NICE National Institute for Health and Care Excellence

Appendix B: Stakeholder consultation comments table

2019 surveillance of Suspected cancer: recognition and referral (2015)

Consultation dates: Thursday, 31 October to Thursday, 14 November 2019

1. Do you agree with the proposal to not update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Association for Clinical Biochemistry and Laboratory Medicine (ACB)	Yes	This response relates specifically to the colorectal cancer component of the guideline and use of the faecal occult blood test. There is no additional evidence in terms of the faecal immunochemical test (FIT) since the DG30 guidance was published in 2017.	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Association of Breast Surgery	No	For breast cancer all symptomatic referrals should be seen within 2 weeks – NHS constitution Handbook states "a maximum 2-week wait to see a specialist for all patients referred for investigation of breast symptoms, even if cancer is not initially suspected" This is unique to breast cancer and GiRFT has demonstrated that referrals to breast services continue to rise rapidly and beyond current capacity in many instances. This is	Thank you very much for your comments. We note that you disagree with the proposal to not update the guideline. You state that you consider that the guideline should be updated so symptoms that might indicate that

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		diverting resources from therapeutic to diagnostic pathways. GiRFT reviews have demonstrated a negative impact of this on the capacity of breast surgical and radiological services for therapeutic pathways. The 2019 summary of evidence from surveillance for NG12 reviewed factors predicting for breast cancer in terms of primary care referral. It did not appear to review data and evidence on factors which might indicate that referral to secondary care might not be required, or attempt to identify if there might be instances where management in primary care would be safe. This is important as if there are specific symptoms and/or signs identified where referral is not immediately mandated from primary care this knowledge and understanding might assist with ensuring current breast secondary care resources on are focused on areas of greatest clinical need. If there is no evidence to assist with this NICE should consider whether this, or a review of breast diagnostic clinic access and assessment pathways, should be the subject of a NICE research recommendation given the significant and proven impact on service capacity and delivery.	referral to secondary care might not be needed are included as well as instances where the management in primary care would be safe. We also acknowledge your concern about the increased number of referrals for breast cancer and the pressures the system currently faces. NICE guideline NG12 covers 'identifying children, young people and adults with symptoms that could be caused by cancer. It outlines appropriate investigations in primary care, and selection of people to refer for specialist opinion [with the aim] to help people to understand what to expect if they have symptoms that may suggest cancer.' We have interpreted your comment as the need to consider the negative predictive value (NPV) of the symptoms, so those that are not associated with suspected cancer are identified (and avoid referrals to secondary care). In the original guideline, the committee agreed on a consensus threshold of a positive predictive value (PPV)>3% to underpin positive recommendations for both referrals for further investigation and urgent direct access investigations. It was acknowledged that although the approach used in NICE guideline NG12 was consensus-based, it was a pragmatic approach that stakeholders found broadly reasonable to managing a primary care guideline that covers many cancers. It was also noted that their decision for using PPV rather than NPV relied on the assumption that for most cancer, prevalence is typically low in the primary care population and that no symptom when absent can accurately preclude cancer.

			In the full text of the guideline and the summary of the new evidence of this surveillance review, we have reported the symptoms/tests that did not reach the PPV 3% threshold for inclusion in a recommendation. The guideline covered the two main questions in each of type of cancer included in the guideline: 1) sign and symptoms of suspected cancer and 2) Which investigations of symptoms of suspected cancer should be done with clinical responsibility retained by primary care. It also included other relevant areas such as safety netting, information on patient support, and the diagnostic process. During the current surveillance review, we covered those areas as well as others highlighted by the topic experts consulted (such as rapid diagnostic centres, among others). Having summarised the evidence and information identified (Appendix A), we concluded that no update was needed at this time. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
British Dental Association	No	As we commented in response to the 2014 consultation on the draft guideline, it is not appropriate for patients with suspected oral cancers presenting to general medical practice to be directed to a primary care dentist for onward referral to specialist services (1.8.3). This introduces unacceptable delays into the pathway and also creates a barrier for patients unwilling or unable to access dental care (due to financial constraints, lack of local NHS service availability, dental anxiety or other reasons). We note also that a formal	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We sympathise with the issue you have raised, and we understand that it is a service delivery issue. In the original guideline, the committee considered that

		process of “referral” to a primary care dentist does not exist as such in England, and that there is no system of registration with dentists under the current NHS contract. The BDA and Cancer Research UK have therefore called for this recommendation to be removed: patients presenting to GP settings should be referred directly to specialist services for suspected oral cancers.	an unexplained lump on the lip or in the oral cavity and a red or red and white patch in the oral cavity which is consistent with erythroplakia or erythroleukoplakia could be symptoms of oral cancer, but with a positive predictive value (PPV)<3%. They considered that in those cases, an assessment by a dentist would increase the PPV of the symptoms previously described, and if confirmed, a referral for suspected cancer could be considered. They acknowledged that the referral to a primary care dentist might introduce some delay. They agreed that the reduction in unnecessary referrals to secondary care resulting from lesions being seen by a more expert clinician outweighed any risk associated with a short delay. No new evidence was identified in this surveillance review to change this view. However, we do agree that the issues raised are important. We will ensure that the information on implementation issues that we have identified in this surveillance review are disseminated via appropriate channels within NICE. We will note your comments so this can be considered as an area of interest in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
British Society of Gastroenterology	Yes	That seems reasonable, there are links in the NICE guidelines’ pages to any specific issues	Thank you for your response. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For

		No specific comments from Gastroduodenal Section. The current guidance is correct on upper GI cancers and there is indeed not need to change it	further information, please see the surveillance report.
UK Cancer Genetics Group	Yes	No Comment	Thank you for your response. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Lancashire and South Cumbria Cancer Alliance	No	No Comment	Thank you for your response. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Sarcoma UK	No	Whilst the guidelines are largely right, there still exist some issues. **Bone Sarcomas (all ages)** We suggest that bone sarcomas for both adults and CYP should have an additional clause added, such as 'Consider urgent MRI if x-ray findings are uncertain and clinical concern persists'. This is due to the fact that x-rays of bone sarcomas can seem to have no clinical concerns. It is imperative that this safety net is put in place to ensure that bone sarcomas are not missed, something which we know is not an unusual occurrence. This would bring it in line with soft tissue sarcomas recommendations in 1.11.	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments below. **Bone Sarcomas (all ages)** We acknowledge your concern about ensuring that bone sarcomas are not missed. You suggest adding a new urgent MRI in cases in which the x-ray findings are uncertain, and clinical concern persists. During the current surveillance review, we did not identify any evidence in relation to MRI for this population in primary care to support the addition of this test in this area. However, we will note your comment as an area of particular interest for the next surveillance review.

		Sarcomas are often misdiagnosed as other conditions, with patients even going on to receive treatments for these misdiagnoses. Therefore, the term 'unexplained' in these settings is problematic, as patients are often given an explanation, but this is incorrect. This delays onward referral. **Soft Tissue Sarcomas (all ages)** The information is not in line with best practice according to the British Sarcoma Group guidelines. 1.11.4 and 1.11.6 do not include the recommended clinical criteria for urgent direct access to ultrasound. As well as the included 'unexplained lump that is increasing in size', it should include patients with soft tissue masses with any of the following features: • Size more than 5 cm (except superficial subcutaneous lipomas) • Painful Masses which are deep or recur after previous excision	Thank you for your comment. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. Please see 'your responsibility' section in the overview page of the guideline. **Soft Tissue Sarcomas (all ages)** Thank you for your comment and the information provided. It is noted that British Sarcoma Group Guidelines recommendations are different from those included in NICE guideline NG12. Organisations could use different methods to develop their guidance meaning they could arrive at different conclusions/recommendations. We recognise that having different recommendations in the same area is not ideal. In NICE, we use an explicit and systematic methodology to develop our guidance that attempts to ensure that the most relevant evidence is used to develop our recommendations. Similar processes are used to guarantee that our guidance is up to date. Although useful, we did not use other guidance as part of our processes. During the current surveillance, we did not identify any new evidence about specific features, pain or masses after a previous excision to warrant an update of the current recommendations. We have considered all stakeholder feedback in detail and retain our proposal to not update the

			guideline at this time. For further information, please see the surveillance report.
Royal College of Nursing	Yes	Large-scale clinical trials are underway regarding faecal immunochemical tests (FIT) but the results will not be published until mid/ late 2020. The findings may instigate a change in referral guidelines, particularly for low risk patients. These could be incorporated into the NICE Diagnostic Guidance (DG30).	Thank you for your comment. We note that you agree with the proposal to not update the guideline. We have identified one relevant ongoing study in this area: FIT— Can a Dipstick Test Rule Out Bowel Cancer? This is a non-randomised diagnostic study assessing the accuracy of FIT to triage symptomatic patients for a suspected cancer referral for bowel cancer in primary care. We plan to regularly check whether this study has published results and evaluate the impact of the results on current recommendations as quickly as possible. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further details, please see the surveillance report.
Stockport Clinical Commissioning Group	No	**Gynaecology**: Remove ascites and pelvic mass from the criteria for suspected ovarian cancer and replace by urgent direct access ultrasound. **Colo-rectal:** Adding back in the specific criteria for FIT testing would be helpful. When FIT testing was recommended in place of FOBt, the criteria for this were left very vague and open to interpretation – just classed as "low risk" symptoms. The role of FIT could be expanded, to incorporate some of the other vague symptoms, eg thrombocytosis **Vague Symptoms:** Consider separate guidance on suggested management of vague symptoms such as fatigue and thrombocytosis, to guide investigations in primary care. Many of these are included in the cancer decision support tools but not actually in any of the suspected cancer pathways.	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed responses below: **Gynaecology** The recommendations in this section of the guideline were incorporated from the NICE guideline on ovarian cancer (NICE guideline CG122). NICE guideline CG122 was checked in November 2017, and it was decided not to update it. During this surveillance review of NG12, we did not identify

			new evidence to warrant an update of the recommendations included in this section. We will note your comment on the Ovarian cancer guideline so it could be considered in the next surveillance review of the guideline. **Colorectal cancer** Thank you for your comment. We have carefully considered your comment and the comments received from other stakeholders in this area. We will include the low-risk symptoms profile that was removed after the DG30 recommendations were included in the NG12 guideline. For further details, please see the surveillance report. **Vague symptoms** Thank you for your comment. We note your view that separate guidance is needed to include recommendations about vague symptoms such as fatigue and thrombocytosis. The guideline includes a section called non-site-specific symptoms. This section includes symptoms or combinations of symptoms that may have a low risk for each cancer, but the total risk of any cancer may be high. In the original guideline, evidence was identified on symptoms such as abdominal pain, deep vein thrombosis, dyspepsia, appetite loss, appetite loss combined with weight loss, or weight loss alone. Recommendations were made for those symptoms with a PPV >3% (unexplained weight loss, appetite loss, and deep vein thrombosis). In this surveillance

			review, we identified new evidence on weight loss, supporting current guideline recommendations. We have also identified new evidence on thrombocytosis, which was summarised Appendix A under the relevant type of cancers (lung cancer, colorectal cancer, Hodgkin's lymphoma in adults). Please note that the guideline presents the recommendations by site or type of suspected cancer and by symptoms and findings. For example, thrombocytosis as a finding is included under the section Primary care investigations/blood test findings. Fatigue as a symptom is included under the section Non-specific features of cancer. Similarly, the NICE pathway on suspected cancer recognition and referral includes 2 different flowcharts: 1) site or type of suspected cancer, and 2) symptoms and findings. So, users can choose which if the best way to find relevant information about a type of cancer or a symptom and sign. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
National Association of Laryngectomee Clubs	Yes	We are satisfied with the evidence presented on our area of concern, head and neck cancer	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.

