National Institute for Health and Care Excellence

Suspected cancer (update)
Guideline Consultation Table
20 November 2014 – 9 January 2015

ID	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
1	Action Against Heartburn	1	Full	60		*(p50-63)* Oesophageal cancer is the sixth most common cause of cancer death in the UK (2011). 70% of the cases relate to adenocarcinoma, the fastest growing tumour in the Western world. The UK has the highest incidence of oesophageal adenocarcinoma in the world. Unusually, oesophageal adenocarcinoma has a precursor condition, Barrett's Oesophagus. Dysplasia within Barrett's Oesophagus can be treated by radio frequency ablation, making opportunities for *preventing* cancer. 71% of oesophageal cancer diagnoses presenting from digestion symptoms (eg reflux/GORD) are treated with curative intent; contrasted with only 49% presenting with dysphagia, a classic symptom indicating later stages when the tumour may have grown two-thirds around the circumference of the oesophagus. Early diagnosis of oesophageal cancer makes a difference to outcomes (75-87% 1 –year survival at early stage; 20-21% at late stage). The Government are launching a *Be Clear on Cancer* campaign for OG cancer on 26 January 2015 based on persistent heartburn, a risk factor for Barrett's Oesophagus.	Thank you for this information. Thank you for this information. Thank you for this information.

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						Planning meetings involving surgeons and others involved in the campaign have been dismayed at the prospect of guidance conflicting with CG184 on Dyspepsia & Gastro Oesophageal Reflux Disease (GORD). The recently revised NICE guidelines CG184 on Dyspepsia and GORD deal with Barrett's Oesophagus and referral for endoscopy, have removed the age criterion and stated the significance of unresolved Gastro Oesophageal Reflux Disease (GORD) so the two sets of NICE Guidelines need to be consistent to maintain credibility and reduce confusion. Therefore there should be more overt references to the significance of diagnosing, monitoring and treating Barrett's Oesophagus as a precursor condition in these guidelines. **Therefore the age and gender criterion for referral for endoscopy for unresolved persistent heartburn should be removed and a cross-reference inserted to Guidelines on CG184 Dyspepsia & GORD because of the relevance for cancer early diagnosis represented by Barrett's Oesophagus. This will ensure that two sets of NICE guidelines are not in conflict with each other.**	CG184 states that this guideline should be referred to when a person presents with symptoms that could be caused by cancer. Comparison of the recommendations in the two documents, does not demonstrate any incompatibility. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
2	Action Against Heartburn	2	Full	54	Table 10	Amongst others, the well-regarded Lagergren study pointed out the link between symptomatic gastro-oesophageal reflux and oesophageal adenocarcinoma. N Engl J Med. 1999 Mar 18;340(11):825-31. http://www.ncbi.nlm.nih.gov/pubmed/10080844	Thank you for providing these references. The suggested papers were not included as they did not meet our pre-specified inclusion criteria, that is, they were not conducted in an unselected population presenting to primary care with symptoms.

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						See also: *Guidelines on the Diagnosis and Management of Barrett's Oesophagus* Fitzgerald RC, di Pietro M, Ragunath K et al**.** http://www.bsg.org.uk/clinical-guidelines/oesophageal/guidelines-on-the-diagnosis-and-management-of-barrett-s-oesophagus.html Lagergren J, Lagergren P. *Oesophageal Cancer – Clinical Review*. BMJ. 2010; 341. O'Doherty MG, Freedman ND, Hollenbeck AR, Schatzkin A, Abnet CC. *A prospective cohort study of obesity and risk of oesophageal and gastric adenocarcinoma in the NIH–AARP Diet and Health Study*. *Gut* 2011;10:1136 A paper by Bhat SK and others concludes that prior identification of Barrett's Oesophagus is associated with an improvement in survival of patients with oesophageal adenocarcinoma . http://gut.bmj.com/content/early/2014/04/03/gutjnl-2013-305506.abstract	Moreover, as we are developing an evidence-based guideline, we do not routinely use other guidelines unless they present original data that meets the inclusion criteria for consideration in this guideline.
3	Action Against Heartburn	3	Full	60	14	*(Section 8.1)* Oesophageal adenocarcinoma can affect people younger than 55 years. 18% of patients diagnosed with Barrett's Oesophagus were 50 years or younger in *Are newly diagnosed columnar-lined oesophagus patients getting younger?* Christine Wall et al *European Journal of Gastroenterology & Hepatology: October 2009 - Volume 21 - Issue 10 - pp 1127-1131* We therefore need to be able to refer patients with unresolved persistent heartburn for endoscopy	Thank you for providing these references. Surveillance in Barrett's Oesophagus is outside the scope of this guideline

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						regardless of age (but this may not be an immediate and urgent investigation for a tumour)	
4	Action Against Heartburn	4	NICE	2		The categories need to be extended to include a category for 'Heartburn and non-heartburn dyspepsia'	The recommendations made are only for dyspepsia with weight loss and make no reference to heartburn. Therefore we do not think this change would be helpful.
5	Action Against Heartburn	5	NICE	61 67	1.2.1	The comments at point number 3 apply	Thank you for providing these references. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
6	Action Against Heartburn	6	NICE	61 68	1.2.3	The comments at point number 3 apply	Thank you for providing these references. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
184	Action on Bladder Cancer	1	NICE	180 39	1.6.4 1.6.7	Not investigating visible haematuria in patients less than 45 years old will result in significant pathology including bladder cancer being missed. All the studies examining haematuria clinics demonstrate that cancers (and other significant pathology) are found in patients with visible haematuria irrespective of age. This recommendation appears to contradict the information from NHS England in their 'blood in pee' campaign'. We would like to see this addressed and it is our view that the guidance should state that all patients with un explained visible haematuria require urgent referral.	The age thresholds in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the younger age groups you mention. In the case of a patient with visible haematuria who was under 45 we would expect primary care clinicians to use their clinical judgement when applying this recommendation. People with persistent symptoms would be covered by the recommendations made on safety netting.
185	Action on Bladder Cancer	2	NICE	180 38	1.6.5	Linking dysuria with non-visible haematuria is helpful. However we are concerned that this will exclude patients with non-visible haematuria and other 'filling' lower urinary tract symptoms. Patients may present with non-visible haematuria, urinary frequency, urgency or pelvic pain. We would like to	The available primary care evidence did not support making a recommendation for non-visible haematuria in combination with these symptoms. We would expect primary care clinicians to apply their clinical judgement in such cases.

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						see the recommendation expanded to 'dysuria and or severe filling lower urinary tract symptoms'.	
186	Action on Bladder Cancer	3	NICE	180 39	1.6.5	The inclusion of a raised white cell count to determine who should be referred along a cancer pathway with nVH appears an unusual inclusion as this is not routinely used in most urological departments. We would be interested to know the evidence base for this.	The primary care evidence showed that the symptom combination of raised white blood cell count and non-visible haematuria had a PPV of 3.9% for bladder cancer (Price 2014). This is documented in the evidence section on page 177 of the full guideline.
187	Action on Bladder Cancer	4	NICE	180 39	1.6.5	Investigating non-visible haematuria represents a significant burden to the NHS and we welcome the re-evaluation of the referral guidance. We welcome the change of not referring asymptomatic non-visible haematuria <60 yo via the cancer 2ww. This would reduce the numbers referred to the rapid access haematuria service. However this will inevitably miss a few cancers. BAUS have previously looked at this in some detail and provide a succinct and clear algorithm for referring patients with non-visible haematuria based upon age, presence of lower urinary tract symptoms and persistence. We acknowledge that linking non-visible haematuria with dysuria is a good step but feel that a broader categorisation of urinary symptoms to include severe frequency and urgency would reduce the number of missed cancers.	Thank you Thank you It is not part of NICE methodology to cross reference information from other organisations in their guidelines. There was insufficient primary care evidence to add qualifying terms to urinary symptoms. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. People with persistent symptoms would be covered by the recommendations made on safety netting.
188	Action on	5	NICE	180	General	The link between smoking and bladder cancer is	We have documented in the introduction,

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	Bladder Cancer			General		very strong and not universally known. As has been done for lung cancer in the document we would like to see reference made to this link. Patients who are heavy smokers with new onset of visible haematuria, filling lower urinary tract symptoms or significant persistent non-visible haematuria should be fast tracked for investigation along a cancer pathway.	there are very few instances where risk factors affect the predictive power of symptoms sufficiently to allow different recommendations to be made for people with the same symptoms. The GDG 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 smoking affected the predictive power of symptoms for bladder cancer.
189	Action on Bladder Cancer	6	NICE	180 General	1.6.5 General	Most referral for non-visible haematuria are actually for dipstick proven haematuria. The document should use the opportunity to state what represent significant non-visible haematuria eg 1 plus on dipstick or >10 RBC / microliter.	The research underpinning the non-visible haematuria recommendations did not specify the level of haematuria. This will be a scenario where the clinician will be expected to use their judgement.
247	Association for Clinical Biochemistry and Laboratory Medicine	1	Full	131	1.3.6 Recommendation	The recommendation says to offer faecal occult blood testing to assess CRC risk in patients without rectal bleeding who have abdominal pain, weight loss and <60y with anaemia. FOB testing, outside the setting of formal CRC screening programmes has been withdrawn by clinical biochemistry laboratories in many UK regions because of its perceived limited predictive value and the fact that symptomatic patients will require endoscopy in any case.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used

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							alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
248	Association for Clinical Biochemistry and Laboratory Medicine	2	Full	258	1.10.5 Recommendation	The Recommendation says to consider very urgent protein electrophoresis [within 48h]. Clarify that the '48h' refers to the interval between the clinical consultation and venepuncture rather than the interval between venepuncture and the serum protein electrophoresis result being available. [The laboratory turnaround time for serum protein electrophoresis may be in excess of 48h]	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
249	Association for Clinical Biochemistry and Laboratory Medicine	3	Full	258	Recommendation	For patients presenting with clinical symptoms suggestive of myeloma, failure to test the urine for Bence Jones protein [in addition to serum protein electrophoresis] might result in missing patients with light chain myeloma [10-15% of total myeloma patients] which may be less easily detected by serum protein electrophoresis.	We have included urine Bence Jones protein in the recommendation.
127	Association of	1	Full	141	11	*(lines 11-12)* It should refer to diagnosis being made by mammography and core biopsy not fine	Thank you. We have amended the introduction where it refers to core

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	Breast Surgery					needle aspiration	biopsy.
171	Association of British Neurologists	1	NICE	240 General	1.9.1 General	We will limit our comments to the recommendations made for adults and some points in the commentary that followed. Recommendation *Consider an urgent direct access MRI scan of the brain (within 2 weeks) to assess for brain or central nervous system cancer in adults with progressive, sub-acute loss of central nervous system function.* Commentary 'The GDG considered recommending an urgent scan instead of a referral to neurology would result in a faster diagnostic process for adults with a tumour because they will be referred straight to a neurosurgeon after the scan instead of first to neurology, then for a scan and then to neurosurgery'. The GDG noted that the recommendation is likely to result in an increase in MRI scanning, a decrease in out-patient appointments and a decrease in GP consultations (due to patients receiving an earlier answer about symptoms and reassurance that they do not have brain cancer, which means they will not re-attend). The GDG agreed that this would not constitute an increase in cost, and may even constitute a small decrease in costs'. **Comments from the Association of British Neurologists:**	Thank you. We will respond to your detailed comments below.

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						For the following reasons, recommending an urgent scan in place of an urgent referral to neurology would result in an overall **increase in costs** and a **delayed diagnosis** for many patients with serious neurological disease. **1. Brain tumours are an uncommon cause of sub-acute progressive loss of neurological function.** The majority of patients with neurological dysfunction have other conditions, the rapid and efficient diagnosis of which requires an appropriate history, examination and targeted plan of investigation. The choice of investigation (eg; a scan of the brain or spine, or neurophysiological tests) requires neurological expertise that GPs would not claim to possess. An approach to progressive neurological impairment which results in indiscriminate MRI scanning of the brain, with the outcome of the vast majority of patients simply being told they do not have a brain tumour, will not help the many patients with other neurological diseases whose diagnosis will be delayed, will raise anxieties in patients with benign symptoms who would be reassured by an expert neurological opinion, and will overwhelm hard-pressed radiology services. An obvious example of a serious clinical error that would arise from implementing the proposed guideline is that patients with progressive leg weakness due to spinal cord compression (eg; from a tumour) would be sent for an MRI brain. **2. These recommendations fail to take into account the biology of brain tumours.** Most patients with brain tumours who develop	We agree that the patient would still need investigating but it is outside the scope of this guideline and we therefore cannot make any recommendations. A patient who is rapidly deteriorating would be managed using the clinical judgement of the primary care clinician.

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						progressive loss of function have high grade gliomas and will usually have deteriorated rapidly, requiring hospital admission before an outpatient scan can be performed. In support of this, research in 2004 showed that the median time to diagnostic scanning for patients with progressive subacute neurological function subsequently found to have a brain tumour was between 2-4 weeks (see J Neurol Neurosurg Psychiatry 2004;75(Suppl II):ii18–ii23). Link http://jnnp.bmj.com/content/75/suppl_2/ii18.full.pdf+html With the wider availability of CT and MRI, we suspect all would be scanned within 2 weeks currently. A guideline suggesting MRI scanning within 2 weeks therefore is unlikely to lead to an improvement in current practice. **3. The fact that the guideline does not recommend same day discussion or an urgent neurology referral where there is clinical concern is alarming.** Most patients with rapidly progressive neurological symptoms will continue to deteriorate considerably while waiting up to 2 weeks for a scan. These patients require an urgent neurology opinion, which the guidelines would actually delay. Most neurology units have rapid access clinics for patients with rapidly evolving problems, which can be accessed by GPs. The Guideline Development Group clearly found it difficult to come up with isolated clinical features on which to pin their referral guidelines. This reflects the heterogeneous and variable pattern of presentation of neurological disease. In doing so	Thank you for your comment. Recommendation 1.9.1 suggests a maximum of 2 weeks which can be seen as an improvement. As above, we would expect primary care clinicians to use clinical judgment. Recommendation 1.16.2 explicitly recommends discussion where there is doubt.

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						they have removed some potentially important symptoms such as rapidly progressive postural headache or papilloedema which would serve as red flags for GPs for significant neurological disease. A r**ecommendation from NICE endorsing the provision of acute neurological advice and assessment services would in our view achieve the stated aim of increasing the speed of diagnosis of brain tumours, provide a valuable service to GPs and benefit all patients with symptoms suggestive of neurological disease.** **4. This recommendation is very unlikely to achieve the stated aim of decreasing the number of outpatient consultations.** Headache, which has up to now accounted for the majority of direct referrals for imaging and subsequent incidental findings, has been removed as an indication for direct referral. However, any increase in the number of MRI scans requested by non-specialists, rather than reducing the traffic of patients to the outpatient clinic will in fact lead to an rise in the number of out-patient referrals to neurology. Incidental findings on MRI brain scans are common in the normal population. Once identified significant time and effort is required to confirm that such findings are indeed irrelevant to the patient's symptoms and to offer appropriate explanation and reassurance. **5. Patients with new onset suspected seizures shoudl already be referred for rapid assessment under the NICE epilepsy guidelines.** Seizures, rather than neurological impairment, are the more common presentation for	Thank you for your comment. We agree 'headache' has been the largest patient group seen by neurologists seen in this context. The absence of a recommendation in the new guideline for 'headache' would be expected to reduce referrals considerably Your comment about incidental findings on MRI leading to increased neurology activity should be viewed remembering this is a highly symptomatic population who have been recommended for MRI. Thus the benefits are likely to outweigh the harms. Thank you for this comment. The PPV for new onset seizures in primary care is lower than 3% therefore no recommendation was made in the context of cancer.

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						patients with lower grade gliomas, and the diagnostic pathway for these patients would not therefore be improved by the suggested guidelines.	
33	Association of Coloproctology of Great Britain & Ireland	1	Full	20	11	As an example at Heart of England Foundation Trust 460 new cases of bowel cancer per year. Using a ppv of 3% 15,333 patients would need to be seen each year. This would be a 3 fold increase on current numbers and completely overwhelm clinic and endoscopy resources	The majority of patients referred will have a PPV higher than 3%, which is a minimum figure, not an average figure. Therefore the expected number of referred patients will be lower than your estimate.
34	Association of Coloproctology of Great Britain & Ireland	2	Full	130	7	The preceding 20 or so pages have been an economical modelling of which is the best test to use to investigate a patient for bowel cancer. Much of this data is historical and ba enema examination has almost ceased. It does not help refine criteria of patients that need referral for lower GI investigations. The conclusions raise the question as to whether a GP should be performing FOB testing on symptomatic patients. The secondary care physician will always chose an endoscopy or CT.	The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling. The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used

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							alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
35	Association of Coloproctology of Great Britain & Ireland	3	Full	130	8	*(line 8-12)* The current clinic view is that a FoBT is not appropriate to investigate a change in bowel habit. Ba enema examination has almost ceased	The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to

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36	Association of Coloproctology of Great Britain & Ireland	4	Full	130	1.3.5 13	The lowering of threshold will result in more patients without cancer being put through potentially harmful tests. The criteria of wt loss and abdominal pain in the >40's will result in everyone with IBS being referred - probably every few years. Offering a PR is not very relevant for those with lower GI symptoms. It is relevant for ano rectal symptoms only. The data in this area is of poor quality and I note the comment that in no instances is the data of	The GDG considered this issue for the recommendations made on every cancer site and determined that an appropriate balance had been struck. This is documented in the Linking evidence to recommendations sections in the full guideline. We would expect primary care clinicians to exercise clinical judgement when applying these recommendations. We would expect primary care clinicians to exercise clinical judgement when applying these recommendations. Thank you we agree. We have made recommendations for further research to

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						high quality There are now 9 different symptom complexes suggesting a 2ww lower GI referral or FOB testing (increase from 5). This makes if far more confusing for GP's. Symptoms of bowel cancer are very vague and non specific. Time and money would be far better spent increasing uptake in the national screening FOB programme and rolling out the bowel scope project rather than lowering referral criteria. The matter of GP's offering FOB to low risk patient groups is worth further exploration. However caution is needed and I enclose a copy of an email from Prof Robert Steele who is an expert in this field: *It is entirely inappropriate to recommend using FOBT in this context without specifying a cut-off for the faecal haemoglobin concentration and the method for measuring it. In addition, although there is an increasing evidence base for using quantitative faecal immunochemical testing (FIT) for haemoglobin in the assessment of the symptomatic patient, the appropriate cut-off has yet to be determined, and may be dependent on age and gender in addition to the symptoms themselves. The way this guidance is worded suggests that a standard qualitative guaiac FOBT could be used to determine the cause of symptoms. This is dangerous, as we know that it will miss around 50% of cancers, in a screening setting at least.*	try to enrich the data in this field. The recommendations for colorectal cancer have been revised to make them simpler and easier to understand. Screening is outside the scope of this guideline. The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real

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							beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. The GDG chose not to stipulate the specifics for administering the test in the recommendation. They would expect people to refer to the manufactures instructions for its use as a diagnostic test.
457	Blackpool Teaching Hospitals NHS Foundation Trust	1	NICE	41 64	1.1.1	Lung & Pleural Cancers: What is the definition of haemoptysis? Is it one episode or recurrent over 'x' number of days?	It is not possible to add precise qualifying terms to haemoptysis as the evidence base did not allow us to do so.
458	Blackpool Teaching Hospitals NHS Foundation Trust	2	NICE	61 67	1.2	Oesophageal Cancer: Currently many of the dyspeptic patients are being referred to clinic for consultation and most of the direct access gastrosocopies are for dysphagia and/or dyspepsia with weight loss. The highlighted indication would easily increase the direct access OGD by at least 40-50/month. I suppose the evidence produced in the draft for this is not strong enough.	The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which

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							they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral.
459	Blackpool Teaching Hospitals NHS Foundation Trust	3	NICE	67 68	1.2.4	Pancreatic cancer: I suspect primary care is not well equipped to deal with interpretation of the CT results (if they do manage to get direct access CT pancreas/abdomen); although onus will be on requesting clinician to act on the results of the CT, it would end up radiologist trying to find a clinician urgently for further management and also numerous telephone/further urgent consultation referrals from GP for incidental and less familiar (to primary care physicians) CT findings.	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
460	Blackpool Teaching Hospitals NHS Foundation Trust	4	NICE	80 68	1.2.6	Stomach Cancer: The indications highlighted in red will again increase direct to test Gastrosocopies (crude approximation of 40-50/month). Majority of these can be dealt with by good clinical consultation. Also, I do not think offering direct access OGD will have much impact on these patients being subsequently referred for gastroenterology opinion.	The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are

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461	Blackpool Teaching Hospitals NHS Foundation Trust	5	NICE	86 69	1.2.12	Gall Bladder Cancer: Agree with recommendations	Thank you
462	Blackpool Teaching Hospitals NHS Foundation Trust	6	NICE	89	1.2.13	Liver Cancer: Agree with recommendations	Thank you
463	Blackpool Teaching Hospitals NHS Foundation Trust	7	NICE	130 70	1.3	Colorectal Cancer: Again we might see a significant increase in referrals for the highlighted indication, may be primary care will start requesting direct access sigmoidoscopy and colonoscopy. Many of the hospitals provide this service, and definitely this will increase the stress on already overstretched endoscopy service for fast track patients.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
464	Blackpool Teaching Hospitals NHS	8	NICE	General	General	General comments received raising concerns with regards to the increase in number of FT referrals when resources are already limited.	Any increased rate of referral to secondary care and consequent resource issues will be addressed by the tariff from NHS England. We recognise that there will be challenges in implementing this

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	Foundation Trust						guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
465	Blackpool Teaching Hospitals NHS Foundation Trust	9	NICE	General	General	Resource: The new Guidelines will potentially increase the number of FT referrals received into each Trust up to 50-100%. In turn, this will have an impact on all diagnostic services, in particular Gastroenterology and Radiology, where additional resources will be needed Cancer Teams/MDT Coordinators and MDT's will also be affected; additional resources and MDT	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable. We recognise that there will be challenges in implementing this guideline

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						planning / attendance time will need to be reviewed and possibly extended (which will also have a further impact on a Radiology)	but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
466	Blackpool Teaching Hospitals NHS Foundation Trust	10	NICE	General	General	In view of the potential increase in the number of 2ww referrals, if no additional resources are available to accommodate the increase, consideration should be given to lowering the National 85% CWT standard	Any increased rate of referral to secondary care and consequent resource issues will be addressed by the tariff from NHS England. National cancer targets are outside the remit of this guideline.
265	Bowel Cancer UK	1	NICE	General	General	Bowel Cancer UK welcomes the update to the guideline on the referral of suspected colorectal cancer. The timely referral of individuals who experience symptoms can lead to the early detection of polyps and tumours. This is essential to saving more lives from bowel cancer. Individuals diagnosed at the earliest stage of the disease are more responsive to treatment and have more chance of surviving than those diagnosed later. Nine out of ten people diagnosed at the earliest stage of the disease will survive for more than five years. We believe the guideline is a step in the right direction to seeing more timely referrals and more people diagnosed quickly with bowel cancer.	Thank you
266	Bowel Cancer UK	2	NICE	130 70	1.3.2	Bowel Cancer UK welcomes the increase in the level of haemoglobin concentration levels for women and men who present with unexplained iron-deficiency anaemia. However we would argue that any level of anaemia should be investigated in the presence of iron deficiency, as recommended by British Society of Gastroenterology guidelines for the management of iron deficiency anaemia. This is because the range used to define anaemia can vary between pathology laboratories. In	The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion. BSG guidelines cover more than just cancer and so their recommendations may not apply in this instance.

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						practice this is <11.5 for women and 13 for men. It would be unreasonable not to refer a patient with evidence of iron deficiency anaemia because their haemoglobin level was 11.2 and not less than 11.0. Therefore the cut-off should be defined by the laboratory conducting the test.	
267	Bowel Cancer UK	3	NICE	130 70	1.3.2	The guideline should make clear whether the haemoglobin level for women is irrespective of menstruation.	Menstruation was not examined in any of the anaemia studies used by the GDG. Therefore we could not make specific recommendations on this. However we would expect primary care clinicians to use their clinical judgement when using these recommendations.
268	Bowel Cancer UK	4	NICE	130 70	1.3.4	Bowel Cancer UK objects to the change in language from "should refer" to "consider a referral" for patients who present with rectal or abdominal mass. We believe this change is a retrograde step and that those who present with rectal or abdominal mass should be referred for further testing.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
269	Bowel Cancer UK	5	NICE	130 70	1.3.6	The guideline suggests that a standard guaiac faecal occult blood test should be used as a diagnostic test in symptomatic patients who present with either abdominal pain, weight loss or those aged under 60 who have a change in bowel habit or iron-deficiency anaemia, without rectal bleeding. Bowel Cancer UK believes that this recommendation on the use of occult blood testing in these symptomatic patients is highly inappropriate and the use of FOBt in this setting should not be encouraged.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to

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							recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
270	Bowel Cancer UK	6	Full	119	13	*(p119-120, lines 13-17, 1-5)* The evidence presented within the guideline does not provide a sound basis upon which to recommend the use of FOBt in the symptomatic patients described by NICE in the guideline. The false-negativity rate quoted in the evidence statement, beginning on page 119, is very high for symptomatic patients. We do not believe that the evidence is strong enough to recommend FOBt in symptomatic patients. Furthermore in a screening setting evidence demonstrates that this test will miss approximately 50 per cent of cancers, compared to a 95 per cent detection rate for colonoscopy. It is therefore entirely inappropriate to recommend the use of FOBt in symptomatic patients. We are very concerned that this recommendation could lead to	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to

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						patients being referred for a poor quality test and could lengthen the time to receiving a definitive diagnosis. It is of upmost importance that patients are referred and diagnosed as quickly as possible.	recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
271	Bowel Cancer UK	7	Full	119	13	Furthermore there is an increasing evidence base for use of quantitative faecal immunochemical testing (FIT) in the assessment of symptomatic patients, although the appropriate cut-off has yet to be determine. We believe that FOBt should not be recommended until an evaluation of the sensitivity of FIT has been completed and this should be considered in the next review of the NICE guideline.	There was insufficient evidence on FIT to make a recommendation for use.
272	Bowel Cancer UK	8	NICE	130 70	1.3.6	Patients with iron deficiency anaemia should not be offered occult blood testing. They should be properly and appropriately investigated. Occult blood testing should be reserved exclusively for screening purposes in asymptomatic patients and not for symptomatic patients.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group

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							receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
273	Bowel Cancer UK	9	NICE	130 70	1.3.6	We are also concerned that the recommendation on the use of FOBt may also mean that alternative innovative pathways, for example Straight To Test (STT), are not used. Pathways such as STT would provide patients with a definitive timely diagnosis.	Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer

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							between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
274	Bowel Cancer UK	10	NICE	130 71	1.3.8	Bowel Cancer UK welcomes the inclusion of recommendations for the referral of patients with symptoms under the age of 50. We believe the recommendation to "consider a referral" for this population to be appropriate and reasonable. Bowel Cancer UK has been campaigning on this issue for some time. Our report "Never too Young" highlighted the issue in detail.	Thank you
275	Bowel Cancer UK	11	NICE	130 71	1.3.8	We strongly recommend that consideration for the referral of symptomatic patients under the age of 50 should also be made if they have a strong risk	We have documented in the introduction, there are very few instances where risk factors allow different recommendations

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						of colorectal cancer, for example, if the patient has one symptom as listed in the guideline and one of the following risk factors: • IBD with extensive colitis for over 10 years • Previous cancer or multiple polyps • Known inherited syndrome, e.g. Lynch syndrome • Family history of colorectal cancer	to be made for people with the same symptoms. The GDG 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 IBD, previous cancer, multiple polyps, known inherited syndromes or family history affected the predictive power of symptoms for colorectal cancer.
276	Bowel Cancer UK	13	Full	129	14-15	We are greatly concerned that the guideline appears to advocate the continued use of barium enema as the next "cost-effective" test. There is good evidence to suggest that barium enema is an inferior diagnostic test, with a high rate of missed cancer. The NICE Clinical Guideline on the diagnosis and management of colorectal cancer is clear: a colonoscopy or flexible sigmoidoscopy should be offered before a barium enema. It also states that CT colonography should be considered as the alternative to colonoscopy and flexible sigmoidoscopy before barium enema.	Barium enema was not recommended by the GDG and so has not been advocated. The section of text to which you refer does not constitute an endorsement of barium enema. It is merely a statement of the modelled results. The diagnostic accuracy data used to inform the barium enema arm was recognised to be of low quality and so the result should not be viewed outside of this context. Furthermore, even in this scenario, barium enema was not the preferred strategy (FOBT was still the test preferred in cost-effectiveness terms).
489	Breakthrough Breast Cancer and Breast Cancer	1	Full	141 General	General	Breakthrough Breast Cancer and Breast Cancer Campaign are dedicated to improving and saving lives through breast cancer prevention, early diagnosis, more targeted treatments and better services for everyone affected by breast cancer. We welcome the opportunity to comment on NICE's draft clinical guidelines for suspected	Thank you for this information.

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	Campaign					cancer. We welcome the change in the structure of the referral guidelines to focus on symptom clusters rather than individual conditions. This will better reflect how patients present in primary care and how a primary care practitioner may approach the information. However, the proposed updates represent huge changes to the existing referral guidelines for breast cancer, and we believe that considerably more thought and explanation are needed before changes of this magnitude are implemented. We will outline our concerns about specific signs and symptoms, but the scale of these changes is represented visually below, where green boxes show breast cancer signs and symptoms that have been added and red boxes show signs and symptoms will no longer be covered by the proposed guidelines:  Due to the scale and potential impact of these changes, we would like to ask for further consultation on the issues that we raise below	Thank you We will respond with your specific comments as you detail them below. NICE does not plan to run a second consultation on this guideline.

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						before a final version of these guidelines is produced.	
490	Breakthrough Breast Cancer and Breast Cancer Campaign	2	NICE	147 26	1.4.1	The proposed guidelines have replaced the multiple references to lumps in the breast in the existing guidelines with one symptom of an unexplained lump in those aged 30 years and older. This is a more straightforward approach that underlines the importance of lumps as a symptom of breast cancer.	Thank you
491	Breakthrough Breast Cancer and Breast Cancer Campaign	3	NICE	147 General	General	We are very concerned by the removal of any references to women under 30, regardless of their symptoms or clinical and family history. This gives an impression that breast cancer does not occur in women under 30 and therefore we do not support this revision. It is essential to highlight that while breast cancer is uncommon in women under the age of 30, it does still occur. Research has shown that younger women with cancer symptoms are more likely to experience repeated GP appointments before being referred for specialist diagnosis and therefore attention must be paid to the possibility of breast cancer in younger women, especially in those with a family history of the disease. Reference: Lyratzopoulos G, Neal RD, Barbiere JM, Rubin GP, Abel GA. (2012). Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *The Lancet Oncology*, 13(4), pp. 353-365.	Thank you for providing this reference. A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made
492	Breakthrough	4	NICE	147 General	General	We are very concerned by the removal of any references to family history and previous breast	Thank you for providing these references. We have documented in the introduction,

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	Breast Cancer and Breast Cancer Campaign					cancer as risk factors for breast cancer. Of all women who develop breast cancer, about one in five has a significant family history of the disease. If there is a history of breast cancer or some other cancers (especially ovarian cancer) this may increase the patient's risk of developing breast cancer, and at a younger age. Similarly, cohort studies show that breast cancer survivors have between two and five times increased risk of developing a second primary breast cancer. Excluding 'second cancers' found within two years of the primary, which may actually be spread from the primary tumour, the risk of second primary breast cancer remains significantly elevated for 20 years from the primary diagnosis. Primary care practitioners should therefore be aware of the relevance of a family and personal history of cancer when assessing potential symptoms of breast cancer. References: Soerjomataram I, Louwman WJ, Lemmens VEPP, et al. (2005). Risks of second primary breast and urogenital cancer following female breast cancer in the south of The Netherlands, 1972–2001. *European Journal of Cancer*, 41(15), pp. 2331-37. Rubino C, Arriagada R, Delaloge S, et al. (2009). Relation of risk of contralateral breast cancer to the interval since the first primary tumour. *British Journal of Cancer*, 102(1), pp. 213-19. Dong C, Hemminki K. (2001). Second primary neoplasms in 633,964 cancer patients in Sweden, 1958–1996. *International Journal of Cancer*, 93(2),	there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG 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 or previous breast cancer affected the predictive power of symptoms for breast cancer. The GDG considered that the symptom profile carried the largest expression of risk irrespective of personal or family history, or other risk factors.

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						pp.155-61.	
493	Breakthrough Breast Cancer and Breast Cancer Campaign	5	NICE	147 37		The proposed guidelines make no specific references to several non-lump skin and surface symptoms (eczema, skin and nipple changes in women under the age of 50 years) as risk factors. It instead includes other changes of concern in one nipple only as a symptom. We are very concerned by these proposals and believe they need revising. What has been proposed is a very different approach to the explicit list of separate non-lump symptoms in both the current guidelines and the advice given by health information providers such as cancer charities. There are many different signs and symptoms; for example, Breakthrough and Campaign both list the following non-lump symptoms of breast cancer: change in size or shape, change in skin texture such as puckering or dimpling of the skin of the breast, change in colour such as the breast looking red or inflamed, rash or crusting of the nipple or surrounding area, bilateral discharge. Clear guidelines on non-lump signs and symptoms are particularly important because, while there is generally high awareness of a breast lump as a possible breast cancer indicator, awareness of non-lump symptoms is lower, and can lead to delays in presentation. In September 2014 Breakthrough commissioned a nationally representative online survey of 1,082 women across GB to ask them about breast cancer symptoms and screening. We found that 85% of women were spontaneously aware that lump(s) in the breast are a symptom compared with 24% – change in the size or shape of the breast, 34% – changes to the skin, 21% – changes to the	A new recommendation has been added to consider a suspected cancer pathway referral for breast cancer in people who have skin changes suggestive of breast cancer. The GDG chose not to describe skin changes with any further precision, because in the absence of evidence it was not possible to create a complete list.

