diagnosis and management in adults

Consultation on draft guideline – deadline for comments 5pm on 18/09/17 **email: PancreaticCancer@nice.org.uk**

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. We would like to hear your views on the draft recommendations presented in the short version and any comments you may have on the evidence presented in the full version. We would also welcome views on the Equality Impact Assessment. We would like to hear your views on these questions: 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. 2. Would implementation of any of the draft recommendations have significant cost implications? 3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) 4. [Insert any specific questions about the recommendations from the Developer, or delete if not needed] See section 3.9 of Developing NICE guidance: how to get involved for suggestions of general points to think about when commenting.
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	[**UK Cancer Genetics Group (UK CGG)**]

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Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	[**None**]
Name of commentator person completing form:	[**Dr Marc Tischkowitz, Chair, UK CGG**]
Type	[office use only]

Comment number	**Document** (**full** version, **short** version or the **appendices**	**Page number** Or **'general'** for comments on the whole document	**Line number** Or **'general'** for comments on the whole document	**Comments** Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Example 1	Full	16	45	We are concerned that this recommendation may imply that ……..
Example 2	Full	16	45	Question 1: This recommendation will be a challenging change in practice because ……
Example 3	Full	16	45	Question 3: Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. Contact…….
1	Pancreatic cancer: NICE guideline	4	24	*BRCA1* should be removed. There is no increased risk of pancreatic cancer associated with inherited mutations in this gene.

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	short version DRAFT (July 2017)			
2	Pancreatic cancer: NICE guideline short version DRAFT (July 2017)	4	22 & 24	The statement is ambiguous. Does it mean offer surveillance to those with:- 1) *BRCA2, PALB2* or *CDKN2A* (*p16*) mutations, regardless of family history of pancreatic cancer, or 2) Only to individuals with such mutations who have a first-degree relative with pancreatic cancer, or 3) Those with a mutation in such genes, plus those who have a first degree relative with pancreatic cancer? We are not aware of any evidence showing that an increased risk of pancreatic cancer only applies to families with inherited mutations in the *BRCA2, PALB2* or *CDKN2A* (*p16*) in which pancreatic cancers have occurred. We would consider all those with inherited mutations in such genes to be equally at risk of pancreatic cancer, albeit that, naturally, patient perception will be influenced by a personal or family history of pancreatic cancer.
3	Pancreatic cancer: NICE guideline short version DRAFT (July 2017)	4 5	27 3, 4	An excess risk of pancreatic cancer is only seen in Lynch syndrome due to inherited mutations in *MLH1*, and then only in individuals over the age of 60y. From the Prospective Lynch Syndrome Database (http://www.lscarisk.org/) with approximately 25,500 patient-years of data, the risk in those with *MLH1* mutations (both genders combined) is:- **Age Risk (%) 95% Confidence interval** 25 0.00 [0 - 0] 40 0.30 [0 - 0.9] 50 1.10 [0 - 2.1] 60 1.70 [0.3 - 3.1] 70 3.90 [1.4 - 6.4] 75 6.20 [2.6 - 9.8] [Møller, Pål, et al. "Cancer incidence and survival in Lynch syndrome patients receiving colonoscopic and gynaecological surveillance: first report from the prospective Lynch syndrome database." Gut 66.3 (2017): 464-472.

				Møller, P., et al. "Incidence of and survival after subsequent cancers in carriers of pathogenic MMR variants with previous cancer: a report from the prospective Lynch syndrome database." Gut 66.9 (2017): 1657-1664. Møller, P., et al. "Cancer risk and survival in path_MMR carriers by gene and gender up to 75 years of age: a report from the Prospective Lynch Syndrome Database." Gut (2017). Jul 28] There is also no evidence in Lynch syndrome that predisposition to any of the cancers it causes is any greater in families in which specific cancers types are reported, i.e. there is no basis for recommending pancreatic surveillance in *MLH1* families because they do have a history of pancreatic cancer, any more than in *MLH1* families without a history. Therefore, **we disagree with the proposition that surveillance for pancreatic cancer should be offered to any patient with Lynch syndrome, and then only in Lynch syndrome patients with a first-degree relative with pancreatic cancer**. Given the low level of increased risk of pancreatic cancer in Lynch syndrome, the risks of surveillance in terms of morbidity and mortality, the costs to healthcare and limited resources, we do not recommend the routine surveillance of individuals with Lynch syndrome for pancreatic cancer. If it should be offered, it should only be to those with (or strongly suspected of having) an inherited mutation in *MLH1,* and then such surveillance should only be offered at an age where the risks of pancreatic cancer outweigh the risks of surveillance, and as part of a properly constituted clinical trial. We do recommend Aspirin prophylaxis in Lynch syndrome as part of the CaPP3 clinical trial [http://www.capp3.org/], given the earlier CAPP2 trial has shown and continues to show a very significant (>50%) reduction in all forms of cancer in Lynch syndrome, and moreover for at least 10 years after the Aspirin was stopped. [Burn, John, et al. "Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial." The Lancet 378.9809 (2011): 2081-2087, and *personal communication*, Prof. Sir John Burn, Newcastle University.]
4	Pancreatic cancer: NICE	General comment	General comment	The utility of pancreatic surveillance is still largely unproven. Signoretti et al, conducted a systemic review and meta-analysis of 16 pancreatic surveillance studies in high-risk groups. A relatively low diagnostic yield of pancreatic cancers and relevant precursor lesions was reported (pooled prevalence; 3.3%) using EUS and MRI as first line

	guideline short version DRAFT (July 2017)			screening tests. A significant proportion (up to 25%) of the screen-detected cancers were also unresectable or metastatic. Some patients underwent surgery for precursor lesions and were not found to have high-risk precursor lesions, and a significant morbidity (up to 40%) and mortality (0.5-6%) has been reported for the surgical treatment of suspicious pancreatic findings. **Therefore, based on the current evidence available, we disagree with the proposition that surveillance for pancreatic cancer should be routinely offered to patients from a high-risk group and would recommend that surveillance should take place within the context of a well –structured clinical trial.** [Signoretti, M. *et al.* Results of surveillance in individuals at high-risk of pancreatic cancer: A systematic review and meta-analysis. *United Eur. Gastroenterol. J.* (2018). doi:10.1177/205064061775218] [Vasen Hans F.A. and Bartsch Detlef. Familial Pancreatic Cancer: To Screen or not to Screen? EBioMedicine 2 (2015)]
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Insert extra rows as needed

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Include page and line number (not section number) of the text each comment is about.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 response from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Underline and highlight any confidential information or other material that you do not wish to be made public.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Spell out any abbreviations you use
- For copyright reasons, comment forms do not include attachments such as research articles, letters or leaflets (for copyright reasons). We return comments forms that have attachments without reading them. The stakeholder may resubmit the form without attachments, but it must be received by the deadline.

You can see any guidance that we have produced on topics related to this guideline by checking NICE Pathways.

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Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory Committees.