The Royal College of Physicians and Surgeons of Glasgow	Yes	The Royal College of Physicians and Surgeons of Glasgow although based in Glasgow represents Fellows and Members throughout the United Kingdom. While NICE has a remit for England, many of the recommendations are applicable to all devolved nations including Scotland. They should be considered by the relevant Ministers of the devolved governments. The College welcomes this Guideline covering Suspected Cancer recognition and referral. However in making these recommendations NICE should be conscious that investigation and management of other life-threatening conditions which can present in similar ways should not be disadvantaged. Examples would be connective tissues diseases, vasculitis, and vascular diseases in general. It is not uncommon for primary care and secondary care results systems to miss abnormal results. Any system within a surgery, hospital department or laboratory should have quality standards in place for acting on results. There should be regular audit to confirm the standards are enforced. In considering symptom presentation, none of the symptoms have considered metastatic spread. For instance many cancers present with bone secondaries which can either be in the spine bones or fracture. The types of cancer mentioned are Pancreas and Myeloma. There is no mention of Breast, Lung or Colon.	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report. We have carefully considered your comments. Please see the detailed responses below: Thank you for your recommendation about NICE being aware of not disadvantaging other disease or conditions which can present in similar ways to suspected cancer. Within its portfolio, NICE provides guidance on different disease and conditions to support health, public health and social care professionals, patients and carers, and relevant stakeholders, among others. So, these resources are available with many of the conditions cited covered in other NICE guidelines. You commented about the need to consider people with metastatic disease. This population is explicitly excluded from the scope of this guideline. When the scope of the guideline was developed, it was considered that recommendations on recurrence or metastases would be better placed in site specific cancer guidance. So, we are not able to make any recommendations on this issue. We would expect

		Pallor is a non-specific symptom of many cancers and other diseases. However only leukaemia is discussed.	primary care professionals to exercise their clinical judgement in these situations. Thank you for your comment about pallor. In the original guideline, the NG12 Committee agreed a consensus threshold of a positive predictive value (PPV) above 3% to underpin positive recommendations for both referrals for further investigations and urgent direct access investigations. Two exceptions to the 3% PPV threshold were also agreed: In children and young people (no explicit threshold value was set in the guideline) and a PPV>2% for symptoms that could have a 'cumulative' PPV value across all the cancer sites. Pallor was discussed in any type of childhood cancer and haematological cancers including leukaemia, non-Hodgkin's lymphoma and Hodgkin's lymphoma. However, it was only included as a symptom in suspected cancer in leukaemia because the guideline committee considered that this symptom was more likely to results from leukaemia than non-Hodgkin's or Hodgkin's lymphoma. In the current surveillance review we did not identify new evidence on pallor to warrant adding to any other guideline recommendations.
Society for Acute Medicine	Yes	No comment	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.

NHS Horsham and Mid Sussex CCG	Yes	Having read the 'Surveillance Review Proposal' and in light of the fact that no new high quality evidence has emerged, I would support the proposal to not update NG12. I have spent a lot of time trying to implement NG12 in my role as a commissioner and early diagnosis lead. In addition, I have travelled to various locations across the UK to teach GPs about this complex guideline. Based on my experiences, I truly believe it would be counter-productive to change NG12 significantly, especially if there is no evidence to support new or revised referral criteria.	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
University Hospitals Leicester NHS Trust	No	Regarding the 2WW recommendations for investigations of suspected endometrial cancer: This pathway is incongruous with other 2WW pathways in that referral is recommended without first performing any screening test. A transvaginal pelvic USS as a first line screening test would be in keeping with BSGC 2017 guidance which recommends further investigation only if the endometrial thickness is ≥4mm at first presentation with PMB. This excludes endometrial cancer in all but 0.9% of women. Women that have a false negative USS screening test will remain symptomatic and will re-present with ongoing bleeding and as per BSGC guidance will be fully investigated at this point, so there would be no clinically significant delay in diagnosis. By comparison the 2WW ovarian pathway recommends 2 screening tests – a CA125 followed by an USS BEFORE referral. This is despite the fact that women with ovarian cancer typically present later in stage 3 or 4 whereas most women with Endometrial cancer present in stage 1. Therefore any delay in diagnosis of EC because the ET was <4mm on the first scan, would be highly unlikely to have any detrimental long-term effect on patient outcome. Introduction of a screening test with USS PRIOR to 2WW would reduce unnecessary referrals on the 2WW pathway by at least 30% according to our audits and would not lead to missed diagnoses of cancer. It would reduce the burden of referral on this pathway, enabling trusts to achieve a "faster diagnosis" in line with planned targets on achieving a cancer diagnosis within 28 days. It would reduce anxiety in this group of women and reduce unnecessary invasive investigations.	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed responses below: You highlighted that NICE guidance is not aligned with other 2ww pathways in that a referral is recommended, particularly the British Gynaecological Cancer Society guidance on endometrial cancer, published in 2017. Different organisations could use different methods to develop their guidance meaning they could arrive at different recommendations. In this particular case, in the diagnostic methods section of the BGCS guidance (p.8) it is mentioned that 'In the UK, recommendations for diagnosis and referral are based on guidance from NICE', and the NICE guideline NG12 is included as part of the references. Similar to NICE guideline NG12, in the BGCS guidance, postmenopausal bleeding is a relevant symptom to offer/consider a suspected cancer pathway referral for an appointment within 2 weeks. New evidence identified in this surveillance review suggests that postmenopausal bleeding has a PPV of

		A prerequisite of a new approach to investigation of women with PMB with USS prior to referral would be that the GP must examine these patients to exclude lower genital tract pathology (in line with BSGC 2017 recommendations). We are aware of a number of trusts have already introduced a straight to test pathway PRIOR to 2WW referral and in spite of the current NICE recommendations and have seen no negative outcomes as a result. We strongly feel that national policy should reflect best evidence (BSGC) as these changes are in the best interests of the patients and would lead to a significant cost saving without detrimental effect on disease progress. I would like to add by comments to those made by Miss Barney. I have been in discussion with my primary care colleagues in Leicester regarding the proposed pathway change to pre-referral USS in PMB. There is considerable resistance to this proposal as it does not concord with current NICE guidance so there will be continued pressure on secondary care services to provide appointments to confirm or refute a cancer diagnosis. When NG12 was introduced the intention as I understand it was to drive down conversion rates to 3% in order to detect more cancers. The capacity in secondary care is not and never will be sufficient to meet the demand that arises from this conversion rate. In Leicestershire and Rutland we have been working on other pathways such as lower GI and prostate to alleviate the pressure on secondary care. In lower GI the investigation of choice to exclude colonic malignancy is CT colon. In our STP we have introduced faecal immunochemical testing prior to referral for patients presenting with isolated change in bowel habit as the evidence indicates its sensitivity is equivalent to colonoscopy. This has resulted in a sustained decline in the number of patients being referred on a 2ww pathway for CTC in the order of 25% whilst effectively excluding malignancy without the need for irradiation or intrusive investigation.	3.7% (above the 3% threshold used in the NICE guideline NG12). So, it supports current guideline recommendations. The scope of NICE guideline NG12 is primary care settings, so further investigations to diagnose cancer in specialist or secondary care are not included. In the original guideline, no evidence on investigations for endometrial cancer in primary care was identified. Similar to other test recommended to be done primary care for other types of cancers, the guideline committee considered that ultrasound scans could have value as an investigation in primary care to determinate if a suspected cancer referral was needed. They felt that the benefits of this test would be to expedite endometrial cancer diagnosis in women whose symptoms may otherwise not be investigated. They considered, based on the evidence, other symptoms different from postmenopausal bleeding, that could fall in this category. They recommend doing an ultrasound scan in those clinical scenarios where an urgent referral was not warranted. You suggested that a direct access ultrasound scans from primary care in symptomatic women (instead of offering a suspected cancer pathway referral) will reduce unnecessary secondary care appointments, tests, patient anxiety and costs. However, no primary care evidence was identified in this surveillance review pertaining to the diagnostic accuracy of ultrasound, where the clinical responsibility was retained by primary care.

		In urology we have recently introduced a second PSA test following exclusion of urinary tract infection to ensure that isolated raised PSA does not result in unnecessary investigation. These primary care instigated investigations play a key role in excluding malignancy without the need for a 2ww referral and can contribute significantly to the achievement of a 3% conversion rate. I would be grateful if you could advise of the timescale for review of the PMB pathway as we hope to introduce the pre-referral scan in January with comprehensive roll out in April 2020. I hope that a general review of NG12 is in the not too distant future with a view to recommending straight to test pathways across tumour sites that can be requested in primary care in order to take pressure of secondary care so that treatment targets can be achieved and the 3% conversion rate realised.	You noted that NG12 was introduced to drive down conversion rates to 3%, so more cancers are detected. However, when NG12 was developed, the guideline committee considered that in order to improve diagnosis of cancer, a PPV threshold >3% was preferable to underpin positive recommendations for both referral for further investigations and urgent access investigations. This change will result in a conversion rate across all cancers >3% (so, it will increase the conversion rate) because many of the symptoms and signs that warrant a suspected cancer pathway referral within 2 weeks have a PPV above 3%. We acknowledge the work you are developing in other areas such as lower GI cancer and prostate cancer pathways. However, we would not take forward an update in these areas because we did not identify evidence to warrant an update of current guideline recommendations. We will note your comments so it will also be considered as an area of interest in next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
University of Exeter	No	The current NICE guideline NG12 excludes important risk factors that do affect a patient's risk of cancer, and should be taken into consideration in the clinical assessment of patients presenting in primary care with symptoms suggesting a possible cancer. The body of evidence for these risk factors and their mechanisms in impacting on the	Thank you for your comment and the information provided. We note that you disagree with the proposal to not update the guideline. We have

		development of cancer has grown, and is continuing to grow, and should be reviewed to inform an update of this guideline.	carefully considered your comment. Please see the detailed response below: As it was mentioned in the original guideline, there were very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The committee actively sought exceptions to this in the evidence searches. Apart from those included in the original guideline (age and smoking in lung cancer), we did not identify any new ones in the current surveillance review. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
The Binding Site Group Limited	No	Please find attached my comments on NG12 – primarily the confusion with newer recommendations in NG35. More recent NG35 (Myeloma Diagnosis and management recommendations, Morris et al 2016) recommendations suggest that a combination of serum protein electrophoresis and serum free light chain analysis is performed to confirm the presence of monoclonal paraproteins in patients suspected of having myeloma. They specifically state that urine protein electrophoresis (Bence Jones Protein analysis) should not be performed due to its well documented inadequacies. NG12 contradicts these recommendations by suggesting that urine protein electrophoresis is still an indicated test. These contradicting recommendations have caused some confusion with clinicians (GP's and those in secondary care) as to which tests should be used (sometimes meaning both are used, adding unnecessary extra cost to the system). Myeloma is the second most common blood cancer and has one of, if not the longest delays to diagnosis from initial presentation with symptoms. The inadequacies of urine protein electrophoresis versus serum free light chain analysis (urine is rarely supplied, unlike serum and the fact that light chains don't always deposit in the urine but always	Thank you for your comment and the information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed responses below: NICE guideline NG12 outlines appropriate investigations in primary care, and selection of people to refer for a specialist opinion. So, the setting is different from the one covered in NICE guideline NG35. NICE guideline NG35 Multiple myeloma, covers the diagnosing and managing of myeloma. It covers adults referred to secondary care with suspected myeloma, including those with monoclonal gammopathy of undetermined significance. So, recommendations included in NG35 are relevant to secondary care settings.