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						appearance of the nipple. Similarly, when choosing from a list of potential symptoms women's knowledge of non-lump signs was also lower: 93% were aware that lump(s) in the breast are a sign, compared with 77% – change in the size or shape of the breast, 69% – changes to the skin, 82% – changes to the appearance of the nipple. The risk of breast cancer increases with age, and for most women getting older is their biggest risk factor for breast cancer. However, surveys have repeatedly shown that older women are often unaware of their increased risk of developing breast cancer. As with younger women they tend not to be aware of non-lump signs and symptoms of breast cancer, but they are more likely to delay seeking help with breast cancer symptoms than younger women. It is therefore important that primary care practitioners are particularly alert to potential non-lump signs or symptoms in older patients. Clinicians are likely to approach non-lump symptoms differently. The National Audit of Cancer Diagnosis in Primary Care in 2009/10 looked at the primary care pathway to cancer diagnosis. Those whose primary presenting symptom was a lump in the breast were more likely to be referred through the two week urgent referral pathway than those presenting with non-lump symptoms e.g. 84 percent of those presenting primarily with lump compared with 73 percent with a change in breast appearance and 67 percent with nipple discharge. The new symptom of changes of concern is very vague and likely to be unclear to clinicians. We	The Linking Evidence to Recommendations section in the full

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						believe that listing specific symptoms (as now) is likely to be much more helpful to clinicians and we would like to see considerably more information on what is, and is not, covered by this term. More specifically, we are concerned about the decision to only recommended urgent referral following changes to the nipple in the over 50s for two reasons: 1) Although the guideline presents evidence for why these symptoms are only being applied to women over 50, it depends on an adjusted guess about the cut-off age for unilateral nipple symptoms based on evidence that did not distinguish between unilateral and bilateral symptoms. Given the limited evidence currently available we believe a lower age should be considered.	guideline documents the GDG's reasons for including the symptom 'changes of concern'. This is as follows: 'The GDG noted, based on their clinical experience, that other nipple symptoms, such as Paget's disease, can be highly predictive of breast cancer. The GDG therefore decided to recommend a suspected cancer pathway referral for 'other nipple change'. However, in order to make a comprehensive and user-friendly recommendation on nipple symptoms, the GDG decided to include 'other changes of concern' in the recommendation already made on nipple symptoms in people aged 50 years or older.' This extract from the Linking Evidence to Recommendations section in the full guideline documents the GDGs decisions around making this recommendation: 'The GDG also noted, based on the evidence, that nipple discharge or nipple retraction are symptoms of breast cancer with positive predictive values that increase with age to the extent that they exceed 3% in women aged 70 years or older and 60 years or older, respectively. However, the GDG also noted that the included studies did not distinguish between unilateral and bilateral breast symptoms and therefore judged that the reported symptoms are most likely to be a mix of unilateral and bilateral symptoms. Moreover, the GDG noted,

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							based on their clinical experience that unilateral symptoms carry a higher risk of breast cancer than bilateral symptoms because breast cancer is usually unilateral. The GDG therefore considered that the positive predictive values presented in the evidence are likely to be higher for unilateral symptoms. The GDG therefore decided to recommend a suspected cancer pathway referral for unilateral nipple discharge or retraction in people aged 50 years or older.' This situation would be covered by the recommendations made on safety netting.
						2) Given that nipple changes are the only symptom given a higher age limit than 30, we would like the guidelines to state that women under the age of 50 who present with nipple changes should be informed that if the symptoms recur later in life that they re-contact their GP. We are concerned that younger women could be reassured that nipple changes are not something to worry about, and may ignore them later in life. Finally, the draft guideline now does not include the recommendation to "encourage all patients, including women over 50 years old, to be breast aware". We do not support this revision; early detection saves lives, so the guideline should not	Raising awareness amongst the public of signs and symptoms is outside the scope of this guideline. However a lay version of the recommendations called 'Information for the public' is produced alongside the

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						miss the opportunity to reinforce breast awareness as a key early detection measure. References: Linsell L, Forbes LJL, Kapari M, Burgess C, Omar L, Tucker L and Ramirez AJ. (2009). A randomised controlled trial of an intervention to promote early presentation of breast cancer in older women: effect on breast cancer awareness. *British Journal of Cancer*, 101 Supplement 2, S40-48. Linsell L, Burgess CC and Ramirez AJ. (2008). Breast cancer awareness among older women. *British Journal of Cancer*, 99, pp. 1221-1225. Macleod U, Mitchell ED, Burgess C, Macdonald S and Ramirez AJ. (2009). Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers, *British Journal of Cancer*, 101, S92-S101. Moser K, Patnick J, Beral V. (2007). Do women know that the risk of breast cancer increases with age?. *British Journal of General Practice*, 57, pp.404-406.	guideline. Thank you for providing these references.
494	Breakthrough Breast Cancer and Breast Cancer Campaign	6	Full	149		All of the recommendations on symptoms of breast cancer in women have been extended to men. We believe this is appropriate because while the condition is rare in men (around 300 men are diagnosed with breast cancer every year in the UK), cases do occur and primary care practitioners should be made aware of this. It might therefore be preferable for the guideline to explicitly refer to 'men and women' rather than 'people', as this could raise more awareness in primary care about male breast cancer.	We were advised by NICE that 'people' was the correct term to use in this instance as it was consistent with terminology used in other NICE guidance.

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495	Breakthrough Breast Cancer and Breast Cancer Campaign	7	NICE	147 26	1.4.3	We are pleased that the proposed guidelines now include a lump in the axilla as a symptom of breast cancer. Axillary lumps or swelling can occur in the absence of clinical breast abnormality as breast cancer that has spread to lymph nodes may result in swelling above or below the collar bone, and it is a symptom of possible breast cancer that should indicate referral. This is in line with the information about breast cancer symptoms given by the NHS, Royal Marsden and cancer charities. Reference: Willett AM, Michell MJ, Lee MJR. (Eds) (Nov 2010). Best practice diagnostic guidelines for patients presenting with breast symptoms.	Thank you
496	Breakthrough Breast Cancer and Breast Cancer Campaign	8	NICE	366 44	1.13.4	The proposed guidelines include deep vein thrombosis (DVT) as a possible indicator of breast cancer. This is not widely referenced as a possible symptom in health information at the moment. The criterion that the Guideline Development Group used for including a symptom was that it must have a positive predictive value (PPV) for the disease of greater than 3 percent; although the PPV of DVT for cancer was 3.49 percent according to the 1 study referenced, for breast cancer it was only 0.93 percent. Including DVT as a possible symptom of breast cancer is therefore inconsistent with the approach taken for other symptoms of breast cancer.	DVT only has a low PPV when single cancers are considered. Cumulatively, the PPV for cancer as a whole exceeds 3%. Breast cancer is only a component of this 3 % so we do not consider there is any inconsistency.
497	Breakthrough Breast Cancer and Breast Cancer Campaig	9	NICE	29 86		Very little information is provided around safety netting procedures. It is essential that this section of the guideline is given careful further consideration to avoid potential delays in diagnosing some possible cancer cases. These guidelines are developed to best understand the potential implications for patients presenting with any signs and symptoms of breast cancer, and it is	It is not appropriate to recommend what should happen at the review because the review should be dependent on the needs, preferences and symptoms of the individual patient.

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	n					vital that all primary care practitioners have the necessary information to be confident in knowing when, and when not, to refer.	
498	Breakthrough Breast Cancer and Breast Cancer Campaign	10	NICE	11		*(p11-12)* We are aware that the following comment is not a breast cancer referral issue but we have highlighted it for consideration by relevant pelvic symptom experts. We feel that the guideline could be strengthened here by clarifying the relevance of abdominal symptoms to previous and on-going cancer treatment. For example, if a woman presents with a pelvic or abdominal mass or pain, or abnormal vaginal bleeding and is being treated with tamoxifen for breast cancer, a doctor should be particularly mindful of the need to rule out endometrial cancer or uterine sarcoma which are rare but known side-effects of this treatment. We would also like the guidelines to consider whether suspected large fibroids should be routinely further tested in these patients, to rule out the possibility of uterine sarcoma. For example, we are aware of a case of a woman being treated for breast cancer with tamoxifen, where a very large mass assumed to be a uterine fibroid was later found to be advanced stage uterine sarcoma. The guideline might be amended along the following lines: 'Refer the woman urgently if physical examination identifies ascites and/or a pelvic or abdominal mass, especially if previous/on-going cancer treatment may have increased the risk of cancer in the pelvic region.' Under 'possible cancer', 'endometrial' and	Thank you In the introduction we have documented that, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that treatment with tamoxifen affected the predictive power of symptoms for ovarian cancer. The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.

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						'uterine' would also need to be added to 'ovarian'.	
610	Breast Cancer Care	1	NICE	General	General	We welcome the change in structure to a focus on symptoms in addition to structuring by cancer type (as in the previous guideline). We agree that this will aid primary healthcare professionals in recognising suspected cancer symptoms.	Thank you
611	Breast Cancer Care	2	NICE	147 71	1.4	*(p71-72)* We welcome the use of the term 'people' rather than 'women' in the breast cancer recommendations, as around 350 men are diagnosed with breast cancer each year. However, we would suggest that at the outset of this section there is a sentence that specifically highlights that men can get breast cancer, as generally the disease is still viewed as one that only affects women.	We have amended the background to strengthen this.
612	Breast Cancer Care	3	NICE	147 71	1.4	*(p71-72)* As the full guideline points out, breast cancer in people under 30 years of age is extremely rare. However, we are concerned that the draft updated guideline may indirectly imply that people under 30 years of age do not get breast cancer. Although it is rare, it is important that those under 30 are still referred promptly. During 2009-2011, the average number of breast cancer cases per year in those aged up to 30 was 219 (Cancer Research UK http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/incidence/#age, January 2015). NHS messaging (e.g. NHS Choices website http://www.nhs.uk/Livewell/Breastcancer/Pages/Breastcancersymptoms.aspx [Accessed January 2015]) currently encourages people to talk to their GP if they have any worrying breast changes, regardless of age. The draft recommendations put	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.

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						forward are inconsistent with this message. The previous guideline recommended that in women aged under 30: • *"with lump that enlarges, or* • *with a lump that has other features associated with cancer (fixed and hard), or* • *in whom there are other reasons for concern such as family history* *an urgent referral should be made"* We are concerned that there is no direction in the draft updated guideline for a primary healthcare professional who is faced with a patient under 30 who presents with these symptoms. Some direction about this is needed.	
613	Breast Cancer Care	4	Full	148	Whole page	As in our comment above, while we appreciate that breast cancer is extremely rare in people under 30, we are concerned by the GDG's decision to therefore only recommend that *'any breast lump with or without pain' should prompt a suspected cancer pathway referral in a person aged 30 years or older'.*	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. A new recommendation has also been added to consider a suspected cancer pathway referral for breast cancer in people who have skin changes suggestive of breast cancer. The GDG had already made a recommendation that an unexplained lump in the axilla should prompt a suspected cancer pathway referral.

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							In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
614	Breast Cancer Care	5	NICE	147 71	1.4.2	We understand the GDG's wish to balance the importance of *'recommending the 'right symptoms' ,in order to minimise the number of people without breast cancer who get inappropriately referred whilst maximising the number of people with breast cancer who get appropriately referred'* (Full version of draft guidance, p.147). However, we have significant concerns about the decision to recommend referrals only in those aged 50 and over for symptoms of nipple discharge, retraction or '*other changes of concern'*. Although more likely in those over 50, we are concerned about this recommendation's implication that only people aged over 50 should be referred if they present with these symptoms. Guidance is needed for primary healthcare professionals on what they should do if people under 50 years of age present with these symptoms. Alternatively, the reference to age should be removed.	The age threshold for nipple changes was based on the evidence in Walker et al. and the clinical experience of the GDG (as documented in the Linking Evidence to Recommendations section) If someone presented with these symptoms under 50, we would expect the GP to use their clinical judgement.
615	Breast Cancer Care	6	NICE	147 71		*(p71-72)* **Breast awareness** The previous guideline included a recommendation that '*Primary healthcare professionals should encourage all patients, including women over 50 years old, to be breast aware in order to minimise delay in the*	As you state, this is outside the scope of this guideline and so we are not able to comment on it.

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						presentation of symptoms' (Recommendation 1.6.4, NICE Clinical Guideline 27). While we appreciate that the scope of the updated guideline is focussed on recognition and management of suspected cancer, the breast awareness recommendation is important and we hope that this will be covered as an introductory sentence in the guideline.	
616	Breast Cancer Care	7	NICE	147 71	1.4 & all lines on pages 10-63	*(p71-72 & 10-63)* **Referral for suspected recurrence or metastases in previously diagnosed cancer** As stated in the scope, the draft updated guideline does not cover referral for suspected recurrence or metastases in previously diagnosed cancer. We know from talking to people living with secondary (metastatic) breast cancer that a major barrier to good treatment and care can be delayed referrals by their GP when they present with possible symptoms of metastatic disease. Once the person has been discharged from active follow-up, non-breast symptoms may not be recognised by GPs as signs of possible metastatic disease and so there are delays in appropriate referrals. More guidance is needed for primary healthcare professionals to support them in recognising the possible symptoms of metastatic breast cancer. While we recognised that this is not in the scope of this guideline, we suggest including a recommendation that primary healthcare professionals be mindful of possible metastatic	As you state, this population is explicitly excluded from the scope of this guideline so we are not able to make any recommendations on this issue. We would expect primary care professionals to exercise their clinical judgement in these situations.

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						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 metastatic disease. This recommendation could be in the form of examples of symptoms of metastatic 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).	
617	Breast Cancer Care	8	NICE	29 86	1.15	**Safety netting** We welcome the inclusion of this recommendation, especially the emphasis this places on patient involvement. We suggest adding a clear sign-post to this section within the symptoms/cancer site sections, to ensure that primary healthcare professionals take this recommendation into account.	Thank you. The short version only contains the recommendations from the guideline so it is not possible for us to include cross references as you suggest. However we have added these to the full guideline.
618	Breast Cancer Care	9	Full	141		*(p141-146)* **Evidence** While we recognise that the methodology used to identify these studies is sound, we have reservations with regards to only six studies being used as a basis for such significant changes to the guidance. We also have reservations regarding the relatively small combined sample size of the studies used.	The GDG was aware of the paucity of the evidence. However, considered it was important to provide guidance to clinicians using what evidence was available.
619	Breast Cancer Care	10	NICE	General	General	We believe it may be helpful for primary healthcare professionals if the updated guidance contained a 'reading map' at the beginning of the document, i.e. a guide that suggests an order of reading, to ensure that sections such 'Recommendations on	Thank you for this suggestion. We have received a large number of comments on the length of the document. Text in the introduction explains about the different sections of the guideline.

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						patient support, safety netting and the diagnostic process' are taken into account.	
777	British Association of Dermatologists	1	General	General		We are concerned that there appears to be no dermatological representation on the GDG to provide greater insight into the impact of the recommendations in the guideline.	This guideline is targeted at primary care where patients suspected of having cancer are identified. Therefore it was appropriate to have a majority of primary care clinicians on the GDG. Given there were 37 separate cancer sites to be investigated, it was unrealistic to have representation from each specialty on the group. When the GDG needed further specialist input to make their recommendation, they called on expert advice. This was not done in the case of dermatology.
778	British Association of Dermatologists	2	General	General		We are also concerned of the seemingly lack of understanding by the GDG of the Skin IOG and referral pathways for skin cancer already in place which are part of local cancer networks.	The recommendations cross-reference the guidance in the IOG. Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG.
779	British Association of Dermatologists	3	General	1	3	We question the need to include *"in children, young people and adults"* in the title and suggest "*in patients of all ages*".	The title of the guideline was set at the scoping stage and we are not able to change it.
780	British Association of Dermatologists	4	NICE	3	3	We believe this is a gross underestimation – it is very likely that there are that many BCCs alone.	We have clarified this figure relates to non-skin cancers. As you acknowledge the figures on skin cancer are large but unreliable.
781	British Association of Dermatologists	5	NICE	3	23	*(lines 23-27)* What about common local pathways requiring primary care CT pre-2ww referrals?	We are unclear what part of the text your comment is referring to.

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782	British Association of Dermatologists	6	Full	29	10	Safety netting: The recommendations suggest either a planned review in an agreed time frame OR patient initiated review. However on page 30 paragraph 4, it states *"that 'safety-netting' would need to involve planned review of the person with symptoms."* Here it seems to state it has to be a planned review with an additional patient initiated review if required. The wordings in these 2 sections seem to be contradictory.	We have amended the text in the Linking Evidence to Recommendations section to clarify that a patient initiated review may occur in the absence of a planned review.
783	British Association of Dermatologists	7	NICE	147 37	9	Symptomatic breast referrals are all under 2ww?	We have made recommendations for which breast symptoms should prompt a suspected cancer pathway referral and which should prompt non-urgent referral.
784	British Association of Dermatologists	8	NICE	198 37	1.6.10 29	There may be local supra-network referral pathways not primarily to local urology unit.	Thank you
785	British Association of Dermatologists	9	NICE	198 37	1.6.11 39	We do not concur, as this broad definition would include all balanitis xerotica obliterans and Zoon's balanitis.	We would expect primary care clinicians to use their clinical judgement when applying these recommendations.
786	British Association of Dermatologists	10	NICE	220 38	8	The impact of the statement will overload 2ww pathways already overstretched, causing significant breaches for trust departments and is also at odds with the Skin IOG. All high-risk BCCs need to be referred directly to the LSMDT under an 18-week wait referral. The referral should be flagged up for rapid access under this pathway, not a 2ww, with the appropriate patients' medical history and skin lesion information. LSMDT core members will review these cases and upgrade the patients accordingly onto designated clinic lists.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine

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							referral is needed. The remit of this guideline is to advise primary care about which patients warrant referral for suspected cancer. The arrangements used by secondary care to manage these referrals are outside the scope of this guideline.
787	British Association of Dermatologists	11	NICE	220 38	20	We suggest replacement of the word "consider" with "refer" as it is a requirement to refer as 2ww for suspicious lesions in line with the Skin IOG.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
788	British Association of Dermatologists	12	NICE	77	16	As above.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
789	British Association of Dermatologists	13	NICE	77	19	As above.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
790	British Association of Dermatologists	14	NICE	220 78	1.7.6 5	We believe this is incorrect – the GDG needs to refer to both the 2006 Skin IOG and the 2010 update.	We have changed the cross reference to refer to the 2010 update as this is the document that covers excision of BCCs.
791	British Association of Dermatologists	15	NICE	279 81	1.11.3 23	We do not know how sensible this is - rather refer as 2ww as this could result in a prolonged pathway.	It was the view of the GDG that the PPV of this scenario was below 3% and therefore did not warrant a suspected cancer referral.

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792	British Association of Dermatologists	16	Full	203	4	We know that GPs are likely to refer many more suspicious lesions – use of the term 'diagnose' is a poor choice and the % 5-year survival rate is inappropriate and showcases poor understanding of the cancer.	This is background text and we consider that the use of the term 'diagnose' here is appropriate.
793	British Association of Dermatologists	17	Full	203	7	We feel there is a missed opportunity to raise red-flag lesions - and for example, recommend including PGs into pathways. Nodular melanomas as are not rare - should this be amelanotic melanoma?	Thank you, this was very helpful. A recommendation has been added about lesions suggestive of nodular melanoma.
794	British Association of Dermatologists	18	Full	203	22	We feel there is a need to differentiate between routine and suspicious pigmented lesions. There is also the need to highlight that not all melanomas are pigmented, and urgent referral is required for new or changing red nodules or ulcerated lesions. Patients with previous history of melanoma should be referred directly to a LSMDT/SSMDT to ensure that they get on the appropriate pathway.	This text describes the evidence that was found. A recommendation has been added about lesions suggestive of nodular melanoma. The arrangements used by secondary care to manage these referrals are outside the scope of this guideline.
795	British Association of Dermatologists	19	Full	204	1	We believe there is a wealth of information out there; the GDG should use data from several rather than predominantly a single article.	We conducted a systematic review of the evidence based on a pre-specified protocol outlining the methodology we would follow, and particularly the inclusion criteria that any relevant study would have to meet in order to be considered as evidence. On that basis, we consider we have included all the directly relevant evidence, as planned.
796	British Association of Dermatologists	20	Full	208	1	We think that a more generic and less specific (product-related) section would be better. Discuss digital dermoscopy, mole-mappping systems, etc. There is a lot of information provided but resulting in weak results and recommendations. Once again there is a broader range of information available and other studies that should be included.	The section you refer to, details the published cost effectiveness evidence that was identified by our review question on the most effective investigations in primary care for malignant melanoma. No cost-effectiveness evidence was found on any of the other interventions of interest

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							so we are not able to document anything about them. This page simply reflects the available evidence and is not intended to promote MoleMate – as detailed in the Linking Evidence to Recommendations section, the GDG agreed not to use this paper when agreeing their recommendations.
797	British Association of Dermatologists	21	Full	208	3	*(lines 3-41)* We have read this section on cost-effectiveness analysis of MoleMate several times and are still not clear what the final conclusion from the analysis is. The first five paragraphs seem to be in favour while the last is not. We think the final conclusion should be made clearer. We suspect the conclusion was that it was not cost-effective as it doesn't figure in the final recommendation. The data on MoleMate adds nothing to the conclusions of the paper by Fiona Walters published in the BMJ in 2012. That showed clearly that MoleMate added no value to clinical examination. We don't understand how these very clear conclusions can be changed by the GDG. Moreover, the results for MoleMate alone, i.e. without structured clinical examination as used in the study, do not give confidence that it would have high positive predictive value for melanoma. This may well be the mode of use in primary care should it be more widely used. Therefore its use cannot be supported on the evidence available, and indeed it may increase risk of misdiagnosis. The use of MoleMate is outside of cancer pathways requirements and its use has escalated increases in referrals under 2ww. Unfortunately,	The perceived discrepancy here relates to the statement of the results and how they were interpreted by the NCC-C health economist. The first three paragraphs state the results of the analysis, which appear to be very favourable. The following three paragraphs attempt to explain the potential limitations of the analysis and how this affects the interpretation of the results. In particular, it was noted that MoleMate was only proven to decrease specificity (i.e. increase false positives) with an associated statistically insignificant increase in sensitivity. Thus, the study effectively demonstrates the cost-effectiveness of being less strict when referring patients (i.e. over-referring) rather than using the MoleMate system itself. We are unsure of what is meant by the GDG changing the conclusions of a paper by Fiona Walters. As you stated, the GDG did not recommend the use of

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						the legal implications for making wrong diagnoses at times by primary and intermediate grade clinicians impact on skin cancer pathways. Currently, conversion rates for 2ww referrals are between 5-20%; the additional increase from MoleMate referrals will have a significant impact on already over-stretched staffing resources and diverts consultant time away from patients with acute inflammatory skin disease.	MoleMate. We can confirm, as stated in the Linking Evidence to Recommendations section, this cost-effectiveness analysis was not utilised by the GDG when making their recommendations.
798	British Association of Dermatologists	22	Full	211	End of the page	Clinical suspicion (aided by using 7PCL) is most important - dermoscopy is not a routine GP tool and training in skin lesion recognition and management would be required (see GPwSI Training programme).	Thank you for this comment. Recommendation 1.7.1. does not recommend dermoscopy, but acknowledges that some primary care clinicians use it. The recommendation covers what to do when dermoscopy suggests malignant melanoma.
799	British Association of Dermatologists	23	Full	212	"Trade-Off"	We do not understand the first sentence; weak conclusion after so much time spent on the Wilson paper.	The section on pg 208-209, details the published cost effectiveness evidence that was identified by our review question on the most effective investigations in primary care for malignant melanoma. No cost-effectiveness evidence was found on any of the other interventions of interest so we are not able to document anything about them. This page simply reflects the available evidence and is not intended to promote MoleMate – as detailed in the Linking Evidence to Recommendations section, the GDG actually agreed not to use this paper when agreeing their recommendations.
800	British Association of Dermatologists	24	Full	216	18	Include keratoacanthomas and uncertain lesions here to include other high-risk, non-melanoma skin cancers. *"Consider a suspected cancer pathway referral (for*	Benign skin conditions are outside the scope of this guideline and so we are not able to include them in a recommendation.

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						an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of squamous cell carcinoma." It is better to make a recommendation based on clinical experience on specific symptoms to trigger a referral, rather than just based on "suspicion". The guidelines have no practical value if it just says "consider a referral when you suspect a BCC/SCC". That is common sense and a given that a GP will refer when they suspect BCC/SCC and it does not require guidelines to say that.	The GDG did not wish to try and describe SCCs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation. This guideline is for all primary care professionals, not just GPs. Therefore it is important that it is sufficiently comprehensive for all users.
801	British Association of Dermatologists	25	Full	217	Signs and symptoms	We suggest the GDG includes rapid expansion, painful lesion in sun-damaged/exposed skin in susceptible patients, plus, some classic keratinous/crateriform.	This text summarises the quality of the evidence and the GDGs deliberations on it.
802	British Association of Dermatologists	26	Full	218	13.3 general	We have seen reports from our membership of a sustained increase in referrals for 2ww consultations for the past 10 years. In one example, this summer the increase was 30% and the volume of referrals has thus far been sustained; their 'winter dip' is yet to transpire. Seeing these patients within 2 weeks has caused a knock-on effect such that low-risk BCCs are struggling to be fitted in within the 18-week pathway and even putting significant pressure on ensuring that the SCCs and melanoma re-excisions are performed in a timely fashion. We do understand the rationale for getting the	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not included in the recommendation.

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						highest risk BCCs seen urgently - those growing rapidly and on the eyelid for instance - but, our concern is that the guidance is not robust enough, and all head-and-neck BCCs plus biopsy proven infiltrative BCCs and incompletely excised BCCs will end up filling the 2ww clinic too. This would most likely break the system, without much benefit for what is, on the whole, not a life-threatening tumour. It is a requirement of the Skin IOG and NHS England peer-review measures to ensure that high-risk BCCs are referred to LSMDT/SSMDT core members within the host hospital to ensure appropriate diagnosis and that the procedure is carried out in the correct setting. The recommendation that suggests some BCCs should be seen via the 2ww route is both illogical and unsustainable. There is no evidence to support that BCCs should be seen in a 2ww clinic. Since BCCs are extremely common, a change in referral pathway for these would have a detrimental effect on patients with a probable melanoma or SCC. Dermatologists would no longer be able to prioritise if all of those patients came through the same route. In line with the national trend, it is proving a major struggle to cope with the demand of the existing 2ww referrals for SCCs and melanomas. If BCCs are added to these cases it will be impossible to cope with this demand given our already struggling services. There is already a mechanism for clinicians to upgrade patients under the 2ww pathway for treatment.	Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
803	British Associati	27	Full	218	Other Consid	We disagree - there has to be a lower threshold and higher suspicion in these patients. Perhaps	We have documented in the introduction, there are very few instances where risk

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	on of Dermatologists				erations	describe immunosuppression (acquired/drug-induced (including past use)/haematopoietic).	factors allow different recommendations to be made for people with the same symptoms. The GDG 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 immunosuppression affected the predictive power of symptoms for basal cell carcinoma.
804	British Association of Dermatologists	28	Full	220	16 blue area	*"Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is concern that a delay may have an unfavourable impact, because of factors such as lesion site or size. [new 2015]."* We think the impact of this recommendation has been underestimated. Although, the number of BCCs referred would probably not change significantly, the proportion referred for appointment within 2 weeks would significantly increase causing strain on departments already struggling with the 2-week referrals. We agree the BCCs on high-risk sites need to be seen earlier than "routine", but how earlier is debatable. We do not think 2-week referrals are practical or necessary. Also, size should not be a criterion for an urgent referral. The importance of size decreases after site has been taken into account, e.g. a 1 cm BCC on the nose needs earlier attention than a 3 cm BCC on the back.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the

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							suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
805	British Association of Dermatologists	29	Full	220	16 blue area – alternative	*"Consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma"* We disagree - who will make this decision? There should be locally agreed pathways for this which are part of the cancer network. Making it a national recommendation will cause havoc and is outside the Skin IOG.	Local pathways will be a matter for implementation of this guideline.
806	British Association of Dermatologists	30	Full	222	1st Paragraph	We suggest "histology" instead of "excision" as it excludes biopsy and alternative treatments.	We have changed 'excision' to 'biopsy'.
807	British Association of Dermatologists	31	Full	222	2nd Paragraph	Again, we think the guideline needs to refer to both the 2006 Skin OPG and the 2010 update.	We have changed the cross reference to refer to the 2010 update as this is the document that covers excision of BCCs.
808	British Association of Dermatologists	32	Full	222	Last Paragraph before references	We disagree - this will change dramatically with the 2ww recommendation and will require additional resources with costs.	The GDG discussed this issue when agreeing their recommendations. They did not consider that the number of people with BCCs being referred on a suspected cancer pathway would be large.
809	British Association of Dermatologists	33	General	General		**<u>General comments on how the draft guideline is at odds with the Skin IOG</u>** 1. We know of no data which support the idea that we can discriminate between BCCs requiring 2ww (if any) and those seen according to current pathways. And how are primary care specialists to make this	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact.

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						distinction?	We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
						2. Dermoscopy is only part of the diagnostic process for melanoma, and one whose use is subject to the same error as other visual diagnostic procedures. The clinical history is a critical determinant of melanoma diagnosis, sometimes the only determinant, as is clinical examination. Emphasising dermoscopy as a sole basis for referral presupposes that it is more powerful than the history and examination findings combined. This is not the case, and in our view this advice is potentially dangerous.	Recommendation 1.7.2. does not recommend dermoscopy, but acknowledges that some primary care clinicians use it. The recommendation covers what to do when dermoscopy suggests malignant melanoma.
						3. There is no advice about the referral of patients with enlarging red nodules, a not infrequent and often-missed presentation of melanoma, SCC, and rare skin cancers such as Merkel cell carcinoma. All of these are potentially lethal. Primary care awareness for this group needs to be increased.	Thank you, this was very helpful. A recommendation has been added about lesions suggestive of nodular melanoma.
						The time spent on MoleMate seems disproportionate, confusing and seemingly comes to no clear conclusion. Concentration on the value of appropriate use of dermoscopy (better/shorter term than 'dermatoscopy') with appropriate training/education would be preferred (it almost	The section you refer to, details the published cost effectiveness evidence that was identified by our review question on the most effective investigations in primary care for malignant melanoma. No cost-effectiveness evidence was found on

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						feels that someone has an interest in promoting the use of sialoscopy/MoleMate).	any of the other interventions of interest so we are not able to document anything about them. This page simply reflects the available evidence and is not intended to promote MoleMate – as detailed in the Linking Evidence to Recommendations section, the GDG agreed not to use this paper when agreeing their recommendations.
						The additional emphasis on opthalmoscopy is also disproportionate; ocular melanomas are rare (on a par with intranasal/vulval/anal so why no mention of other techniques of special area examination).	We have reviewed the text and can only find mention of opthalmoscopy in the Linking Evidence to Recommendations section, where we document the discussion had by the GDG. Opthalmoscopy is only mentioned once and no recommendations were made about this intervention so we do not think there has been a disproportionate emphasis on this technique.
						Routine referral for BCC versus 2/52-week inclusion if unfavourable impact on outcome, will lead to over-saturation of shortage 2/52 slots by BCCs as there will be a failure to discriminate. It would be better to suggest that BCCs should all be referred on a soon basis and those with perceived high risk on a very soon or urgent basis with justification on an individual basis rather than a mandatory 2/52 wait.	The GDG discussed this issue when agreeing their recommendations. They did not consider that the number of people with BCCs being referred on a suspected cancer pathway would be large.
						14-1C-111j Skin Measure Patient Pathways for Primary Care/ Community Services and MDTs 'that GPs should refer suspected cases of skin cancer requiring treatment, including BCCs, to the contact point of the relevant named MDTs in the	Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG.

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						network configurations, or for cases of low-risk BCC, there is the option of referral to the contact point of a relevant GP-based service'. **<u>14-1D-101j Provision of Clinics for Immunocompromised Patients with Skin Cancer</u>** Please note referral requirements for immunocompromised patients in line with the Skin IOG and skin measure require: There should be a regular clinic in one of the hospitals of the locality which should: • be identified on the hospital outpatient department clinic list or timetable as a clinic for immunocompromised patients with skin cancer; • have bookable numbered clinic slots identified for the immunocompromised patients; • have a dermatologist core member of a named MDT with direct patient care sessions for the clinic in their job plans; • have a nurse specialist member of a MDT with the clinic specified as part of their work plan or job description. Referral pathways need to reflect the clinical criteria and models of practitioners working within the levels of care defined in the 'skin measures' since 2008. Descriptions of the models and types of BCC which make up these lists are classified from the point of view of peer-review and referral for treatment specified in clinical terms, here since *initial* decisions in primary care, regarding referral for treatment need to be made before histology is	Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG. The organisation of services in secondary care is outside the scope of this guideline.