		deposit in the serum etc) has been indicated as a common cause of missed/delayed diagnosis in myeloma. The NHS has identified the need to improve early diagnosis rates in cancers such as myeloma through its new 10-year plan, and myeloma itself formed a key part of an All-Party Parliamentary Group on Blood Cancer as something in urgent need of improving, for the reasons outlined above. Therefore, to improve early diagnosis rates for patients with myeloma and avoid confusion with clinicians, it may be prudent to align the two sets of recommendations, NG12 and NG35.	During this surveillance review, we did not identify any new evidence in this area to warrant an update of the recommendations. We will note your comment so it will also be considered as an area of interest in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Royal College of General Practitioners	No	The committee should consider updating the guidance to include For head & neck cancer: Inclusion of referral guidance on cervical dysphagia, odonophagia, recurrent or persistent pharyngitis as risks for H&N cancer as within H&N cancer guidelines in Canada, USA and Scotland. For prostate cancer: Clarity on suspected prostate cancer referral guidance which remains contentious amongst urologists leading to confusion for GPs regarding repeat testing of raised PSA and thresholds. Review of the evidence of this to reach a consensus would help clinicians in primary care. For Sarcoma: Consideration of adding the British Sarcoma Group guidance on Sarcoma criteria.	Thank you for your comment and the information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comment. Please see the detailed responses below: **Head and neck cancer:** You suggested that dysphagia, odynophagia, recurrent or persistent pharyngitis are symptoms of suspected head and neck cancer. Also, that they are included in other guidelines developed in other countries and Scotland. Note that different organisations could use different methods to develop their guidance meaning they could arrive at different recommendations. In this guideline, the committee agreed a consensus threshold of positive predictive value (PPV) > 3% to underpin positive recommendations for both referral for further investigations and urgent direct access investigations (note that some exceptions were made for children and young people, and for symptoms that could have

			a 'cumulative PPV across all the cancer sites'). Similar to the original guideline, in the current surveillance review, we did not identify evidence showing that dysphagia, odynophagia, recurrent or persistent pharyngitis have a PPV>3% for inclusion in the guideline recommendations. **Prostate cancer:** We note that your comment refers to adding more clarity about PSA referral guidance and conducting a second test after an abnormal result. In the original suspected cancer guideline, the committee noted that there was no strong primary care evidence available on which to base a recommendation for what level of PSA should prompt a suspected cancer pathway. So, they agreed to accept the age-specific reference range. In the current surveillance review, we did not identify any new evidence in the area to warrant an update of current guideline recommendations. We recognise the issues with the recommendation, and we will aim to address them. Regarding your second point about retesting after an abnormal result, we did not identify any new evidence in this area to warrant an update of current guideline recommendations. **Sarcoma:** You suggested that the Sarcoma criteria included in the British Sarcoma Group guidance should be considered for inclusion in the NICE guideline NG12 recommendations. Different organisations could use different methods to develop their guidance meaning they could arrive

			at different recommendations. In NICE, we use an explicit and systematic methodology to develop our guidance to ensure that the most relevant evidence is used to develop our recommendations. Similar processes are used to guarantee that our guidance is up to date. In the current surveillance review, we did not identify any new evidence in this area to warrant an update of the current recommendations in the area. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Accelerated Access Collaborative	No	The Accelerated Access Collaborative (AAC) strongly recommends that NG12 is reviewed by NICE in order to help resolve ongoing challenges in the uptake for the Faecal Immunochemical Tests (FIT) in the diagnosis of colorectal cancer. The AAC chose FIT as one of the seven rapid uptake products because it is NICE approved, delivers significant patient and system benefits and was failing to reach the level of patient access expected. As part of the AAC's engagement workshops (with representatives from the companies, NICE, Office for Life Sciences, NIHR, AHSNs and NHS England & Improvement and input from laboratory scientists and clinicians) confusion between NG12 and DG30 was identified as the most important on-going barrier to patient access to FIT. An update to the guidance could remove that confusion by clarifying the appropriate use of FIT in the implementation of the colorectal cancer pathway, thereby speeding up our ability to improve patient access to FIT. Specific concerns were flagged in the confusion around DG30 and NG12 which could be resolved through a review of NG12. In particular, a review of NG12 would enable the guidance to move away from high and low risk symptoms, and support referral	Thank you for your comment and the information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comment and the comments received from other stakeholders in this area. We will refresh the recommendation 1.3.4 and include the low-risk symptoms profile that was removed after the DG30 recommendations were included in the NG12 guideline. We will pass your comments about your submission to the Medical Technologies Evaluation Programme (MTTOG) to update DG30 to the Diagnostic Assessment Programme at NICE. We will note your comment so it will also be considered as an area of interest in the next surveillance review of the guideline.

		based on risk, primarily determined by: FIT results, age and gender. We are aware that there will be a significant tranche of new data available on the use of FIT available shortly, which NICE would have access to at the start of the review process. In preparation for this data the AAC, in collaboration with the National Cancer Programme at NHS England and NHS Improvement, recently submitted a request to the medical technologies topic oversight group (MTTOG) to update guidance on the use of quantitative faecal immunochemical tests (FIT) to guide referrals of suspected colorectal cancer in primary care. This submission was received positively at the recent MTTOG meeting. Finally, if a review of NG12 does not take place at this stage then this may put further mixed messages into the system. Separate reviews concerning the use of FIT and any subsequently update to NG12 introduces a risk of not providing a unified approach going forward. We therefore disagree with the NICE recommendation to not update NG12.	
Breast Cancer Now	Yes	<u>Breast cancer specific guidance</u> Specifically regarding the current content of section 1.4 Breast cancer: We agree with the decision not to update this content. <u>New Faster Diagnosis Standard</u> NHS England is currently undertaking a Clinically-led Review of NHS Access Standards, including cancer standards. The interim report proposed introducing a Faster Diagnosis Standard which would replace the two-week wait suspected cancer pathway, and the breast symptoms (where cancer is not initially suspected) pathway. If these changes are	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report. Thank you for the information about the New Faster Diagnosis Standard. We are aware that NHS England has published its Long Term Plan for Cancer in 2019. The NHS Long Term Plan includes, among other relevant areas, the creation of new rapid diagnostic centres (RDC) and the introduction of new, faster diagnosis standards. We will not update the guideline now because we did not identify new evidence to

		introduced across 2020/21, the guideline would need to be significantly updated. It's important that the guideline is updated in a timely manner in line with the introduction of any new national targets.	warrant an update of current recommendations and these changes are still being implemented into the system. We will monitor and track this area, so we can assess any impact on NICE guideline NG12 in future surveillance reviews.
British Association of Dermatologists	No	You may wish to consider reviewing NG12 Suspected cancer: recognition and referral. There are significant concerns in the NHS over the growing number of 2 week wait referrals for skin cancer which now make up 21%[1] of all two week wait referrals delivered almost exclusively by dermatology services. Since the 2015 Skin cancer update, around half of all UK cancer is skin cancer[2,3,4] and this figure is doubling every 15 years. The commonest referral to this pathway is for benign lesions which are not accurately diagnosed in primary care due to lack of adequate training in the early detection of skin cancer. The commonest benign lesion referred is a seborrhoeic keratosis which clinically to the untrained eye can present very similar to malignant melanoma. Most trained	Thank you for your comment and all the detailed information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the responses below: Thank you for the data provided about the increasing number of referrals for skin cancer and skin cancer diagnosis in the UK. You note that most of the referrals are benign lesions not accurately diagnosed in primary care due to a lack of training. This area is covered in the recommendation 1.16.1 included in the diagnostic process section of the guideline. The recommends reads 'take part in continuing education, peer review

[1] NHS England, Waiting Times for Suspected and Diagnosed Cancer, 2018-19 Annual Report
[2] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/non-melanoma-skin-cancer, Accessed November 2019
[3] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/melanoma-skin-cancer, Accessed November 2019
[4] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk, Accessed November 2019

		Dermatologists will make this diagnosis clinically without the need for further histopathology, preferable since histopathology services are also over stretched. Basal Cell cancers are the commonest type of cancer and these do not require urgent treatment but can be difficult to differentiate from squamous cell cancers which do. More confusingly under the microscope the histology of both cancers might be present. The current NICE guidance indicates that GPs should refer some high risk BCCs under the 2-week wait skin cancer pathway. This overall lack of diagnostic accuracy is driving an increasing number of 2ww skin cancer referrals. There are a number of trusts who have had to close their services to all 18-week referrals or restrict their services to only local referrals, to accommodate demand. This has had a knock-on effect for other local services which are then left to cope with the influx of these patients who have nowhere else to go. This has led to intermittent closure of routine services in some areas of England. The pathway and particularly its service provision therefore needs a significant rethink The British Association of Dermatologists is working hard to increase the diagnostic accuracy of these skin lesions in primary care so that low risk BCCs are triaged to an 18-week pathway and fewer benign lesions such as seborrheic keratoses are referred into secondary care service but this is a longer term project. Teledermatology is being developed by many Dermatology services to triage these patients more effectively and this may be a solution in the longer term.	and other activities to improve and maintain clinical consulting, reasoning and diagnostic skills, in order to identify at an early stage people who may have cancer, and to communicate the possibility of cancer to the person'. Please also note that the NICE guideline NG14 Melanoma: assessment and management as well as the NICE cancer service guideline CSG8 and currently being updated, which will provide useful updated recommendations in the area. For further information, please see the website of the update. In the basal cell carcinoma section of the guideline, the committee considered that basal cell carcinoma was exceptionally rare, with the main advantage from an early diagnosis being less extensive treatment. They also felt (and as you noted in your comments) that a diagnosis of a typical basal cell carcinoma is often possible visually. Still, a confirmation of the diagnosis is generally made by excision biopsy in accordance with NICE guidance. Given that basal cell carcinomas are slow growing, and do not often metastasise, the committee agreed to recommend a routine referral in these cases. They recognised that this approach could result in a delay in referral for someone with a squamous cell carcinoma that had been misdiagnosed as a basal cell carcinoma. Still, they considered that this was unlikely to have significant adverse consequences. So, they included a recommendation that the referral could be expedited in case of clinical concern because of the site or the size of the lesion.

Table 1 - Outpatient Attendance Dermatology

Year	Treatment Specialty	Treatment Specialty Code Description	Attended first appointment	Attended first tele consultation	Attended subsequent appointment	Attended subsequent tele consultation	Attended but first / subsequent / tele unknown	Follow-up attendances for each first attendance	All Attendances	Percentage of all attendances
2012-13	257	Paediatric Dermatology	28,972	29	60,462	44	-	2.1	89,507	0.1%
2012-13	330	Dermatology	863,714	413	2,218,209	3,530	-	2.6	3,085,866	4.1%
2013-14	257	Paediatric Dermatology	36,014	7	74,270	34	-	2.1	110,325	0.1%
2013-14	330	Dermatology	914,318	3,664	2,315,579	5,565	4,038	2.5	3,243,164	4.0%
2014-15	257	Paediatric Dermatology	38,702	17	78,467	69	-	2.0	117,255	0.1%
2014-15	330	Dermatology	979,760	4,082	2,386,776	7,026	-	2.4	3,377,644	3.9%
2015-16	257	Paediatric Dermatology	41,153	24	83,229	403	3	2.0	124,812	0.1%
2015-16	330	Dermatology	1,000,981	5,073	2,443,244	10,540	52	2.4	3,459,890	3.9%
2016-17	257	Paediatric Dermatology	44,694	27	87,759	552	-	2.0	133,032	0.1%
2016-17	330	Dermatology	1,032,717	6,550	2,473,583	17,488	9	2.4	3,530,347	3.8%
2017-18	257	Paediatric Dermatology	45,696	81	87,371	682	198	1.9	134,028	0.1%
2017-18	330	Dermatology	1,011,138	6,279	2,389,208	21,916	3,753	2.4	3,432,294	3.7%
2018-19	257	Paediatric Dermatology	48,222	254	95,068	565	153	2.0	144,262	0.1%
2018-19	330	Dermatology	1,071,934	10,642	2,444,030	26,847	5,691	2.3	3,559,144	3.7%

Data source: HES Outpatient Data for all attendances of routine, urgent and 2ww

The increase in new attendances has a direct impact on follow-up management of patients on longer term treatment pathways such as biologics and systemic therapies, phototherapy, patch testing, PDT, day case therapies.

Table 2 - 2WW Cancer Waiting times data for suspected skin cancer and skin surgery

Year	2WW	Total Breach Days	31 Days	Total Breach Days	62 Days	Total Bre Days
2012-13	210618	10263	35011	561	18290	
2013-14	245947	12605	37302	670	20423	
2014-15	290156	20026	40289	979	22720	1
2015-16	329376	19999	43847	1092	25438	1

We are very grateful for all the detailed information provided on the outpatient attendance in dermatology, the 2ww cancer Waiting times date for skin cancer and skin surgery, and the trends of the number of new attendances for patients referred under a 2ww for suspected cancer. We sympathise with the issues raised particularly the one related to the increasing demands on general practice and secondary care. We also understand that it is more issue pertaining to the resources available in the system than with the recommendations themselves.

In the current surveillance review, we did not identify relevant evidence that indicates that an update of the recommendations was needed at this time.

We identified some evidence on decision supports tools for skin cancer and primary care, but it was considered that more research is needed in this area before updating the guideline.

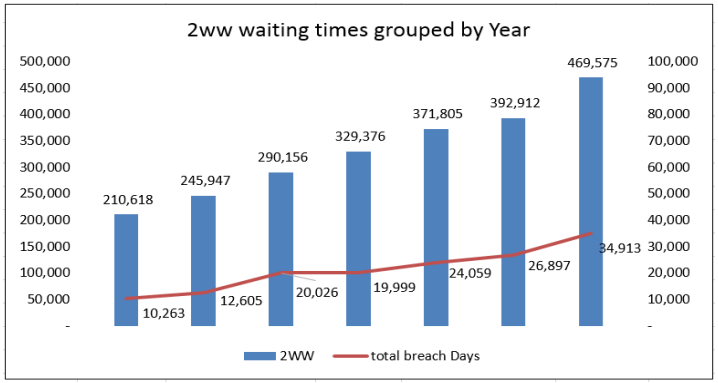
We will note your comment so it will also be considered as an area of interest in the next surveillance review of the guideline.

We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.

2016-17	371805	24059	46733	1209	27839	1216
2017-18	392912	26897	48366	1224	29192	1270
2018-19	469575	34913	53304	1486	32913	1558
Grand Total	**2310389**	**148762**	**304852**	**7221**	**176815**	**7461**

Data source: NHS England, Cancer Waiting Times

This represents the number of new attendances for patients referred under a 2ww for suspected skin cancer with the majority of sent to Dermatology (the rest to plastics). This data shows a substantial increase in the number of referrals being generated by GPs to skin cancer units and centres.



Comments received in the course of consultations carried out by NICE 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 submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

		References [1] NHS England, Waiting Times for Suspected and Diagnosed Cancer, 2018-19 Annual Report [1] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/non-melanoma-skin-cancer, Accessed November 2019 [1] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/melanoma-skin-cancer, Accessed November 2019 [1] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk, Accessed November 2019	
Cancer Research UK	No	General Cancer Research UK welcomes the opportunity to comment on this proposal. We want to highlight how important the recommendations included in NICE guidance are for influencing and supporting the work of primary care. Specifically, for us it has been valuable to be able to reference the guidance within materials and tools we and others develop for primary care. However, the importance placed on the guidance does mean that where gaps exist, they do make a difference. As noted in a previous consultation we welcome the use the 3% positive predictive value (PPV) threshold in order to cast the net wider and ensure more cancers are diagnosed earlier. However, there are instances throughout the guidance where we feel that certain recommendations could be strengthened in order to support earlier diagnosis. In some cases, this is based on new evidence, and in others it is because we feel that there is an	Thank you for your comments and all the detailed information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the responses below: Thank you for your feedback about the importance of NICE guideline NG12 for the system. You comment that you support the use of the positive predictive value threshold, but you suggest that there are areas in the guideline that need to be updated. During the surveillance review of the guideline, we looked for new information and evidence that indicated that an update was required. The summary of the new evidence identified is summarised in the Appendix A and the reasons for

		opportunity to optimise the interfaces and interactions between different recommendations and to remove any unnecessary barriers to a swift diagnosis.	final proposal to not update the guideline are detailed in the surveillance review.
		We would welcome more clarity from NICE as to when and how the guidance is going to be updated in future. We encourage NICE to consider other frameworks for reviewing guidance e.g. the National Screening Committee's annual call for new and emerging screening areas. A more frequent review would facilitate timelier assessments of emerging evidence and then could enable NICE to reflect the evolving health system landscape across England, Wales and Northern Ireland. Further clarity on review timescales would also allow us/others to prepare comprehensive responses in advance of the consultation opening.	You note that NICE needs to be more explicit about how their products are kept up to date, and you suggest the use of other frameworks for reviewing guidance. You also mention that more frequent reviews are needed, as well as more clarity on the review timescales. NICE has in place processes and methods for regularly checking that published guidelines are up to date. The NICE surveillance programme regularly checks different sources of information and evidence to decide if a specific guidance needs to be updated. For more details about how NICE keep their guidance up to date, please see Developing NICE guidelines: the manual. Please note that as a part of our standard process, we only consult on proposals to not update the guideline or to partially update the guideline. We notify stakeholders about the consultation of surveillance decision between 8 and 10 working days before the consultation is opened. The stakeholders also received an email on the day that the consultation is opened. A reminder is sent to them before the consultation period is closed. We will pass your comments to the Surveillance project team so they can assess how this process can be improved.
		We strongly recommend keeping the title of NG12 if NICE do commit to a light touch review now and annual reviews in future. The term NG12 is well recognised and has	Thank you for your comment about the title of the guideline. We don't plan to change the guideline title

		traction within primary care as what they need to do to ensure timely recognition and referral of suspected cancer. Safety netting Guidance noted in 1.15.2 of NICE continues to be important, but we recommend NICE consider additional literature (below) on safety-netting that has been published since 2015. More guidance on the specific safety-netting actions GP's could take would be welcome especially following referral and test results. Jones, D., et al., Safety netting for primary care: evidence from a literature review. BJGP, 2019. 69(678): p. e70-e79. Tompson et al. Quality improvements of safety-netting guidelines for cancer in UK primary care: insights from a qualitative interview study of GPs. BJGP 2019 Nicholson, B.D., D. Mant, and C. Bankhead, Can safety-netting improve cancer detection in patients with vague symptoms? BMJ, 2016. 355: p. i551 We also recommend NG12 include more specific mentions of safety-netting actions within certain symptom/cancer site guidance e.g. respiratory symptoms/lung cancer and action after negative chest x-rays. Laryngeal cancer NICE should consider new evidence from Hamilton et al. on symptoms associated with laryngeal cancer, which have a PPV of higher than 3%	at this time, but we will note your comment in case there is an intention to do so in the future. **Safety netting** Thank you for your comments and the studies provided. You note that more guidance is needed about specific safety netting actions, mainly linked to symptoms/test results in certain cancers sites such as lung cancer. In the original guideline, the committee recognised that almost any symptoms could potentially indicate cancer, but it would not be possible to 'safety-net' all patients with symptoms. They noted that it was difficult to define a specific set of symptoms which should prompt 'safety netting' because they considered that any list of symptoms would be incomplete. They also agreed that it was important to clarify that responsibility extends beyond ordering of the test through to the review of results and actions appropriately on the results received. We acknowledge the relevance of this area, but no new information was identified at the surveillance review to warrant an update of current recommendations. The references provided have been carefully considered. Please note that in line with our surveillance review process, we only assess the abstracts of the relevant studies identified: 1) Jones D et al 2019. This study was not identified in our literature searches and would not have been eligible based on the type of publication. It is a narrative review which aimed

		https://www.bmj.com/content/364/bmj.l435 & https://bjgp.org/content/69/679/e127 Oral cancer The guidance states, 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for oral cancer by the community dental service in people with an unexplained lump on the lip or in the oral cavity that has not been assessed by a dental surgeon.' We are concerned that this guidance adds another barrier to diagnosis by including another primary care professional into the pathway with the potential to delay diagnosis. https://bjgp.org/content/69/679/e112 This is a concern, especially for high risk patients. We also believe that many of the most deprived patients who may be at greater risk of oral cancer may not have access to a community dental service and so this extra barrier would disproportionately affect them. The guidance also states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a lump extent in the symptom guidance but NICE should consider ways to incorporate this into recommendations ordered by cancer site.	to provide a conceptual framework on safety-netting in primary care. The methodology followed is not clearly described in the abstract. It describes information about how safety netting is defined in the studies included. In also provides information about the main aspects included in the safety-net interventions. For example, information to patients about the disease, symptoms and when to consult, as well as follow-up of investigations and referrals. All this information is broadly covered in the patient information and support, safety netting and diagnostic process sections of the NICE guideline NG12. Based on the information provided in the abstract, we consider that it supports current guideline recommendations. 2) Tompson A et al. 2019. This qualitative study was not identified in our literature searches. The study presents the results of semistructured interviews conducted in the UK to 25 GPs. The aim was to explore their views on the proposed safety netting guidelines for suspected cancer in the UK. It was unclear in the methods section of the abstract which guidelines were assessed, but the results showed that GPs support current guidelines in the area, but their main concern is about the resources needed to implement them better. Based on the information provided in the abstract, we consider that the study does not have an impact on current guideline recommendations.

			3) Nicholson B.D et al 2016. This study was not identified in our literature searches, would not have been eligible based on the type of publication. The abstract is not available, so it is not considered for further assessment. **Laryngeal cancer** The primary study cited in your comment, Shephard EA et al. 2019 was identified in our searches and included. This observational study described single symptoms and symptom combinations associated with laryngeal cancer, most of them with a positive predictive value <3%. In the original guideline, results from case-control studies were regarded with caution because this type of design has been shown to be associated with an overestimation of test accuracy parameters compared with studies that incorporate random or consecutive patient selection. Given this limitation and that no other studies were identified, we considered that the evidence is limited to warrant an update of the recommendation at this time. For further details, please see Appendix A. **Oral cancer** We sympathise with the issue you have raised, and we understand that it is a service delivery issue. In the original guideline, the committee considered that an unexplained lump on the lip or in the oral cavity and a red or red and white patch in the oral cavity which is consistent with erythroplakia or erythroleukoplakia could be symptoms of oral cancer, but with a positive predictive value (PPV)<3%. They considered that in those cases, an

			assessment by a dentist would increase the PPV of the symptoms previously described, and if confirmed, a referral for suspected cancer could be considered. They acknowledged that the referral to a primary care dentist might introduce some delay. They agreed that the reduction in unnecessary referrals to secondary care resulting from lesions being seen by a more expert clinician outweighed any risk associated with a short delay. No new evidence was identified in this surveillance review to warrant an update of the recommendations at this time point. In reference to the study cited in your comment [Grafton-Clarke C et al. 2019], it was not identified in our searches. The study was described as a systematic review, but no specific methods were described in the abstract. A total of 16 studies reporting data on oral squamous cell carcinoma diagnosis in primary care were included. The length of delay reported was similar between GPs and dentist in the majority of the studies included (no further details were given in the abstract). The authors concluded that more studies were needed, and that GPs performed similarly to the dentist (but no information to which aspects they referred to were given in the abstract). It is considered that this study does not have an impact on current guideline recommendations. We will ensure that the information on implementation issues that we have identified in this surveillance review are disseminated via appropriate channels within NICE. We will note your comments

			so this can be considered as an area of interest in the next surveillance review of the guideline. **Recommendations organised by symptoms** We understand that your comment about lumps refers to the recommendations organised by symptom section of the guideline. In this section, lumps and masses as symptoms and specific features are linked to possible cancer sites, and the recommendations included in the guideline which we think covers the point raised.
Greater Manchester Health and Social Care Partnership	No	Prostate cancer guidance is not in line with best-timed pathway Lung cancer guidance relies heavily on Chest X-ray which is unreliable. Need to consider instances to refer when Chest X-ray is normal Lower GI guidance does not include FIT Guidance on raised platelets, VTE, weight loss needs to be updated and include reference to RDCs	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed responses below: **Prostate cancer** We understand that your comments refer to the Prostate cancer diagnostic pathway published by NHE in 2018 (https://www.england.nhs.uk/wp-content/uploads/2018/04/implementing-timed-prostate-cancer-diagnostic-pathway.pdf). On page 3 of the document, it is stated that 'Rapid diagnostic and assessment pathways illustrate how timely and effective care can be provided to patients presenting with cancer symptoms...[the handbook] sets out how diagnosis within 14 days and diagnosis within 28 days can be achieved for the prostate cancer pathway.' In the same page, it is also states that 'This guidance complements existing resources such as NICE guidelines (including NG12) and should therefore be read alongside such guidance.' We