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						available. The Skin IOG, either explicitly or by implication, effectively specifies six levels of care, differing in the degree of specialisation and service consolidation needed. The personnel foreseen as offering these levels range from any GP, through specifically authorised and trained community practitioners, local and specialist MDTs to supra-network MDTs. All this is incorporated into the network referral guidelines and network infrastructure for skin cancer, set out in the measures. Therefore, the cancer referral guideline must triangulate and comply with the Skin IOG, and any update made outside of these requirements need to be removed from this consultation. This draft and update of the cancer referral guidance does not reflect the necessary guidance and referral pathways which have been implemented since its inception in 2005. It is with some urgency that we must insist the GDG reviews the necessary documentation and references to these requirements laid out in the Skin IOG and skin measures 2014.	Thank you for this information Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG. Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG.
58	British Association of Endocrine & Thyroid Surgeons	1	Full	230	5	5y survival for all thyroid cancer is not 80% but 97.8% (seer.cancer.gov). This is because the vast majority of patients present with stage 1 or 2 differentiated thyroid cancer where survival is measured over 20y not 5y where it is close to 98% as already stated. Poorly differentiated cancer is even rarer but does feature a worse prognosis.	We have amended this to 'over 90%'

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59	British Association of Endocrine & Thyroid Surgeons	2	Full	230	6	*(lines 6,13,14)* Clinical features suggestive of thyroid cancer are actually very well known and can be found in any relevant clinical textbook. The simple presence of a lump does not itself raise the immediate concern of malignancy. As the document itself declares, thyroid malignancy is rare but benign thyroid lumps are extremely common. Around 6% of the population will have palpable thyroid lumps. This can rise to almost 50% of elderly patients. Declaring all of these scenarios as potential malignancies will not benefit patients nor the NHS.	This is factual background text, and does not constitute recommendations
60	British Association of Endocrine & Thyroid Surgeons	3	Full	231	1	If a patient has a "community" ultrasound requested by the GP, it will inevitably be repeated by the secondary care physician within the hospital. Upto 35% of patients will have ultrasound visible thyroid nodules. If GPs were to refer all such patients for assessment of potential malignancy the numbers would be huge. This would inevitably negatively impact those patients who were to have malignancy.	No recommendations relating to ultrasound and thyroid cancer were made.
61	British Association of Endocrine & Thyroid Surgeons	4	Full	393		a 2 week suspected cancer referrel pathway is suggested for all thyroid lumps It is noted with a degree of dismay that there is no reference to the recently published British Thyroid Association guidelines on thyroid cancer (www.british-thyroid-association.org/guidelines/) which is the template for thyroid cancer MDTs in the UK. We are surprised that the British Thyroid Association are not stakeholders in this venture and we are disappointed at the total lack of	The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop

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						references which in turn fail to provide evidence to justify a change in policy regarding the timing of referring patients with a thyroid lump. In the recent (2014) BTA guidlines document (www.british-thyroid-association.org/guidelines/) it is made clear that the commonest presentation of thyroid cancer is a lump, but that 95% of thyroid lumps that present are benign. Furthermore the prognosis for those patient harbouring thyroid cancer is excellent. There is clear guidance regarding those patients who should be referred within 2wks - an associated hoarse voice - age under 16 years - the presence of cervical lymphadenopathy - rapid enlargement of the goitre over a period of weeks. We further note the lack of evidence for the NICE guidance which finds an investigation with a PPV of only 3% to be significant. Nevertheless we applaud the recommendation that patients with new thyroid lumps should be referred to secondary care. We suggest that all patients with a new thyroid lump should be seen because regardless of the probability of malignancy, we wish to allay the fears of the majority who will have benign disease. There are many Units that do not have the capacity to see all patients within this time-frame and the BAETS would suggest a maximum timeframe of 4 weeks for all referrals.	recommendations for a guideline targeted at a primary care population. It is not part of NICE methodology to cross reference guidance from other organisations in their guidelines. The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline. Thank you We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the

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							timeliness and quality of cancer diagnosis.
277	British Association of Oral and Maxillofacial Surgeons	1	Full	228	1.8.3 Recommendations	We would be very concerned that directing patients with oral lesions through the community dental service (CDS) would introduce another level of bureaucracy and potential delay to the pathway. The CDS clinicians treat patients with special needs and children, and in general have no postgraduate training in oral and maxillofacial pathology. Significant resource would need to be invested in the CDS to undertake this additional role, in the context of clinical time and training. Overall, we do not feel this proposed change would enable the earlier recognition, diagnosis and treatment of oral cancer.	Whilst we acknowledge this may introduce some delay, the GDG agreed that reduction in unnecessary referrals to cancer services resulting from lesions being seen by a more expert clinician, outweighed any risks associated with a short delay. In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'
278	British Association of Oral and Maxillofacial Surgeons	2	Full	229	Recommendations	We would recommend that biopsies should only be undertaken in specialist centres. It is crucial that the area is measured, photographed if possible and the patient assessed fully prior to any biopsy, by properly trained staff.	Thank you for this information. We do not make any recommendations about biopsy.
250	British Association of Urological	1	NICE	180 39	1.6.4 1.6.7	We have some concerns about not investigating visible haematuria in <45. We appreciate there may be a low yield of patients with cancer following investigation but there will inevitably be a few missed cancers and this seems to be contrary	The age thresholds in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the younger age groups

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	Surgeons					to recent public health campaigns for example the DH Blood in Pee campaign. There are a significant number of patients under the age of 45 with renal cancer and bladder cancer and some have disease that presents with haematuria rather than an incidental finding. These young patients will be greatly disadvantaged by this new guidance. We would suggest that consideration should be given to saying that all adult patients (? Greater than 20 years old) should be referred urgently if they have visible haematuria, however it is reasonable to say that they are only referred via the 2WW if >45.	you mention. In the case of a patient with visible haematuria who was under 45 we would expect primary care clinicians to use their clinical judgement when applying this recommendation. People with persistent symptoms would be covered by the recommendations made on safety netting.
251	British Association of Urological Surgeons	2	NICE	180 39	1.6.5	Generally we welcome this change, ie to not investigate asymptomatic NVH >60, which will reduce the numbers referred to the rapid access haematuria service. We will inevitably miss a few cancers but currently we do investigate a lot of people with asymptomatic NVH so on balance this seems reasonable. Primary care must ensure that patients are still considered for referral on non-urgent pathways. These guidelines are an opportunity to expand on what is significant nVH, it would be helpful if the guidance could state what is significant dipstick haematuria ie 1+ or trace etc. BAUS did quite a lot of work on an algorithm for managing nVH with respect to age, symptoms and persistence and it is a shame this has not been introduced into the guidelines at all, (see http://www.baus.org.uk/Resources/BAUS/Documents/PDF%20Documents/BAUS%20in%20general/haematuria_consensus_guidelines_July_2008.pdf) .	Thank you The research underpinning the non-visible haematuria recommendations did not specify the level of haematuria. This will be a scenario where the clinician will be expected to use their judgement.

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						Linking NVH to dysuria seems reasonable but potentially excludes patients with nVH and frequency, urgency etc. What is the evidence for investigating asymptomatic NVH in patients who have a raised white blood cell count?	The evidence for non-visible haematuria plus raised white cell count came from Price (2014) and is documented on pg 177 of the full guideline.
252	British Association of Urological Surgeons	3	NICE	169 39	1.6.2	*(p39-41)* We think DRE and PSA are mandatory, not optional, in men with LUTS, ED and VH. Getting into age/life expectancy >10 years could cause difficulty for the referrer but it is reasonable to suggest that a PSA should not be done in men >80 unless DRE is abnormal.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. Thank you for this comment. We agree with you that assessment of life expectancy is difficult. The evidence base included patients above 80 years, so it would be inappropriate for this guidance to suggest an upper age limit for investigation.
253	British Association of Urological Surgeons	4	NICE	180 41	1.6.6	We agree with the recommendation for referral of recurrent/persistent UTI in >60, particularly as we know women may present in this way and the evidence shows they are often referred late with bladder cancer but it must be recognised that this will add considerably to the workload in flexi clinics / USS / CT scans.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
254	British Association of Urological	5	NICE	196 40	1.6.8	Non-painful enlargement of the testis. An average GP will see 1 testis cancer over an entire career. Therefore, benign swellings, which are much more common, are frequently referred by 2 week rule which is a waste of resource. Non-operative	Thank you. You will recognise that the changed guidance does partly reduce urology referrals. We would expect primary care clinicians to exercise their judgement in the likelihood of intra-scrotal

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	Surgeons					management with reassurance is a frequent outcome for epididymal cysts for example. We would propose a direct access ultrasound service for all non-painful scrotal enlargement as well as for non-acute orchalgia. The cancer diagnoses will be referred by radiology straight to MDT and cancer clinicians and so the pathway might be quicker than a 2 week rule referral. There is an opportunity to reduce unnecessary referrals to secondary care.	swellings being testicular or otherwise.
255	British Association of Urological Surgeons	6	NICE	180 General		We note that you are using a PPV of .3% as the cut off for recommendation. However we notice that you do not include any stats for smokers/history of industrial exposure. If stratified for this the PPV value of some symptoms would go up. The document is an opportunity to again stress the link between bladder cancer and smoking. Would it be possible to include a line "Patients with a history of smoking are at increased risk of urological malignancy and this should be considered when deciding on whether to refer a patient for further investigation.	We have documented in the introduction, there are very few instances where risk factors affect the predictive power of symptoms sufficiently to allow different recommendations to be made for people with the same symptoms. The GDG 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 smoking or a history of industrial exposure affected the predictive power of symptoms for bladder cancer.
166	British Dental Association	1	Full	226		*(p226-230)* Greater emphasis should be given to the identification of high-risk patients. (Brocklehurst PR, Baker SR, Speight PM. (2010) Factors which determine the referral of potentially malignant disorders by primary care dentists. *J Dent*; **38**, 569-78.) Smokers, smokeless tobacco users and those who consume alcohol to excess can be identified through medical history taking.	Thank you for providing this reference. We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (lung cancer) of sufficient impact on the

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							predictive power of symptoms to require different recommendations.
167	British Dental Association	2	Full	226		*(p226-227)* Although it has rightly been rejected, we are concerned that the use of brush biopsy has been considered as a diagnostic test. The technique is intended to be used for the exclusion of low-risk cases that do not merit biopsy, and its routine use in diagnosis would introduce delay into the referral pathway.	The GDG considered the evidence on a range of possible investigations. No recommendation was made on brush biopsy.
168	British Dental Association	3	Full	228		The use of the word "consider" in the guidance on referral appears weak; we believe all of the recommendations for referral of suspected oral cancer should be strengthened to "refer" or "offer a suspected cancer pathway referral".	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
169	British Dental Association	4	Full	228		Erythroplakia and erythroleukoplakia (red and speckled patches) in the oral cavity that have been present for more than two weeks and assessed by a dental surgeon should be specified as criteria for referral. These lesions have high predictive value, since they occur rarely but approximately half harbour early cancer. (This is in contrast with leukoplakias, which have low predictive value and are correctly excluded from the referral criteria.) The survival rate for oral cancers increases from approximately 50 to 90 per cent with early diagnosis, and dentists are trained in early detection of malignant lesions. Lumps and ulcers are signs of late-stage cancer, though it should be noted that there are also many possible benign diagnoses for lumps.	We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation.
170	British Dental Associati	5	Full	228	1.8.3	"Consider an urgent referral (for an appointment within 2 weeks) for assessment for oral cancer by the community dental service in people with an	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an

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	on					unexplained lump on the lip or in the oral cavity that has not been assessed by a dental surgeon." The suggestion that non-dental health professionals should refer suspected cancers to the community dental service (CDS) is not appropriate. Firstly, it would introduce an unacceptable delay into the pathway and secondly, the CDS does not have the required skill mix, contract or facilities to handle such referrals in most areas of the country. We recognise the pressure to provide a dental opinion that is free to the patient, and would point out that the normal NHS dental charges do, in fact, apply in the CDS. Moreover, the above proposals will not be consistent with the planned structure of NHS dental services once Tier 2 and 3 specialist services are commissioned. Referral to a Tier 2 specialist practitioner in Oral Medicine or Oral Surgery, or directly to secondary care, would be more appropriate. We note, however, that the draft commissioning framework for Oral Surgery and Oral Medicine assumes that patients will continue to be referred directly to Head and Neck Cancer Treatment Centres, though this framework is still in development. We would urge the GDG to give further consideration to the referral pathway for suspected oral cancers by non-dental healthcare professional and the place of dentists within it. If primary care dentists were to act as gatekeepers, the criteria for referral could be defined more precisely with specialist terminology to improve their predictive value; however, this may cause confusion for any non-dental professionals. This system also risks	urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'

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						causing delays in diagnosis, in comparison to direct referral to secondary care, and dentists involved must possess the appropriate skills. (Brocklehurst PR, Baker SR, Speight PM. (2010) Factors which determine the referral of potentially malignant disorders by primary care dentists. *J Dent*; **38**, 569-78.) Referral to dental hospitals, which provide primary care in a secondary setting, could be considered if appropriate in areas where these are available.	
119	British Gynaecological Society	1	Full	151	onwards pertaining to gynae cancer	Ovarian Cancer – NICE guidelines in 2011 recommend symptom triggered testing in Ovarian Cancer. Is the GDG aware that both prospective studies evaluating this have not shown evidence of stage shift in diagnosis (Gilbert, lancet Oncology, 2012 and Goff, Obstetrics and Gynaecology 2014. Ovarian cancer – NICE could take this opportunity to clarify actions where Ca125 is raised and ultrasound is normal (repeat Ca125 in 6 weeks) and indeed what constitutes an ultrasound suspicious of ovarian cancer as that would provide clear guidance to primary care. Endometrial Cancer - They look fairly sensible. However in the endometrial guidelines the document misses out the pre-menopausal irregular or heavy bleeding group and RCOG recommendation that those over 45 should have endometrial sampling, even if they come through urgent rather than 2WW pathway. This is an important group, who feel let down as frequently are diagnosed after prolonged symptoms.	Thank you for this information. It has been passed on to the surveillance team at NICE for when the Ovarian cancer guideline is considered for an update. The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations. There was no primary care evidence to support making a recommendation for abnormal menstrual bleeding in younger women.

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						Cervical cancer The section on cervical cancer mentions an abnormal looking cervix as being a referral criteria but it should also say under what circumstances the cervix should be inspected. This would help to avoid the current situation in many premenopausal patients where women present with abnormal bleeding and pain but are not examined because their symptoms are attributed to menstrual problems. If there isn't the evidence to say when patients should be examined then a group of experts should be asked.	We state in the introduction that there is an expectation that 'the clinician will have taken an appropriate history and performed an appropriate physical examination'. We consider this adequately covers the situation you describe.
						As it stands, the draft guidance (i.e. if a cervix looks like cancer then pt should be referred) is likely to do nothing to help women be diagnosed earlier than they are now because I suspect virtually all clinicians would already refer a pt if they thought the appearance of their cervix looked like cancer.	There was insufficient evidence on the PPVs of symptoms of cervical cancer to make a more specific recommendation. The recommendation made was based on the GDGs clinical experience that a cervix with the appearance of cervical cancer was likely to have a PPV of 3%, had it been studied. The GDG agreed that no other symptoms were likely to have a PPV of 3% given that the symptoms were common and cervical cancer is relatively rare. This has been documented in the Linking Evidence to Recommendations section.
						Further comments – specific lines P151 referral recommendation - mass not due to fibroids (add or a pregnancy)	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes.

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						P152 recommendation raised CA125 and N USS – recommended to see GP if symptoms persist (suggest repeat CA125 6 weeks) I have no published evidence – just an audit of our practice. P153 table – what does 'flow and timing' mean? P155 why an age limit of 55? Why refer if thrombocytosis, why haematuria, why high blood sugar? No evidence is presented. P157/160 why is IMB not considered for endometrial or cervical cancer? What evidence is there either way? P160 IMB/ PCB not associated with cervical cancer? No evidence is presented.	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes. This means that it is unclear if all patients are accounted for in the study that was appraised. This clarification has been included in the Methodology chapter of the full guideline. The age thresholds and symptoms in the recommendations were derived from the evidence on PPVs which is reported in section 11.2. We have not recommended that the symptoms you cite should prompt referral – we have recommended a direct access ultrasound scan. No primary care evidence was found for this symptom. It was the view of the GDG that the PPV of IMB was below 3% and therefore did not warrant a suspected cancer referral. No primary care evidence was found for these symptoms. It was the view of the GDG that the PPV of IMB/PCB was below 3% and therefore did not warrant a suspected cancer referral.
120	British Gynaecological	2	Full	General		Why have the guidelines agreed a PPV of 3% as a cut of for a suitable diagnostic test *(1 in 33!)*? Normally a cut off of 10% is usually used (example	This comment seems to confuse two separate situations. The first is the use of genetic testing in an asymptomatic

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	Society					- as in genetic testing for a risk of 10% and above) .	individual for screening purposes. The second is what the guideline has done, which establishes a threshold for referral for suspected cancer in symptomatic people. The rationale for this is detailed in the introduction to the full guideline.
202	British Sarcoma Group	1	Full	272 General	General	The British Sarcoma Group (BSG) is a Society formed of clinicians, scientists and others whose main interest is in treating patients with sarcomas. Early diagnosis is key to improving outcomes for patients with sarcomas. Despite the two earlier guidance documents, delays in diagnosis of both bone and soft tissue sarcomas (STS) are common and the average size of sarcomas at diagnosis remains at almost 10cm. As size is critical for prognosis, this large size leads to the UK having worse outcomes than many other countries, particularly for STS. The latest draft guidance causes us great concerns as it would appear that no one with any knowledge or experience of sarcomas has been involved in developing the guidance. The latest guidance appears to ignore the two previous guidance documents and the numerous publications that have been produced trying to improve on these. The most surprising thing is the	Thank you for this information. This guideline is targeted at primary care where patients suspected of having cancer are identified. Therefore it was appropriate to have a majority of primary care clinicians on the GDG. Given there were 37 separate cancer groupings to be investigated, it was unrealistic to have representation from each specialty on the group. When the GDG needed further specialist input to make their recommendation, they called on expert advice. The description of soft tissue sarcomas in the IOG were taken from CG27. This guideline is updating CG27. No primary care evidence was found on symptoms

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						lack of acknowledgement of the NICE Improving Outcomes Guidance (IOG), published in March 2006 on Improving Outcomes for People with Sarcoma, which sets out very clearly the symptoms and signs suspicious of a bone or soft tissue sarcoma and clear recommendations concerning urgent referral to a specialist centre for appropriate investigations, including biopsy.	with a PPV consistent with referral. The GDG agreed, on the basis of their clinical judgement, that it was appropriate to make the recommendations they did. The prior recommendations in CG27 were explicitly reviewed by the GDG and the new recommendations were agreed to be more appropriate. Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG.
203	British Sarcoma Group	2	Full	273		*(p273-5)* Since the IOG was published there has also been a concerted effort to implement the recommendations that sarcomas should be cared for in dedicated specialist centres. The IOG was prepared after extensive literature searches and broad consultation. Instead this new guidance has apparently been based on 7 articles (bone) and 3 for STS. Reading these articles reveals that most have nothing to do with sarcomas whatsoever and their inclusion in the document results in a complete loss of credibility of the GDG who appear to have accepted these and made use of them. In particular: Deyo 1988. Cancer as a cause of back pain - sarcomas hardly ever arise in the back - myeloma and metastases do. Dommett 2012. Childhood cancer in primary care. Minimal relevance Dommett 2013a. Risk of childhood cancer with symptoms. Some use but only for children. Dommett 2013b. Cancer in TYA. Excellent but very non specific, lumping bone and STS together	Thank you for providing these references. The clinical questions have all been answered in a transparent and consistent manner according to established systematic reviewing methodology that has attempted to ensure that the most relevant evidence has been identified for the identification of symptoms in primary care that are associated with an increased risk of sarcoma (and other cancers). While the identified studies all have a number of limitations, they nevertheless represent the best available, most relevant evidence for this question as agreed in the review protocols.

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						and not detailing the actual symptoms (e.g. what are musculoskeletal symptoms). Henschke 2009. Spinal pathology in low back pain. Irrelevant Pharisa 2009. Neck complaints in children. Irrelevant Suarez-Almazor 1997. Xrays for LBP. Irrelevant The selection of these articles completely seems to miss the point about the incidence and age patterns and locations for sarcomas. Four of the articles are about spinal problems - and less than 3% of sarcomas arise in or near the spine. Four are about children and yet less than 6% of all STS arise in children under the age of 16 and less than 6% in the TYA category. For bone tumours almost 45% arise around the knee, 32% in the pelvis or hip and 12% in the shoulder girdle. Knee, shoulder or hip pain (with a limp) are thus key worrying features. Night pain is a huge clue for a possible bone tumour.	
204	British Sarcoma Group	3	Full	275	1.11.111	We do agree that symptoms of bone sarcomas are often very non specific to start with and we agree with the modified recommendation: **Consider an urgent access Xray within 2 weeks to assess for bone sarcoma or other bone malignancy in any patient with unexplained bone pain or swelling.**	The reason the recommendation specifies children and young people, and excludes adults, is that the anticipated PPV of this clinical presentation in adults being a bone sarcoma would be extremely low. We have amended the LETR to make this more explicit.
205	British Sarcoma Group	4	Full	275	1.11.211	we would feel however that guideline 2 should be: **Make a suspected cancer pathway referral (for an appointment within 2 weeks) for people if an Xray suggests the possibility of bone sarcoma.**	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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206	British Sarcoma Group	5	Full	275	1.11.211	finally, about 10% of patients with a bone tumour will have an Xray that is either normal or reported as normal. If symptoms persist we would advise: **Consider urgent referral for any patient with persisting unexplained bone pain or swelling (even if the Xray is reported as normal).**	The GDG did not consider that the PPV in this scenario would be high enough to warrant recommending an urgent suspected cancer referral. However, we would expect that primary care clinicians would use their clinical judgement in such situations. People with a negative X-ray but persistent symptoms would be covered by the recommendations made on safety netting.
207	British Sarcoma Group	6	Full	388		The recommendation about investigating fracture on page 388 suggests that myeloma is the only cause of pathological fracture and can be excluded. However, this is clearly not the case as sarcomas and metastatic bone disease may also lead to unexplained (ie pathological) fracture	This guideline covers people presenting to primary care with symptoms.
208	British Sarcoma Group	7	Full	276		There is no proven value for any blood test in diagnosing bone sarcomas.	The GDG considered the evidence on a range of possible investigations. No recommendation was made on blood tests.
209	British Sarcoma Group	8	Full	277		*(p277-9)* **For Soft tissue sarcomas** We note that the predictive score for referral for cancer has been lowered to 3%. The GDG do not seem to be aware that the current two week wait criteria generally result in a 10-15% diagnosis of sarcoma (see references). We accept that no study has yet been done in general practice to identify the frequency of the criteria mentioned in previous guidance documents but we are concerned that the GDG are throwing out the old guidance without any justification. Whilst the	As we have detailed in the introduction, we have used primary care evidence to formulate our recommendations. The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop

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						articles by Dommett are of some help the symptoms identified were so non specific as to be useless and furthermore only referred to young peoples who are unlikely to get STS. We believe that the distillation of experience thus far would suggest that the following criteria are the most valid and should prompt referral. **Any person with a lump that is:** **increasing in size** **or** **bigger than 4cm** **or** **deep to the fascia,** **should be referred on a suspected cancer pathway for investigation.** (We have used 4cm as various articles submitted for publication have indicated that this is just as effective as 5cm as predicting the possibility of malignancy).	recommendations for a guideline targeted at a primary care population. No primary care evidence was found on symptoms with a PPV consistent with referral. The GDG agreed, on the basis of their clinical judgement, that it was appropriate to make the recommendations they did. The prior recommendations in CG27 were explicitly reviewed by the GDG and the new recommendations were agreed to be more appropriate.
210	British Sarcoma Group	9	Full	279	1.11.311	We note that the suggested guidance is: Consider an urgent direct access ultrasound scan (within 2 weeks) to assess for soft tissue sarcoma in people with an unexplained lump that is increasing in size. We have several concerns about this: 1. We remain very unclear of the availability of two week ultrasound	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first

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							would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
						2. We are unaware of the general expertise of ultrasonographers in identifying possible STS from the multitude of other lumps and bumps. Our day to day experience suggests that many patients are diagnosed with haematomas, fibrous lumps or lipomas following ultrasound when in fact they have a STS. Has there been a national training scheme to teach the very varied appearance of STS and to raise awareness of this possible diagnosis? 3. What is an unexplained lump? Our	Making recommendations for training in secondary care is outside the scope of the guideline. There was insufficient primary care evidence to add qualifying terms to lump.

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						patients all tell us that on the multiple attendances at the GP surgery prior to diagnosis they have been told not to worry and that their lump is a lipoma or a cyst or a haematoma. In other words the GP is falsely reassuring both themselves and the patient. Putting in the words 'unexplained' will stop patients being referred rather than encouraging it. 4. One common complaint we hear from patients diagnosed with STS is that they saw multiple different health care professionals on the pathway to diagnosis. It is very rare for any of these to have actually measured a lump, so there is no objective evidence of 'increase in size'. We would therefore suggest the following additional comment: **Any patient presenting with a lump should have the size of this recorded to aid future assessment of whether it has grown or not.**	We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. Thank you for this information. We hope that this guideline will go some way to helping resolve this issue. We have documented this issue in the introduction and do not consider that further recommendations are needed.
211	British Sarcoma Group	10	Full	279	1.11.4 11	We do agree however with the final modified recommendation: **Make a suspected cancer pathway referral (for an appointment within two weeks) to assess for soft tissue sarcoma in people with an unexplained lump that is increasing in size, bigger than 4 cm or deep to fascia.**	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. There was insufficient primary care evidence to add qualifying terms to lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.

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212	British Sarcoma Group	11	Full	General	General	Finally, we remain committed to the concept of diagnostic centres where soft tissue lumps can be referred and evaluated. These should be established in conjunction with sarcoma centres but need not be run by them.	Thank you for this information
213	British Sarcoma Group	12	Full	General	General	We are very concerned that the current suggested guidelines are far too 'wishy-washy' and hope that the GDG will consider our suggestions. Finally, the BSG confirms that it would be delighted to work with investigators in primary care to identify the frequency of our suggested "worrying symptoms" in the normal population and to see how effective they are in predicting sarcomas.	Thank you, we have responded to your detailed comments above. Thank you for your support.
214	British Sarcoma Group	13	Full	General	General	Suggested references of relevance: Smith GM, Johnson GD, Grimer RJ, Wilson S. Trends in presentation of bone and soft tissue sarcomas over 25 years: little evidence of earlier diagnosis. Ann R Coll Surg Engl. 2011 Oct;93(7):542-7 Grimer RJ, Briggs TWR. Earlier diagnosis of bone and soft-tissue tumours. J Bone Joint Surg(Br) 2010;92-B:1489-92 Taylor WS, Grimer RJ, Carter SR, Tillman RM, Abudu A, Jeys L. "Two-week waits"-are they leading to earlier diagnosis of soft-tissue sarcomas? Sarcoma. 2010;2010. pii: 312648. Epub 2010 Sep 26 George A, Grimer R. Early symptoms of bone and soft tissue sarcomas: could they be diagnosed	Thank you for providing these references. They were not included for the following reasons: - Smith: Population does not meet the inclusion criteria as it is cancer patients and not unselected patients presenting to primary care with symptoms. - Grimer: Narrative review with no new data. - Taylor: Population does not meet the inclusion criteria as it is referred patients and not unselected patients presenting to primary care with symptoms. - George: Population does not meet the inclusion criteria as it is cancer patients and not unselected patients presenting to primary care with symptoms. - Clark: Population does not meet the inclusion criteria as it is referred patients and not unselected patients presenting to

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						earlier? Ann R Coll Surg Engl. 2012 May;94(4):261-6 Clark MA, Thomas JM. Delay in referral to a specialist soft-tissue sarcoma unit. Eur J Surg Oncol. 2005 May;31(4):443-8. Epub 2005 Jan 21. Brouns F, Stas M, De Wever I. Delay in diagnosis of soft tissue sarcomas. Eur J Surg Oncol. 2003 Jun;29(5):440-5. Hussein R, Smith MA. Soft tissue sarcomas: are current referral guidelines sufficient? Ann R Coll Surg Engl. 2005 May;87(3):171-3. Johnson CJ, Pynsent PB, Grimer RJ. Clinical features of soft tissue sarcomas. Ann R Coll Surg Engl. 2001 May;83(3):203-5. Datir A, James SL, Ali K, Lee J, Ahmad M, Saifuddin A.MRI of soft-tissue masses: the relationship between lesion size, depth, and diagnosis. Clin Radiol. 2008 Apr;63(4):373-8; discussion 379-80. doi: 10.1016/j.crad.2007.08.016. Epub 2007 Dec 21. Lakkaraju A, Sinha R, Garikipati R, Edward S, Robinson P. Ultrasound for initial evaluation and triage of clinically suspicious soft-tissue masses. Clin Radiol. 2009;64(6):615-21	primary care with symptoms. - Brouns: Population does not meet the inclusion criteria as it is cancer patients and not unselected patients presenting to primary care with symptoms. - Hussein: Population does not meet the inclusion criteria as it is cancer patients and not unselected patients presenting to primary care with symptoms. - Johnson: Population does not meet the inclusion criteria as it is referred patients and not unselected patients presenting to primary care with symptoms. - Datir: Population does not meet the inclusion criteria as it is referred patients and not unselected patients presenting to primary care with symptoms. - Lakkaraju: Population does not meet the inclusion criteria as it is referred patients and not unselected patients presenting to primary care with symptoms.
215	British Society for Oral and Maxillofa	1	Full	226	General	*(p226-230)* The British Society for Oral and Maxillofacial Pathology welcomes the opportunity to respond to the NICE consultation on the Clinical Practice Guideline on Suspected Cancer.	Thank you for this information

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	cial Pathology					The Society's members provide specialist pathology services to Head and Neck Cancer centres and its members have particular expertise in **oral cancer** and **precancer** and undertake research ranging from epidemiology to molecular oncology, including diagnostic methods and the diagnostic pathways.	
216	British Society for Oral and Maxillofacial Pathology	2	Full	226	5	The statement that oral cancer "rarely" presents as advanced disease with regional lymphadenopathy seems incorrect. This would seem a fairly frequent presentation; overall 60% of patients present at Stage III or IV (UICC Staging). The DAHNO National audit data in the ninth report for 2013 shows one third of tongue cancers presenting with a positive neck and a further 16% of the apparently N0 necks being upstaged on treatment. There needs to be increased emphasis on neck metastasis as it is very frequently the presenting sign of HPV-positive tonsil, base of tongue and oropharyngeal carcinomas, whose incidence is increasing dramatically and for which the primary carcinoma is often subclinical.	We have deleted the term 'rarely'. The GDG did not find any evidence suggesting that neck metastasis had a PPV high enough to warrant referral.
217	British Society for Oral and Maxillofacial Pathology	3	Full	226	General	*(p226-230)* Currently just over half of referrals come from medical and just under half from dental practitioners.	Thank you for this information
218	British Society for Oral and Maxillofa	4	Full	226	General	Pages 226-227 discuss in detail two US studies of one specific method of assessing an oral brush biopsy. The technique is correctly rejected but for the wrong reasons. As noted the study has significant defects. However, the technique should	The GDG considered the evidence on a range of possible investigations. No recommendation was made on brush biopsy.

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	cial Pathology					be excluded from the review because it is not designed to be a test for suspected cancer and should not be used in this situation as it introduces delay in referral and diagnosis. The test is intended as a diagnostic adjunct or secondary screening test, primarily to exclude lesions of low risk that do not merit formal scalpel biopsy. Its use in primary care environments, efficacy, cost effectiveness and value in the diagnostic pathway have not been defined or evaluated. The document mentions the one large multicentre study but there is a considerable body of evidence of lower level that shows a poor predictive value, sensitivity and specificity. Note the studies only refer to one method of assessing a brush biopsy, others are being used in the UK in specialised centres. There are also many other adjunctive methods to assist diagnosis (eg. methods of illumination, vital stains etc.) which have been extensively evaluated, but have not been reviewed and would need to be considered in any evaluation of brush biopsy.	
219	British Society for Oral and Maxillofacial Pathology	5	Full	228	General	The new recommendations concentrate on oral ulcers and lumps. However, these are late signs of oral carcinoma, and are signs of established rather than suspected cancers. Red patches (erythroleukoplakia and speckled leukoplakias) should have been included using the phraseology: **Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a red or red and white patch in the oral cavity that has been present for more than 2 weeks and has been assessed by a dental surgeon to be consistent with oral cancer or precancer.**	We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation. We did not find any primary care evidence to support retaining these recommendations as part of the update.

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						This is the most important change we suggest. Epidemiological data suggests that approximately a half of erythroleukoplakia and speckled leukoplakias harbour early cancer but these lesions are rare overall so that the predictive value of this sign for cancer is high. Dentists are trained in assessing such lesions and identification of oral cancer at this early stage is the best predictor of successful treatment. The positive predictive value of this referral criterion would be much higher than that for lumps, given the large number of possible benign diagnoses for lumps. White lesions are correctly excluded as a referral criterion as the predictive value is too low, only speckled leukoplakia and erythroleukoplakia should be included.	
220	British Society for Oral and Maxillofacial Pathology	6	Full	230	General	At the top of page 230 it is stated that *The GDG estimated that the recommendations would result in an increase in costs within the community dental service*…… It should be recognised that most referrals will not come from the Community Dental Service and that the CDS does not necessarily have the appropriate skill mix to deal with this referral load. We recognise the imperative to find a free dental opinion to make the new criteria practicable, but have reservations about the suitability of the Community Dental Services to undertake and evaluate this referral caseload as their target groups are children and special needs groups. Most CDS services do not have the appropriate mix of skills and, in most areas, are contracting. The suggestion fails to take into account changes in the General Dental Services now that tier 2 and	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'

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						3 specialist services are to be commissioned. In a few areas the CDS might be an appropriate referral pathway, but in almost all cases a better pathway for URGENT REFERRAL for a dental opinion would be to a Tier 2 or 3 specialist practitioner in Oral Medicine or Oral Surgery (which would involve a patient charge under current proposals) or direct to an Oral Surgeon or Oral Physician in a Dental Hospital in secondary care. Cases to be referred on the SUSPECTED CANCER PATHWAY should be referred to a Head and Neck Cancer Team in secondary care. Commissioning models for Tier 2 and 3 (Dentists with special interests) Oral Surgery and Oral Medicine services are in development but the draft commissioning framework produced to date has sidestepped cancer referral assuming that patients will continue to be referred direct to a Head and Neck Cancer Treatment Centre. As they stand, the NICE proposals do not align with the planned structure of NHS dental services. There is a balance to be struck between either defining better referral criteria to allow immediate referral to secondary care or using dentist 'gatekeepers' in primary care. If dentists are to be used as a primary screening service then the predictive value of the criteria could be considerably enhanced using more specific oral and dental terminology, though this may prevent non-dental healthcare professionals from understanding them. We also feel this two tier pathway needs further discussion as it risks introducing delay and leaves the dentists in the second stage of the process without defined onward referral criteria. Does the	

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						clock restart at review by a dentist? Does the patient enter a 2 week wait pathway on referral to the dentist or after leaving the dentist for secondary care? Evidence from use of the current criteria shows that referral to a primary care dentist is often a cause of delay in diagnosis so selection of those with the correct skills is paramount (Brocklehurst PR, Baker SR, Speight PM. Factors which determine the referral of potentially malignant disorders by primary care dentists. J Dent. 2010;38:569). We will feed back information on the guideline to the commissioning group and NHS England and we recommend further discussion of the pathway with the Chief Dental Officer and commissioners. For the proportion of the population living within referral distance of a Dental Hospital these would also provide a free assessment service through their primary care dental emergency services. Though these centres are few, they are almost all located in large population centres.	
221	British Society for Oral and Maxillofacial Pathology	7	Full	226	General	*(p226-230)* There is insufficient attention to the concept of the high risk patient, particularly smokers aged over 45 and those of Asian culture who use betel quid (paan), the latter a particularly potent and easily identifiable risk factor. Evidence from primary care suggests these factors are useful in referral. (Brocklehurst PR, Baker SR, Speight PM.Factors which determine the referral of potentially malignant disorders by primary care dentists. J Dent. 2010;38(7):569-78).	Thank you for providing this reference. We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG 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 smoking or using betel quic affected the predictive power of

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							symptoms for oral cancer.
222	British Society for Oral and Maxillofacial Pathology	8	Full	226	General	*(p226-230)* The British Society for Oral and Maxillofacial Pathology will be pleased to provide any specialist advice that NICE feels may be helpful.	Thank you for your offer of assistance.
172	British Society for Oral Medicine	1	Full	228	14.2 Oral cancer Recommendations	RESPONSE: This recommendation should also include a "red patch" or a "mixed red and white patch" persisting for more than 2 weeks after being seen by a dental surgeon. Perhaps also persistent for more than 2 weeks white patches on floor of the mouth and sides of the tongue could be considered There are also other previous recommendations in NICE (2005) that are missed out in this update. For example . non- healing socket more than 2 weeks and excessive mobility of a tooth / teeth when other teeth are sound	We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation. We did not find any primary care evidence to support retaining these recommendations as part of the update.
173	British Society for Oral Medicine	2	Full	226	12	*(lines 12-13, 14.2)* GDG REPORTED: No primary care evidence was identified pertaining to the risk of oral cancer in patients presenting with symptoms in primary care. RESPONSE: One study in the UK has .examined what factors or cues primary care dentists (PCDs) take into account when diagnosing and referring PMD. This study confirmed that risk factors were statistically significant in their ability to predict a referral decision. The study was on potentially	Thank you for providing this reference. We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. The proposed paper did not report such data and was therefore not included.