			understand that a more detailed timed diagnostic process is described in the Prostate cancer diagnostic pathway, including an explicit service model. Other stakeholders also highlighted that pathways for lung, oesophago-gastric, and colorectal cancer are also available. In this surveillance review, we did not identify new evidence to warrant an update of the recommendations. We acknowledge that the Cancer Waiting Times Guidance is being reviewed by the National Cancer Programme, and a further review is undergoing as part of the Clinical Review of Standards. So, any results of the review will be considered in a future surveillance review of the guideline. We will also note your comment so it will be also considered as part of the next surveillance review. **Lung cancer** In the original guideline, no primary care evidence assessing the diagnostic accuracy of chest x-ray, CT, sputum cytology, or bronchoscopy in patients with suspected lung cancer in primary care. The guideline committee considered, based on their clinical experience, that chest x-ray was a reasonably reliable test for lung cancer, although they acknowledge it has a false negative rate. The false negative group are covered by the recommendations made on safety netting. The recommendation 1.15.1 explicitly states that people should be aware of the possibility of false negative results for chest x-rays. Haemoptysis was the only single symptom with a positive predictive value above 3%. However, the

			committee also considered that there were a collection of other signs and symptoms that were indicative of lung cancer and needed to be included. Their clinical consensus was that those patients should be investigated in primary care to decide if a suspected cancer pathway referral was required. We identified evidence through this surveillance review on x-rays. However, it was from a systematic review that only included 2 small case studies (results described narratively), and no data on the PPV were reported, but sensitivity was between 77% and 80%. We identified one study on low- dose CT scan in primary care. The findings suggested that low-dose CT scans do not have an impact on the diagnosis of lung cancer in symptomatic patients in primary care. It was considered that until the evidence base matures in this area, an update was not needed. However, we will continue to look at it as an area of interest in the guideline. **Lower gastrointestinal tract cancers** The recommendation 1.3.4 links to the NICE guidance on quantitative faecal immunochemical test to guide referrals for colorectal cancer in primary care. Please note that this recommendation will be amended. For further details, please see the surveillance report. **Rapid diagnostic centres** NHS England and NHS Improvement informed us that that the rapid diagnostic centre (RDC) service model will start to be implemented across England from 2019/2020 and that it is expected to be fully

			implemented by 2028. They will evaluate the RDC programme, and the results are likely to be published in the second half of 2020. One of the topic experts consulted during this surveillance review also highlighted the emergence of rapid diagnostic centres and the need for guidance in this area. We looked for evidence in this area, but no new evidence was identified in this surveillance review. We will note your comment so it can be considered in the next review of the guideline or before if the results of the RDC programme evaluation are published. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
NHS England and NHS Improvement	No	From a CYP perspective this [not to update] makes sense. (MC) Agree not to update (DS) The National Cancer Programme has published its Vision and 2019 Implementation Specification for Rapid Diagnostic Centres (RDCs). This new service model outlines a referral pathway for patients with non-site-specific symptoms. Previously, patients with these symptoms tended to see their GP multiple times before referral and were often referred on multiple urgent pathways, with resulting inefficiencies in healthcare provision. Where RDCs are available, patients with non-site-specific symptoms can be referred directly to a holistic diagnostic service to receive a broad assessment of symptoms,	Thank you for your response. We note that you answered that you disagree with our proposal but in your comments, you agree with it, particularly from a children and young people perspective. We have carefully considered your comments. Please see the detailed responses below: Thank you for the information provided about the Vision and 2019 Implementation Specification for Rapid Diagnostic Centres (RDCs) of the National Cancer Programme. We note that the RDC service model will start to be implemented across England from 2019/2020 and that it is expected to be fully implemented by 2028. We also note that an evaluation of the RDC programme will be conducted,

		coordinated testing, and timely diagnosis and referral. RDC services will be rolled out across England from 2019/20 with full implementation expected by 2028. We suggest referencing the RDC service model in NG12 1.13 on NSSS and including that, where available, patients with non-site-specific symptoms can be referred to an RDC for diagnosis. The National Cancer Programme plans to conduct a National Evaluation of the Rapid Diagnostic Centre Programme. This will be undertaken by an external evaluation partner, with publication of initial results is projected for Summer/Autumn 2020. Within the current NG12 guidance, GPs retain clinical responsibility for patients who need a direct access test. Once the patient has had that test, they are reviewed again by their GP before referral for suspected cancer. There has been significant confusion on how this is operationalised, and it is possible that a number of these patients are not receiving the same timely diagnosis as patients referred directly for suspected cancer. The National Cancer Programme is reviewing Cancer Waiting Times Guidance v10 for direct access patients with abnormal test results, including an approach for 'escalating' patients (see s.2.6 of Guidance). Further review is taking place as part of the Clinical Review of Standards to ensure all patients receive equitable and fast diagnosis. The National Cancer Programme would welcome a review of the NG12 guideline in the light of changes to CWT guidance and the Clinical Review of Standards, in order to align documentation for direct access patients. (LM)	and the results are likely to be published in the second half of 2020. One of the topic experts consulted during this surveillance review also highlighted the emergence of RDC and the need for guidance in this topic. We have looked for new evidence in this area, but no new evidence was identified in this surveillance review. We will note your comment so it can be considered in the next review of the guideline or before if the results of the evaluation of the RDC programme are published. We acknowledge your concern on patients having further tests not receiving the same timely diagnosis than patients directly referred for suspected cancer. The recommendation 1.15.1 included in the safety netting section of the guidelines states mechanism should be in place to 'ensure that the results of investigations are reviewed and acted upon appropriately, with the health professional who ordered the investigation taking or explicitly passing on responsibility of this'. So, it is expected that mechanisms are in place to avoid unnecessary delays. We note that the National Cancer Programme is reviewing the National Cancer Waiting Times Monitoring Dataset Guidance v10 and a further review is ongoing as part of the Clinical Review of Standards to guarantee that patients are receiving an equitable and quick diagnosis. In the current surveillance review, we did not identify new evidence that indicates we need to update the recommendations at this time, but we will review the results of the assessment once they are published to

			determine the impact on current guideline recommendations. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Novartis Pharmaceuticals (UK)	Yes	None	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Pancreatic Cancer UK	No	We do not agree with NICE's decision to not update the Suspected cancer: recognition and referral (NG12) guideline for pancreatic cancer. The current referral criteria do not allow for or achieve pancreatic cancer diagnoses at an early stage. Currently only 20% of people with pancreatic cancer are diagnosed at an early stage (stage 1 and stage 2) and nearly half (44%) are diagnosed as an emergency[5]. Very few people are diagnosed through the two-week wait (21%) or through GP referral (21%), where survival is three times higher than emergency presentation (*NCRAS Routes to diagnosis 2016*).	Thank you for your response. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed responses below: We acknowledge your concern about pancreatic cancer not being diagnosed in an earlier stage. We note that around 80% of the people with pancreatic cancer are diagnosed at a late stage (data from England and Wales 2014). We also note that the analysis of the pancreatic cancers diagnosed from 2006 to 2016 in England showed that 46% were

[5] NCRAS, Survival by Stage (2017)

		People with pancreatic cancer often have multiple appointments with GPs before referral (*Keane et al 2014*)[6], re-attend with the same symptom and attend with symptoms months before diagnosis, showing that the current referral criteria is not able to pick up people with pancreatic cancer quickly or effectively. The current referral criteria is too restrictive and is too dependent on weight loss for referral despite only 10% of patients presenting with weight loss (Stapley *et al 2012*, *Keane et al 2014)*. The 40 years age threshold for jaundice and the 60 years threshold for other symptoms also means that younger patients are not referred and may be 'missed'.	emergency presentations, 15% were through 2ww route, and 21% through routine and urgent referrals where the patient was not referred under the 2ww rout (NCRAS, Routes to diagnosis 2016/Percentage of diagnoses by route - 2006 to 2016). This section of the guideline was updated in 2015 and the low survival rate of pancreatic cancer was noted. The guideline committee acknowledge that pancreatic cancer could present with a number of different symptoms, and there are often multiple symptoms simultaneously. When making the recommendations, they considered that a potential benefit of recommending which symptoms should prompt a suspected cancer pathway referral would be a more rapid identification of the people with cancer. Also, the relevance of recommending the right symptoms so the people with suspected cancer will be appropriately referred. Jaundice was the only symptom with a positive predictive value (PPV) above 3%, so a suspected cancer pathway referral for pancreatic cancer was recommended. The guideline committee considered that the evidence on jaundice was established in a population aged 40 years and above, and that jaundice in people below this age is more likely to be cause by other

[6] https://bmjopen.bmj.com/content/4/11/e005720#ref-6

			conditions. They also noted that these cases would usually be referred on non-cancer related pathways. You comment that the current referral criteria are restrictive and reliant on weight loss. I understand your comment refers to the recommendation 1.2.5. When developing the recommendations, the guideline committee thought that considering further testing in people whose symptoms may otherwise not be investigated will provide clinical benefits and expedite the diagnosis of pancreatic cancer. Based on evidence, they recommended to consider urgent direct access CT scan or an urgent ultrasound scan if CT is not available in people aged 60 and above presenting with weight loss diarrhoea, back pain, abdominal pain, nausea/vomiting, constipation or new diabetes. In the current surveillance review, the new evidence identified was considered unlikely to change current guideline recommendations. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Prostate Cancer UK	No	Reference to age-specific reference ranges in paragraph 1.6.3 should be removed. Age-specific reference ranges have been removed from PHE's Prostate Cancer Risk Management Programme (PCRMP) and NG131 due to a lack of evidence. The PCRMP suggests a PSA referral value of 3ng/mL for men aged 50-69.	Thank you for your comments and the information provided. We note that you disagree with the proposal to not update the guideline. We have carefully considered your comments. Please see the detailed response below: We understand that your comment refers to the Prostate cancer risk management programme

		For men under 50, Prostate Cancer UK's clinical consensus suggests a referral value of 2.5 ng/mL. The PCRMP also suggests decisions should not be based on PSA alone, but should consider other factors: • prostate size • DRE findings • age • ethnicity • family history of prostate cancer • body weight/BMI • co-morbidities • history of any previous negative biopsy • any previous PSA history Prostate Cancer Risk Management Programme: https://www.gov.uk/guidance/prostate-cancer-risk-management-programme-overview Prostate Cancer UK PSA consensus: https://prostatecanceruk.org/about-us/projects-and-policies/consensus-on-psa-testing/psa-consensus-for-health-professionals	(PCRMP): benefits and risks of PSA testing, published by PHE in 2016 and the NICE guidance NG131 prostate cancer published in 2019. The PHE guidance on PSA testing refers to screening of asymptomatic men, and the NICE guideline NG131 prostate cancer refers to the diagnostic and management of people referred from primary care for investigations of possible prostate cancer. So, both groups are excluded from the scope of NICE guideline NG12. In the original suspected cancer guideline, the committee noted that there was no strong primary care evidence available on which to base a recommendation for what level of PSA should prompt a suspected cancer pathway in people presenting with symptoms in primary care. So, they agreed to accept the age-specific reference range. In the current surveillance review, we did not identify any new evidence in the area to warrant an update of current guideline recommendations. We recognise the issues with the recommendation, and we will aim to address them. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Royal College of Paediatrics and Child Health	Yes	This document was assessed from the view of paediatric cancers. There are no further known updates and the presentation has been similar in the reviewers years of practice.	Thank you for your response. We note that you agree with the proposal to not update the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the

			guideline at this time. For further information, please see the surveillance report.
Target Ovarian Cancer	No	Ovarian cancer The guidance for ovarian cancer should be updated. The NHS Long Term Plan sets out the ambition the proportion of cancers diagnosed at stages 1 and 2 will rise from around half now to three-quarters of cancer patients. If this ambition is to be achieved for ovarian cancer the diagnostic pathway should be reviewed. The CA125 blood test has limitations, while approximately 80 per cent patients with advanced ovarian cancer have elevated concentrations of CA125 in the blood serum, no more than 50 per cent of patients with clinically detectable stage I disease have elevated CA125 levels[7]. This means women with early stage ovarian cancer are less likely to be referred for an ultrasound so may not be diagnosed until the disease has spread. Due to these limitations the current diagnostic pathway should be reviewed and shortened. In Scotland women with suspected ovarian cancer are referred for a CA125 blood test and an ultrasound at the same time, a far shorter pathway than the rest of the UK where an ultrasound can only be conducted after a CA125 [8]. Bringing the pathway in England in line with best practice in Scotland would lead to a reduction in the time women	Thank you for your comments and the information provided. We note that you disagree with the proposal to not update the guideline. **Ovarian cancer** Thank you for the information provided. The recommendations in this section were incorporated from the NICE guideline on ovarian cancer (CG122). In the ovarian cancer original guideline, the committee recognised that 'no single test on its own adequately selected a manageable number of women for referral to secondary care. The combination of raised serum CA125 and sequential ultrasound of the abdomen and pelvis reduced significantly the number of women who would be referred'. They considered that a sequential testing was a sensible strategy and a cost-effective one: CA1245 was the most cost-effective first test compared to ultrasound or ultrasound and serum CA125 combination. The ovarian cancer guideline was checked in 2016 and 2017 (exceptional review) to see if an update was needed and it was concluded no update was needed.