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						malignant disorders but would reflect on their decision for cancer referrals too. Brocklehurst PR, Baker SR, Speight PM. Factors which determine the referral of potentially malignant disorders by primary care dentists. J Dent. 2010 Jul;38(7):569-78.	
174	British Society for Oral Medicine	3	Full	227	14.2 Oral cancer Evidence statement	GDG QUOTED Transepithelial oral brush biopsy study from USA. RESPONSE: This is not relevant for the UK as the method is not recommended by UK Pathologists	The GDG considered the evidence on a range of possible investigations. No recommendation was made on brush biopsy.
175	British Society for Oral Medicine	4	Full	228	14.2 Oral cancer Quality of the evidence	Signs and symptoms of oral cancer GDG statement; No evidence was found pertaining to the positive predictive values of different symptoms of oral cancer in primary care. Cochrane review gives sensitivity and specificity of dental practitioners finding cases in primary care: REF : Walsh T, Liu JL, Brocklehurst P, Glenny AM, Lingen M, Kerr AR, Ogden G, Warnakulasuriya S, Scully C. Clinical assessment to screen for the detection of oral cavity cancer and potentially malignant disorders in apparently healthy adults. Cochrane Database Syst Rev. 2013 Nov 21;11:CD010173. doi: 10.1002/14651858	Thank you for providing this reference. The Cochrane review was not included because the included studies were all screening studies, which are outside of the scope of this guideline.
176	British Society for Oral Medicine	5	Full	228	14.2 Oral cancer Quality of the evidence	GDG STATEMENT: No evidence was found for this outcome RESPONSE: Despite some controversial evidence, there is one study in the UK (not quoted in the GDC) that has assessed the predictive value of two week wait Head and neck (oral cancer) initiative using existing NICE guidelines for referral from primary care; Ref:	Thank you for providing this reference. The suggested study was not included because it did not meet the inclusion criterion pertaining to the study population: It was conducted in a referred population, that is, not in an unselected primary care population presenting with symptoms to primary care, which was an

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						Singh and Warnakulasuriya 2006: Citation: Singh P, Warnakulasuriya S. The two week wait cancer initiative on oral cancer; the predictive value of urgent referrals to an oral medicine unit. Br Dent J. 2006;201 :717- 20. With reference to current NICE Guidelines, this study found 6/76 referrals from primary care with an urgent referral (7.9%) and 6/25 (24%) of suspected malignancy referrals had cancer diagnosed by biopsy. Predictive values are given.	eligibility criterion for the clinical questions dealing with the cancer risk of signs and symptoms.
177	British Society for Oral Medicine	6	Full	230	14.2 Oral cancer Other considerations	GDG statement: Noted that the community dental Service (CDS) is free, available in all areas, and provides more standardised care than individual dental practitioners, but the GDG recognised that it is currently only set up to treat children and people with special needs and not people with suspected cancer RESPONSE : This is exactly why community dental service is unsafe to handle this urgent need. CDS is the most difficult service to access, though it is free. To qualify to attend CDS it may take moths not days as the appointments beyond children, and special needs have to be approved by the managers. There appears to be a lack of rigour among many CDS practitioners when screening for oral cancer or potentially malignant disorders as very few cases arrive in secondary care from CDS. The recommendation should be to seek a dental practitioner but if that is considered costly for the patient to seek help from their GP. Triage through CDS is unsafe, will cause further delays to the cancer journey	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'

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178	British Society for Oral Medicine	7	Full	228	14.2 Oral cancer Trade-off between clinical benefits and harms	GDG set a positive predictive value (PPV) of 3% Response: This PPV is likely too low; it should be set at 5%	The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline.
179	British Society for Oral Medicine	8	Full	226	2	GDG stated: Most oral cancers are diagnosed by dental surgeons. RESPONSE: This is not so. Many referrals in our experience do come from GPs. This is important to recognize in generating proposals for referrals, as patient choice is still to see their GP for any non-dental symptom in their mouths such as ulcers.	We have changed this to 'many'.
180	British Society for Oral Medicine	9	Full	226	6	GDG stated; Oral cancer can present as advanced disease with regional lymphadenopathy. RESPONSE: In secondary care we still encounter many (close to 50%) with regional (neck) lymphadenopathy in stages 3 or 4	We have deleted the term 'rarely'.
147	British Society of Gastroenterology	1	NICE	80 69	1.2.8	What is the evidence for a cut off of 55 for urgent investigation if weight loss and upper GI symptoms? Why choose 55 for one scenario but over 40 rather than 55 for upper abdo pain with nausea and vomiting with weight loss (1.2.8)? Is there good evidence to support these different thresholds, because if not, it looks very confusing for GPs?	The recommendations for upper GI cancers have been revised to make them simpler and easier to understand. The age thresholds in the recommendations are now the same

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148	British Society of Gastroenterology	2	NICE	80 69	1.2.9	The differences between 1.2.8 and 1.2.9 are difficult to understand (and will be confusing to GPs): why should a patient with weight loss, abdo pain and vomiting over 40 be offered a direct access OGD within 2 weeks (1.2.8) while if they just have nausea and vomiting with weight loss they have to be over 55 to merit direct access Endoscopy – and then only 'non-urgent'? Also patients with weight loss and upper abdominal pain (no duration specified) over 55 are offered urgent 2WW Endoscopy (1.2.8) while in 1.2.9 the same patients, if they have symptoms for more than 2 weeks, are to be offered non-urgent Endoscopy? This is VERY confusing.	The recommendations for upper GI cancers have been revised to make them simpler and easier to understand.
149	British Society of Gastroenterology	3	NICE	130 70	1.3.1	This implies that a single, isolated, episode of bleeding could trigger a 2ww referral, and is too broad. The bleeding needs to be recurrent, or accompanied by other symptoms, to warrant any form of invasive investigation.	There was insufficient primary care evidence to add qualifying terms to rectal bleeding. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
150	British Society of Gastroenterology	4	NICE	130 70	1.3.2	We suggest the standard cut off of 115g/L for women and 130g/L for men be used	The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
151	British Society of Gastroenterology	5	NICE	130 70	1.3.3	This seems very broad, and would include everyone with infective gastroenteritis, and people with longstanding symptoms. We suggest it should be modified, to specify an acute change but of duration over 2 weeks.	There was insufficient primary care evidence to add qualifying terms to change in bowel habit. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
152	British Society of Gastroen	6	NICE	130 70	1.3.4	The use of the word 'consider' here seems odd-particularly given the more didactic language used elsewhere, and 'hardness' of this clinical finding, which should be the strongest of all criteria for	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE

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	terology					referral mentioned.	recommendations please see p 6 of the short version.
153	British Society of Gastroenterology	7	NICE	130 70	1.3.6	FOBT has low specificity, sensitivity, PPV and NPV, and is not a suitable investigation in those with symptoms or anaemia. FOBT should be reserved exclusively for screening activities and not used for, often false reassurance, in anyone with symptoms and certainly not for iron-deficiency which should be fully and appropriately investigated. Please note that a number of other sections of the BSG (endoscopy and oesophageal) and individual members raised concerns about this particular recommendation including the Director of the Eastern Hub of the Bowel Cancer Screening Programme. We suggest the standard cut off of 115g/L for women and 130g/L for men be used - otherwise it is confusing for users.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may

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							decide that they warrant a routine referral. The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
154	British Society of Gastroenterology	8	NICE	130 71	1.3.7	See above comments about FOBT	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states

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							in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
155	British Society of Gastroenterology	9	NICE	130 71	1.3.8	We suggest the standard cut off of 115g/L for women and 130g/L for men be used - otherwise it is confusing for users.	The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
156	British Society of Gastroenterology	10	NICE	130 71	1.3.9	DRE is part of a complete assessment of a patient with lower GI symptoms but is not proven to provide any diagnostic benefit/yield in patients without rectal bleeding or anal symptoms.	The recommendation on digital rectal examination for colorectal cancer has been deleted.
157	British Society of Gastroenterology	11	NICE	136 71	1.3.10	The use of the word 'consider' here seems odd- particularly given the more didactic language used elsewhere, and 'hardness' of this clinical finding, which should be the strongest of all criteria for referral mentioned. In addition: The studies included for "flexi-sig" are archaic. Indeed two include rigid sigmoidoscopy i.e. will only have examined the rectum. For the age group at which this is targeted it should not be in the	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. This guideline used data from primary care studies as it was important to know the performance characteristics of investigations when performed in a primary care population. These studies

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						algorithm. Good for young, pr bleeding but little else. Barium enema is outdated and should be removed. Duration of symptoms is important and should be made explicit. With regard to **patients under 50 years of age**, perhaps consideration for referral could also be made if they have a significant risk factor for colorectal cancer i.e. rectal bleeding plus 1 other symptom as per consultation document, OR 1 symptom plus 1 risk factor as per the list below; • IBD with extensive colitis for over 10 years • Previous cancer or multiple polyps • Known inherited syndrome, e.g. Lynch Syndrome • Family history of colorectal cancer	were all that was available in this patient population. However we do not make any recommendations about the use of primary care flexible sigmoidoscopy. The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling. There was insufficient primary care evidence to add qualifying terms to the recommendations. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that IBD, previous cancer, multiple polyps, known inherited syndromes or family history affected the predictive power of symptoms for colorectal cancer.
158	British Society of	12	NICE	67 68	1.2.4	We feel the sentence should be completed with: "and a diagnosis of biliary colic due to gallstones is thought to be unlikely."	The PPV for jaundice in pancreatic cancer is one of the highest for any symptom in any cancer. If a GP has a

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	Gastroenterology					(It is important to include a clinical assessment of what likely diagnoses may be as not all cases will be due to cancer and hence would not be appropriate to be on cancer pathway. Gallstones is the most likely other diagnosis).	clearly correct alternative diagnosis we would expect them to exercise their clinical judgement.
159	British Society of Gastroenterology	13	NICE	67 68	1.2.5	Apart from the latter, we feel it is important to state that a clinical assessment of underlying pathology is needed as these symptoms could be due to gastric or colorectal cancer in which endoscopic evaluation is need. Possible sentence to include may be "in patients over 60 years with weight loss and any of the symptoms below with normal endoscopic assessments of the gastrointestinal tract, pancreatic cancer should be considered by investigating with CT scan".	The symptom based section shows the range of recommendations that are appropriate for people with particular symptoms. GPs will need to use their clinical judgement to decide which is the most appropriate cancer to exclude first.
429	British Thoracic Society	1	General	32	10	*(lines 10-12)* It should be acknowledged that lung cancer can often be asymptomatic at presentation, especially early stage lung cancer.	This guideline covers people presenting to primary care with symptoms.
430	British Thoracic Society	2	General	32	12	The text is confusing regarding use of CT. All patients with suspicious chest X-rays will have CT and most units would CT smokers > 40 with persistent haemoptysis even if the CXR is normal.	This background text is a reflection of current practice in primary care. Secondary care investigations follow different practice which is not germane to this introduction.
431	British Thoracic Society	3	General	32	16	The most common biopsy is CT guided lung biopsy. Thoracoscopy not commonly used to diagnose lung cancer. Suggest change to "Definitive diagnosis requires biopsy, usually via CT lung biopsy or bronchoscopy.	We have amended the text
432	British Thoracic Society	4	General	32	16	*(lines 16-18)* This is out of date. Patients are most likely to have a diagnostic biopsy via CT guided biopsy or bronchoscopy/EBUS. Thoracoscopy is only used as a diagnostic tool in a small proportion	We have amended the text relating to biopsy, but do not consider further detail is required for a primary care guideline.

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						of patients. It should include the fact that PET scanning is frequently used in guiding diagnostic sampling and staging.	
433	British Thoracic Society	5	General	41	1.1.2 – 1.1.5 17	The recommendations are quite complicated and could be confusing for GPs as to when to refer in and when to do a FBC and CXR. Recommend the format is changed to have two separate boxes – one titled "when to refer for 2 week wait appointment" and a one titled "when to offer FBC and CXR". There should be a statement to say "Do not refer patients under 40 with haemoptysis and normal CXR for urgent 2 week wait cancer appointment". These referrals clog up cancer clinics and inappropriately tie up resource as part of 2 week wait pathway.	The recommendations for lung cancer have been revised to make them simpler and easier to understand. We have clarified in the recommendations that people 40 and over with unexplained haemoptysis should be referred using a suspected cancer pathway referral. The GDG did not think it was appropriate to make the recommendation you have suggested because although unlikely it is possible that someone under 40 with haemoptysis may need a cancer referral. Making a negative recommendation might impact in such situations. We expect primary care clinicians to exercise clinical judgment in applying these guidelines.
434	British Thoracic Society	6	General	45	13	The text is confusing re use of CT. All patients with suspicious pleural abnormality on CXR should have CT.	We have not made any recommendations on the use of CT in lung cancer.
435	British Thoracic Society	7	General	45	16	*(lines 16-17)* Once again, a large number of mesotheliomas are now diagnosed with US and Ct guided pleural biopsies. The thoracosopy route is usually Video-assisted VATS, Open thoracosopy is rarely used for diagnosis.	The text on thoracoscopy has been deleted.

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436	British Thoracic Society	8	General	46		Clarify the mesothelioma recommendations so that all of the symptoms listed are to prompt a CXR in the first instance, not a direct referral.	The recommendations are now clear that symptoms should prompt a chest X-ray. If the chest X-ray shows findings suggestive of mesothelioma this should prompt a referral on a suspected cancer pathway.
87	Cancer Research UK	1	Full	General	General	Cancer Research UK welcomes the opportunity to comment on the updated guidance. Early diagnosis and having access to optimal treatments are crucial to improving clinical outcomes for cancer patients. The UK continues to have lower cancer survival than some other developed nations. There is some evidence that later stage diagnosis in the UK compared to other countries is contributing to this trend, notably for lung and colorectal cancer. We also know that there is variation across Clinical Commissioning Groups for the proportion of cancers diagnosed at an early stage, from 40 – 60%. Updating this guidance is therefore an important step in improving our cancer outcomes. We recognise that the introduction of the 3% positive predictive value (PPV) threshold is an attempt to 'cast the net wider' and ensure more cancers are diagnosed earlier, which we welcome. However, there are instances throughout the document when we feel that the recommendations are not in keeping with the aim of a 3% PPV, for example the cervical guidance recommends 'consider' a two week referral if the cervix has an appearance consistent with cervical cancer. We believe this should be strengthened. It is essential that the guidance is joined up with –	Thank you Thank you for this information. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. We agree that co-ordinated attempts to

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						and complements - other efforts to improve the early diagnosis of cancer, such as public awareness campaigns, the National Awareness and Early Diagnosis Initiative (NAEDI) and the Accelerated, Co-ordinated, Evaluated (ACE) programme which will help us to understand how the NHS can give patients the best possible chances of being diagnosed and treated early. Furthermore, in order for this guidance to be effective, it is essential that it is made accessible to, and useable by, its target audiences. It should also be matched with the necessary resources – both at the primary and secondary care levels – to ensure the health system has the capacity to meet rising demand. We are also concerned that the guidance makes the assumption that efficient access to diagnostics exists across the country but we know that – unfortunately – this is not the case. We believe that action should be taken to ensure equal and efficient access to diagnostics across England so that the guidance can be implemented effectively. We welcome efforts to reflect the evidence base throughout the guidance but have some concerns that there is inconsistency across cancer types as to which recommendation ('consider', 'offer' or 'refer') is used.	improve cancer diagnosis are worthwhile. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. However, it is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable. The wording in the recommendations reflects the strength of the evidence. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						There are also concerns that this guidance is occasionally at odds with other symptom-specific NICE guidance, for example the oesophageal guidance seems to be inconsistent with NICE's dyspepsia guidance. Finally, whilst we acknowledge the decision to focus less on risk factors within this guidance, we feel there is a missed opportunity to link up considerations of symptoms with an assessment of risk factors. For example, when considering possible symptoms associate with prostate cancer we would expect primary care professionals to take into consideration ethnicity of the patient (as a known risk factor). We would welcome further clarity from NICE as to how there can be better linkage between symptoms and risk factors to support professionals in their clinical assessments.	This is a guideline about referral of people with suspected cancer from primary care. As such it covers a slightly different population to the dyspepsia guideline and there is therefore no direct conflict in the recommendations. As documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that ethnicity affected the predictive power of symptoms for prostate cancer.
88	Cancer Research UK	2	Full	7	11	*(lines 11-12)* The guidance states that it will be 'reviewed and updated as is considered necessary.' We would welcome clarification on what 'as is considered necessary' entails, and how this decision is made. Ten years is a long time to wait to update this guidance. Cancer Research UK commented on the scope nearly three years ago. While we appreciate the pressures NICE is under and the thoroughness with which guidance is reviewed, the evidence is constantly accumulating. Ideally guidance could be updated on a rolling basis as evidence mounts.	NICE has a process for reviewing and updating guidelines. This can be found on the NICE web site.
89	Cancer	3	Full	7	37	*(lines 37-39)* The guidance states that it is	This guideline covers 37 different

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	Research UK					'relevant to all primary healthcare professionals who come into contact with people suspected of having cancer, as well as to the people with suspected cancer themselves and their carers'. The guidance will have no impact at all unless it is regularly used by healthcare professionals and understood by the public. It is therefore of the utmost importance that thought is given to how best to present the guidance in an accessible form for these diverse audiences. Primary care professionals are incredibly busy and only see, on average, around eight new cases of cancer each year. They will also see many patients who have symptoms that turn out not to be cancer. They therefore cannot be expected to know the symptoms of 200+ types of cancer in detail, nor can they be expected to read and digest 400+ pages of guidance. We would like to hear from NICE on plans to make the guidance useable by primary care professionals. For example, it could be converted into a searchable computer-based tool. Any work in this area should link up with existing decision support tools (which would require updates in any case) and the stakeholders involved in this work to ensure it has the greatest possible impact and is not duplicative. Similarly, the guidance in its current form is very	cancers. As a consequence it contains a lot of information. By producing a section of the guideline focused on symptoms, the GDG have sought to make this information more easy to navigate by primary care clinicians. In addition, NICE are exploring ways that we can improve usability of the document. The short version of the guideline only contains the recommendations and none of the supporting evidence. Primary care professionals may find this version more useable. There is also a NICE pathway on the NICE website that presents all of the guidance provided by NICE and any related NICE guidance. NICE also produce a version of the guideline for the public which contains all of the recommendations in lay terms. This will be published at the same time as the other guideline documentation. The creation of clinical decision support software based on these recommendations is outside the scope of this guideline and will be a matter for implementation. However, NICE are exploring ways that we can improve usability of the document. NICE also produce version of the

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						technical and it cannot be expected that the general public will either take the time to read such a weighty document or easily understand its contents. We would therefore like to hear from NICE on plans to make the contents of this guidance understandable for a lay audience, as well as people from different cultural backgrounds and people with learning difficulties. Cancer Research UK would be pleased to work with NICE on plans to disseminate the guidance.	guideline for the public which contains all of the recommendations in lay terms. This will be published at the same time as the other guideline documentation. Thank you for your support.
90	Cancer Research UK	4	Full	7	39	*(lines 39-40)* The guidance states that it '…will be of value to those involved in clinical governance in both primary and secondary care to help ensure that arrangements are in place to deliver appropriate care to this group of people'. As above it is important that the guidance is also made accessible for these audiences. Furthermore, the relevance of this guidance to secondary care professionals cannot be understated. It needs to be clearly communicated to all parts of the health service that the impact of the updated guidance will be an increase in referrals, in order that the service can prepare accordingly.	Thank you, we agree. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
91	Cancer Research UK	5	Full	19	from line 40	*(p19-20)* We welcome the ambition to diagnose cancer earlier and understand the rationale behind introducing the threshold value of 3% PPV. However, we appreciate that there is a balance to be struck between enabling earlier diagnosis and not overwhelming an already stretched system. We urge NICE and others to work together to	Thank you The GDG understand your concerns. However the implementation of this guideline in primary and secondary care is outside the scope of this guideline.

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						understand how the threshold can best be communicated to – and used by - primary care professionals, and assimilated into existing decision support tools. In addition, the new threshold should be communicated to secondary care professionals and commissioners so that they do not believe a potential increase in referrals is the result of inappropriate referral behaviour from primary care. We are already aware of anecdotal evidence of certain referrals being 'refused' or discouraged as it is. The wider system needs to be engaged to cope with increased demand. NICE should liaise with NHS England to help understand the knock-on effects on the whole cancer services system and to ensure that there are enough resources for the system to cope with increased demand. We know that services are already beginning to struggle (Measuring up? The health of NHS cancer services. Cancer Research UK. September 2014) and this guidance has the potential to place even more demand upon the system, so it is essential that these conversations happen now. We also believe that the impacts of setting the threshold at this level (i.e. whether the potential benefits of earlier diagnosis of cancer and other conditions outweigh the potential harms of increased anxiety, overdiagnosis, unnecessary tests and treatment) should be monitored and evaluated so that the evidence base is built up and can inform future practice. Additionally, it is important that, if they are suspicious, GPs have the flexibility to refer patients	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. We agree Recommendations in NICE guidelines do not replace clinical judgement. We would

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						for tests who may not fit all the guidelines.	expect GPs to use their knowledge and experience when applying these recommendations, and have made this explicit in the introduction in the full and short versions.
92	Cancer Research UK	6	Full	29	General	*(p29-30)* Cancer Research UK believes that there needs to be enough flexibility in the system so that primary care professionals can monitor patients when they may not fit all of the guidelines and ensure they are referred if symptoms persist and are believed to be consistent with suspected cancer. We therefore welcome the addition of 'safety-netting' to the guidance. However, through our work with GPs, we understand that there are concerns that the section is a little vague regarding its implementation and we would welcome further detail on this. The guidance states that, "No evidence was found pertaining to the effectiveness of any safety-netting strategies…" We therefore believe that this recommendation should be monitored and evaluated in order to build the evidence base of what works (and what doesn't). This should help to inform future practice. It is also important that test results are followed up within primary care so that the GP who requested the test sees and acts on the results in a timely manner. Furthermore, there is nothing in the guidance about safety netting for patients who have been referred. Simple measures such as following	Thank you The GDG consider that the wording of the recommendation on safety-netting is clear and will be understood. Delivery of this recommendation will be a matter for implementation. This will be a matter for future research. We agree. The GDG did not consider that this situation was specific to referral for suspected cancer. They therefore did not

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						patients up to ensure they have been seen can help to make sure they do not get lost in the system. It would also be helpful to ask GPs to consider reviewing patients for ongoing symptoms who have had a negative 2 week wait referral.	investigate a review question on this issue and are not able to make any recommendations. It was not possible for the GDG to provide comprehensive guidance on this issue, however this will be addressed in part through the symptom based approach, which suggests alternative actions for a particular symptom.
93	Cancer Research UK	7	Full	31	General	The National Cancer Peer Review programme is being reviewed. It is important that this programme is maintained in some form to ensure that services can improve in line with the guidance's recommendation.	Thank you for this information
94	Cancer Research UK	8	Costing report to support the guideline	General	General	Cancer Research UK believes that it is very difficult to estimate the changes in referral patterns with any degree of certainty. This is why we believe that as far as possible, the recommendations in the guidance are monitored and evaluated in order to inform future practice. However, we do believe that the costs of implementing the guidance (estimated at £18m to £36m) should be considered in the context of savings that will be gained from diagnosing cancer at an earlier stage when it is easier to treat. A recent report (Saving lives, averting costs: An analysis of the financial implications of achieving earlier diagnosis of colorectal, lung and ovarian cancer. Incisive Health, September 2014) suggested that achieving the level of early diagnosis comparable with the best in England	Further work to identify savings as result of this guideline is being undertaken.

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						across colon, rectal, ovarian and lung cancer could deliver treatment savings to the NHS of over £44 million, and benefit more than 11,000 patients.	
95	Cancer Research UK	9	Full	42	1.1.5 17	The guidance states, 'Consider an urgent full blood count and chest X-ray (within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following: • finger clubbing or • supraclavicular lymphadenopathy or persistent cervical lymphadenopathy or • chest signs compatible with lung cancer.' We believe this should be 'offer' as if a patients has chest signs compatible with lung cancer, 'consider' does not feel strong enough. We feel that this would be consistent with the aim to cast the net wider as suggested by the 3% threshold. We are also concerned that the guidance does not prompt consideration of lung cancer in patients under the age of 40. While we know it is rare, and appreciate the fact that the guidance states that GPs should have the ability to use clinical knowledge to override guidance as appropriate, we would welcome the inclusion of a sentence that reflects this.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. The GDG did not find any evidence suggesting high PPVs for lung cancer in people under 40. We agree that GPs should use their clinical judgement when assessing patients and have mentioned this in the introduction to the full guideline.
96	Cancer Research UK	10	NICE	45	Various	*(p45,47,51)* It is extremely positive to see children's symptoms accounted for so extensively, however with the new standalone symptoms of fatigue (p.45) and parental concern (p.51) it is crucial that genuinely integrated diagnostic pathways (possibly through the use of diagnostic hubs) are established to avoid repeat tests for children.	Thank you for your comment. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.

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97	Cancer Research UK	11	Full	60	1.2.1 14	The guidance states, 'Offer urgent direct access upper gastrointestinal endoscopy (within 2 weeks) to assess for oesophageal cancer in people: • with dysphagia or • aged 55 and over with weight loss and any of upper abdominal pain or reflux or dyspepsia.' We are concerned that the major symptom for referral is dysphagia as we know that the majority of patients with this symptom will have advanced disease at this stage. The previous guidance didn't require dyspepsia to be accompanied by another sign/symptom before referral. We feel that maintaining the previous wording would be more consistent with the aim to cast the net wider as suggested by the 3% threshold. We are also concerned that the new recommendation is not consistent with NICE dyspepsia guidance in which the cut off age of 55 has been removed. Furthermore, when PHE and DH developed the creative for the Be Clear on Cancer oesophago-gastric campaign, they had a group of experts from	We agree that dysphagia is a significant symptom but our recommendations also cover several other symptoms. This recommendation was based on primary care evidence. Meta-analysis of dyspepsia alone gave an estimated PPV of 0.25%. Consequently no recommendation for referral for this symptom alone was made. This guideline deals with suspected cancer, whereas GC184 covers all conditions that could cause dyspepsia. As such it covers a slightly different population to the dyspepsia guideline and there is therefore no direct conflict in the recommendations. It should be noted that CG184 states that this guideline should be referred to when a person presents with symptoms that could be caused by cancer. Our recommendation was based on primary care evidence. Meta-analysis of dyspepsia alone gave an estimated PPV

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						primary and secondary care to help inform the decision on which symptoms to focus on and the consensus was that to identify early stage disease, dyspepsia should be the trigger symptom for investigation. We believe that the guidance should more closely align with this message.	of 0.25%. Consequently no recommendation for referral for this symptom alone was made.
98	Cancer Research UK	12	Full	130	1.3.3 13	The guidance states, 'Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if they are aged over 60 and have unexplained changes in their bowel habit'. In the previous guidance, 'change in bowel habit' was defined as, 'looser stools and/or increased stool frequency' yet this qualification is missing in the new recommendation. On page 96 of the new guidance, it says, 'Several symptoms have been reported, with rectal bleeding, diarrhoea, constipation (sometimes referred to as 'change of bowel habit')'. We would welcome clarification in the current guidance as what should count as a 'change in bowel habit'. In addition, the timeframe of 6 weeks has been removed from the current guidance. However, we do not believe patients should be referred if they have had a change in their bowel habit for a couple of days so would welcome the inclusion of guidance on the timeframe. We also believe that thought should be given to how best to communicate this guidance to the public – how should they interpret this and know when to take	There was insufficient primary care evidence to add qualifying terms to change in bowel habit. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. We have amended the background text to remove any possible ambiguity. There was insufficient primary care evidence to add qualifying terms to change in bowel habit. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations

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						action if they have a change in their bowel habit?	
99	Cancer Research UK	13	Full	131	1.3.6 13	The guidance states, 'Offer testing for occult blood in faeces to assess for colorectal cancer in people without rectal bleeding who: • have abdominal pain or • have weight loss or • are aged under 60 and have a change in bowel habit or iron-deficiency anaemia (with haemoglobin levels of 12 g/dl or below for men and 11 g/dl or below for women).' We are concerned that the suggestion that GPs consider FOBt in symptomatic patients (albeit without rectal bleeding) might be confusing for GPs and blur the lines between asymptomatic screening and symptomatic diagnosis. We believe that a colonoscopy should be offered to these patients rather than FOBt.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may

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							decide that they warrant a routine referral.
100	Cancer Research UK	14	Full	141	1.4.2 10	The guidance states, 'Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer if they are aged 50 and over with any of the following symptoms in 1 nipple only: - Discharge - Retraction - Other changes of concern We are concerned that this implies that only breast lump or nipple changes warrant referral. This text: *'The GDG noted that McCowan (2011) reported a PPV of 11.1 for breast thickening. The GDG noted that this was a difficult symptom to make sense of as it was unclear whether it meant thickening of the skin of the breast or of the breast tissue itself. The confidence intervals reported in McCowan (2011) for this symptom were also extremely wide, reflecting small numbers. Given these issues the GDG agreed it was better to group all 'changes of concern' in the breast together,'* suggests that 'other changes of concern' is meant to apply to breast changes other than those relating to the nipple, but we feel that this is not clear in the recommendation. We would welcome clarification of this within the guidance.	A new recommendation has been added to consider a suspected cancer pathway referral for breast cancer in people who have skin changes suggestive of breast cancer. The GDG chose not to describe skin changes with any further precision, because in the absence of evidence it was not possible to create a complete list. We have amended the text in the Linking Evidence to Recommendations section to clarify that 'changes of concern' relates to nipple symptoms.
101	Cancer Research UK	15	Full	147	6	The old guidance had recommendations for what to do for women aged under 30 suspected of having breast cancer but this has been omitted	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30

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						from the updated guidance. We believe this should be retained.	and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
102	Cancer Research UK	16	Full	155	11	The old guidance had recommendations around bleeding in women who are on tamoxifen but this guidance does not. Similarly, the new guidance does not mention how to approach pre-menopausal abnormal bleeding that could be endometrial cancer. We believe both should be retained.	We have documented in the introduction, there are very few instances where risk factors impact sufficiently on the predictive power of symptoms to allow different recommendations to be made for people with the same symptoms. The GDG 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 treatment with tamoxifen affected the predictive power of symptoms for endometrial cancer. There was no primary care evidence to support making a recommendation for abnormal menstrual bleeding.
103	Cancer Research UK	17	Full	159	1.5.142	The guidance states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for women if the appearance of their cervix is consistent with cervical cancer.' We believe this should be strengthened to 'Refer'.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						This would make the cervical recommendations consistent with the prostate recommendations, which state, 'Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their prostate feels malignant on digital rectal examination.'	
104	Cancer Research UK	18	Full	210	1.7.21	The old guidance for malignant melanoma stated, 'if there are strong concerns about cancer, any one feature is adequate to prompt urgent referral' but the proposed new guidance does not include this. We believe the new guidance should retain the old wording as this would be consistent with casting the net wider as implied by the shift to the 3% threshold. The new guidance also only mentions 'pigmented lesions' which risks excluding some types, e.g. non-pigmented nodular melanomas, which have a particularly poor outcome. We believe this should be included within the guidance.	These recommendations were based on the available evidence in primary care. We would expect primary care clinicians to use their clinical judgement when dealing with skin lesions. A recommendation has been added about lesions suggestive of nodular melanoma.
105	Cancer Research UK	19	Full	216	17	The guidance states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of squamous cell carcinoma.' We believe this should be strengthened to 'refer' or 'offer' as 'consider' does not seem strong enough if a GP suspects cancer. Furthermore, we believe the guidance should also specifically reference non-healing lesions.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. The GDG did not wish to try and describe SCCs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their

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							clinical judgement when applying this recommendation.
106	Cancer Research UK	20	Full	228	1.8.3 17	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. 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 on the lip or in the oral cavity that has been assessed by a dental surgeon to be consistent with oral cancer.' We believe that this should be 'Refer' or 'Offer', as if a patient has symptoms consistent with oral cancer, 'consider' does not seem strong enough. The guidance also states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for oral cancer in people with unexplained ulceration in the oral cavity lasting for more than 14 days.' And,	Whilst we acknowledge this may introduce some delay, the GDG agreed that reduction in unnecessary referrals to cancer services resulting from lesions being seen by a more expert clinician, outweighed any risks associated with a short delay. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for oral cancer in people with a persistent and unexplained lump in the neck' The strength of this recommendation appears to have been downgraded, which does not seem consistent with casting the net wider as implied by the introduction of the 3% threshold. All oral cancer recommendations are at the level of 'consider' and we believe these should be strengthened to 'offer' or 'refer'. There is also no explicit reference to leukoplakia or erythroplakia, which are associated with an increased risk of oral cancer. We believe both should be incorporated into the guidance.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation.
107	Cancer Research UK	21	Full	275	1.11.211	The guidance states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people if an X-ray suggests the possibility of bone sarcoma.' We believe that this should be 'Refer' or 'Offer', as if an x-ray suggests the possibility of bone sarcoma then 'consider' does not feel strong enough.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
108	Cancer Research UK	22	Full	279	1.11.411	The guidance states, 'Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people if they have ultrasound scan findings that are suggestive of soft tissue sarcoma or if ultrasound findings are uncertain and clinical concern persists.' We believe that this should this be 'Refer' or 'Offer'	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						as if findings are suggestive of soft tissue sarcoma then 'consider' does not feel strong enough.	
437	Children's Cancer and Leukaemia group	1	General	General	General	We as a group are very concerned by the proposed updated Guidelines for Suspected Cancer. Paediatrics is mixed in mostly with adults, and the guidelines are nothing like as user friendly as the old version. Furthermore, no paediatric input is visible in the guideline development group membership. It is our impression from conversations we have had so far, that there is universal agreement that these guidelines are not suitable for children as	This guideline is targeted at primary care where patients suspected of having cancer are identified. Therefore it was appropriate to have a majority of primary care clinicians on the GDG. Given there were 37 separate cancer groupings to be investigated, it was unrealistic to have representation from each specialty on the group. When the GDG needed further specialist input to make their recommendation, they called on expert advice. The GDG discussed whether they needed to have paediatric input and agreed that the very different spectrum of patients seen in paediatric services from those seen in primary care would reduced the usefulness of such input. They therefore did not request expert paediatric advice. In addition, one of the lay members had a paediatric interest. The GDG considered the evidence and made recommendations that were consistent with that evidence. This guideline is targeted at primary care and therefore secondary care evidence is of limited usefulness. This matter is discussed in the introduction in the full guideline. The GDG were tasked with producing recommendations for all ages. Childhood cancers are given a specific separate

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						they stand, and a separate set of guidelines for paediatrics is required. Whilst we have included some specific comments returned by our membership on this proforma, at this stage, as the guidelines seem so suboptimal, we do not feel that further detailed comments are until we can review a draft guideline with appropriate paediatric input.	chapter. We therefore consider that these guidelines are suitable for children. We have responded to these specific comments
438	Children's Cancer and Leukaemia group	2	Full	General	General	The paediatric diagnoses specifically included are Wilm's (this is mis-spelled - it should be Wilms or possibly Wilms'), retinoblastoma and neuroblastoma. Whilst it is not unreasonable to include these, it is not adequate and gives an impression that these are the only concerns. A far greater concern is the delay of diagnosis for primary CNS tumours (30% of all tumours), and other sarcomas.	We have corrected the spelling of Wilms'. The GDG have made a separate recommendation for children for primary CNS tumours in chapter 15. We have amended chapter 18 to make it clearer where children-specific recommendations for cancers that affect both adults and children appear in the guideline.
439	Children's Cancer and Leukaemia group	3	Full	General	General	Referral guidelines which include the two-week wait process are not useful. There is good evidence that this pathway does not work for paediatric patients. Referral of a child for suspected cancer needs to involve a telephone call today to a local paediatrician or paediatric oncologist.	The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
440	Children's Cancer and Leukaemia group	4	Full	General	General	There is no recommendation for spinal cord compression in children, as a presenting feature of spinal tuours. This is specifically excluded from the adult guideline document, and so there is a gap.	There was no evidence on spinal presentation of malignant CNS tumours in adults or children. It should be noted that benign spinal tumours are outside the scope of this guideline.
441	Children's Cancer and Leukaemia group	5	Full	General	1.10.1 General	48 hour referral for unexplained bleeding or petechiae is inappropriately slow, although this is referred to as "Very Urgent". If a blood count is indicated, it should happen today.	Recommendation 1.10.3 is for immediate specialist assessment for unexplained petechiae. A full blood count within 48 hours has been recommended for unexplained bleeding.