[7] Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, Kiserud T, Halvorsen T, et al. Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. Br J Obstet Gynaecol 1996;103(8):826-31
[8] SIGN 2018, SIGN 135 • Management of epithelial ovarian cancer.

Comments received in the course of consultations carried out by NICE 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 submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

		wait for a diagnosis and would help ensure that more women are diagnosed with early stage disease. The Faster Diagnosis Standard is due to be rolled out from April 2020 and a shortened diagnostic pathway will be crucial to achieving the target of diagnosing or ruling out cancer within 28 days.	In this surveillance review, we did not identify new evidence to warrant an update of current guideline recommendations. We will note your comment so it will also be considered in the next surveillance review of the ovarian cancer guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Teenage Cancer Trust	No	No comment	Thank you for your response
2. Do you have any comments on areas excluded from the scope of the guideline?			
Stakeholder	Overall response	Comments	NICE response
Association for Clinical Biochemistry and Laboratory Medicine (ACB)	No	No comment	Thank you for your response.
Association of Breast Surgery	No	No comment	Thank you for your response.
British Dental Association	No	No comment	Thank you for your response.

British Society of Gastroenterology	No	No comment	Thank you for your response.
UK Cancer Genetics Group	Yes	There should be a recommendation in the document to say that a GP should check the family history if person presents with symptoms,	Thank you for your comment. We have carefully considered your comment. Please see the response below: In the introduction of the original guideline it was documented that there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The committee of the original guideline actively sought exceptions to this in the evidence searches, finding only age and smoking (lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that family history affected the predictive power of symptoms for different cancers. In this surveillance review, we did not identify any new evidence either. Your comments will be noted so it will also be considered as an area of interest in the next surveillance review. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Lancashire and South Cumbria Cancer Alliance	Yes	1. It does not take into account new evidence that has emerged since publication in 2015 e.g. the risk factors for laryngeal cancer, FIT and lower GI, PSA values	Thank you for your comments and the information provided. We have careful considered your comments. Please see the detailed responses below: 1. All the relevant new evidence identified in the different areas covered in NICE guideline NG12 was

		2. There have been considerable developments in urgent access to diagnostics and the relevant merits of test v 2ww e.g. CT scans for suspected lung cancer and new understanding of the negative predictive value of CXR for lung cancer. 3. The need to clarify actions on none specific symptoms and the emerging rapid diagnostic centres. 4. More detail on safety netting for lower risk patients and the importance of advice and guidance systems. Perhaps the way forward is not a complete re-write. This would actually cause confusion and a huge amount of work in amending referral forms and processes. However I would advocate either an appendix for 2020 or added new paragraphs in relevant tumour type and symptom sections where important new information is available that improves earlier diagnosis of cancer.	summarised in appendix A, including alarm symptoms of laryngeal cancer and the effectiveness of faecal immunochemical tests (FIT) in symptomatic patients in colorectal cancer. We did not identify any relevant evidence on PSA values. Please note that specific inclusion and exclusion criteria were used, and they are described in the section Summary of evidence from surveillance included in appendix A. 2.I n the original guideline, no primary care evidence assessing the diagnostic accuracy of chest x-ray, CT, sputum cytology, or bronchoscopy in patients with suspected with lung cancer in primary care. The guideline committee considered, based on their clinical experience, that chest x-ray was a reasonably reliable test for lung cancer, although they acknowledge it has a false negative rate. The false negative group are covered by the recommendations made on safety netting. The recommendation 1.15.1 explicitly states that people should be aware of the possibility of false negatives results for chest X-rays. Haemoptysis was the only single symptom with a positive predictive value (PPV) above 3%. However, the committee also considered that there were a collection of other signs and symptoms that were indicative of lung cancer and needed to be included. Their clinical consensus was that those patients should be investigated in primary care to decide if a suspected cancer pathway referral was required. We identified evidence through this surveillance review on x-rays. However, it was from a SR that only included 2 small case studies (results described

			narratively), and no data on the PPV were reported, but sensitivity was between 77% and 80%.ris We identified evidence on low- dose CT scan in primary care, evidence from one study identified in this area. The findings suggested that low-dose CT scans do not have an impact on the diagnosis of lung cancer in symptomatic patients in primary care. It was considered that until the evidence base matures in this area, an update was not needed. However, we will continue to look at it as an area of interest in the guideline. 3. We understand that your comment is related to the section on non-site-specific symptoms. NHS England and NHS Improvement informed us that that the rapid diagnostic centre (RDC) service model will start to be implemented across England from 2019/2020 and that it is expected to be fully implemented by 2028. All Cancer Alliances are expected to set up at least one RDC for patients with non-site-specific symptoms and one for a cohort of patients with site-specific symptoms in which services have been identified as underperforming in the 2 weeks wait or 62-day pathway. It is estimated that the RDC will be fully implemented by 2028. They will evaluate the RDC programme, and the results are likely to be published in the second half of 2020. We looked for evidence in this area, but no new evidence was identified in this surveillance review. We will note your comment so it can be considered in the next review of the guideline or before if the results of the RDC programme evaluation are published.

			4. We understand that your comment is related to the safety netting section of the guideline. No new evidence was identified in this section of the guideline to warrant an update of the recommendations. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Sarcoma UK	No comment	No comment	Thank you for your response.
Royal College of Nursing	No	No	Thank you for your response.
Stockport Clinical Commissioning Group	No	No comment	Thank you for your response.
National Association of Laryngectomee Clubs	No	No comment	Thank you for your response.
The Royal College of Physicians and Surgeons of Glasgow	Yes	Although not directly related to this guidance, screening for both Bowel Cancer (using FIT or Occult Blood) and Prostate cancer are both areas which are changing and these areas will need review.	Thank you for your response and the information provided. Please note that screening is out of the remit of the guideline.

Society for Acute Medicine	No	No comment	Thank you for your response.
NHS Horsham and Mid Sussex CCG	Yes	NG12 recommends patients to be referred for an appointment within 2 weeks if they have a PSA above age-specified range but it doesn't clarify what the PSA reference range is. As a result, many parts of the country are using different ranges and this has set up a post-code lottery for patients. Please could some guidance be released – for GPs and pathology labs – regarding when PSAs should be considered abnormal (for all age ranges, not just men aged 50-69)? Many thanks	Thank you for your comments and the information provided. We considered your comment in detail. Please see the response below: In the original suspected cancer guideline, the committee noted that there was no strong primary care evidence available on which to base a recommendation for what level of PSA should prompt a suspected cancer pathway in people presenting with symptoms in primary care. So, they agreed to accept the age-specific reference range. In the current surveillance review, we did not identify any new evidence in the area to warrant an update of current guideline recommendations. We recognise the issues with the recommendation, and we will aim to address them. Please note that we have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
University Hospitals Leicester NHS Trust	No	No comment	Thank you for your response.

University of Exeter	Yes	The introduction to the current NICE guideline NG 12 states that "…risk factors do not affect the way in which cancer presents." Based on this assumption, all risk factors outside of age, asbestos exposure, and smoking status were not included in the guidance. We believe that risk stratification needs to be broadened to include other key risk factors in the assessment of a patient presenting in primary care with symptoms suggesting a possible cancer. Overweight and obesity is a particular risk factor that should be considered. For example, obesity increases the risk of upper gastrointestinal cancers (including oesophageal, stomach, and pancreatic), and some of the signs highlighted for these cancers in NG12 such as a palpable upper abdominal mass may not be as reliable in overweight and obese people. Age recommendations in the guideline may also result in patients below these thresholds having a delayed diagnosis of cancer if they have developed it earlier due to their excess weight.	Thank you for your response. We have considered your comments in detail. Please see the response below: As mentioned in your comment, in the introduction of the original guideline it was documented that there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The committee of the original guideline actively sought exceptions to this in the evidence searches, finding only age and smoking (lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that overweight and obesity affected the predictive power of symptoms for different cancers. In this surveillance review, we did not identify any new evidence either. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
The Binding Site Group Limited	No	No Comment	Thank you for your response.
Royal College of General Practitioners	No	The committee should consider updating the guidance to include referral guidance for nasal/sinus cancer	Thank you for your response. We have considered your comment in detail. Please see the response below:

			In the original guideline, the guideline committee agreed to cover the top 30 cancers according to the incidence plus any additional cancers that had been covered by CG27 but did not appear in the top 30. They reason behind that was that it was not possible for the guideline to cover all cancers. We will note your comment, so it will also be considered as an area of interest in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Accelerated Access Collaborative	No	No comment	Thank you for your response.
Breast Cancer Now	Yes	Referral for suspected metastases in previously diagnosed cancer As stated in the scope, the guideline does not currently cover referral for suspected metastases in previously diagnosed cancer. As we highlighted previously in 2015, we feel that the scope should be updated to include this. We know that people with secondary breast cancer often face delays in diagnosis. This is, broadly, for two main reasons: 1) delays in getting a referral from their GP for further investigative tests when presenting with potential symptoms of secondary disease, as secondary disease is not initially suspected	Thank you for your comments. We have carefully considered them. Please see the response below: We acknowledge your concerns around the referral for suspected metastases in previously diagnosed cancer. As it was mentioned, this group of patients have been explicitly excluded from the scope of the guideline. When the scope of the guideline was developed, it was considered that recommendations on recurrence or metastases would be better placed in site specific cancer guidance. We will note your comment so it will also be considered in the next surveillance review of our breast cancer guidance.