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442	Children's Cancer and Leukaemia group	6	Full	263 General	1.10.8 General	2 week wait for a suspected Non-Hodgkin Lymphoma is much too slow. Same day referral	The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
443	Children's Cancer and Leukaemia group	7	Full	240 General	1.9.2 General	2 week wait for new abnormal cerebellar or other central neurological function deficit is much too slow. Same day referral.	Our recommendation for abnormal cerebellar function or other central neurological function is for a very urgent referral within 48 hours, not a 2 week wait.
444	Children's Cancer and Leukaemia group	8	Full	General	General	There is no clarity around ages – for example does "below 50" with PR bleeding include children?	For all recommendations, we would expect the GP to use their clinical judgement in determine the appropriate action for a specific patient.
445	Children's Cancer and Leukaemia group	9	Full	240 General	General	We have concerns about the GDGs recommendations for referral for brain tumours, which relate to the threshold for referral according to particular symptoms or signs. There is considerable discussion about the likelihood of particular signs being associated with cancer, which rather misses the point. For example, a patient with definite new cerebellar symptoms has a significant neurological abnormality, which needs to be investigated promptly. One cause is a primary CNS tumour, and if the cause is indeed a tumour, the patient is at risk of acute severe deterioration. Such a patient needs to be seen immediately, and probably will require an MRI within 24 hours.	We have documented the GDG's deliberations when agreeing the timescale for this recommendation in the Linking Evidence to Recommendations section. We would expect primary care clinicians to use their clinical judgement when applying this recommendation.
446	Children's Cancer and Leukaemia group	10	Full	240 General	General	A second concern, which is not addressed, is the frequent difficulties of establishing whether a patient does indeed have a particular sign. Fundoscopy can be impossible in children. Recognition of a specific neurological deficit may	We accept that examination of a sick child can be difficult. We would expect primary care clinicians to use their clinical judgement in such situations.

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						require specific paediatric examination skills, which are not universally present.	
447	Children's Cancer and Leukaemia group	11	Full	240 General	General	The perception that inappropriate referral casues undue stress for parents is not that seen in clinical practice. One member added 'Whenever I see parents whose child has been referred to exclude a diagnosis of cancer, there is general appreciation of the GP's concerns. In contrast, on the numerous occasions when I see patients who have been seen repeatedly without being referred, there is anger and distrust.'	Thank you for this information. We have tried to make recommendations that get the balance right of referring those people who do have cancer, whilst not referring those that do not.
448	Children's Cancer and Leukaemia group	12	NICE	263 35	1.10.8	Suspected NHL if symptomatic should be significantly less than 2 weeks	The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
449	Children's Cancer and Leukaemia group	13	NICE	35		*(lines 35-36)* Back pain in child that is unexplained and persistent must be a red flag Bone pain/swelling unexplained should be xrayed within in 48 hours not within a 2 week window	No evidence was identified in spinal presentation in children, however whilst back pain in children is an important symptom it is not specific to cancer, and therefore a recommendation has not been made. The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
450	Children's Cancer and Leukaemia group	14	NICE	279 63	1.11.4	Imaging suspicious of STS – in CTYA this should provoke immediate referral	The recommendations have been amended to clarify that the action for children (and young people where appropriate) should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
451	Children'	15	Full	245	1.10.3	I'm at a loss to understand why a child with	As documented in the Linking Evidence

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	s Cancer and Leukaemia group				14	petechiae needs an urgent specialist opinion to rule out leukaemia. They simply need a full blood count like the adults and every other symptom listed. There is no evidence or sense base for this recommendation that I can see.	to Recommendations section, the GDG agreed that unexplained petechia in children may indicate severe marrow suppression. They agreed that this was a medical emergency and therefore warranted immediate specialist assessment.
452	Children's Cancer and Leukaemia group	16	Full	275	11	Seems a little odd that child with abnormal bone lump ? sarcoma only needs X-ray within 2 weeks – when a few petechiae scores a cons haematologist in <24 hours.	We have amended the recommendation so that it is for a very urgent X-ray (within 48 hours).
453	Children's Cancer and Leukaemia group	17	General	General	General	The document is difficult to navigate in its current format. The symptom based structure means that the CTYA sections are difficult to find	Thank you for your comments. A symptom based section for CTYA has now been added.
454	Children's Cancer and Leukaemia group	18	NICE	233 79		We fully accept that the primary care evidence base has not grown but a level of detail appears to have been lost in these revised guidelines. This is noticeable in the Brain and CNS tumour section where specific symptoms are no longer detailed and this does not reflect the guidance in the Headsmart campaign. Also of note is that the only eye sign mentioned is leukocoria.	We acknowledge that none of the symptoms in the evidence had a PPV that met the 3% threshold. For this reason the GDG did not make any recommendations on these symptoms. The evidence available did not contain PPV values for the symptoms in recommendation 1.9.1. The GDG agree that these symptoms were likely to have had a PPV of 3% or above, on the basis of their clinical judgement.
455	Children's Cancer and Leukaemia group	19	NICE	293 82		The advice regarding abdominal masses in children is important. We appreciate that the guidance cannot be exhaustive but recognition that tumours such as Neuroblastoma can present in other ways than just with an abdominal mass is important.	There was very little evidence in this area. Thus, the GDG considered this was better left to the clinical judgement of the individual clinician.
456	Children's Cancer	20	NICE	36		Wording is also an issue and there is a risk of misleading the user in some sections e.g Bone	The design of the symptom based section has been amended to make it simpler

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	and Leukaemia group					pain – persistent and unexplained (children and young people)-Leukaemia. Bone pain in childhood leukaemia can be intermittent/fluctuating and by stating 'persistent' it may not be taken seriously.	and easier to understand.
7	Clinical Reference Group for Sarcoma Specialised Commissioning	1	Full	272 General		Sarcomas are a rare and diverse group of tumours with a wide range of presentations: evidence for the PPV of symptoms is therefore lacking. However, we are concerned that diagnostic delays remain and many patients fail to access specialist services. We believe these factors lead to poorer outcomes in the UK than in other countries. A poor diagnostic experience is the norm for many patients with sarcoma. Our approach is therefore to encourage early referral and assessment even where the perceived risk of sarcoma is low. Furthermore sarcomas can be difficult to diagnose histologically and therefore expert pathology review is often required. The service specifications for specialised sarcoma are designed to support the rapid assessment and expert treatment of patients with sarcoma and include the requirement for diagnostic services within or allied to specialist MDTs. These guidelines should reflect that service provision and encourage referral to appropriate diagnostic services under the guidance of a sarcoma MDT.	Thank you for this information Our recommendations do not specify to whom referral should be made.
8	Clinical Reference Group for Sarcoma Specialised Commiss	2	Full	275	1.11.211	An x-ray should ALWAYS be requested for patients with unexplained bone pain, regardless of age.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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	ioning						
9	Clinical Reference Group for Sarcoma Specialised Commissioning	3	Full	275	1.11.211	An X-ray suggesting the possibility of bone sarcoma should ALWAYS lead to urgent referral to one of the specialised commissioned treatment or diagnostic centres.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. Our recommendations do not specify to whom referral should be made.
10	Clinical Reference Group for Sarcoma Specialised Commissioning	4	Full	279	1.11.311	An urgent direct access ultrasound scan to assess for soft tissue sarcoma should be requested for an unexplained lump that is increasing in size. Unfortunately, this is a highly operator dependent test, and we would therefore recommend that USS for sarcoma are performed only by those who are associated with or have been trained by a sarcoma MDT. Furthermore, as the explanation for lumps is often incorrect, we recommend the word "unexplained" is removed.	Making recommendations on who performs the ultrasound is outside the scope of this guideline. It would be inappropriate to recommend an ultrasound for all lumps that are increasing in size, so the word 'unexplained' is a sensible qualifier.
11	Clinical Reference Group for Sarcoma Specialised Commissioning	5	Full	279	1.11.411	A suspected cancer pathway referral to a specialised centre should ALWAYS be made for people with ultrasound findings suggestive of soft tissue sarcoma.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
12	Clinical Reference Group for Sarcoma Specialised	6	Full	279 General		The diagnostic criteria for referral of a soft tissue mass are in the IOG and the service specifications, and are: a lump>5cm, increasing in size, deep to fascia or painful. Present IOG recommendations are that any one of these should trigger an urgent referral. Between 6 and 12% of patients referred under the two week wait guidance which includes	The description of soft tissue sarcomas in the IOG were taken from CG27. This guideline is updating CG27. No primary care evidence was found on symptoms with a PPV consistent with referral. The GDG agreed, on the basis of their clinical judgement, that it was appropriate to

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	Commissioning					these criteria have sarcomas, and a further proportion have other malignant tumours. We are concerned that these draft recommendations will potentially undermine existing efforts to improve referral pathways by promoting an alternative message.	make the recommendations they did. The prior recommendations in CG27 were explicitly reviewed by the GDG and the new recommendations were agreed to be more appropriate.
427	CoppaFeel!	1	Full	147	1.4.16	Recommendation to refer people using a suspected cancer pathway referral (for an appointment with 2 weeks) for breast cancer if they are aged 30 and over and have an unexplained breast lump with or without pain. We are extremely concerned that people under 30 are being excluded from this pathway referral and that this will encourage general practice to defer from referring women with symptoms under the age of 30 for further investigation leading to late diagnosis of breast cancer. The GDG notes that breast cancer in people under 30 is extremely rare – this does not mean that it does not occur and that those who do have cancer and present with early signs and symptoms of breast cancer to their GP will not be referred for the further investigations they require. We would like to see guidance given that includes people under 30 years of age. The GDG also note that they are making the recommendation to make the age 30 as a cut off in regard to 'an unexplained lump in the axilla' as a symptom of breast cancer to 'make this recommendation easier to implement' CoppaFeel! exists to encourage women –	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.

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						particularly those under 30 to know their own breasts, the signs and symptoms of breast cancer and to present early to their GP. This new guidance appears to counter act all this advice and will make it more difficult for those people with breast cancer under the age of 30 to benefit from an earlier diagnosis.	
679	County Durham and Darlington NHS Foundation Trust	1	Full	General	General	This Trust has concerns that the implementation of these guidelines will impact severely on capacity in key trust services in line with previous and current demand being experienced as a result of the various cancer awareness campaigns. Unless additional resource is provided at the points where pressure of service demand is predicted to be high; namely Endoscopy, CT, MRI, US and Pathology it is highly likely that the quality and timeliness of such services for patients will necessarily be affected. Resources to expand Cancer Tracking teams will also need to be provided otherwise it will be increasingly difficult to proactively manage pathways for the cohort of patients who do go on to be diagnosed with cancer. In addition it will become increasingly more difficult to meet key NHS waiting times targets with resultant potential for censure from commissioners and MONITOR. This will almost certainly have a negative effect on the general public's perception of trusts and the wider NHS.	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable. Implementation of these recommendations in secondary care and target setting by other organisations are beyond the remit of this guideline

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680	County Durham and Darlington NHS Foundation Trust	2	NICE	42 31	1.1.4 Mentioned in several places	*(p31-2)* I am surprised by the recommendation to undertake FBC only for never smokers 40 and over to investigate lung cancer.	The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended.
681	County Durham and Darlington NHS Foundation Trust	3	Full	41 General	General	I anticipate the increased awareness will result in more referrals and as a result a reduction in the conversion of 2ww to actual cancers. Clinic capacity is such that we either have more chest physicians undertaking clinics, or a greater proportion of the current slots are given to 2ww thus reducing capacity for non- malignant conditions. This will be the consequence of doubling referrals.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
682	County Durham and Darlington NHS Foundation Trust	4	Full	224 General	General	There is nothing in the guidelines about dysphagia or odynophagia possibly being related to an oropharyngeal Head and Neck cancer (and this is one of the more frequent presenting symptoms in this group)	There was no primary care evidence base to support adding recommendations relating to these symptoms.
683	County Durham and Darlington NHS Foundation Trust	5	Full	210 General	General	There is no mention of amelanotic melanoma, new single pink lesions are those most often missed by GP's.	We have amended the background to include these.
684	County Durham and Darlington NHS Foundati	6	Full	130 General	General	If these recommendations are implemented in their current form and 2ww referrals doubled there would be considerable pressure exerted on services which are already running over capacity, ie endoscopy and colorectal outpatient clinics. There would need to be significant work done to	The GDG consider that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for

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	on Trust					increase resources, working on capacity and demand both in these areas and also on the support services such as radiology, histology. There would also presumably be a knock on effect for surgical capacity too. Hopefully the timescales for implementation would allow this work to happen before the recommendations are adopted.	endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG also consider that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral.
685	County Durham and Darlington NHS Foundation Trust	7	Full	General	General	I have looked specifically at the proposals for UGI Cancer (for both Oesophago-gastric and pancreatic) and adoption of the recommendations of the national guidelines would be recommended.	Thank you
686	County Durham and Darlington NHS Foundation Trust	8	Full	General	General	These recommendations now require us to provide access to **direct to test endoscopy and CT scans** for an expanded list of indications (new to 2015) for these two conditions and this is likely to result in a considerable further increase in demand, and resulting capacity issues for both endoscopy and Radiology across the Trust.	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of

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							people with these cancers and improve patient experience. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
687	County Durham and Darlington NHS Foundation Trust	9	NICE	147 26	1.4.1 Mentioned in several places	I would query the lower age threshold of 30 for referral as we see quite a few breast cancer patients in a much younger age group.	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
688	County Durham and Darlington NHS Foundation Trust	10	Full	General	General	I don't anticipate much of a change in the referrals we will receive. The majority of our referrals appear to fit the criteria recommended in this document. I'm sure there will continue to be the occasional inappropriate referral that doesn't, but that I'm sure will be the same with all specialities. I certainly can't see that there will be a decrease in referrals but obviously time will tell.	Thank you for this information.
689	County Durham and Darlington NHS Foundati	11	NICE	155 73	1.5.10 1.5.13 Last 5 lines, first 6 lines	*(p73-4)* The age 55 limit for PMB concerns me as does the direct access to USS for GP's - wasting resources and clogging up the service.	There are two recommendations for post-menopausal bleeding; the former for women aged 55 and over are for referral using a suspected cancer pathway. The latter – for women under 55, is a 'consider' recommendation, also for

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	on Trust						referral under the same pathway. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. Arrangements for direct access ultrasound will be a matter for implementation.
48	Department of Health	1	General	General	General	The Department of Health has no substantive comments to make, regarding this consultation	Thank you
332	East Lancashire Hospitals NHS Trust	1	NICE	General	General	**General** The timing of the consultation document coincided with the December winter pressures and the Christmas/New Year holidays. This has reduced our opportunity to comment. With this in mind, would NICE consider a lengthening of the consultation period to enable everyone to have a fair opportunity to evaluate and respond?	The standard consultation period for a guideline is 6 weeks. Due to the proximity to Christmas, the consultation period for this guideline was extended to 7 weeks..
333	East Lancashire Hospitals NHS Trust	2	NICE	General	General	**General** Whilst the objective of these guidelines is to provide GPs with the opportunity to increase the number of suspected cancer referrals ("double the number"), there appears to have been little consideration as to the effect this will have on secondary care providers.	When making recommendations, the GDG explicitly considered the cost consequences of these recommendations and the likely impact on service delivery. This has been documented in the Linking Evidence to Recommendations sections in the full guideline.
334	East Lancashire Hospitals NHS Trust	3	NICE	General	General	**Primary Care** In secondary care we note persisting considerable non compliance by patients and we feel it is important that the necessity to attend hospital appointments to eliminate the possibility of cancer needs to be strongly emphasised by primary care.	We consider that these issues are covered by recommendations 1.14.1. and 1.16.5.

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335	East Lancashire Hospitals NHS Trust	4	NICE	General	General	**Diagnostic Procedures** With the threshold of referral being reduced from a positive predictive value of 5% to 3%, patients are likely to experience more referrals and investigations for suspected cancer. There is therefore the risk of over investigation and the potential harm this can cause to patients (including increased patient anxiety).	The GDG considered this issue for the recommendations made on every cancer site and determined that an appropriate balance had been struck between lowering the threshold for referral whilst providing more targeted referrals. This is documented in the Linking evidence to recommendations sections in the full guideline and the methodology section. In addition, there is strong published evidence that patients support a move to lowering the previous PPV threshold, so the GDG did not agree that this potential harm was likely to be realised.
336	East Lancashire Hospitals NHS Trust	5	NICE	General	General	**Diagnostic Procedures** Increasing suspected cancer referrals does not just equate to an increase in out-patient clinic capacity – we anticipate over 80% of these referrals will have at least one diagnostic test. See Appendix 1	The GDG considered this issue in their deliberations on the resource requirements of the recommendations. This is documented in the Linking Evidence to Recommendations sections in the full guideline.
337	East Lancashire Hospitals NHS Trust	6	NICE	General	General	**Diagnostic Procedures** The implications of the "at least one diagnostic test" requirement include not just radiology diagnostics. They include the full range of endoscopy diagnostics, including bronchoscopy, cystoscopy, colonoscopy, flexible sigmoidoscopy and CT guided biopsies. Very urgent blood tests, urgent endoscopies, US scans, abdominal CT scans and brain MRI scans will also experience increased demand. See Appendix 1 & 2	The GDG considered this issue in their deliberations on the resource requirements of the recommendations. This is documented in the Linking Evidence to Recommendations sections in the full guideline.
338	East Lancashire	7	NICE	General	General	**Diagnostic Procedures** The guidance makes reference to "increased straight to test" facilities for GPs but does not consider the operational	We acknowledge that there may be operational challenges but this will be a matter for implementation of the

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	Hospitals NHS Trust					challenges this presents. To illustrate, with a requirement for patients to go "straight to colonoscopy" the questions arise of who will (a) counsel the patient (b) prescribe the bowel prep (c) ensure the patient understands the need for effective preparation. Without the appropriate information many patients will present "straight to test" not fully prepared. This may mean the appointment will have to be rebooked with a slot wasted. For a health locality to establish a "middle man" to reduce this risk (for example nurse triage / telephone triage) additional resources will be required. Have these been considered in the costing of this proposal?	guideline. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
339	East Lancashire Hospitals NHS Trust	8	NICE	General	General	**Diagnostic Procedures** The majority of Trusts already provide "straight to test" opportunities for OGD and flexi sigmoidoscopy. As a result the savings predicted in the costing paper are inaccurate. What does need to be included and costed is the predicted increase in Upper GI referrals which will go straight to test ie there will be an increase in OGD tests which need to be costed.	The GDG consider that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. However, the GDG acknowledge that the broadening of eligibility within our recommendations will increase the number of people who qualify for

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							investigation for a suspected upper GI cancer
340	East Lancashire Hospitals NHS Trust	9	NICE	General	General	**Diagnostic Procedures** Adoption of the new guidance could see a significant increase in the number of biopsies required. This is turn will require additional staff and equipment.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
341	East Lancashire Hospitals NHS Trust	10	NICE	General	General	**Secondary Care** A thorough evaluation is required of the capacity of providers to provide all the additional tests that this guidance suggests. Is this capacity available – is this achievable?	The GDG considered the issue of capacity in their deliberations on the resource requirements of the recommendations. The GDG also considered the balance between lowering the threshold for referral whilst providing more targeted referrals. This is documented in the Linking Evidence to Recommendations sections in the full guideline. Capacity to provide tests will be a matter for implementation of the guideline. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
342	East Lancashire Hospitals NHS Trust	11	NICE	General	General	**Primary Care** From a GP perspective the introduction of the guidance would result in increased consultations and time spent with each patient explaining reasons for referral and providing information about 'direct to test referral' and increased follow up to communication when the results are received back with the GP'. There will be increased administrative implications on the	The GDG considered the issue of increased GP time in their deliberations on the resource requirements of the recommendations. This is documented in the Linking Evidence to Recommendations section that accompanies the recommendations in section 4.1 of the full guideline.

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						GP practice team which will require resourcing. There is an increased risk of litigation if GPs don't follow the guidelines, particularly when it states 'offer' investigation or referral.	
343	East Lancashire Hospitals NHS Trust	12	NICE	General	General	**Primary Care** Changes will be required to both management and education processes to enable the adoption of the new guidelines	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
344	East Lancashire Hospitals NHS Trust	13	NICE	General	General	**Secondary Care** There does not appear to have been any consideration given to the vast increase in clerical support this guidance will require. For example, every Trust in the UK is going to require a significant increase in the number of cancer trackers/cancer MDT coordinators (band 3 and band 4). Whilst NICE accept the conversion rate will not significantly increase, and may even reduce, it must be recognised that every patient referred as a 'suspected cancer' is tracked from the date the referral is received into secondary care. This is to ensure (a) the 14 day target is achieved and (b) the 62 day target is achieved. Whilst a significant number of referrals will not convert to cancer these will still require tracking through to the point "no cancer diagnosis, remove from the cancer pathway" is reached. This will require an increase in the number of cancer trackers and the costing guidance does not make any allowance for this. The NHS will need to find resources to (a) accommodate these extra staff [increasing the pressure on NHS Acute Trusts office space] and (b) set up costs [PCs, desks, office equipment]. Neither of these potential costs	This level of detail was not included in the costing report as the NHS England tariff incorporates all the ancillary costs. It should be noted that in some tumour groups where additional tests take place in primary care, referrals may reduce due to the test ruling out cancer. The issue of other resource pressures such as training and office accommodation will be noted in the 'other considerations' section of the final costing report.

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						appear to have been included in the costing report. Additionally, there will need to be a 'lead in' time to allow for the training of such additional staff. Further increased staff costs may occur within out-patient clinic, endoscopy and radiology booking teams if additional capacity is required, again this does not appear to have been included within the costings.	
345	East Lancashire Hospitals NHS Trust	14	NICE	220 General	General	**Secondary Care** BCCs have never been included in cancer waits and, from a clinical point of view, do not need to be seen within 2 weeks. These should be excluded from the proposal or allowing of local flexibility to redesign skin cancer pathways.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
346	East Lancashire Hospitals NHS Trust	15	NICE	General	General	**General** There were virtually no secondary care representatives on the guidance group. Out of a total of 36 only 2 were indicated as representing secondary care and we do not therefore feel this is sufficient representation for the organisations that will be severely affect by these changes	The scope of this guideline was to make clinical recommendations on referral for suspected cancer from primary care. We consider that the GDG was constituted appropriately to deliver this task. For information, out of the 14 members of the GDG, 3 were from secondary care. The constituency of the GDG was agreed at the scoping phase. The secondary care members of the GDG fed into the secondary care issues.
347	East Lancashire	16	NICE	General	General	**General** Should this guidance be passed, please may we request that serious consideration be given to the start date. To implement such	This guideline will publish in May 2015 and implementation will follow. The timescale for implementing this guideline

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	Hospitals NHS Trust					significant changes with, potentially, a vast increase in the number of referrals by May 2015 is unrealistic and could be seen as being unfairly biased against secondary care providers. Imposition of the guidance in its current format and in the timings suggested may lead to an initial decrease in the quality of patient care. A further consequence could be an immediate decrease in compliance with the NHS Cancer Waiting Times which goes against Government policy.	is not dictated by the GDG or NICE. It is not within the remit of a guideline to make recommendations on the way organisations perform against national targets and the way that performance is evaluated.
348	East Lancashire Hospitals NHS Trust	17	NICE	General	General	**General** With the anticipated increased workload this will create, the cancer tracking staff will have to track a significant increase in patients who will subsequently not have a cancer. The time and capacity of undertaking diagnostics and tracking patients through the system will place severe pressure on the NHS cancer waiting time targets which are already not being achieved within the current system. This is also likely to impact on other NHS targets eg the 18 week target and actually be a detriment on other disease groups of equally high need.	The GDG considered the balance between lowering the threshold for referral whilst providing more targeted referrals when forming their recommendations. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
349	East Lancashire Hospitals NHS Trust	18	NICE	198 37	1.6.11 Last paragraph	Persistent penile symptoms affecting the glans or foreskin would make up 100% of the male patients I see and it would be inappropriate to suggest referring them all via the 2 week rule. Fast track referral should be confined to elderly uncircumcised males with persistent nodules, ulceration or plaques on the penis not responding to treatment, especially if asymmetric, isolated or hyperkeratotic lesions. (response from Dermatologist)	We would expect primary care clinicians to use their clinical judgement when applying these recommendations.

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350	East Lancashire Hospitals NHS Trust	19	NICE	General	General	There is no commentary in the guidance that exactly how NICE believe the referral guidance will change mortality or result in cancer presentation at an earlier stage. If it doesn't do this - and it can't clearly be shown that there has been a change from 'the old system' of referral - then it isn't an improvement.	We disagree. The introduction to the full guideline makes it clear that late diagnosis is implicated in cancer mortality. CG27 (2005) was followed by considerable improvements in cancer mortality and we expect this guideline to build on them.
351	East Lancashire Hospitals NHS Trust	20	NICE	General	General	Similarly, what evidence has been used to show that lowering the PPV of individual symptoms to below 5% will improve clinical outcomes? Is this just a NICE consensus view? Or driven by a government requirement? The document does include some evidence but this particular aspect does not appear to be evidence-based.	The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline. By definition, a lower PPV will find more cases and deliver fewer late diagnoses. Given that late diagnosis is an important factor in cancer mortality, lowering the PPV may reduce cancer mortality overall.
352	East Lancashire Hospitals NHS Trust	21	NICE	General	General	The lack of formal economic evaluation studies to underpin the whole process is very worrying.	It was not feasible to conduct a cost-effectiveness analysis covering all recommendations in the guideline. The main barrier preventing such an analysis was a lack of evidence on the effectiveness of changes in referral criteria. Lowering the referral threshold is thought to lead to an increase in the number of cancer cases detected and/or an increased number of cancer cases detected at an earlier stage. However, the challenge in a cost-effectiveness analysis would be *quantifying* these changes. As discussed and agreed by the GDG, it

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							was thought that it was not possible to reliably estimate these aspects and as such any economic analysis would be fundamentally flawed. The cost-effectiveness of tests used in the diagnosis of colorectal cancer was prioritised as a key area and thus a de novo economic analysis was conducted for this topic. In addition, the cost impact of recommendations was considered in a separate analysis by NICE.
353	East Lancashire Hospitals NHS Trust	22	NICE	General	General	The lack of proper evidence on the impact of these changes on other important hospital resources and services, given (obviously) finite resources, is similarly worrying. Are such studies planned and do NICE consider this important?	The impact of the guideline recommendations on non-cancer hospital resources and services will be a matter for implementation of the guideline. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
354	East Lancashire Hospitals NHS Trust	23	NICE	224 78	1.8.2	Why are neck lumps being linked to laryngeal – should just read "make a H&N referral"	The purpose of this guideline is to make recommendations on what symptoms should prompt referral for suspected cancer. We do not specify in our recommendations to whom referrals are made.
355	East Lancashire Hospitals NHS	24	NICE	General	General	*(an Excel table was provided on the pro forma)* **Comments relating to predicted/estimated costings above:** • All figures are estimates, based on a consensus view of expected increases	Thank you for your comments We will consider your anticipated increase alongside other estimates for

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	Trust					given the significance of changes in guidance for each tumour site. Certain 2WW pathways will have high increases (lung), others little and some virtually none (eg breast). • We are particularly concerned about the impact on ultra sound • We are particularly concerned about the impact on dermatology (skin cancer) services (inc skin cancers seen within the Head & Neck team) • The Costings above do not include any costing for endoscopy. With only limited time it has not been possible to predict the impact on this service other than we anticipate: (i) Flexi sigmoidoscopy: at 50% increase there will be a requirement for 2 additional lists per week at 66% increase there will be a requirement for 3 additional lists per week (ii) Colonoscopy: at 50% increase there will be a requirement for 2.5 additional lists per week at 66% increase there will be a requirement for 3.33 additional lists per week (iii) ODG: at 50% increase there will be a requirement for 5.5 additional lists per week at 66% increase there will be a requirement for 7.3 additional lists per week	national costing. The final costing tool will be such that it can be adapted to reflect local circumstances This issue will be highlighted in the costing report as a possible barrier to implementation This issue will be highlighted in the costing report for consideration at a local level Where additional activity is anticipated for endoscopy additional costs will be estimated. Costs will be based on national tariff where possible. The providers implications will be highlighted as appropriate

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						The above implications for endoscopy will require additional staff and additional equipment (eg scopes and revenue (maintenance, sterilisation costs etc) • Implications for pathology (based on additional diagnostic biopsies) (i) Based on 25% uplift: 332 extra histologies @ 3 RCPath points each = 996 extra points per month = 27 extra reporting sessions Staffing costs 1 consultant post, 2 x Band 4 post Equipment 1 consultant microscopes	
256	Heart of England NHS Foundation Trust	1	Full	20	11	As an example at Heart of England Foundation Trust 460 new cases of bowel cancer per year. Using a ppv of 3% 15,333 patients would need to be seen each year. This would be a 3 fold increase on current numbers and completely overwhelm clinic and endoscopy resources	The majority of patients referred will have a PPV higher than 3%, which is a minimum figure, not an average figure. Therefore the expected number of referred patients will be lower than your estimate.
257	Heart of England NHS Foundation Trust	2	Full	130	7	The preceding 20 or so pages have been an economical modelling of which is the best test to use to investigate a patient for bowel cancer. Much of this data is historical and ba enema examination has almost ceased. It does not help refine criteria of patients that need referral for lower GI investigations. The conclusions raise the question as to whether a GP should be performing FOB testing on symptomatic patients. The secondary care physician will always chose an endoscopy or CT.	The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling. The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under

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							CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
258	Heart of England NHS Foundation Trust	3	Full	130	8	*(lines 8-12)* The current clinic view is that a FoBT is not appropriate to investigate a change in bowel habit. Ba enema examination has almost ceased	The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling. Your comment does not take account of the different patient group in which FOB

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							is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
259	Heart of England NHS Foundation Trust	4	Full	130	1.3.5 13	The lowering of threshold will result in more patients without cancer being put through potentially harmful tests. The criteria of wt loss and abdominal pain in the >40's will result in everyone with IBS being referred - probably every	The GDG considered this issue for the recommendations made on every cancer site and determined that an appropriate balance had been struck. This is documented in the Linking evidence to

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						few years. Offering a PR is not very relevant for those with lower GI symptoms. It is relevant for ano rectal symptoms only. The data in this area is of poor quality and I note the comment that in no instances is the data of high quality There are now 9 different symptom complexes suggesting a 2ww lower GI referral or FOB testing (increase from 5). This makes if far more confusing for GP's. Symptoms of bowel cancer are very vague and non specific. Time and money would be far better spent increasing uptake in the national screening FOB programme and rolling out the bowel scope project rather than lowering referral criteria. The matter of GP's offering FOB to low risk patient groups is worth further exploration. However caution is needed and I enclose a copy of an email from Prof Robert Steele who is an expert in this field: *It is entirely inappropriate to recommend using FOBT in this context without specifying a cut-off for the faecal haemoglobin concentration and the method for measuring it. In addition, although there is an increasing evidence base for using quantitative faecal immunochemical testing (FIT) for haemoglobin in the assessment of the*	recommendations sections in the full guideline. We would expect primary care clinicians to exercise clinical judgement when applying these recommendations. We would expect primary care clinicians to exercise clinical judgement when applying these recommendations. Thank you we agree. We have made recommendations for further research to try to enrich the data in this field. The recommendations for colorectal cancer have been revised to make them simpler and easier to understand. Screening is outside the scope of this guideline. The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is

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						symptomatic patient, the appropriate cut-off has yet to be determined, and may be dependent on age and gender in addition to the symptoms themselves. The way this guidance is worded suggests that a standard qualitative guaiac FOBT could be used to determine the cause of symptoms. This is dangerous, as we know that it will miss around 50% of cancers, in a screening setting at least.	evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. The GDG chose not to stipulate the specifics for administering the test in the recommendation. They would expect people to refer to the manufactures instructions for its use as a diagnostic test.
260	Heart of England NHS Foundation Trust	5	Full	220	15	Dermatology - there is absolutely no justification on clinical or health economy grounds for suggesting that the 2WW pathway should be used for any BCC and that BCCs should therefore be excluded.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact.

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							We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
261	Heart of England NHS Foundation Trust	6	Full	231	9	Thyroid - British Association of Thyroid and Endocrine surgeons (BAET) have issued new guidelines for management of thyroid cancer. In chapter 21, page 86, there are explicit recommendations for 2WW referral. NICE should incorporate these.	Thank you for this information. It is not part of NICE methodology to incorporate recommendations from other organisations into their guidelines.
262	Heart of England NHS Foundation Trust	7	Full	180	1.6.46	Frequency of 'recurrence' should be defined to avoid overzealous or unnecessary referrals.	There was insufficient primary care evidence to add qualifying terms to urinary infection. We would expect primary care clinicians to exercise their clinical judgement when applying the recommendations.
51	Heartburn Cancer UK	1	Full	60	1.2.114 – recommendations	The age 55 is stated for urgent direct access for endoscopy to assess for oesophageal cancer in people with weight loss and any of upper abdominal …….. reflux or dyspepsia. The Be Clear on Cancer D of H oesophago-gastric cancer campaign gives no age. The Dyspepsia/GORD guidelines had the age 55 removed and replaced with 'of any age ..' regarding referral to specialist services in the review published in September 2014. The Suspected Cancer guidelines are therefore going to cause complete confusion in primary care to the detriment of the patient. There will be inconsistency of information between these guidelines the D of H oesophago-gastric BCCC and Dyspepsia/GORD guidelines if the age 55 (or any specific age) remains in the recommendations.	This guideline deals with suspected cancer, whereas GC184 covers all conditions that could cause dyspepsia. As such it covers a slightly different population to the dyspepsia guideline and there is therefore no direct conflict in the recommendations. It should be noted that CG184 states that this guideline should be referred to when a person presents with symptoms that could be caused by cancer.