		2) a lack of information provided to patients on the signs and symptoms of secondary breast cancer after finishing treatment for primary breast cancer, meaning they are unaware of what to look out for It is crucial that people with secondary breast cancer are diagnosed promptly so that they can begin treatment and access supportive care as quickly as possible. Timely access to treatment and care can relieve symptoms and have a dramatic impact on quality of life. One person living with secondary breast cancer told us: *'Being diagnosed quickly would have saved me four and a half months of pain, suffering and anxiety. I was constantly worrying about what was wrong with me.'* (Quote from Aliya, included in Breast Cancer Now's *Unsurvivors* report, 2019) Regarding GP referrals, research from Breast Cancer Now in 2019 has found that delayed diagnosis of secondary breast cancer continues to be an issue. Our survey of over 2000 people living with a diagnosis of secondary (metastatic) breast cancer found that: • 24% of those who previously had breast cancer had to see their GP three or more times before they were diagnosed • 20% of those who had previously had breast cancer were initially treated for a different condition by their GP before eventually being diagnosed with secondary breast cancer These figures show that the picture has not improved since our previous research in in 2016, which found that 21% of those who had had a previous diagnosis of primary breast cancer were first treated for another condition by their GP when presenting with symptoms of secondary breast cancer. In response to our initial call for inclusion of suspected recurrence and metastases in 2015, the NICE view was that *'We would expect primary care professionals to exercise clinical judgement in these situations'* (NICE, 2015). However, it's clear that, in the context of unprecedented time and resource pressure, GPs are struggling to effectively identify	We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.

		secondary breast cancer in a significant number of cases. Support is needed to help GPs recognise cases of secondary breast cancer as quickly as possible. This guideline is ideally placed to provide such support, without needing to create additional, new guidance. We suggest including a recommendation that primary healthcare professionals be mindful of possible secondary disease and that they refer people on for appropriate tests if they have had a previous breast cancer diagnosis and present with possible symptoms of secondary disease. This recommendation could be in the form of examples of symptoms of secondary disease within the breast cancer specific section of the guidance, or ideally, reference to possible metastatic breast cancer within each of the relevant symptom areas (e.g. skeletal symptoms for breast cancer which has spread to the bones). Breast Cancer Now would like to work in partnership with NICE to progress this issue further. References: Breast Cancer Care (2016). *Secondary. Not Second Rate. Secondary breast cancer part one: diagnosis* [online]. Available at: https://breastcancernow.org/sites/default/files/secondary-breast-cancer-report-part-1.pdf Breast Cancer Now (2019). *The Unsurvivors* [online]. Available at: https://breastcancernow.org/sites/default/files/bcn_theunsurvivors_campaignreport_oct2019.pdf NICE (2015) Suspected cancer (update) Guideline Consultation Table 20 November 2014 – 9 January 2015 [online] Available at: https://www.nice.org.uk/guidance/ng12/documents/suspected-cancer-update-guideline-consultation-table-with-responses2	

British Association of Dermatologists	No	No comment	Thank you for your response.
Cancer Research UK	No	No comment	Thank you for your response.
Greater Manchester Health and Social Care Partnership	No	No comment	Thank you for your response.
NHS England and NHS Improvement	Yes	The current NG12 guidance includes only smoking as a risk factor to consider during referral. In practice, other risk factors, such as family history, as well as genetic testing results, can inform GP referral decisions and could be considered in NG12 surveillance exercises. (LM)	Thank you for your response. We have carefully considered your comments. Please see the detailed response below: In the introduction of the original guideline, it was documented that there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The committee of the original guideline actively sought exceptions to this in the evidence searches, finding only age and smoking (lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that other risk factors (i.e. family history or genetics) have an impact on the predictive power of symptoms for different cancers. In this surveillance review, we did not identify any new evidence either. Genetic testing in another evolving area but no new evidence was identified through this surveillance review to inform an update to the

			guideline. We will note your comment as an area of interest so it will also be considered in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Novartis Pharmaceuticals (UK)	No	None	Thank you for your response.
Pancreatic Cancer UK	Yes	Rapid Diagnostic Centres (RDC) We are concerned that the NICE Guideline (NG12) review has excluded reference to the newly set up Rapid Diagnostic Centres (RDCs) in the NG12 guideline. Rapid diagnostic centres form an integral part of the NHS Long term plan and is an important component for delivery of earlier and faster diagnosis and a two year pilot from Cancer Research UK[9] has demonstrated that pancreatic cancer is the second most common cancer to be diagnosed. We believe that RDCs should be integrated as a key referral route for pancreatic cancer.	Thank you for your response. We have carefully considered your comments. Please find the response below: **Rapid diagnostic centres** Thank you for all the information provided about rapid diagnostic centres (RDC) and pancreatic cancer. We are aware that they form an integral part of the NHS Long Term Plan. We understand that it showed promising results in a pilot. We were informed that the RDC service model will start to be implemented across England from 2019/2020 and that it is expected to be fully implemented by 2028.

[9] https://www.cancerresearchuk.org/sites/default/files/ace_programme_mdc_interim_report_may_2018v2.4.pdf

		The RDCs are designed for symptoms that may be high risk but are not specific enough to indicate a single diagnostic pathway. RDCs are geared towards diagnosing hard to detect cancers such as pancreatic cancer, where the symptoms are vague and non-specific and as such have low PPVs (positive predicative values). The RDCs predominantly diagnosed cancers with a broad symptoms range with varying or low predictive value. This is particularly important for pancreatic cancer that is a hard to diagnose cancer because of the non-specific symptoms, such as abdominal and back pain, unexplained weight loss, indigestion, loss of appetite, jaundice, nausea and changes of bowel habits. NICE adheres to a PPV risk threshold to determine if a symptom triggers an investigation or referral, however, this excludes many symptom combinations that can be indicative of pancreatic cancer as they fall below the PPV threshold such as: • Nausea/vomiting and new onset diabetes 0.7 (0.5-1.0) [10] • Loss of weight 0.8 (0.7-1.0) • Abdominal pain/new onset diabetes 0.9(0.7-1.1) • Abdominal pain/nausea vomiting 0.9 (0.7-1.2) • Abdominal pain twice 1.0 (0.8-1.2) • Weight loss and malaise 0.9 (0.4-2.1).	Also, that an evaluation of the RDC programme will be conducted, and the results are likely to be published in the second half of 2020. RDC were also highlighted as an area of interest by topic experts contacted during this surveillance. We actively searched for evidence in this area, but no new relevant evidence was identified. We will note your comment so it can be considered in the next review of the guideline or before if the results of the evaluation of the RDC programme are published.

[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388562/

		If NICE will not include these symptom combinations for suspected pancreatic cancer referral, then they should add into the pancreatic cancer specific NG12 guidance that these symptom combinations should trigger referral to RDCs. The RDC model is designed for these non-specific and vague symptom combinations, that have a low PPV for a single cancer but still require investigation. As mentioned above, the RDC model have already shown to be effective for diagnosis of pancreatic cancer. Pancreatic cancer has been reported as the second most common diagnosed (8.5%) cancer in the RDC pilot[11]. In addition to diagnoses of cancer, the RDCs are also able to detect a broad range of non-cancer conditions. Age threshold for jaundice We are concerned that NICE has decided not to update the Suspected cancer: recognition and referral (NG12) guideline for pancreatic cancer. As we argued in the original consultation on NICE Guideline 12 (NG12), there should not be an age threshold for suspected cancer referral for people with jaundice. Stapley *et al* 2012[12], upon which the current NG12 pancreatic cancer referral criteria is based, found that jaundice, as a single symptom, has a PPV of 12.9 (7.89-27.1) in the whole study population but crucially the study population excluded people below the age of 40 up front as only cases ⩾40 years were included in the study. Therefore, the current age threshold primarily exists due to the methodology of this study.	**Age threshold for jaundice** Thank you for all the detailed information provided. The study published by Keane et al 2014 was identified in our literature searches. We assume that the study published by Schmidt-Hansen et al 2016 you are referring to is this one and it was also included in our literature searches. Both studies were considered relevant and included in the summary of the evidence. Based on the new evidence identified it was concluded that no update was needed at this time (for further details please see the Appendix A). As it was mentioned in our response to your previous comment, when making the

[11] https://www.cancerresearchuk.org/sites/default/files/ace_programme_mdc_interim_report_-_v2.4.pdf
[12] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388562/

		Keane *et al* 2014 found that jaundice had a PPV of 4.11 (2.98-5.63), although age range was not reported[13]. Keane *et al* 13 (2014) did not report PPVs but reported sufficient data to allowed Schmidt-Hansen *et al* to calculate those using Bayesian statistics. Given that, jaundice has a very high PPV for pancreatic cancer in the studied populations, significantly higher than for other pancreatic cancer symptoms, it is very likely that people below 40 would also have a PPV for jaundice above the 3% threshold or at least higher than other symptom combinations that are currently included in the NG12 referral criteria. Jaundice at any age is a serious condition that will require investigative diagnostics and treatment, regardless of cancer diagnosis or not. The differential diagnosis would include hepatitis, liver diseases that cause hepatitis including alcoholic liver disease and autoimmune diseases, or biliary blockage due to cholelithiasis or cholangiocarcinoma. The CT scan is not a wasted diagnostic tool for the jaundiced patient in any case. Even if no malignancy is uncovered by investigation, a common alternative explanation for jaundice is stones in the biliary system, and these are also worth identifying without undue delay. There is a promising rapid access diagnosis clinic for jaundice that exists in Wigan that ensures timely referral of patients with jaundice to diagnose or rule out pancreatic cancer[14].	recommendation, the committee considered that people below 40 years has an extremely low risk of pancreatic cancer. Also, in line with your comment, it was highlighted that the cause of jaundice in people below 40 years is more likely to be linked to other conditions such as alcoholism or hepatitis. The also noted that those cases would usually be referred on non-cancer related pathways. Having done those considerations, the guideline committee agreed the recommendation. In the current surveillance review we did not identify evidence that contradict current guideline recommendations. We acknowledge the current implementation of RDC. As it was mentioned before, no new relevant evidence was identified in this area. We will note your comment so it can be considered in the next review of the guideline or before if the results of the evaluation of the RDC programme are published.

[13] https://bmjopen.bmj.com/content/4/11/e005720.full

[14] https://www.pancreaticcancer.org.uk/media/1845103/rapid-access-jaundice-clinic.pdf

		Lower threshold for referral from 60 to 50 We feel strongly that the age-thresholds for referral with suspected pancreatic cancer should be removed, however, if thresholds are to remain, a lowering of the 'age 60 or above threshold to 50 would help to reduce the number of 'missed' patients for non-jaundice symptoms. We acknowledge that Stapley *et al* study found that the PPV was only over 1% for weight loss in combination with diarrhoea, back pain, abdominal pain, nausea, vomiting, constipation or new-onset diabetes in people over the age of 60. However, single symptoms of diarrhoea, back pain, abdominal pain, nausea, vomiting, constipation or new-onset diabetes are all still significantly associated with pancreatic cancer across the whole study population ($P<0.001$ except for back pain, $P=0.004$). [15] There were 1232 people under 59 diagnosed with pancreatic cancer, which represents 14% of all pancreatic cancer cases in 2017 (ONS cancer registration, 2017). Lowering of the age '60 or above' threshold would help reduce the number of 'missed' patients for non-jaundice symptoms. 913 new cases of pancreatic cancer were diagnosed in England in 2017 in patients between the ages of 50 and 59. Pancreatic Cancer UK undertook a survey in 2015, which found that nearly 60% of patients would not have been referred for a CT scan based on the cluster of symptoms	**Lower threshold for referral from 60 to 50, new onset diabetes and weight loss as the reference symptom** Thank you for all the detailed information provided and your rationale about why we need to update the recommendation 1.2.5. In the original guideline, the age thresholds and symptom combinations included in the recommendation were evidence based. When developing the recommendation, the guideline committee thought that considering further testing in people whose symptoms may otherwise not be investigated will provide clinical benefits and expedite the diagnosis of pancreatic cancer. They recommended considering urgent direct access CT scan or an urgent ultrasound scan if CT is not available in people aged 60 and above presenting with weight loss, diarrhoea, back pain, abdominal pain, nausea/vomiting, constipation or new diabetes (all of them with a PPV≥2). There was no evidence of a PPV high enough to warrant action in other groups

[15] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388562/

		and age thresholds in the NICE referral guidelines for suspected cancer. This is either because they did not have weight loss AND at least one of the symptoms selected as an alarm symptom by NICE, or if they did have weight loss and one of the other symptoms they were under the age threshold of 60 years old. [16] Whilst the guidance makes clear that GPs should be using their own experience and intuition to refer, there is a real possibility that such clear age thresholds deter or delay GPs from referring younger patients for diagnostic tests. <u>Weight loss as the reference symptom</u> Weight loss only occurs in around 10% of patients (Stapley *et al 2012*, *Keane et al 2014)*, therefore, by only allowing other symptoms in combination with weight loss, most patients will not be eligible for urgent direct access to CT scan, and therefore weight loss should not be the first reference symptom, which triggers suspicion. We have serious concerns at how presenting symptoms that could trigger a scan investigation/referral are all limited to being combined with weight loss. As mentioned above, weight loss is reported in only 10% of pancreatic cancers. Other combinations of symptoms are worthy of investigation. Keane *et al (2014)* demonstrated several single symptoms with substantial ORs that should act as alarm symptoms. • Weight loss (10.5% of patients, 6.6 OR) • Abdominal pain (43.9%, 6.38)	or symptom combination. In the current surveillance review, the new evidence identified was considered unlikely to change current guideline recommendations.

[16] https://www.pancreaticcancer.org.uk/media/409005/3047_pcuk_symptomsdiagnosis_survey.pdf

		• Nausea and vomiting (16.6%, 3.43) • Dyspepsia (20%, 2.56) • New onset diabetes (13.6%, 2.46) • Change in bowel habits (27.4%, 2.17) • Lethargy (10.5%, 1.42) • Back pain (16%, 1.33) One problem with the above is that jaundice and loss of weight are reported by a minority of patients with pancreatic cancer. Therefore, relying on a policy of (rapid) investigation of these 2 symptoms inevitably means many patients with pancreatic cancer will be diagnosed belatedly after the onset of nonspecific symptoms. New Onset diabetes The current guidance only investigates new-onset diabetes in the presence of unexplained weight loss. New onset diabetes is associated with pancreatic cancer and can be detected in the pre-symptomatic phase (Ben *et al.*, *(2011)*) The current guideline means that people with only new onset diabetes would not be considered for pancreatic cancer. People can only be investigated once they have weight loss and new onset diabetes. At this stage the cancer may have progressed and be diagnosed at a later stage. The guideline should allow for a broader and more flexible referral of people with new onset diabetes, this could include new onset diabetes and with another symptom, and this could allow more people to be diagnosed at an earlier stage. NICE should depart from the strict adherence to PPV measures to determine guidelines, particularly for less survivable cancers such as pancreatic cancer where there is a low	

		evidence base for symptoms, most people are diagnosed late and survival is poor and has not changed in the last five decades. Keane *et al (2014)* identified lethargy as a symptom with overall risk (1.42) that is not currently in the NICE NG12. NICE should consider expanding the measures it considers to include overall risk rather than only PPV. NICE should be more flexible around the PPV threshold for hard to detect and less survivable cancers such as pancreatic cancer. This could allow more people with pancreatic cancer to be diagnosed at an earlier stage. If the PPV threshold was more flexible, Stapley *et al* research would include an additional 6 symptoms/combinations to be included in the guideline: • Nausea/vomiting and new onset diabetes 0.7 (0.5-1.0) [17] • Loss of weight 0.8 (0.7-1.0) • Abdominal pain/new onset diabetes 0.9(0.7-1.1) • Abdominal pain/nausea vomiting 0.9 (0.7-1.2) • Abdominal pain twice 1.0 (0.8-1.2) • Weight loss and malaise 0.9 (0.4-2.1).	

[17] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388562/

Prostate Cancer UK	No	No comment	Thank you for your response
Royal College of Paediatrics and Child Health	No	No comment	Thank you for your response
Target Ovarian Cancer	No comment	No comment	Thank you for your response
Teenage Cancer Trust	Yes	Teenage Cancer Trust would like to see a review of the guideline that considered young people as a distinct patient group. Young people get a distinct range of cancers and have specific emotional needs. We understand that in the coming months there are papers due to be published on the multiple symptoms young people with cancer may experience. We believe that the guidance should be reviewed in light of any new evidence specific to young people's cancer. We recognise there are changes planned to referral time targets through the Faster Diagnosis Standard recommended in the NHS Long Term Plan, it feels appropriate to review the context that this guidance would be considered in at this time.	Thank you for your response. We have fully considered your comments. Please see the responses below: NICE guideline NG12 includes specific aspects related to children and young adults as a patient group: • Positive predictive value (PPV) thresholds: the committee agreed that PPV threshold to make recommendations made for children and young people should be below the 3% agreed for adults. The guideline committee considered that children and young people have longer to live than adults therefore a successful cancer diagnosis leading to cure should yield more years of life gained. • Cancers affecting children and young people: Cancers almost entirely restricted to children are given specific recommendations in a section of the guideline. Recommendations for other

			common cancers affecting children and young people were included in subsections of the specific type of cancers. During the surveillance review, we searched for new information or evidence covering all the patient groups included in the scope of the guideline (children from birth up to 15y, young people 16-24y, and adults). We sympathise with your concern and acknowledge each patient group could have their own needs. We also understand the challenges to identify evidence specific for young people given that studies could use different age ranges. We will note this as an area of particular interest so it can also be considered in the next surveillance review. We will also track the development in the NHS Long Term Plan to assess the impact on the guideline recommendations. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
3. Do you have any comments on equalities issues?			
Stakeholder	Overall response	Comments	NICE response
Association for Clinical Biochemistry and	No	No comment	Thank you for your response.

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Laboratory Medicine (ACB)			
Association of Breast Surgery	No comment	No comment	Thank you for your response.
British Dental Association	Yes	The requirement for GPs to direct suspected oral cancer cases to primary care dental services disproportionally disadvantages patients who are vulnerable and unlikely to attend, are unable to afford NHS dental charges or live in an area where there is an access problem. We strongly urge NICE to update the guideline to remove this requirement.	Thank you for your response and your comment. We have addressed this issue in our response to your previous comment above. Here the response to your previous comment: 'We sympathise with the issue you have raised, and we understand that it is a service delivery issue. In the original guideline, the committee considered that an unexplained lump on the lip or in the oral cavity and a red or red and white patch in the oral cavity which is consistent with erythroplakia or erythroleukoplakia could be symptoms of oral cancer, but with a positive predictive value (PPV)<3%. They considered that in those cases, an assessment by a dentist would increase the PPV of the symptoms previously described, and if confirmed, a referral for suspected cancer could be considered. They acknowledged that the referral to a primary care dentist might introduce some delay. They agreed that the reduction in unnecessary referrals to secondary care resulting from lesions being seen by a more expert clinician outweighed any risk associated with a short delay. No new evidence was identified in this surveillance review to change this view. However, we do agree that the issues raised are important. We will ensure that the information on

			implementation issues that we have identified in this surveillance review are disseminated via appropriate channels within NICE. We will note your comments so this can be considered as an area of interest in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.'
British Society of Gastroenterology	No	No comment	Thank you for your response.
UK Cancer Genetics Group	No Comment	No	Thank you for your response.
Lancashire and South Cumbria Cancer Alliance	No	No Comment	Thank you for your response.
Sarcoma UK	No comment	No Comment	Thank you for your response.
Royal College of Nursing	No	No	Thank you for your response.
Stockport Clinical Commissioning Group	No	No comment	Thank you for your response.

National Association of Laryngectomee Clubs	No	No comment	Thank you for your response.
The Royal College of Physicians and Surgeons of Glasgow	No	No Comment	Thank you for your response.
Society for Acute Medicine	No	No comment	Thank you for your response.
NHS Horsham and Mid Sussex CCG	Yes	My comment relates to the point highlighted above – if NICE (through its helpful Clinical Knowledge Summary) has produce a PSA reference range for men aged 50-69, why has it not produced a PSA reference range for the other age brackets? This unfairly disadvantages some men, based on their age.	Thank you for your response. We have addressed this issue in our response to your previous comment above. Here the response to your previous comment: 'In the original suspected cancer guideline, the committee noted that there was no strong primary care evidence available on which to base a recommendation for what level of PSA should prompt a suspected cancer pathway in people presenting with symptoms in primary care. So, they agreed to accept the age-specific reference range. In the current surveillance review, we did not identify any new evidence in the area to warrant an update of current guideline recommendations. We recognise the issues with the recommendation, and we will aim to address them.

			Please note that we have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.'
University Hospitals Leicester NHS Trust	No	No comment	Thank you for your response.
University of Exeter	Yes	Gender differences in certain cancer types in terms of delayed diagnosis and survival outcomes warrant consideration to inform guidance. For example, women experience greater delay in the diagnosis of bladder cancer compared to men. Woman will also be more likely to develop certain cancers (i.e. lung, bladder) compared to men in the coming years due to demographic and lifestyle changes, such as smoking and obesity rates, which may need to be factored into clinical assessment and guidance.	Thank you for your response and the information provided. We have carefully considered your comments. Please see the detailed response below: In the introduction of the original guideline, it was documented that there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The committee of the original guideline actively sought exceptions to this in the evidence searches, finding only age and smoking (lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that overweight and obesity affected the predictive power of symptoms for different cancers. In this surveillance review, we did not identify any new evidence either. We will note your comment as an area of interest so it will also be considered in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the

			guideline at this time. For further information, please see the surveillance report.
The Binding Site Group Limited	No	No comment	Thank you for your response.
Royal College of General Practitioners	No	No comment	Thank you for your response.
Accelerated Access Collaborative	No	No comment	Thank you for your response.
Breast Cancer Now	No	No comment	Thank you for your response.
British Association of Dermatologists	No	No comment	Thank you for your response.
Cancer Research UK	No	No comment	Thank you for your response.
Greater Manchester Health and Social Care Partnership	No	No comment	Thank you for your response.

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NHS England and NHS Improvement	Yes	The National Cancer Programme has received feedback from charity partners that age thresholds can restrict access for younger patients. NICE could consider the inclusion of age thresholds in NG12 as a surveillance item, focusing on the potential need for safety netting to ensure that patients who fall below age thresholds but who are still at risk of cancer receive appropriate referrals. (LM)	Thank you for your response and letting us know that charities are concerned about the impact that the age thresholds used in some of the recommendations could have on restricting the access for a suspected cancer pathway referral in younger patients. In the original guideline, the age thresholds were derived from the evidence on positive predictive values (PPVs). If there was no mention of younger age groups, it was because there was no evidence of a PPV high enough to warrant action in this population (for example, haematuria in people <45 for bladder or renal cancer). In the current surveillance review, we did not identify new relevant evidence to update the recommendations at this time. We will note the age thresholds in younger patients as an area of interest for future surveillance reviews.
Novartis Pharmaceuticals (UK)	No	None	Thank you for your response.
Pancreatic Cancer UK	Yes	We believe that NICE should remove 'the one size fits all' approach and be less restrictive for hard to diagnose and hard to treat cancer such as less survivable cancers, including pancreatic cancer. We acknowledge the difficulty in diagnosing cancers with vague and non-specific symptoms, but given that less survivable cancers claim around half of all common cancer deaths, it is important to show flexibility and reduce threshold restrictions if we want to see improvements in survival.	Thank you for your response. We have carefully considered your comments. Please see the detailed response below: When the guideline was updated, the committee considered whether the PPV threshold should be varied in recognition of the fact that some cancers have a poorer prognosis than others. They agreed to keep the same PVV threshold for suspected cancer referral in all type of cancers in adults. They

			considered that 'for many of the cancers with poorer prognosis, there is neither clinical evidence nor agreement in the wider clinical community that earlier detection would improve prognosis, nor evidence that there are highly effective treatments that could be employed to improve prognosis in individual cases.' In this surveillance review, we did not identify any relevant evidence in the area. We will note your comment, so it will also be considered as an area of interest in the next surveillance review of the guideline. We have considered all stakeholder feedback in detail and retain our proposal to not update the guideline at this time. For further information, please see the surveillance report.
Prostate Cancer UK	No	No comment	Thank you for your response.
Royal College of Paediatrics and Child Health	No	No comment	Thank you for your response.
Target Ovarian Cancer	No comment	No comment	Thank you for your response.
Teenage Cancer Trust	No	No comment	Thank you for your response.

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