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62	Lancashire Teaching Hospitals NHS Foundation Trust	1	Full	General	General	We are disappointed that the guidelines make little reference to patients who may present with signs of metastatic spinal cord compression (MSCC). It is know that 23% of patients present with MSCC as the first presentation of their cancer. The importance of a full neurological examination and guidelines for referral need to be highlighted more.	The GDG examined the primary care presentations of cancer and there was no evidence supporting spinal cord compression as a presentation approaching a 3% PPV.
379	Lancashire Teaching Hospitals NHS Foundation Trust	2	Appendices	100		*(p100-101)* Lung cancer section seems astoundingly sensible	Thank you
380	Lancashire Teaching Hospitals NHS Foundation Trust	3	Appendices	115		*(p115-118)* The proposals are seriously flawed. Siascopy is an expensive complicated and very inaccurate tool that doesn't answer what simple visual triaging can do far more cost-effectively. I have raised this with our Regional Dermatology Audit meeting yesterday, who agree. Fast-tracking BCC's is not only un-necessary medically, but it is a complete waste of precious resources. I raised this with the President of the British Association of Dermatologists (BAD) at their Roadshow at the Annual UK Dermatology Consultant's course on 21st November, and who concurred the BAD would argue against this impractical and unnecessary measure.	The information on Siascopy in the guideline simply reflects what evidence was found. We do not make any recommendations that it should be used. The guideline does not recommend a suspected cancer pathway referral for all basal cell carcinomas. We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as

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							the first recommendation in this section to highlight that in most cases, only routine referral is needed.
381	Lancashire Teaching Hospitals NHS Foundation Trust	4	Appendices	121		No comments and am happy to accept the recommendations	Thank you
382	Lancashire Teaching Hospitals NHS Foundation Trust	5	Appendices	104		*(p104-5)* Thanks for this. I note this document is over 400 pages long, so not surprisingly I haven't read it all, though I have had a look at the GI sections. So far as I can tell there is at least one important change: The current BSG guidleines on indications for lower GI endoscopy are fairly clear: change of bowel habit *to looser* is an indication for colonoscopy: constipation isn't. So far as I can see these new NICE guidelines will change the goalposts slightly (to a PPV of 3%), but enough to change that - constipation now WILL be an indication for colonoscopy (specifically, NICE will not differentiate between a change to looser bowels and a change to constipation - all being grouped together as "change in bowel habit"). This has potentially huge implications for demand for lower GI endoscopy in a service already stretched (nationally).	The symptoms in the recommendations were derived from the evidence on PPVs. We would expect primary care clinicians to use their clinical judgement when applying these recommendations. Access to endoscopy will be a matter for implementation.
383	Lancashire Teaching Hospitals NHS Foundati	6	Appendices	113		*(p113-115)* I am in agreement with the guidance	Thank you

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384	Lancashire Teaching Hospitals NHS Foundation Trust	7	Appendices	125		*(p125-133)* I have a number of comments: 1. The 48h FBC referral for a whole list of symptoms is unworkable. I would suggest limiting this to unexplained bruising. Children that are acutely unwell should be referred to the ward. 2. "Palpable abdominal mass" needs to specifically exclude faecal loading. I would suggest that these children be referred to the ward. 3. Most haematuria children is not malignancy. I would suggest RAC clinic review within two weeks as previous. I am not sure about the benefits of a 400 page guideline… I will not pretend I have read it all. I saw the suggested changes to the paediatric brain tumour guide, and I am in agreement. I think urgent referral would be required, even if they don't have a brain tumour. I highlighted the comment I very much agree should be taken out: A GP should be able to examine a child. (1.14.15) I think the short statement is more helpful than what was mentioned before.	These were the symptoms, supported by evidence that the GDG agreed should prompt a 48 hour FBC. We would expect primary care clinicians to use their clinical judgements when applying these recommendations. The rationale for using a lower PPV in children is made in the introduction. This guideline covers 37 different cancers. As a consequence it contains a lot of information. . In addition, NICE are exploring ways that we can improve usability of the document. Thank you Thank you Thank you
385	Lancashire	8	Appendices	110		*(p110-113)* I have already expressed my concerns to BAUS section of oncology re the Prostate	This guidance relates to the selection of patients for referral or investigation. The

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	Teaching Hospitals NHS Foundation Trust					Cancer guideline changes as the new guidance is suggesting all men with 1 abnormal age specific PSA should be referred, regardless of age or fitness. European Association of Urology guidelines clearly state 6.3 Prostate biopsy *6.3.1 Baseline biopsy* The need for a prostate biopsy should be determined on the basis of the PSA level and/or a suspicious DRE. The patient's age, potential co-morbidities (American Society of Anesthesiologists' physical status classification index [ASA] and Charlson co-morbidity index), and the therapeutic consequences should all also be considered (25). Risk stratification is becoming an important tool for reducing unnecessary prostate biopsies (25). The first elevated PSA level should not prompt an immediate biopsy. The PSA level should be verified after a few weeks by the same assay under standardized conditions (i.e. no ejaculation, no manipulations such as catheterisation, cystoscopy or transurethral resection, and no urinary tract infections) in the same diagnostic laboratory, using the same methods (26,27) (LE: 2a). i.e. patients should have 2 PSA tests before referral to a rapid access biopsy service, If the new guidance is issued in it's current format we will be inundated with potentially inappropriate	choice of investigative strategy after referral outside the scope of this guidance.

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						referrals and men will be biopsied on the basis of a single abnormal result or breach the cancer targets if biopsy is delayed – unless they are specifically put on surveillance, assuming this is possible under the current cancer monitoring regulations. The one stop prostate biopsy service will become even more inefficient with biopsy slots being wasted and delays therefore increasing in time to diagnosis and treatment which presumably is not the intention of the changes to the NICE guidelines. The changes to the Haematuria referral guidelines is welcomed as this will remove asymptomatic dipstix haematuria from the 2 week referral targets	
386	Lancashire Teaching Hospitals NHS Foundation Trust	9	Appendices	118		*(p118-121)* The new guidelines are very vague and do not appear to be helpful for primary care colleagues. The old guidelines should be left in as these are far clearer. (1.11.1, 1.11.2, 1.11.3, 1.11.4, 1.11.5, 1.11.12,) Not everyone has access to a dentist. 1.11.14 replaced by the general statement without further guidance would be a retrograde step	We disagree. The recommendations made are based on the best available evidence. We think that they will be helpful when referring people who have symptoms suspicious of cancer
387	Lancashire Teaching Hospitals NHS Foundation Trust	10	Appendices	108		*(p108-11)* Since the revisions to the guidance in 2011, practice has not been formally audited and it is our experience that the majority of referrals do not follow the recommended pathway and further education is required in primary care. Also, further evidence of the false/positive evaluation of the CA125 test is required.	Thank you. Your comment about referral pathways and audit falls outside the scope of this guidance. Education is specifically included in recommendation 1.6.1. We agree it would have been useful to know the performance characteristics of CA125.
527	London Cancer	6	NICE	130 70	1.3.6	We have major concerns about the use of FOBt in the investigations of patients with colorectal	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in

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	Alliance					symptoms. Whilst we appreciate that this recommendations is backed by few studies but we have concerns that a negative FOBt in patients with symptoms will provide GPs and patients with a false sense of security and the reassurance not to refer or be referred. We believe that FOBt should only be used in the screening of asymptomatic population and as such has no place in investigating the symptomatic patient.	the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
522	London Cancer	1	NICE	General	General	The LCA Colorectal Pathway Group welcomes this long awaited radical shake up of the existing	Thank you

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	Alliance					referral guidelines, which is needed if the UK is to diagnose colorectal cancer early and close the wide gap in survival figures with the rest of the western world.	
523	London Cancer Alliance	2	NICE	General	General	Whilst the removal of the duration component is a welcome change so that patients do not have to wait to have 6 weeks of symptoms before referral, the introduction of several age limits make the guidelines complex and not easy to follow. All of this is likely to confuse general practitioners making the guidelines impractical and unusable or at least not used as intended. We would recommend using a one cut off age of 40 years instead of the 40, 50 and 60 age limits with some of the recommendations. The LCA working with Transforming Cancer Services in London and other stakeholders have obtained agreement on the introduction of guidance for referral of symptomatic patients in the Capital from the age of 40. Early diagnosis of cancer is the only way to improve outcomes and survival. We would wish to see this emulated nationally.	The ages included in the recommendations reflect the evidence that was available on the positive predictive value of symptoms. It would therefore not be appropriate to apply the same age group to all recommendations.
524	London Cancer Alliance	3	NICE	130 General	General	There is no mention of referral for investigations of high risk groups for colorectal cancer and who have bowel symptoms. Such high risk groups including those with inflammatory bowel disease, history of cancer or polyps or a personal family history of colon cancer.	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that inflammatory bowel disease, family history or history of cancer/polyps affected the predictive power of symptoms for colorectal cancer.

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525	London Cancer Alliance	4	NICE	130 70	1.3.2	The introduction of an age limit to referring patients with iron deficiency anaemia is a retrograde step. Furthermore patients with iron deficiency anaemia as defined by the laboratory performing the test irrespective of the levels should be referred for investigations.	The primary care evidence on haemoglobin levels and iron deficiency was examined in detail and used to select the age threshold values in this guideline.
526	London Cancer Alliance	5	NICE	130 70	1.3.4	We have concerns about the term "Consider" rather than "refer" for patients with abdominal or rectal mass. These patients "should" be referred	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
528	London Cancer Alliance	7	Full	41-42 32	General	*(p32-44)* The changes are not far reaching enough. Other risk factors should be brought into the decisions eg previous other cancer, family history of lung cancer, pack year history of smoking, exposure to asbestos as these all increase the chance of development of lung cancer	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that previous other cancer, family history, pack year history of smoking or exposure to asbestos affected the predictive power of symptoms for lung cancer.
529	London Cancer Alliance	8	Full	41-42 32	General	*(p32-44)* Given that some patients with lung cancer have a normal CXR more guidance needs to be given for patients who have persistent symptoms and signs.	The GDG considered that someone with persistent symptoms but a negative chest X-ray would be covered by the recommendations on safety-netting.
530	London Cancer	9	Full	41-42 32	General	*(p32-44)* More information should be put very prominently in the document of a patient's risk of	The guideline relates to identifying in which patients cancer is suspected and

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	Alliance					lung cancer with pack year smoked, current smokers and years since quitting	what action should be taken. The prevention of cancer and its association with lifestyle factors are outside the scope of this guideline.
531	London Cancer Alliance	10	Full	46 45	General	*(p45-49)* The referral for lung cancer and mesothelioma should be put together as the symptoms and signs that are being described are the same for both types of tumour and in the section here there is little made of the history of asbestos exposure and chest pain which are the most distinguishing characteristics, but only investigation will finalise this. At primary care level this distinction is unnecessary as the same specialist teams will be seeing the patients.	At the time of constructing the review questions for this guideline, the GDG did not know if lung cancer and mesothelioma would have separate symptom profiles. Therefore we set two separate review questions and have maintained this separation in the guideline to ensure transparency of process.
532	London Cancer Alliance	11	Full	41-42 32	10	Persistent chest infection – this needs defining as if it is a cough with yellow sputum this could be due to undiagnosed asthma	We agree there is wide differential diagnosis for apparent persistent chest infection. As lung cancer is one of the diagnoses it is included in this recommendation. Other potential non-cancer diagnoses are outside the scope of this guideline.
533	London Cancer Alliance	12	Full	32	16	Thoracoscopy is not a useful test for lung cancer unless the patient has a pleural effusion. Mention needs to be made of percutaneous biopsy of a lung mass.	Thoracoscopy has been removed from this text. It is always difficult to decide how much additional information about secondary care procedures to give in the background. The risk with being specific - like the good point you make - is that things change. This guideline is for selection of patients for investigation, not the precise investigation modality. So, while we fully accept your point, we prefer to err on the side of simplicity throughout the background sections and have not made this change.
534	London Cancer	13	Full	32	16	*(lines 16-17)* The sentence regarding sputum cytology is inappropriate at this point and would be	We have made this change

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	Alliance					better after the following sentence.	
535	London Cancer Alliance	14	Full	41	1.1.1 17	Haemoptysis should be defined as either on more than one occasion if tiny streak or single episode if larger volume. Consideration needs to be given for advising against referring patients known to have bronchiectasis. These patients should have a chest X-Ray	The recommendation has been amended to clarify that it is 'unexplained haemoptysis'. There was insufficient primary care evidence to add any further qualifying terms to haemoptysis. We would expect primary care clinicians to exercise their clinical judgement when applying the recommendations.
536	London Cancer Alliance	15	Full	41	17	*(p41-42)* Often patients with lung cancer have shoulder pain so consideration should be given to stating chest or shoulder pain	There was no specific evidence to support including shoulder pain in a recommendation.
537	London Cancer Alliance	16	Full	42	17	If we are to get patients diagnosed with lung cancer earlier then we should recommend doing the creatinine which is needed for a contrast enhanced scan, and look for hyponatraemia which is quite common in patients with lung cancer	Contrast enhanced scanning, and therefore the use of creatinine testing is not part of the diagnostic process for lung cancer in primary care. Therefore it is outside the scope of this guideline. The evidence reviewed for this guideline did not indicate that hyponatraemia was predictive of lung cancer in the primary care population.
538	London Cancer Alliance	17	Full	42	1.1.5 17	Chest signs compatible with lung cancer are not very instructive. The signs are due to changes in the lungs from an obstructing lesion or a pleural effusion. There needs to be some explanation of this in the text.	We consider it is more important to highlight the signs rather than to explain the underlying pathophysiology.
539	London Cancer Alliance	18	Full	45	3	Surely there should be some reference to the fact that mesothelioma is increasing in incidence owing to the amount of asbestos in use 30 years ago. There is no mention of asbestos in either part of this guidance until the last paragraph	The increasing incidence of mesothelioma is mentioned in the background to this section.It was agreed that given the high relative risk of mesothelioma in people exposed to asbestos, a known history of exposure to asbestos was likely to increase the predictive value of symptoms for

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							mesothelioma and therefore needed to be included in the recommendation.
540	London Cancer Alliance	19	Full	45	10	A common symptom of mesothelioma is sweats and this might be worth mentioning	The symptoms listed in the background are examples and not intended to be exhaustive or to pre-empt the recommendations.
541	London Cancer Alliance	20	Full	46	1	Mesothelioma is often associated with raised inflammatory markers. Should this be an added blood test.	There was no primary care evidence to support the use of inflammatory markers in the diagnosis of mesothelioma.
542	London Cancer Alliance	21	Nice	41 64	1.1.1	*(p64, 30, 100)* Advising referral of patients with haemoptysis who have never smoked and have a cough is not helpful. Haemoptysis by definition is expectoration but with blood.	The recommendations for lung cancer have been revised to make them simpler and easier to understand. We now recommend a suspected cancer pathway referral for people aged 40 and over with unexplained haemoptysis
543	London Cancer Alliance	22	Nice	41 66	1.1.1	Chest signs which could be caused by lung cancer would more appropriate	We have amended the text to 'consistent with' for consistency with terminology used in the rest of the guidelines.
544	London Cancer Alliance	23	NICE	46 66	1.1.8-9	*(p66-7)* Why not add inflammatory markers to the requested tests. Cheap but would require further investigation if abnormal	There was no primary care evidence to support the use of inflammatory markers in the diagnosis of mesothelioma.
545	London Cancer Alliance	24	Nice	42 30	1.1.6	Chest infection requires definition	We consider this is best left to the judgement of the individual clinician.
546	London Cancer Alliance	25	NICE	130 101	5th rec 1.3.5	This paragraph should be nearer the beginning of the document,	This is now included in recommendation 1.3.1.
547	London Cancer Alliance	26	Nice	224 33	1.8.1	Persistent hoarseness needs defining and these patients should have a chest x-ray if they are smokers as this is a relatively common presentation of lung cancer also.	There was no primary care evidence to allow the GDG to add qualifying terms to hoarseness. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. Some of the primary care studies included hoarseness, but when studied

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							alongside other chest symptoms it did not retain statistical significance. In other words, isolated hoarseness appears not to be a feature of lung cancer, though it may accompany other symptoms.
548	London Cancer Alliance	27	Full	141	11	*(lines 11-12)* Should replace 'fine needle aspiration' with "A diagnosis of breast cancer is made using mammography, ultrasound and image guided core biopsy…"	Thank you. We have amended the introduction where it refers to core biopsy.
549	London Cancer Alliance	28	Full	147	1.4.1 Below 6 in recommendation	Use of term 'unexplained' unhelpful – open to varied interpretation – anything from lump previously assessed with imaging and biopsy and unchanged to new lump in patient with history of cysts which could be a cancer	We would expect primary care professionals to exercise their clinical judgement in applying these recommendations
550	London Cancer Alliance	29	Full	147	1.4.3 recommendations	Clinical experience would suggest that cut off age of 30 for axillary lumps is too low – 40 may be better	As documented in the Linking Evidence to Recommendations section, the GDG agreed to use the same age threshold as in their recommendation on breast lumps to make implementation easier.
551	London Cancer Alliance	30	Full	147	1.4.1 recommendations	Consider using the word persistent breast lump as many "lumps" will disappear after a period i.e. Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer if they are aged 30 and over and have an unexplained persistent breast lump with or without pain	There was insufficient primary care evidence to add qualifying terms to breast lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
551	London Cancer Alliance	30	Full	147	1.4.1 recommendations	Consider using the word persistent breast lump as many "lumps" will disappear after a period i.e. Refer people using a suspected cancer pathway	There was insufficient primary care evidence to add qualifying terms to breast lump. We would expect primary care clinicians to exercise their clinical

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						referral (for an appointment within 2 weeks) for breast cancer if they are aged 30 and over and have an unexplained persistent breast lump with or without pain	judgement when using the recommendations
552	London Cancer Alliance	31	Full	148	Second to last paragraph under the recommendations- titled: Trade-off between clinical benefits and harms	Term 'other nipple change' too vague – previous description of unilateral eczematous change not responding to topical treatment much more helpful	We would expect primary care clinicians to exercise their clinical judgement when applying these recommendations.
553	London Cancer Alliance	32	Full	147 Breast Chapter general	Breast chapter general	Suggest to include: All patients regardless of symptoms need to be seen under 2WR. Diagnostic clinics are overwhelmed with breast referrals of which <10% will be cancer. It would be helpful if guidance could include symptoms which do not require referral to a breast clinic due to low predictive value e.g. breast pain, bilateral nipple discharge, galactorrhea, breast skin lesions such as sebaceous cysts, gynaecomastia. These symptoms should be managed in primary care. This would allow all patients with suspected cancer to be seen in a timely fashion without risk of	We have focused on positive recommendations as 'do not use' recommendations were outside the aim of this guideline. It should be noted that the symptoms included in our recommendations are fewer than in previous guidance, as well as being based on primary care evidence.

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						breaching.	
554	London Cancer Alliance	33	Full	220	Recommendations – 2nd Paragraph	The Group are unable to identify an evidence base for this statement. Grave concern is raised regarding this statement as it essentially gives primary care an opportunity to use this urgent pathway indiscriminately. It is the belief of the Pathway Group that this statement should be removed totally. Improvements in the provision of community dermatology services and appropriately accredited individuals to diagnose and treat basal cell carcinomas would further help to address this issue.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
555	London Cancer Alliance	34	Full	169	1.6.2 Recommendations – 2nd	The Pathway Group does not support the recommendation that erectile dysfunction should act as an indicator for a PSA test. There is no inclusion of evidence that directly supports this link and will result in unnecessary testing and resultant	The evidence review on pg167 shows a PPV of 3% for impotence.

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					Paragraph	referrals irrespective of the age profile guidance for elevated PSA levels.	
556	London Cancer Alliance	35	NICE	General	General	The LCA Haematology Oncology Pathway Group supports the need for increased referral of patients with suspected haematological malignancies and as such agrees that a low bar for referral is not unreasonable.	Thank you
557	London Cancer Alliance	36	Full	246	1.10.1 Recommendations	The recommendations for adult leukaemia should also include "persistent or unexplained bone pain" as it does for children and TYA	There was no primary care evidence to support this symptom warranting action in adults. It is expected that clinicians will exercise their clinical judgement in such a scenario.
558	London Cancer Alliance	37	Full	243	Leukaemia section	*(p243-247)* There is no mention of MDS and MPN in here – MDS is quite similar to symptoms/signs for Leukaemia in general, but MPN is different. So the LCA Haematology Oncology Pathway Group wonders what NICE thinks about including this as a "cancer" or "leukaemic syndrome"?	The scope of this guidance did not cover pre-malignant conditions. so did not include either of these conditions.
559	London Cancer Alliance	38	Full	243	Leukaemia section	*(p243-247)* Any reference to "bone marrow suppression" should really be "bone marrow failure" as this is what it is and is a more precise term. "Bone marrow suppression" has other connotations to it to which this guidance does not pertain	We have made this change.
560	London Cancer Alliance	39	Full	257	1.10.4 Recommendations	The word "persistent" should be defined more clearly. The LCA Haematology Oncology Pathway Group proposes that this should be people over 60 with bone pain that has persisted for over six weeks, particularly back pain or unexplained fracture.	There was insufficient primary care evidence to add qualifying terms to persistent pain. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
561	London Cancer Alliance	40	Full	257	1.10.4 Recommendations	Myeloma should also be considered in people under 60 presenting with bone pain, if there are other worrying features and no history of trauma or injury	There was insufficient primary care evidence to add qualifying terms to persistent bone pain. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.

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562	London Cancer Alliance	41	Full	260	Non-Hodgkin's Lymphoma and Hodgkin's Lymphoma sections	*(p260-270)* The LCA Haematology Oncology Pathway Group feels it is important to clarify the purpose of the referral for patients with potential lymphoid malignancies. In the event that a haematological malignancy is excluded, the pathway for further investigation leading to a definitive diagnosis for this patient needs to be explicit. The LCA Haematology Oncology Pathway Group believes that robust onward pathways need to be developed as an integral part of diagnostic services for "lumps" to ensure appropriate onward referral can be facilitated in a timely manner, through consultant to consultant referral, streamlining the time to diagnosis for the patient. Current commissioning arrangements (such as the need for GPs to initiate consultant referrals as opposed to consultant to consultant referrals) may hinder such pathways and delay diagnosis. The Pathway Group feels that this should be included as a priority even though it may appear to be outside the intended scope of this document – without clarity, there is potential for haematological services to be overloaded with patients with lumps who do not have a haematological malignancy, causing delay for patients who do have a haematological malignancy.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
563	London Cancer Alliance	42	Full	155	1.5.10 Recommendations	The LCA Gynaecology Oncology Pathway Group recommends that all women (irrespective of age) with post- menopausal bleeding should be referred using a suspected cancer pathway referral	There are two recommendations for post-menopausal bleeding; the former for women aged 55 and over are for referral using a suspected cancer pathway. The latter – for women under 55, is a 'consider' recommendation, also for referral under the same pathway. The use of the term 'consider' reflects the strength of the evidence base upon which

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							the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
564	London Cancer Alliance	43	Full	159	1.5.14 Recommendations	The LCA Gynaecology Oncology Pathway Group recommends that patients with symptoms such as post-coital or inter-menstrual bleeding, post-menopausal bleeding or offensive blood-stained vaginal discharge, with or without a suspicious cervix, and irrespective of smear result, should be referred to the gynaecologist for further investigations for suspicion of cancer.	The GDG did not identify any primary care evidence that reported PPVs for these symptoms that would warrant action.
565	London Cancer Alliance	44	Full	General	General	The LCA Children and TYA Pathway Group recommend that where cancer is suspected in a child, onward referral should NOT be made using the suspected cancer referral pathway. Use of the 2ww referral form for suspected childhood cancers can result in delay to definitive diagnosis and treatment. The Group recommends that the child should be referred to a local paediatrician as an urgent referral who will triage and refer to the appropriate provider as necessary.	The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
566	London Cancer Alliance	45	Full	240	1.9.1 Recommendations – 1st Paragraph	The LCA Brain and CNS Pathway Group is not supportive of this recommendation. The supporting evidence included in the consultation document highlights that none of the positive predictive values exceeded the 3% threshold for referral and there is no evidence available to support this recommendation. It is unlikely that introducing direct access to MRI for patients with a suspected brain or CNS cancer	We acknowledge that none of the symptoms in the evidence had a PPV that met the 3% threshold. For this reason the GDG did not make any recommendations on these symptoms. The evidence available did not contain PPV values for the symptoms in recommendation 1.9.1. The GDG agree that these symptoms were likely to have had a PPV of 3% or above, on the basis of their clinical judgement. The GDG considered that the majority of people referred urgently for certain

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						will improve the pickup rate. This is more likely to increase the burden on MRI scanners and acute radiology departments. The LCA has identified the improvement of early diagnosis rates for patients with a brain or CNS cancer as a priority. Improving direct access to MRI and CT within A&E departments to improve the presentation to diagnosis rate for patients presenting acutely will be associated with a higher pick up rate. Existing triage through neurology departments with headache and first fits clinics already provide access to MRI.	cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
567	London Cancer Alliance	46	Full	General	General	The Head and Neck Pathway Group is supportive of the majority of the recommendations made regarding the suspected cancer referrals, however feels that smoking and tobacco consumption history should be included as a consideration as part of the risk factors for patients, particularly those in the >45 age bracket.	As we have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different

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							recommendations. We did not find any primary care evidence that enabled us to make differential recommendations based on smoking history for head and neck cancers.
568	London Cancer Alliance	47	Full	231	Recommendations	The LCA Head and Neck Pathway Group does not support the general recommendation regarding unexplained thyroid lumps. The Pathway Group strongly recommends that the NICE guidance aligns with the British Thyroid Association clinical guidelines which advise that only patients who meet the following clinical criteria should be referred on an urgent cancer pathway: - a thyroid nodule in a child - A rapidly enlarging, painless, thyroid mass over a period of weeks - Stridor associated with a thyroid mass	There was no primary care evidence available, The consensus of the GDG was that an 'unexplained thyroid lump' would have sufficient risk of cancer to warrant action.
654	Macmillan Cancer Support	1	Full	General	General	Macmillan Cancer Support seeks to ensure that people with cancer are diagnosed earlier so their chances of survival are improved and the risks of more severe consequences of treatment are reduced. While we recognise achieving this will be complex, part of the solution must be ensuring that GPs are supported and enabled to make timely referrals to diagnostic tests if they suspect cancer. We welcome that NICE has undertaken the review of the clinical guidelines on suspected cancer and published the draft document for consultation, Particularly with respect to the fact that over 50% of cancers are diagnosed outside of the 2WW route. [i] We appreciate the amount of time, effort and expertise has been devoted to this process to date.	Thank you for this information.

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						It is essential that we get these guidelines right. We know that the UK's cancer survival rates for almost all common cancers are worse than the overall European average. [ii] At the moment, one in three (32%) people with cancer die within a year of diagnosis. [iii] One in four people with cancer are diagnosed via an emergency route, and those diagnosed this way are on average around twice as likely to die within a year of diagnosis than those diagnosed via an urgent GP referral. [iv] We believe getting the right guidelines in place, that are workable for busy GPs, will be an important part of improving this situation. In light of the importance of the revised guidelines, however, we are disappointed about the length of time we have been given to submit comments, especially as the period covered the Christmas break. Macmillan has worked with its medical community of over 200 primary care clinicians together with our tumour site specific consultant advisors, to inform this submission. We consider the input from clinicians across the entire pathway to be imperative in achieving the best outcomes for patients. We would welcome and look forward to continue working with you to refine the document before it is published in its final version. We have included throughout our comments copies of our tumour site specific "Rich Picture" documents to support our comments. Please see the link our Rich Picture on People living with Cancer http://be.macmillan.org.uk/be/p-22333-the-rich-picture-on-people-with-cancer.aspx	The standard consultation period for a guideline is 6 weeks. Due to the proximity to Christmas, the consultation period for this guideline was extended to 7 weeks.

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						[i] Emery. Assessment of cancer risk in men and women. British Journal of GPs 2013: 63(606) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3529272/ [ii] De Angelis et al. Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5-a population-based study. Lancet Oncology 2014: 15: 23-34 [iii] Office for National Statistics. Cancer Survival Index for Clinical Commissioning Groups, Adults Diagnosed 1996-2011 and Followed up to 2012, http://www.ons.gov.uk/ons/rel/cancer-unit/a-cancer-survival-index-for-clinical-commissioning-groups/adults-diagnosed-1996-2011-and-followed-up-to-2012/index.html (accessed April 2014) [iv] Average one-year survival rate for 15 selected cancer types (which includes the 10 most commonly diagnosed in the UK) is 72% for people diagnosed via the two-week-wait route compared with 40% for people diagnosed via an emergency admission. Source: Elliss-Brookes L *et al*. Routes to diagnosis for cancer – determining the patient journey using multiple routine data sets. *Br J Cancer* 2012; 107: 1220–1226 http://www.nature.com/bjc/journal/v107/n8/full/bjc2012408a.html	Thank you for providing these references.
655	Macmillan Cancer Support	2	Full	General	General	We welcome the GDG's decision that a PPV threshold lower than 5% was preferable in order to improve the diagnosis of cancer. Macmillan Cancer Support's electronic cancer decision support tool (eCDS) based upon much of the evidence considered within this guidance review has already shown beneficial outcomes for a reduction in PPV.	Thank you for this information.

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						(http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/EarlyDiagnosis/CDSExecSummary.pdf)	
656	Macmillan Cancer Support	3	Full	General	General	We note and acknowledge the GDG's approach to the use of risk factors as well as symptoms; however, we do consider that it is important to highlight that in some 4clinical situations there are risk factors that, when considered alongside relevant symptoms, would significantly influence the decision and speed of referral. We refer to this later in response to breast symptoms (point 5).	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations.
657	Macmillan Cancer Support	4	Full	General	General	We welcome the increased emphasis to direct access to diagnostics to improve the patient pathway and we would be keen for consideration and alignment with the Access to Diagnostics Guidance of 2012 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216503/dh_133511.pdf	Thank you
658	Macmillan Cancer Support	5	Full	General	General	We welcome the approach to increasingly addressing symptoms as opposed to specific tumour sites; however we also note that in some instances this has contributed to complexity within the guidance. We would be keen to support any attempts to retain the symptoms based approach whilst attempting to clarify and simplify the guidance wherever possible to ensure successful and widespread implementation.	Thank you for your support of including a symptom based section in the guideline. The GDG also considered that it was important to include it to improve usability. Following comments received during consultation the recommendations for several cancer sites have been simplified to aid implementation.
659	Macmillan Cancer Support	6	Full	General	General	We recognise the breadth of evidence base that has contributed to the development of this guidance. We also note that on some occasions the suggested guidance has been derived from the	Thank you

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						clinical experience of the GDG. We would wholeheartedly support and endorse the importance of clinical consensus when developing guidance such as this and in formulating our response we have consulted with Macmillan's clinical community of primary and secondary clinicians.	
660	Macmillan Cancer Support	7	Full	General	General	We have noted throughout the submission a number of occasions where there are deletions from the previous guidance, NICE guidance CG27. In some cases the rationale for this is not explicitly clear and having discussed this with yourselves over the phone earlier this week, we have been informed that these decisions may have been derived from clinical consensus. We recognise that you are not asking for comments on the previous guidance (NICE Guidance CG27) but in order to support successful implementation of this guidance it will be important to be able to explain the rationale regarding any deletions and we would be grateful for your consideration.	The full version of the guideline contain an Appendix which documents the proposed changes to the recommendations from CG27. Where a recommendation has been deleted and not replaced by anything new, a reason for this has been given. Where recommendations have been deleted because the topic has been updated, the new recommendations that have replaced the old ones have been cited.
661	Macmillan Cancer Support	8	Full	General	General	We would welcome and look forward to continue working with you to refine the document before it is published in its final version. We have previously supported the implementation of NICE guidance CG27 and Access to Diagnostics Guidance in particular, through the development of an interactive Rapid Referral Guideline PDF document, (http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/PCCL/Rapidreferralguideline	Thank you

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						s.pdf) We have already planned to update this in 2015 once the guidance is finalised.	
662	Macmillan Cancer Support	9	Full	41	General (Lung)	Lung was reviewed in 2011 as a pathway and no update deemed necessary at that time. These recommendations have increased the complexity of referral criteria which has the potential to delay lung cancer diagnosis. It is unclear as to why symptom changes and varying age boundaries for specific symptoms have altered. For example: the differentiation of when to request FBC **and** chest X Ray or simply FBC in people aged 40 +. Specifically we would welcome clarity regarding the removal of the symptoms "hoarseness" and "shoulder pain". We welcome the inclusion of the symptom thrombocytosis. This is a metric already incorporated into the Mac eCDS; however we feel that thrombocytosis should be explicit in the advice as opposed to simply suggesting a FBC so that clinicians are aware that it is the platelet count within the FBC that is of considerable significance. Since 2011 much work has progressed regarding routes to diagnosis and there are numerous models for requesting chest X-ray and responding appropriately to either indeterminate or abnormal results and a direct route on to 2WW. The pathways have been demonstrated to increase lung resection rates and patient experience since investigations are available when a patient first attends an urgent 2WW appointment. There are numerous models e.g. as outlined in the Access to	The recommendations in the lung guideline came from CG27. When the lung guideline was updated, these recommendations were not prioritised for update as it was known that CG27 was also going to be updated. As specified in the scope of this guideline our recommendations on lung cancer will update those in the Lung Cancer guideline. The recommendations for lung cancer have now been revised to make them simpler and easier to understand. Thank you. The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended. Thank you for this information.

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						diagnostics guidance: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216503/dh_133511.pdf This guidance does not reflect or encourage this behaviour. Indeed there are inconsistent recommendations regarding the timing of Chest X ray requests and no specification regarding times for reporting (which were detailed in the previous 2005 guidance (NICE guideline CG27; 1.3.2) which we know vary significantly across the country. For chest X ray a recent survey by Macmillan of GPs across 100 CCGs demonstrated that the average wait for both for investigation and subsequent returned results was each 7 days with 14 GPs stating that it can take over 2 weeks to get results back. We would reiterate that this guidance has increased complexity with potential for delay in diagnosis. The Be Clear on Cancer National lung campaign (BCOC) using simple symptom guidance resulted in significant increase not only in the diagnosis of lung cancer but also at an earlier stage. http://www.cancerresearchuk.org/about-us/cancer-news/press-release/2013-12-09-early-trip-to-the-gp-gives-big-boost-to-lung-cancer-patients http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/update/RP-People-with-lung-cancer.pdf	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. The recommendations for lung cancer have been revised to make them simpler and easier to understand.
663	Macmillan Cancer Support	10	Full	147	1.4.1 General (breast)	We are concerned at the introduction of an age descriptor for breast lumps and we note that the GDG felt that the PPV would drop sharply below the age of 40. However the recommendations of	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with

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						NICE guidance CG27 did discriminate between specific features of a breast lump on clinical examination that would make a diagnosis of cancer more likely irrespective of age and recommended: *1.6.5 – The features of a lump that should make the primary healthcare professional strongly suspect cancer are a discrete, hard lump with fixation with or without skin tethering. In patients presenting in this way a referral should be made irrespective of age* We are also concerned about the introduction of an age descriptor for unilateral nipple changes. We noted an omission of guidelines for erythema+/- swelling the breast failing to respond to antibiotics. We also note that 1.6.7 from NICE guidance CG27 which took into account family history has also been withdrawn. Retention of these criteria would help to support a higher PPV in the age group under 40. http://be.macmillan.org.uk/be/p-22314-the-rich-picture-on-people-living-with-breast-cancer.aspx	or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made. The age threshold for nipple changes was based on the evidence in Walker et al. and the clinical experience of the GDG (as documented in the LETR) We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in 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 breast cancer. The GDG considered that the symptom profile carried the largest expression of risk irrespective of personal or family history, or other risk factors.

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664	Macmillan Cancer Support	11	Full	151	General (ovarian)	We welcome the retention of the criteria for ovarian cancer and Macmillan Cancer Support has worked to support the implementation of this guidance through promoting best pathways to access to diagnostics tests and by including the recommended criteria within our eCDS tool.	Thank you for your support
665	Macmillan Cancer Support	12	Full	161	General (vulval)	We support the guidance as proposed, however referring to some of our general comments, as outline previously, the NICE guidelineCG27 did also give advice beyond a 2WW pathway regarding symptoms that should be reviewed or safety netted. *2011 1.7.12, vulval cancer may also present with Pruritus or pain. For a patient who presents with these symptoms it is reasonable to use a period of "treat, watch and wait" as a method of management. But this should include active follow up until symptoms resolve or a diagnosis is confirmed. If symptoms persist the referral may be urgent or non urgent depending on the symptoms and the degree of concern about cancer.*	Thank you for your support of the safety netting recommendations. The GDG considered whether separate safety netting recommendations could be made for different cancer sites. However they agreed that a single recommendation for all patients being safety netted was the best strategy, to aid clarity and because low risk symptoms often span many cancers.
667	Macmillan Cancer Support	14	Full	155	1.5.10 General (Endometrial)	We are concerned about the introduction of an age discriminator for PMB. We note that the GDG considered the evidence and felt that there was a lack of evidence to support lowering the age limit. We can report that a recent audit of endometrial cancer cases in one of the major gynaecological cancer centres demonstrated that 32% of patients were under the age of 55 at diagnosis and 14% were under the age of 50. Based on this real world data, following these updated recommendations, 20% of cases would not have been referred urgently. We welcome the support for direct access to ultrasound scan but would also welcome guidance on consensus regarding endometrial	There are two recommendations for post-menopausal bleeding; the former for women aged 55 and over are for referral using a suspected cancer pathway. The latter – for women under 55, is a 'consider' recommendation, also for referral under the same pathway. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						thickness to support primary care clinicians in interpreting the results. Macmillan has had feedback from our Cancer Voices regarding late stage diagnosis of womb cancer and they are concerned about the proposed deletion from NICE guideline CG27: *an urgent referral should be considered in a patient with persistent IMB and a negative pelvic exam (1.7.9)* The deletion of persistent IMB would fail to protect the 496 menstruating women who each year develop womb cancer (Evidence: Office for National Statistics Cancer Statistics Registration, England (Series MB1), no. 43, 2012: Total of 496 patients under 50 were diagnosed with malignant neoplasm of corpus uteri in 2012. Total of 1058 patients under 55 were diagnosed with same) As stated previously, guidance of 2011 did highlight some specific issues over and above urgent referral guidance and we would support retention of the profile given to increased risk in patients taking particular medications e.g. Tamoxifen. http://be.macmillan.org.uk/be/p-22317-the-rich-picture-on-people-living-with-cancer-of-the-uterus.aspx	It was outside the scope of the guideline to define test abnormalities. In this instance, it would be expected that the reporting radiologist would give appropriate advice. No primary care evidence was identified that persistent intermenstrual bleeding was a symptom of endometrial cancer requiring a suspected cancer pathway referral. We have documented in the introduction, there are very few instances where risk factors impact sufficiently on the predictive power of symptoms to allow different recommendations to be made for people with the same symptoms. The GDG 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 treatment with tamoxifen affected the predictive power of symptoms for endometrial cancer.

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668	Macmillan Cancer Support	15	Full	169	General (prostate)	We welcome the prostate guidance which is clear and lends itself to straightforward implementation. However to further support implementation it would be helpful to retain some of the guidance around appropriate timing of PSA testing as in NICE guidance CG27. We would welcome clarification of the GDG's consensus regarding the removal of bone pain and back pain as important symptoms as previously included in NICE guidance CG27 1.8.3 http://be.macmillan.org.uk/be/p-22315-the-rich-picture-on-people-living-with-prostate-cancer.aspx	The GDG did not identify any primary care evidence that reported PPVs for these findings that would warrant action.
669	Macmillan Cancer Support	16	Full	180	General (Bladder)	We understand that the GDG having reviewed a significant amount of evidence have agreed different age thresholds for different symptoms. However, this does increase the complexity for implementation by primary care clinicians. Reviewing the breadth of evidence considered, there is evidence to support investigation of some of the symptoms outlined in younger age groups. We would welcome clarification regarding the removal of the criterion of abdominal mass, 1.8.4 NICE guidance CG27. We recognise that this guidance relates to suspected cancer, however, NICE guidance CG27 1.8.2 is helpful to primary care clinicians in clarifying referral routes appropriate beyond suspicion of cancer e.g. symptoms and signs that would require onward referral to a renal physician. http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/update/RP-People-with-bladder-cancer.pdf	The GDG did not identify any primary care evidence that reported PPVs for abdominal mass that would warrant action. We would expect primary care clinicians to use their clinical judgement when applying these recommendations. Non-cancer diagnoses are outside the scope of this guideline.

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670	Macmillan Cancer Support	17	Full	196	General (Testicular)	We welcome the guidance on testicular cancer. In addition we would suggest that an ultrasound scan is requested at the time of referral to ensure that maximum benefit can be accrued from the 2WW referral.	This will be a matter for local implementation
671	Macmillan Cancer Support	18	Full	130	General (Colo-rectal)	We are concerned that guidance is too complex and would be unworkable within primary care and therefore it may not achieve the desired outcome of earlier diagnosis of cancer. We welcome the change in thresholds as outlined regarding unexplained iron deficiency anaemia. We are surprised to see that rectal or abdominal mass suggests "considering" a referral and suggest this be replaced with "offer". We understand the breadth of evidence that has been considered in order to derive the age thresholds, however, this will be extremely complex to implement across primary and secondary care, particularly with the increasing emergence of direct access clinics. The colorectal screening programme offers testing to asymptomatic people at age 55 and yet this guidance still suggests that some symptomatic patients will not be investigated until age 60.	The recommendations for colorectal cancer have been revised to make them simpler and easier to understand. The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. The recommendations in this guideline on the management of people with symptoms are drawn from the evidence on the different predictive value of symptoms in different patient cohorts and from a cost-effectiveness analysis of different testing strategies. The remit of the GDG did not include screening and we are unable, therefore to comment on the evidence base underlying the national screening programme. Even so, it is well recognised that screening populations

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						As we know mortality from colorectal cancer is strongly linked to stage of diagnosis. We also know that 50% of colorectal cancer patients did not meet the previous NICE criteria for referral (BMJ 2013, 346 F3172). The overarching request would be to streamline the diagnostic pathway for these patients and we would encourage consideration of the DoH direct access to diagnostic tests 2012. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216503/dh_133511.pdf http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/update/RP-People-with-colorectal-cancer.pdf	and symptomatic populations differ, so it would not be expected that the age ranges for recommendations should be the same. The recommendations for colorectal cancer have been revised to make them simpler and easier to understand.
672	Macmillan Cancer Support	19	Full	275	General (Sarcoma)	We welcome the increased clarity provided by this updated guidance.	Thank you
673	Macmillan Cancer Support	20	Full	332	General (Childre n's cancer)	We welcome the increased clarity provided by this updated guidance. We would seek to amplify the recommendation made on page 332 and to add that it is important in such circumstances to ensure a full examination of the child is undertaken since in relation to the specific tumour sites, they would be recognised by signs on examination in many instances as opposed to reporting of symptoms.	We state in the introduction that there is an expectation that 'the clinician will have taken an appropriate history and performed an appropriate physical examination'. We consider this adequately covers the situation you describe.
674	Macmillan Cancer Support	21	Full	210	1.7.2 General (Skin/malignant melanoma)	*(p210, 216, 220)* We welcome the updated guidance in line with the 7 point checklist and indeed Macmillan Cancer Support has facilitated the integration of this into our electronic cancer decision support tool	Thank you

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						Squamous cell carcinoma: We recognise that the GDG acknowledge there was no specific evidence relating to specific features but some guidance would still be helpful for primary care professionals as in NICE guidance CG27, 1.10.10. Without any guidance at all there is the potential to overstretch dermatology services and de-prioritise the highest risk cases. Basal cell carcinoma: We welcome the updated guidance on this. We would encourage the inclusion of a recommendation for safety netting for any skin lesion that is not deemed appropriate for urgent referral. http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/update/RP-People-with-malignant-melanoma.pdf	The GDG did not wish to try and describe SCCs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation. Thank you The GDG considered whether separate safety netting recommendations could be made for different cancer sites. However they agreed that a single recommendation for all patients being safety netted was the best strategy, because low risk symptoms often span many cancers.
675	Macmillan Cancer Support	22	Full	240	1.9.2 General (Brain and CNS)	We acknowledge that the GDG have reported that all symptoms for brain cancer have a low PPV. However we also know that almost 60% of brain tumours are currently diagnosed through an emergency route and only 1% are referred via 2WW.(http://www.ncin.org.uk/publications/data_briefings/routes_to_diagnosis) We welcome the GDG comment that for some patients, access to investigation, as opposed to an appointment, in the first instance, would be more beneficial. We would refer to the Access to Diagnostics guidance (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216503/dh_133511.pd	Thank you for this information. We consider that our recommendations will help to address this. It is not part of NICE methodology to cross reference information from other organisations in their guidelines.

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						f) for GPs which was developed by both primary care and secondary care clinicians including radiologists and is in alignment with the RC of radiologists MBUR7. This gives more detailed advice regarding the relevant specific symptoms along with timescales for direct access to MRI. Regarding abnormal cerebellar or other central neurological function of children and young people, we understand the feedback from the GDG in this regard but suggest the recommendation could be that a GP speaks to a paediatrician on the same day as the child presents to confirm the degree of urgency.	Recommendation 1.16.2 allows this option
676	Macmillan Cancer Support	23	Full	60	General (Upper GI)	We welcome the recognition of individual tumour sites and specific symptoms that relate to them. However as acknowledged within the evidence reviewed there is significant overlap across tumour sites pages 61, 80 quality of evidence: *it was noted that a number of the included studies had merged stomach and oesophageal cancer making it difficult to tease out the specifics related to oesophageal cancer* This adds another layer of complexity for primary care professionals when trying to identify appropriate investigation/referral which could ultimately lead to timely delays. We are concerned that guidance is too complex and would be unworkable within primary care and therefore it may not achieve the desired outcome of earlier diagnosis of cancer.	Thank you The issue is less complex than it would seem, the diagnostic test for both oesophageal and stomach cancer is usually the same. The recommendations for upper GI cancers have been revised to make them simpler and easier to understand.

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						Macmillan Cancer Support has effectively integrated upper GI symptoms into the eCDS to support ease of identification of patients requiring ongoing investigation/referral.	Thank you for this information.
						We welcome the GDG's suggestion of increased GP access to endoscopy. However as reported, access and timely access to endoscopy is not available to all and therefore create an inequitable service. We would therefore be concerned about removing the recommendation of urgent cancer referral and replacing it solely with direct access to endoscopy.	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
						We recognise that the GDG has considered the evidence of PPV's for both individual and combinations of symptoms however the complexity of the advice as suggested would be very difficult to realistically implement in practice and has the potential to cause significant delay for the cohorts of patients suggested to refer for endoscopy routinely. The NICE guidance CG27 gave greater clarity to primary care professionals.	The recommendations for upper GI cancers have been revised to make them simpler and easier to understand.
						(p 67) Pancreatic: We welcome the recommendation of direct access to CT and the highlighting of symptoms relating to pancreatic cancer as a specific tumour site. This is particularly important with respect to the fact that presently only 13% are diagnosed through 2WW and 47% through emergency routes (http://www.ncin.org.uk/publications/data_briefings/routes_to_diagnosis)	Thank you we agree.
						Whilst we welcome the recommendation of direct	The decision to include ultrasound, where

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						access to CT, we have concerns that where direct access to CT for GPs is not available, the recommendation is for abdominal ultrasound which as acknowledged within the evidence, will miss tumours less than 3cm in diameter. Regarding direct access to diagnostics, We would therefore suggest that just CT should be the only recommendation (we are aware that significant diagnostic advances are being made with respect to endoscopic ultrasound)	CT was unavailable, was based on the lack of directly relevant data to analyse cost-effectiveness of the choice between the two modalities. This is detailed in the Linking Evidence to Recommendations section.
677	Macmillan Cancer Support	24	Full	224	General (Head and neck)	Laryngeal: We appreciate clear guidance in relation to age. We understand the definition of the term "persistent" as used by the GDG but feel for the specific symptom of "hoarseness" a specified time period of duration would support the referral process as per NICE guidance CG27 We also encourage the retention of chest X Ray to support triage and ensure patients benefit from being on the correct pathway as soon as possible Oral: we support the recommendation for an identified cancer referral pathway for a lump in the neck but would also note that this symptom is not solely indicative of oral cancer. We think the guidelines should reflect this. As with other tumour sites we would welcome clarification regarding the removal of symptoms where we cannot see that the GDG has explained	There was no primary care evidence to allow the GDG to add qualifying terms to hoarseness. We would expect primary care clinicians to exercise their clinical judgement when applying the recommendations We appreciate the differential diagnosis of some symptoms such as hoarseness includes both head and neck cancers and thoracic cancers. CXR recommendations are placed in the lung/mesothelioma section, not here. The symptom based guideline will help. The guideline also makes recommendations on lump on the lip or in the oral cavity and unexplained ulceration in the oral cavity. There was no primary care evidence available on this area. It was the opinion of the GDG, based on their clinical

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						rationale for this: e.g. • Unexplained tooth mobility • Persistent unilateral head pain • Persistent sore throat We acknowledge the GDG discussion around dental care not being free to all and that a community dental service exists, however there is not equity of access to this service. This impacts significantly on the implementation of this guidance and ultimately our concern is that this will almost certainly result in delays. Thyroid: we welcome the updated guidance regarding thyroid cancer which will be clear for primary care professionals and straightforward to implement. http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/update/RP-People-with-head-and-neck-cancer.pdf	experience and input from an expert advisor, that these symptoms would not have a high enough PPV to warrant action In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...' Thank you
678	Macmillan Cancer Support	25	Full	263	General (haematology)	*(p263, 268)* Lymphoma: We welcome the separation of the different haematological malignancies with myeloma and leukaemia however we feel that it is unnecessary to separate out referral guidance for different types of lymphoma. We would also suggest that all guidance for leukaemia should be to "offer" a FBC rather than to	At the time of constructing the review questions for this guideline, the GDG did not know if the two main types of lymphoma would have separate symptom profiles. Therefore we set two separate review questions and have maintained this separation in the guideline to ensure transparency of process. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For

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						"consider". It would also be useful to include some guidance recommending a discussion of the results of FBC between GP and haematologist to appropriately triage necessary speed of ongoing referral. Myeloma: we welcome the guidance relating specifically to myeloma. It is recognised that a patient with myeloma may have a normal ESR and we suggest it would be helpful to include protein electro-phoresis in the initial investigations for all patients in whom there is a suspicion of myeloma. It would also be helpful to highlight the many possible presentations of myeloma. Some cases will require either "immediate" or "very urgent" attention as opposed to an urgent 2WW referral e.g. Patients with hypocalcaemia, renal failure, spinal cord compression and pathological fracture. Again discussion with the haematologist could guide urgency of referral.	more information on the wording of NICE recommendations please see p 6 of the short version. As documented in the Linking Evidence to Recommendations section, the GDG agreed to recommend the tests in a 'phased' approach to try to focus the patient group to those who had a higher likelihood of cancer, given the generic nature of the symptoms. The GDG was aware of the multiple presenting complaints for myeloma. However, the evidence review did not find any symptom pattern (including the ones you have listed) meeting the 3% threshold for suspected cancer referral. This matter is covered in recommendation 1.16.2
190	Manchester Cancer	1	Full	32	11	*(lines 11-15)* We feel it is important to quantify the false negative rate for CXR in primary care (e.g.Stapley et al Br J Gen Pract. 2006 Aug;56(529):570-3) and highlight the importance of not assuming a normal CXR = no cancer. The GPs on our board thought it important to issue guidance on what to do when with a "normal" CXR – e.g. when to repeat (and what time interval, when to refer). Line 15 suggests that primary care has access to CT scans which is not standard in the UK	We do not think that this level of detail is relevant to include in the background information. We have clarified that CT scans are 'often' available.

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191	Manchester Cancer	2	Full	33		*(p33-41)* PPV were considered a useful tool for giving reassurance or reasoning to patients, although there is concern that many of the PPVs listed in the document are from studies with small patient numbers/events. Where possible, it would be useful to include a single PPV (from best evidence) for each symptom/combination in the final NICE guidance.	Meta-analysis was undertaken for symptoms where possible. However this was only possible for a limited number of symptoms and therefore adding a summary PPV to each recommendation would not be possible.
192	Manchester Cancer	3	Full	41	1.1.3 17	(3rd bullet point) "…have smoked in the past" needs to be quantified as this would include, for example, people who smoked for a few weeks as a teenager – is this the intention?	We would expect GPs to use their clinical judgement in defining who is an 'ex-smoker'
193	Manchester Cancer	4	Full	42	1.1.4	*(p42, 46)* It is concerning that a FBC alone (without a CXR) is recommended for patients > 40yrs who have never smoked with unexplained cough, shortness of breath, chest pain, weight loss, or appetite loss. It was considered by the group that a CXR would be an important diagnostic (not just cancer diagnosis) investigation in this setting.	The PPVs of these single symptoms in non-smokers are very low. The purpose of the FBC is to identify any thrombocytosis. These symptoms in combination with thrombocytosis have PPVs that would warrant further investigation.
194	Manchester Cancer	5	Full	42	1.1.5	*(p42, 46)* "Consider an urgent full blood count and chest X-ray (within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:.." suggests that it is acceptable to wait longer than 2 weeks for the FBC and CXR in previous recommendations on this page. We believe that all blood counts and CXR in these settings should be considered **very urgent** (and in reality are often available as an immediate walk-in service).	The GDG considered that these symptom combinations were not strongly predictive of cancer and therefore did not recommend an urgent cancer pathway, but rather testing to refine the PPV for the individual patient. The GDG did not make a recommendation for urgent investigation across the board as the large majority of cases would not have cancer but, as the recommendations on the diagnostic pathway state, it is expected that primary care clinicians use their clinical judgement in such cases.
195	Manchester Cancer	6	Full	42	1.1.6	"Persistent or recurrent chest infection." – persistent is defined in the "Terms used…", but not recurrent, What is considered "recurrent" can be subjective, and therefore a definition would be	We consider this is best left to the judgement of the individual clinician.

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						helpful.	
196	Manchester Cancer	7	Full	44		We do not consider concern over "access and use" of spirometry to be a legitimate reason for excluding it from the list of recommended investigations in primary care, and we argue that GPs should ensure access to spirometry, particularly as COPD is listed as a QOF. Whilst we acknowledge the inconsistency of spirometry PPVs in the data presented, this is likely to be a function of the small number of events. Furthermore, spirometry is commonly listed in the composite-risk assessment models for lung cancer (see comment number 11).	We have deleted this sentence.
197	Manchester Cancer	8	Full	46 45		*(p45-47)* We were concerned that the GDG decided not to make recommendations based on asbestos exposure but do stratify for smoking history. We believe that evidence of previous asbestos exposure is likely to lead to more rapid investigation/referral for patients with borderline symptoms for mesothelioma, and should therefore be included in the recommendations. The GDG is right to acknowledge that it can be difficult to ascertain if previous asbestos exposure has occurred, and that mesothelioma should be considered in patients without exposure. The GDG can mitigate against these concerns by issuing a warning to this effect with the recommendations.	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. However, it was agreed that given the high relative risk of mesothelioma in people exposed to asbestos, a known history of exposure to asbestos was likely to increase the predictive value of symptoms for mesothelioma and therefore needed to be included in the recommendation.
198	Manchester Cancer	9	Full	46	1.1.10	Due to the multidisciplinary target-audience of these guidelines, it would be useful to define "chest signs compatible with pleural disease".	We consider it is more important to highlight the signs rather than to explain the underlying pathophysiology.
199	Manches	10	NICE	General	General	The GPs on our board agreed that the guidelines	This guideline covers 37 different

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	ter Cancer					in their current form would be unusable in primary care. They raised concern that the 133 page document would be digested by only the most committed GPs (who arguably are the least critical target) and left unread on the shelf by the majority. Perhaps a more effective approach would be releasing guidance for each separate tumour type at intervals (for example, there are 12 different cancer-types included in this document – releasing one each month over 1 year) in a simplified format which could be quickly referred to in a clinical setting.	cancers. As a consequence it contains a lot of information. By producing a section of the guideline focused on symptoms, the GDG have sought to make this information easier to navigate by primary care clinicians. In addition, NICE are exploring ways that we can improve usability of the document.
200	Manchester Cancer	11	Full	41 General		Our board is concerned that these update guidelines don't move things forward in the early detection of lung cancer, and continue to rely on presentation of symptoms to trigger investigation/referral for lung cancer. It should be acknowledged that most patients with relevant symptoms, (with the probable exception of haemoptysis), are already likely to be incurable. We would therefore be keen to see this update take a more radical approach to promote the early identification/referral of lung cancer patients (as prioritised in NICE QS17) and recommend the introduction of **a risk-stratifying approach (e.g. composite risk scores) to identify patients more at risk of lung cancer** which would facilitate earlier detection, and is more likely to save lives.	Your suggestion describes screening which is outside the scope of the guideline.
63	Manchester Cancer	12	NICE	220 77	1.7.5 and 1.7.4	There has been a sustained year on year increase in 2WW referrals for many years. The 2WW referrals have a knock on effect on severe inflammatory conditions that get delayed in being seen and treated and repeated audits show most 2ww referrals are for clearly benign lesions. The volume of 2WW referrals can put pressure on the management of the actual SCCs and melanomas	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they

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						meaning departments struggle to treat them in a timely fashion BCCs are the most common type of human tumour. Adding BCCs, even only certain types, means there is a very real risk the 2ww system for skin cancer will break and BCCs no matter even high risk sites and histology are not at all life threatening tumours. Is this necessary??	have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed. Re-configuration of services will be a matter for implementation.
374	NHS Bowel Cancer Screening Programme Southern Hub	1	NICE	130 70	1.3.6 21	Faecal occult blood (FOB) test is a term for a collection of measurement systems that have very different analytical and clinical characteristics. Any recommendation must specify which analytical system it refers to. Analytical methods include guaiac and faecal immunochemical testing (FIT). FIT testing can be qualitative or quantitative.	It is recognised that all tests use different assay techniques but this was not the focus of the question and so no recommendations have been made on which assay to use.
375	NHS Bowel Cancer Screening Programme Southern Hub	2	NICE	130 70	1.3.6 21	Faecal occult blood (FOB) testing has poor PPV, NPV, sensitivity and specificity. In the UK the common test used is guaiac which is a qualitative test. The poor diagnostic characteristics of this test mean it no longer has a place in routine laboratories and a large, and increasing, number of laboratories in the UK no longer offer FOB for this reason. The high false negative rate provides false reassurance.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to

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							recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
376	NHS Bowel Cancer Screening Programme Southern Hub	3	NICE	130 70	1.3.6 21	The guaiac FOB test is a subjective test, relying on visualisation of a colour change. Not all guaiac tests are the same with kits from different manufacturers having different cut off values to report positive and negative. It is the test used in the bowel cancer screening programme where a complex algorithm is used looking at spot patterns and repeat testing if required. Guaiac FOB is suitable as a screening test but it is not the preferred method and is being replaced internationally in screening programmes with quantitative FIT, in line with European Guidelines.	It is recognised that all tests use different assay techniques but this was not the focus of the question and so no recommendations have been made on which assay to use. There was insufficient evidence on FIT to make a recommendation for use. Making recommendations on the standardisation of laboratory assays is outside the scope of this guideline. People with a negative FOB but persistent symptoms would be covered by the recommendations made on safety netting. These recommendations now

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						A large variability in performance between labs is observed with guaiac FOB, as demonstrated in both external quality assurance schemes and in data available from the bowel cancer screening programme.	explicitly state that people should be aware of the possibility of false negatives with this test.
377	NHS Bowel Cancer Screening Programme Southern Hub	3	NICE	130 70	1.3.6 21	Quantitative automated FIT are currently primarily in place only in screening laboratories but are the most reliable analytical systems. In the future there may be a place for using FOB testing with the introduction of quantitative FIT to replace the guaiac test but we don't have the evidence yet to recommend such practice.	There was insufficient evidence on FIT to make a recommendation for use.
378	NHS Bowel Cancer Screening Programme Southern Hub	4	NICE	71	1	*(lines 1-3)* See comments 1,2 and 3 for comments in respect to FOB test	Please see our responses to these comments
52	NHS Choices	1	General			We welcome the guideline and have no comments as part of the consultation.	Thank you
810	NHS Dorset CCG	1	Appendices	General	General	Concern that the threshold would be lowered too far with conversion rate of 3%	The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline.
811	NHS Dorset CCG	2	Appendices	General	General	The role of GPs to manage risk may be affected in addition to their gatekeeping role	We do not expect this to be a significant outcome from the update of this guideline.
812	NHS Dorset CCG	3	Appendices	General	General	Guidelines felt to be prescriptive and a fair amount of repetition and the lay-out rather confusing - incorporation of all the variations into 2WW	The format of the guidance is well outlined in the introduction, and it is made very clear that the clinician is expected to

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						protocols/proformas would be similarly confusing. If NICE is recommending a referral for the wide variety of symptoms that 'may' but certainly are not, pathognomonic of 'cancers', this removes a certain degree of autonomy from the GP. Concern regarding the amount of 'referrals' for investigations may overload secondary care services. (concern that such a prescriptive approach to cancer can open doors to complaint and litigation)	use their clinical judgement. This argument can be made for any clinical guidance. The issue of secondary care services is a matter for implementation
813	NHS Dorset CCG	4	Appendices	31		This approach seemingly will also necessitate multiple more referrals e.g. pg 31 - offer fbc and cxr to someone with cough +/- fatigue, SOB, CP. although relatively cheap investigations when these extend to CT scans, referrals etc this becomes much more costly.	When making recommendations, the GDG explicitly considered the cost consequences of these recommendations and the likely impact on service delivery. This has been documented in the Linking Evidence to Recommendations sections in the full guideline.
814	NHS Dorset CCG	5	Appendices	General	General	Inclusion of all these symptoms and referral advice onto a 2WW pro forma may become hugely time consuming and possibly binding? It can also confuse the picture where multiple explainable symptoms are being associated with cancers which could have a profound impact on patient presentation and ultimately referral, when often not necessary -thereby increasing pressures on Primary and Secondary care. There appear to be very few guidelines regarding 'length of time of symptoms'.	The GDG had to make a balance between simplicity and inclusiveness. It is not surprising that such a large – and important – subject with diverse cancers led to multiple recommendations. The inclusion of the symptom-based section should go some way to address your concerns. There was insufficient primary care evidence to add qualifying terms to the symptoms. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations

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815	NHS Dorset CCG	6	Appendices	General	General	Whilst better access to CT and MRI for GPs must be commended serious thought must be given to expectation and urgent direct access	We agree.
816	NHS Dorset CCG	7	Appendices	General	General	There could be more reference to patients who have multiple attendance without resolution of nebulous symptoms needing referral/investigation.	These patients would be covered by our recommendations in chapter 5 on safety netting.
817	NHS Dorset CCG	8	Appendices		1.14	1.14 raises some questions (specifically 1.14.5) about who should be providing this information. This was brought up during the Breast Risk Stratification meeting - who is best placed to offer this and who will take responsibility for it - the patient doesn't care….just so long as it is done!!	We would anticipate that the primary care clinician would provide this information.
818	NHS Dorset CCG	9	Appendices	General	General	It is unclear whether Primary Care is going to be expected to do research but if so the call for primary care research needs to be coordinated and commissioned through academic units, CRUK, RCGP etc.	We have made recommendations for research in four areas. These can be found at the start of the full guideline. We agree that there would need to be a co-ordinated approach to doing this, but it is beyond the scope of this guideline to make a recommendation on who conducts the research.
819	NHS Dorset CCG	10	Appendices	General	General	Concern regarding the capacity of the system to deal with increase in activity The 3% threshold might be valid for consideration of investigation at primary care level but our secondary care providers could not currently cope/generate the capacity to manage a 3% conversion rate from 2WW clinics. They currently struggle with the volume of referrals that currently generate approx 13% conversion. .	The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline. It should be noted that prior guidance is estimated to have PPV threshold of 5%.
820	NHS	11	Appendic	General	General	Proposals re access to diagnostics welcomed	Thank you for your support

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	Dorset CCG		es				
821	NHS Dorset CCG	12	Appendices	General	General	The emphasis could more usefully be on improving selectivity of referral and, in particular avoiding missing cancer diagnoses.	We consider an evidence-based guideline like this does improve selection of patients, and thus should reduce missed cancer diagnoses.
822	NHS Dorset CCG	13	Appendices	General	General	It is welcomed that thrombophilia is suggested as a trigger to consider cancer in various scenarios.	Thank you
823	NHS Dorset CCG	14	Appendices	General	General	There are some attempts to define terms like 'prolonged' symptoms at the beginning but they are still fairly woolly - and will no doubt be abused in litigation.	There was insufficient primary care evidence to add qualifying terms to rectal bleeding. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
824	NHS Dorset CCG	15	Appendices	General	General	It is disappointing that the document does not highlight the need to identify earlier markers for lung and pancreatic cancers.	A recommendation for research to estimate the PPVs of different symptoms for several cancers, including pancreatic, has already been included in the guideline. There is an ongoing programme of research in biomarkers for lung cancer therefore the GDG did not consider a recommendation for further research was needed.
690	NHS England	1	Full	29	21	Clear guidance for safety netting including written information for patients would be a good step forward particularly for more experienced GPs who may feel more comfortable with watchful waiting	It is not appropriate to recommend what information is needed because the information needs will be dependent on the needs, preferences and symptoms of the individual patient.
691	NHS England	2	Full	41	1.1.2 – 1.1.5 17	I think this is too complex – since both CXR and FBC are easily ordered in general practice I would suggest that both are ordered in anyone over 40 with symptoms on the list whether they have smoked or not. The key is to bring the patient back for the results or to ensure that there are adequate recall systems for this in the practice.	The recommendations for lung cancer have been revised to make them simpler and easier to understand.

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						For haemoptysis the 2 wk referral pathway should be used	Thank you, we agree and this is what we have recommended.
692	NHS England	3	Full	46	1	I would be interested to know where it is not possible to get a CXR within a few days as a routine never mind urgent. This would be a question for CCGs regarding commissioning of diagnostics	We are unclear which part of the text your comment relates to.
693	NHS England	4	Full	60	16	Direct access upper GI endoscopy is not universally commissioned. This may have implications in terms of commissioning.	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
694	NHS England	5	Full	67	1.2.5 12	I think a 2 week referral would be more appropriate to ensure that the patient is in the correct pathway, there is a risk that the CT appointment could delay diagnosis and also that there may not be correct pathways from the (possibly private) provider into the NHS cancer pathway, also transfer of the images can be complex	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The precise mechanism for communication of the results of imaging will be a matter for implementation. It is worth noting that all of the direct

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							access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
695	NHS England	6	Full	80	9	Where direct access endoscopy is available both options for referral would be appropriate. The direct access endoscopy may be offered through a private provider so effective onward referral direct to NHS provider is required to avoid delay in the pathway if cancer is diagnosed	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
696	NHS England	7	Full	89	1.2.13	This would be expected – if a liver edge is found on examination an urgent ultrasound referral would be appropriate from the GP	Thank you.
697	NHS England	8	Full	130	1.3.9 13	Recommend that the final recommendation is put at the top of the list	The recommendation on digital rectal examination for colorectal cancer has been deleted.
698	NHS England	9	Full	136	15	Recommendation is appropriate	Thank you
699	NHS England	10	Full	147	6	Recommendation is appropriate	Thank you
700	NHS England	11	Full	155	11	Recommendation is appropriate but will need to be widely communicated to GPs	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
701	NHS England	12	Full	159	2	Recommendation is appropriate	Thank you
702	NHS England	13	Full	161	6	This would potentially lead to 2 wk pathway being overwhelmed by bartholins cyst, cyst of duct of skene, first herpes presentation etc – would it be appropriate to put an age limit on this eg >40 as vulval cancer very rare in younger women. Please	Given the lack of evidence in this area the GDG were not able to put an age limit on their recommendations. We would expect primary care clinicians to use their clinical judgment when applying these

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						compare with recommendations re penile cancer referral	recommendations. Consequently we do not think the suspected cancer pathway would be overwhelmed.
703	NHS England	14	Full	163	22	This could lead to referral for warts or bartholins potentially. Could the word 'unexplained' be added?	We would expect primary care clinicians to use their clinical judgment when applying these recommendations.
704	NHS England	15	Full	169	9	Recommendation is appropriate	Thank you
705	NHS England	16	Full	180	6	Recommendation is appropriate	Thank you
706	NHS England	17	Full	193	12	Recommendation is appropriate	Thank you
707	NHS England	18	full	196	6	Recommendation is appropriate	Thank you
708	NHS England	19	Full	198	24	Recommendation is appropriate	Thank you
709	NHS England	20	Full	210	1	Recommendation is appropriate	Thank you
710	NHS England	21	Full	216	17	Recommendation is appropriate	Thank you
711	NHS England	22	Full	220	15	Recommendation is appropriate	Thank you
712	NHS England	23	Full	224	25	Recommendation is appropriate	Thank you
714	NHS England	24	Full	231	9	Recommendation is appropriate	Thank you
715	NHS England	25	Full	240	1.9.1 12	Recommendation is appropriate although direct access Brain MRI is not universal and would have commissioning implications	Thank you
716	NHS England	26	Full	245	14	Recommendation is appropriate	Thank you
717	NHS England	27	Full	258	14	Recommendation is appropriate however it could take 3 GP appointments to make the diagnosis if the tests are requested in series. It may be more appropriate to add protein electrophoresis to the initial tests if myeloma is suspected to avoid	As documented in the Linking Evidence to Recommendations section, the GDG agreed to recommend the tests in a 'phased' approach to try to focus the patient group to those who were most

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						diagnostic delay	likely to have cancer, given the generic nature of the symptoms.
718	NHS England	28	Full	263	11	Recommendation is appropriate	Thank you
719	NHS England	29	full	268	15	Recommendation is appropriate	Thank you
720	NHS England	30	Full	275	11	Recommendation is appropriate	Thank you
721	NHS England	31	Full	279	11	Recommendation is appropriate	Thank you
722	NHS England	32	Full	293	10	Recommendation is appropriate	Thank you
723	NHS England	33	Full	306	10	Recommendation is appropriate however this referral could also be made by optometrist/ health visitor thus avoiding delay in making a GP appointment	We agree. This guidance and it's recommendations pertain to all clinicians working in primary care.
724	NHS England	34	Full	319	10	Recommendation is appropriate	Thank you
725	NHS England	35	Full	332	10	Recommendation is appropriate	Thank you
726	NHS England	36	Full	366	1.13.37	Recommendation is appropriate although large overlap with psychological cause of lost appetite so may be advisable to add PHQ 9 to elicit symptoms of depression /could be confounding?	We think this decision is best left the clinical judgement of the primary care clinician.
727	NHS England	37	Full	41 General	General	These comments are made by the newly established NHS England Clinical Reference Group for lung cancer. This group was set up primarily to advise NHSE on the clinical aspects of commissioning high quality care and the recognition and referral of suspected lung cancer is an essential part of the pathway. It has particular importance in early diagnosis as a way of improving survival and reducing the high number of patient diagnosed through the emergency route. The CRG is prioritising early diagnosis and reducing variation in care and it is essential that	Thank you for this information

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						guidance facilitates both of these by ensuring applicability to all patient groups. The group does not believe that the recommendations, in the current form, will serve to improve on the existing guidance. This is because: a) the recommendations are too complicated (see specific members comments below); b) the reliance on the evidence to make recommendations is too heavily reliant on one study of relatively few patients; c) the applicability of the recommendations to all people with suspected lung cancer is compromised by the applicability of the evidence used. Several members of the group are GPs and GP	The recommendations for lung cancer have been revised to make them simpler and easier to understand. Several relevant papers on lung cancer were identified in the searches and critically appraised. Every study, as part of the critical appraisal, is assessed for its generalisability to the population in the review question. The Hamilton paper was assessed to be generalisable to the population. The GDG had no reason to consider that the predictive power of clinical findings elsewhere in the UK would be substantively different from that in the study population. Furthermore, the critical appraisal did not identify any reasons why the Hamilton paper should not be used when drafting recommendations. The primary care based research showed a positive predictive value, and confidence intervals, that was consistent with recommendations for action. Considerable caution should be used in extrapolating secondary care findings to the primary care population. The recommendations for lung cancer

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						commissioners and all commented that the guideline as a whole would be unusable in the current format and would lead to confusion and potentially to a lengthening of the initial pathway. The comment was made that the guidelines were unduly intricate and precise.	have been revised to make them simpler and easier to understand.
728	NHS England	38	Full	32		*(32-41)* We also have comments about the way data have been presented in the full guidance as set out below. Evidence review The National Collaborating Centre for Cancer have, as usual, done an excellent job in identifying the key papers on the subject, it is the interpretation that is, in the view of the CRG, suboptimal. Many of the recommendations stem from the analysis of the paper by W Hamilton et al, particularly concentrating on the positive predictive value of using two factors together. This has led to complicated recommendations but these are often based on only a few events. The paper by Hamilton studied patients in 21 GP practices in Exeter and there were 247 lung cancer cases (237 histologically confirmed) compared with 1235 controls. Whilst this is a very useful paper, it is surprising that applicability concerns were low (although bias was thought to be high). In Exeter, the lung cancer incidence and mortality rate is almost the lowest in the whole of England. Whilst it might be argued that this would not affect the incidence of symptoms of lung cancer, this does not take into account the way people may declare symptoms and interact with primary care. This may be very different in the higher incidence areas with high levels of socio-economic deprivation where	Several relevant papers on lung cancer were identified in the searches and critically appraised. Every study, as part of the critical appraisal, is assessed for its generalisability to the population in the review question. The Hamilton paper was assessed to be generalisable to the population. The GDG had no reason to consider that the predictive power of clinical findings elsewhere in the UK would be substantively different from that in the study population. Furthermore, the critical appraisal did not identify any reasons why the Hamilton paper should not be used when drafting recommendations. We agree that it is possible that factors such as deprivation may affect the presentation of cancer. For this reason we have made a research recommendation on this topic. The primary care based research showed a positive predictive value, and confidence intervals, for thrombocytosis that was consistent with a recommendation for action. Considerable caution should be used in extrapolating

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						both patients and GPs may influence how and when symptoms are recorded. Socio-economic deprivation, and the factors that are associated strongly influence the early outcome of people with lung cancer[1]. 21% of cases were small cell carcinoma, double the rate in the UK, as measured in the National Lung Cancer Audit. This may simply be a reflection of the low numbers but highlights the problem of over-interpretation of smaller studies. By way of illustrating how this has led to complex recommendations it may be helpful to look at the recommendation to use a full blood count to investigate for suspected lung cancer in people with other suggestive symptoms. This was based on the Hamilton paper alone and on 34 (19%) cases of thrombocytosis vs 19 (1.5%) controls. In fact platelet count was measured in 32% of controls and 52% of cases, so of measured cases the percentages were 4.8% and 26% respectively. The latter is a much higher rate than lung cancer physicians see in people with lung cancer at presentation in everyday clinical practice. The explanation may lie in the higher rate of small cell lung cancer or in, potentially, later stage disease or it may be a spurious finding. Thus this recommendation should be re-worded or removed from the lung cancer section.	secondary care findings to the primary care population. The recommendations for lung cancer have been revised to make them simpler and easier to understand.
729	NHS England	39	Full	33		*(p33-41)* Presentation of evidence The tables showing the positive predicative values and those summarising the individual papers should show clear the number of events and the total numbers of patients in each group, so that the reader can judge for themselves the strength of the data. Double symptom / sign complex vs. composite	The number of events (true positives) and totals (total number of positives) have now been added where the data were available to allow this. The GDG decided to only look at positive

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						scores. The other papers reviewed looked at much larger and less selected cases of lung cancer. Hipplesley-Cox et and Iyen-Omofoman et looked at the Health Improvement Network and both derived composite scores with similar AUC of over 0.9 for predicting lung cancer. The numbers of cases in these studies were 3785 and 12,074. The Iyen-Omofoman et al paper exclude all symptoms recorded 4 months or less prior to diagnosis, as this was the time when CXR rate increased in cases compared with the 120000 controls and was therefore the time when GPs were suspecting a diagnosis of lung cancer and recording of symptoms would be subject to ascertainment bias. In reality, the composite prediction models developed were similar and either of these would be likely to perform better than more complicated symptom combinations. Indeed Iyen-Omofoman calculated that using their score 119 CXRs would be required to detect one lung cancer vs 421 if the 2005 NICE guidelines were used. The original 2005 paper by Hamilton showed that patients attend their GPs multiple times before referral and a recent paper by O'dowd et al confirmed this for over 20000 lung cancer patients in the THIN dataset[2]. They also showed that a targeted approach to the use of CXR was needed as simply doing more CXRs was not associated with earlier diagnosis (the reverse was shown, likely due to ascertainment bias) 1. Peake MD: **Deprivation, distance and death in lung cancer.** *Thorax* 2014. 2. O'Dowd EL, McKeever TM, Baldwin DR, Anwar S, Powell HA, Gibson JE, Iyen-	predictive values. Therefore other measures, such as AUC and number of chest X-rays, were not considered. We have outlined in the methodology chapter that clinical decision tools were not considered in this guideline and the reasons for this. Thank you for providing these references.

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						Omofoman B, Hubbard RB: **What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK?** *Thorax* 2014.	
730	NHS England	40	Full	41 General		The CRG would therefore like to see the area of GP selection of patients for referral for lung cancer moved on by this Guideline. It is a major priority as set out in the NICE QS17 on Lung cancer to ensure that people at risk of lung cancer are identified early and referred promptly. To do this GPs need tools that easily fit with their difficult job – and these need to help all GPs, not just the enthusiasts. A recommendation is therefore suggested, which can either be a research recommendation but preferably a recommendation to drive service development, as follows: **Use a GP software-based composite risk score to identify patients who are likely to have lung cancer and investigate with a chest radiograph; consider urgent referral of high-risk people with normal chest radiographs that have on-going symptoms.** This recommendation would link directly to commissioning recommendations and is likely to move this stalled area of lung cancer care on significantly.	Your suggestion describes screening which is outside the scope of the guideline.
731	NHS England	41	Full	41	8	*(lines 8-10)* Several members of the group commented about the statements regarding the concept of direct access to CT and noted that this is not available to the majority of GPs.	We do not make any recommendations for direct access CT for lung cancer.

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						It was noted that the statement that there is no primary care evidence about the accuracy of CXR or CT in the diagnosis of lung cancer is one that ignores a plethora of evidence in other setting that is easily and appropriately extrapolated. CT is a highly sensitive test, as shown in numerous screening studies and CXR far less so. These data area available for high risk populations.	The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop recommendations for a guideline targeted at a primary care population. In the absence of primary care evidence the GDG agreed by consensus that chest X-ray was a useful test, though the possibility of false negatives was a concern.
						The question remains as to when CT is used either as a first test (i.e. bypassing CXR) or after a normal or near normal CXR. This will depend on if and how CT screening is adopted for lung cancer, where the baseline risk of lung cancer will determine whether CT is appropriate. It should also be noted that direct to CT for high risk patients can potentially avoid the need for visits to secondary care but can also result on confusion for GP and patient. There would thus need to be clear protocols so that the correct CT is done and a pathway for dealing with abnormal findings. There was general agreement that CT should be done before the first appointment, where a 2WW referral has been made. A suggestion for a recommendation was: Where a CXR in primary care is reported as	We agree that there is debate about the optimum initial test for lung cancer (CXR/CT). In the absence of primary care evidence to address this or any established practice, the GDG agreed not to make a recommendation about direct access CT. The scope of the guideline was to identify those patients needing referral for

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						suspicious of lung cancer that a direct access CT scan of the chest and upper abdomen is arranged simultaneously with a 2WW referral being made. This might be extended to: **Ensure all patients that fulfill criteria for urgent referral for suspected lung cancer have a CT of the lower neck, thorax and upper abdomen with the administration of intravenous contrast prior to attendance at the first outpatient appointment**. In reality, this is what many centres have been doing for years.	suspected cancer. It was not within the scope to make recommendations on what tests may assist secondary care with their evaluation.
732	NHS England	42	Full	32	16	*(lines 16-18)* The CRG felt the comments about the diagnostic tests reflected the lack of expertise on the guideline development group. Thoracoscopy is less commonly used to make a diagnosis and there was no mention of CT guided biopsy. Suggested re-wording: Definitive diagnosis requires obtaining a tissue biopsy or cytology of the primary tumour or a metastasis. Common techniques used to confirm the diagnosis and guide treatment are bronchoscopy, CT-guided biopsy, pleural aspiration and biopsy and endobronchial ultrasound-guided fine needle aspiration. These techniques are performed in secondary care.	Thoracoscopy has been removed from this text, but we do not consider further detail is required for the background in a primary care guideline.
733	NHS England	43	Full	46 45		*(p45-57)* The CRG was surprised to see in the recommendations consideration of smoking history but not for asbestos exposure. Assessing asbestos exposure is important and could lead to earlier investigation of borderline symptoms such as persistent, but not severe chest pain. The recommendations should therefore include asbestos exposure as a consideration but also warn that up to 50% of people with mesothelioma	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking of sufficient impact on the predictive power of symptoms to require different

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						will not at first, report exposure.	recommendations. However, it was agreed that given the high relative risk of mesothelioma in people exposed to asbestos, a known history of exposure to asbestos was likely to increase the predictive value of symptoms for mesothelioma and therefore needed to be included in the recommendation.
734	NHS England	44	Full	General	General	The Colorectal Cancer Clinical Reference Group (CRG) supports new guidance lowering of the threshold for GPs to refer patients with colorectal symptoms for urgent investigation. This should improving outcomes for patients with colorectal cancer by facilitating early diagnosis. The recommendations, when implemented, will have an impact increasing the workload of clinical teams, colonoscopy and radiology services. Resources may be better managed by increasing the use for straight to test pathways for investigation.	Thank you. The management of resources will be a matter for implementation.
735	NHS England	45	NICE	130 70	1.3.1	The Colorectal Cancer CRG agrees with this new guideline that simplifies the decision making for referring doctors to colorectal diagnostic services.	Thank you
736	NHS England	46	NICE	130 70	1.3.2	This guideline could be improved by removing the haemoglobin levels in parenthesis. Iron deficiency anaemia is an indication for investigation in a man at any age and for post-menopausal women.	The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
737	NHS England	47	NICE	130 70	1.3.3	This simplified the guideline for referral as in 1.3.1. Patients with unexplained new onset colorectal symptoms should be referred for investigation following their first presentation to primary care.	Recommendations 1.3.1 and 1.3.3 cover different groups of people so we do not consider that there is a conflict.
738	NHS	48	NICE	130	1.3.4	The Colorectal Cancer CRG recommends patients	The use of the term 'consider' reflects the

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	England			70		presenting with an abdominal or rectal mass must be referred for investigation. The change from "should refer" to "consider a referral" for patients who present with rectal or abdominal mass does not give clear guidance to GPs. This guideline would be improved if it started with the word refer as for 1.3.1-3 and 5.	strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
739	NHS England	49	NICE	130 70	1.3.5	The CRG supports this guideline as it may assist identifying patients electively who currently present late via the emergency pathway.	Thank you
740	NHS England	50	NICE	130 70	1.3.6	Patients and their referring doctors want a definitive diagnosis for their symptoms. The Colorectal Cancer CRG recommends the removal of guaiac Faecal Occult Blood Testing (FOBT) from the NICE guidelines for investigating patients with colorectal symptoms. This test does not provide a definitive diagnosis and has false negative rates presented in the Full Guidance between 25 and 100%. There are currently insufficient data and laboratory experience to support Faecal Immunological Testing. The use of FOBT should be limited to the National Bowel Cancer Screening Programme where FIT would be preferable to the guaiac test.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are

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							covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. We agree that there is insufficient primary care evidence to recommend FIT and have specified this in the Linking Evidence to Recommendations Section.
741	NHS England	52	NICE	130 71	1.3.7	Guaiac FOBT should not be used for symptomatic patients and FIT should not be used outside a randomised trial supported by appropriate expertise.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations.

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							All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. There was insufficient evidence on FIT to make a recommendation for use.
742	NHS England	53	NICE	130 71	1.3.8	The Colorectal Cancer CRG supports consideration a 2-week wait referral for patients under 50 with colorectal symptoms. Men of any age with iron deficiency anaemia should be referred for investigation.	Thank you. The primary care evidence on iron deficiency was examined in detail. The age cut-offs in the recommendations reflect the evidence.
743	NHS England	54	NICE	130 71	1.3.9	The Colorectal Cancer CRG agrees with guideline.	Thank you
744	NHS England	55	Full	29 General	General	We are pleased to see the introduction of recommendations on safety netting of patients with 'grey area' symptoms not quite reaching 2WW referral criteria We are strongly supportive of the increased emphasis on increased GP-initiated diagnostic testing ('Straight to test') but emphasise that development of these services is best done in	Thank you for your support. We agree. Development of pathways will be a matter for implementation of this guideline.

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						conjunction with local secondary care providers, to ensure seamless and timely onwards pathways for patients where the tests confirm or increase suspicion of a cancer diagnosis and to ensure efficient use of and planning for local diagnostic capacity.	
745	NHS England	56	Full	General	General	It would be of greater value if NICE make it a specific point to support GPs in recognising that cancer diagnosis in primary care isn't always straight forward, and some patients present in convoluted way and only in hindsight does it fit together, therefore inevitably some cancers do take 3-4 consultations before the penny drops – it is too often stated that GPs are failing the patient in these cases and it isn't always so. Denmark has a similar system of primary care /secondary care to UK Gate keepers' role of GP is the same. Same cancer issues as UK - outcomes/late presentation. Work in Denmark has demonstrated that only 40%of cancers are diagnosed using the tumour specific route. Led to a 3 legged diagnostic strategy. NICE is asked to consider recommendations for those who do not fit nicely in to a tumour specific route but suspicion exists.	We agree. The difficulties in cancer diagnostics are covered in the introduction to the full guideline. The GDG discussed at length the difficulty of patients with unclear presentations. This is partly addressed by the symptoms based and the non-specific symptoms sections in the guideline. The configuration of cancer diagnostics in secondary care is beyond the scope of this guideline.
746	NHS England	57	NICE	General	General	Whilst the removal of the duration component is a welcome change so that patients do not have to wait to have 6 weeks of symptoms before referral, the introduction of several age limits make the guidelines complex and not easy to follow. All of this is likely to confuse general practitioners making the guidelines impractical and unusable or at least not used as intended. We would	The ages included in the recommendations reflect the evidence that was available on the positive predictive value of symptoms. It would therefore not be appropriate to apply the same age group to all recommendations.

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						recommend using a one cut off age of 40 years instead of the 40, 50 and 60 age limits with some of the recommendations. The LCA working with Transforming Cancer Services in London and other stakeholders have obtained agreement on the introduction of guidance for referral of symptomatic patients in the Capital from the age of 40. Early diagnosis of cancer is the only way to improve outcomes and survival. We would wish to see this emulated nationally.	
747	NHS England	58	Full	41	8	*(lines 8-10)* Included in the feedback of the NHSE lung CRG: It was noted that the statement that there is no primary care evidence about the accuracy of CXR or CT in the diagnosis of lung cancer is one that ignores a plethora of evidence in other setting that is easily and appropriately extrapolated. CT is a highly sensitive test, as shown in numerous screening studies and CXR far less so. These data are available for high risk populations. A suggestion for a recommendation was: Where a CXR in primary care is reported as suspicious of lung cancer that a direct access CT scan of the chest and upper abdomen is arranged simultaneously with a 2WW referral being made. This might be extended to: **Ensure all patients that fulfill criteria for urgent referral for suspected lung cancer have a CT of the lower neck, thorax and upper abdomen with the administration of intravenous contrast prior to attendance at the first outpatient appointment**. In reality, this is what many centres have been doing for years.	The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop recommendations for a guideline targeted at a primary care population. In the absence of primary care evidence the GDG agreed by consensus that chest X-ray was a useful test., though the possibility of false negatives was a concern. The scope of the guideline was to identify those patients needing referral for suspected cancer. It was not within the scope to make recommendations on what tests may assist secondary care with their evaluation.

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748	NHS England	59	Full	42		On the lung cancer section, there is mention of Cough and thrombocytosis – positive predictive value > 3% - unclear whether this guideline warrants a direct 2WW referral or not e.g. – are gps being advised that if a patient presents with a cough and their platelets are high – but the CXR is normal – would that qualify for a 2WW referral? (being clear will really help GPs)	The current recommendation is to perform an urgent chest X-ray on all patients with thrombocytosis. If the chest X-ray shows finding suggestive of lung cancer the guideline recommends a suspected cancer pathway referral.
749	NHS England	60	Full	46		On mesothelioma – it would be very useful if NICE can give clearer guidelines on what to do when pleural plaques are commented on in a chest x-ray report. Do they go for a CT chest next, chest clinic referral (routine /2WW) it's a grey area.	We have added a recommendation on what should happen if chest X-ray findings are suggestive of mesothelioma. Lesser abnormalities (including pleural plaques) will be a matter for clinical judgement.
750	NHS England	61	Full	67		Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for pancreatic cancer if they are aged 40 and over and have jaundice. [new 2015] (P67) - do they really mean this ?? there are differing types of jaundice – e.g. conjugated / unconjugated bilirubinaemia e.g. after acute hepatitis – do they really want 2WW to be triggered as over 40 years old gets viral hepatitis too	The PPV for jaundice in pancreatic cancer is one of the highest for any symptom in any cancer. If a GP has a clearly correct alternative diagnosis we would expect them to exercise their clinical judgement.
751	NHS England	62	Full	60	14	**OG cancers** open access investigations seems to be is a way of extending the 2WW process into primary care – e.g. the guidelines on upper GI/oesophageal cancers seems to suggest that patients presenting with dysphagia - GPs should use open access endoscopy –it specifically doesn't mention a cancer referral pathway as it does for other cancer elsewhere which makes me think they feel that endoscopy requests must go up in order to detect more upper GI cancers and to help off load 2WW clinics gps should first use open access (which in	The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected

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						principal is fine except that most gps would ask for open access endoscopy in cases where they feel cancer is low risk not No risk, and the guideline is suggesting open access for the cohort that traditionally is being referred directly into 2WW upper GI clinics. There is little consideration that this will increase work load in primary care (except for one statement on page 30 saying it will lead to greater number of consultations (particularly gps).	cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG considered the issue of increased GP time in their deliberations on the resource requirements of the recommendations. This is documented in the Linking Evidence to Recommendations section that accompanies the recommendations in section 4.1 of the full guideline.
752	NHS England	63	Full	240	1.9.1-2	**Brain and CNS cancers** Loss of central neurological function' is too vague a term. Clarify what constitutes 'abnormal cerebellar signs' Seizures (mentioned in 2005 version and NICE guidance CG37 on Epilepsy, January 2012) are not mentioned. Furthermore, headache and progressive sub-acute cognitive decline (both mentioned in 2005) have been dropped.	The GDG did not wish to try and describe loss of central neurological function or cerebellar signs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation. The PPV for seizures and headache were below the 3% threshold for suspected cancer. Sub-acute cognitive decline is subsumed into the term 'progressive sub-acute loss of neurological function'.
753	NHS England	64	Full	257	1.10.4	**Haematological cancers** The guidance around back pain is insufficiently detailed. Although 'persistent' pain is cited as a trigger for further investigation, the definition of persistence is not given. Other factors that might necessitate earlier investigation (e.g. thoracic site,	There was insufficient primary care evidence to add qualifying terms to persistent pain. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.

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						presence of other warning symptoms) are not addressed comprehensively. Back pain is one of the most common complaints GPs deal with and it was our view that more information was required in this area. Myeloma accounts for about 10-15% of cases of malignant spinal cord compression and this is often a presenting feature. The presenting symptoms of impending cord compression were not included.	None of the available evidence reported a PPV for this symptoms that would warrant action.
754	NHS England	65	NICE	130 70	1.3.2	Men at any age and post-menopausal women should be referred with iron deficiency anaemia. Cut offs for anaemia to be determined by testing laboratory There is a need to clarify if the Hb level for referral for women is irrespective of menstruation.	Menstruation was not examined in any of the anaemia studies used by the GDG. Therefore we could not make specific recommendations on this. However we would expect primary care clinicians to use their clinical judgement when using these recommendations. The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
755	NHS England	66	NICE	130 70	1.3.4	Patients presenting with an abdominal or rectal mass must be referred for investigation. Object to the change from "should refer" to "consider a referral" as new version does not give clear guidance. This guideline would be improved if it started with the word refer.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
756	NHS England	67	NICE	130 70	1.3.6	Guaiac FOBT has false negative rates of 25-100% in the evidence in the full guidance. There is insufficient evidence to support the use of faecal immunological testing for symptomatic patients. Objection to recommending FOBT to patients	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group

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						presenting with new onset colorectal symptoms (change in bowel habit, abdominal pain, weight loss) with preference for an investigation that will give a definitive diagnosis e.g. colonoscopy. Objection to recommending FOBT to patients with iron deficiency anaemia urging proper and appropriate investigation to determine the aetiology. Concern that recommending introduction of FOBT complicates the colorectal diagnostic pathway and may negatively impact the implementation of Straight To Test diagnostic pathways.	receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
757	NHS England	68	Full	123	4	The 'full model structure' shown in the figure includes FOBT and Barium enema as guideline approved investigations for change in bowel habit. This very complex diagnostic pathway will result in unacceptable variation in patient care and time to definitive diagnosis: 'A false negative detected at 1	The full model structure is not intended to show the guideline approved investigations. It merely illustrates the structure of the economic model that was used to conduct the cost-effectiveness analysis.

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						year' will be referred for a colonoscopy other patients would have had within weeks of referral. FOBT does not provide a definitive diagnosis. Barium enema has been widely removed from clinical guidelines and replaced by CT Colonography. Commissioners in London have stated that Barium Enema should not be used as a first line test for CRC within current commissioning intentions.	The recommendations made by the GDG show the 'guideline approved investigations' and it can be seen that barium enema was not recommended. Testing for occult blood in faeces was recommended but it should be noted that it was not used by itself to provide a definitive diagnosis. In the economic analysis, patients with a positive FOBT result then go on to receive a colonoscopy where the patient would be diagnosed or identified as a false positive
758	NHS England	69	NICE	130 71	1.3.8	Strongly recommend consideration of referral of symptomatic patients under the age of 50 if they have a strong risk of colorectal cancer (IBD with extensive colitis for over 10 years, previous cancer or multiple polyps, known inherited syndrome or family history)	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG 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 IBD, previous cancer, multiple polyps, known inherited syndromes or family history affected the predictive power of symptoms for colorectal cancer.
759	NHS England	70	Full	85		Gall bladder cancer guidelines make no mention of surveillance of gallbladder polyps. It would be useful for NICE to comment on this. Gall bladder polyps may be premalignant. It is curious NICE guidance on gall bladder cancer fails to mention gall bladder polyps - perhaps there is no firm consensus. There is a useful article on this	Surveillance of non-cancerous lesions is outside the scope of this guideline

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						subject via this link http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3359430/r	
760	NHS England	71	Full	147	1.4.1	**Breast Cancer:** Concern was expressed with the 30 years of age cut off. It avoids the young benign but could delay under 30's with a suspicious lump.	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
761	NHS England	72	Full	155	1.5.13 11	Consider a direct access ultrasound scan to assess for endometrial cancer in women aged 55 and over with visible haematuria and any of the following: • low haemoglobin levels or • thrombocytosis or • high blood glucose levels. [new 2015] (would be good to have this explained)	The evidence on which this recommendation was based, was on the blood glucose level being above the local laboratory's normal range.
762	NHS England	73	Full	165		**Urological cancers** London Cancer: In general agreement with the proposed guidelines. However the guidance starts with suspected cancer rather than the symptoms; leading to several different possibilities for a GP to follow if a patient presents with visible hematuria. This should be clarified.	A symptom based section has also been included in the guideline which shows the range of recommendations that are appropriate for people with particular symptoms.
763	NHS England	74	Full	181	Para 5	The GDG acknowledged that the positive predictive values associated with urinary tract infections presenting in primary care were inconsistent for bladder cancer and that there was no evidence on recurrent (greater than two) urinary	We have clarified that this is a non-urgent referral.

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						tract infections. However the GDG considered that this was a population in which cancer can be missed and therefore referral should be considered for people with this symptom. - be really useful if they can be specific – is this a 2WW referral or routine outpatients for cystoscopy	
764	NHS England	75	Full	220	15	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is concern that a delay may have an unfavourable impact, because of factors such as lesion site or size. [new 2015] - This guidance Is potentially confusing for gps as we have been traditionally taught not to use 2WW for BCCs – what do they mean by this – unfavourable impact of site of lesion???	The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs.
765	NHS England	76	Full	391		London Cancer supports the use of CA125 and USS simultaneously in cases of suspected ovarian cancer.	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.
713	NHS England	77	Full	228	1.8.5 17	Recommendation is appropriate however it assumes that all referrals have to go through GP which could introduce delay into the process, it would be ideal if GDP could make direct 2 week referrals to head and neck	This guideline is for all primary care clinicians. We do not consider that our recommendations would require a dentist to refer to a GMP before a suspected cancer referral could be made.
766	NHS England	78	Full	General	General	Limited cost-effectiveness evidence and economic modelling have been presented. It would be useful	The primary barrier that prevented further cost-effectiveness analysis being

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						to understand to what extent further economic evaluation and economic modelling can be undertaken if these were prioritised. What are the key barriers? The evidence is important to justify the additional resources. Some previous modelling has been undertaken on cost-effectiveness of earlier diagnosis which may be of use: ○ Economic modelling carried out by Frontier Economics on the behalf of the Department of Health (2011) The likely impact of earlier diagnosis of cancer on costs and benefits to the NHS. ○ A report prepared by Incisive Health for Cancer Research UK (2014) Savings lives, averting costs.	conducted was a lack of evidence on the effectiveness of changes in referral criteria. It is usually assumed, perhaps reasonably, that lowering the referral threshold will lead to an increase in the number of cancer cases detected and/or an increased number of cancer cases detected at an earlier stage. However, the challenge in a cost-effectiveness analysis would be *quantifying* these changes. At present, it was thought that it was not possible to reliably estimate these aspects and as such any economic analysis on this issue would be fundamentally flawed. Previous economic analyses, such as the ones that you have mentioned, have relied heavily upon assumptions to plug this evidence gap. It was for this reason that they were not included in the review of the economic evidence.
767	NHS England	79	Full	General	General	Assumptions • The assumptions used in the costing report are not always clear, for example, anticipated total increase for specific diagnostic tests and their unit costs. It would be useful if further details could be provided on these. Numbers of referrals	Thank you for your comment. The increase in the number of tests and unit costs will be made clear in the final costing tool.

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						• There are references to capacity issues e.g. urgent endoscopies (pg. 63); urgent CT scans (pg. 70) but no further analysis. Capacity is a concern for NHS England and further work is required to understand this. There is a concern that if there is a shortage of diagnostic capacity lowering the PPV threshold could increase waiting times for high-risk patients.	This issue will be highlighted in the costing report as a possible barrier to implementation
						• Baseline or business as usual (BAU) referrals are assumed to remain at 2012/13 levels. Historical data suggests there have been an upward trend in numbers of referrals. Further analysis is required to assess the impact on costs of the proposed NICE guidance if the upward trend in BAU continues.	This will be reviewed for the final costing report
						• Current referrals for suspected cancer are based on 2012/13 data of 1.2m. Data for 2013/14 are now available with referrals at 1.4m (1,361,345; pg. 8 of cancer waiting time annual report).	The latest available data for referrals will used for the final costing report
						• The referrals have been apportioned across the different tumour groups on the basis of the split of referrals for Q4, 2012/13. It is not clear why Q4 data was used instead of annual report though the impact is likely to be small.	The latest available data for referrals will used for the final costing report and if annual data is available it will be used
						• The potential increase in referrals and diagnostic tests are based on clinical judgement. To what extent have	The costs relate to the recommendations in this guideline only

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						interactions of cancers and other conditions been taken into consideration (e.g. if symptoms and diagnostic tests are the same then costs overlap (though for non-cancers the two week wait does not apply))? This is important to identify additionality. Costs • Costs have been included for an outpatient appointment and diagnostic tests only. The full range of costs needs to be identified as far as possible including treatment costs and costs on primary care to understand resource and any capacity issues. • There are references to cost savings, for example, decrease in the number of emergency admissions. Can volumes and costs be estimated?	The scope of this guideline is for referral for suspected cancer. The costs are intended to reflect the scope. Further work to identify savings as result of this guideline is being undertaken.
501	NHS Gloucestershire CCG	1	Full	20		We would not agree that that tests such as PSA should be used with a PPV below 3% - this gets dangerously close to screening which is nor supported by evidence and would generate huge cost pressures – as it has in the USA – with a very poor return	We disagree. This guideline covers people with symptoms and as such the use of tests such as PSA cannot be described as screening.
502	NHS Gloucestershire CCG	2	Full	31		We would strongly support the advocating of both 'Advice and Guidance' systems that allowed clinician to clinician discussion of 'grey cases' and helped deliver more efficient and effective assessments, investigations and particularly where (as is increasingly the case) patients are very frail and may not benefit from a very fast track and	The guideline did not investigate a review question on advice and guidance systems. Therefore the evidence on these has not been appraised and we are unable to make any recommendations on this issue.

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						target driven pathway.	
503	NHS Gloucestershire CCG	3	Full	31		we would strongly support systems that ensure non-urgent letters are assessed so that suitable patients can have an accelerated pathway or investigations if an expert feels this is more appropriate. A system that allows all such episodes to be captured and missed warning signs collated, shared and audited would be even better.	This is covered by recommendation 1.16.3.
504	NHS Gloucestershire CCG	4	Full	42		We would advocate that Performance Status is recorded in all referrals.	We consider that this is covered by recommendation 1.16.6
505	NHS Gloucestershire CCG	5	Full	42		We would advocate that details of Smoking Cessation advice and where appropriate referral is included in all referrals.	This guideline is about referral of suspected cancer from primary care. Prevention of cancer is outside the scope.
506	NHS Gloucestershire CCG	6	Full	130	1.3.2	the anaemia should be confirmed as iron deficient with a ferritin and a TT glutaminase completed and guidance should be given as to suspicious levels of ferritin when there are co morbidities that may cause potentially misleading acute phase protein elevations.	The identification of non-cancer conditions is outside the scope of this guideline.
507	NHS Gloucestershire CCG	7	Full	130		nothing about asking for family history – HNPCC etc.? – in younger patients.	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that family affected the predictive power of symptoms for colorectal cancer.

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508	NHS Gloucestershire CCG	8	Full	130	1.3.6	not sure about FoBT testing if patients have iron deficiency anaemia – would you not investigate if the FoBT was negative and there was no other obvious cause?	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine

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							referral.
509	NHS Gloucestershire CCG	9	Full	169	1.6.2	PSA testing in a patient with LUTS is considered by many as 'screening' and has no evidence to support its utility or benefit, though screening is meant to be for asymptomatic individuals	Thank you. The cause of the symptoms must be known in order for them to be offered treatment choices. This is not screening.
510	NHS Gloucestershire CCG	10	Full	169	1.6.3	Insisting on immediate TWW referral of all patients on a single test who are above the age specific range sounds over-prescriptive and will cause significant problems.	The evidence for the performance of PSA is detailed on p168-9. It is clear that an abnormal PSA equates to a sufficiently high risk of prostate cancer to warrant investigation.
511	NHS Gloucestershire CCG	11	Full	180	1.6.5	TWW referral for all patients with non-visible haematuria seems excessive. There is no evidence to support this. BMJ article 'investigating asymptomatic invisible haematuria' 17.11.14 BMJ2014:349:g6768 doi:1136/bmj.g6768 seems to have a much more measured approach.	Our recommendation is to refer for people over 60 who have non-visible haematuria as well as either dysuria or a raised white cell count. We have not recommended that everyone with non-visible haematuria should be referred.
512	NHS Gloucestershire CCG	12	Full	193		Our local Urologists would strongly advocate imaging before referral in patients with haematuria – many GPs have received strongly worded letters to that effect! The Urologist will always request imaging so seems perverse not to organise it before or at the time of referral?	This will be a matter for local implementation
513	NHS Gloucestershire CCG	13	Full	196	1.6.9	direct access USS for testicular lumps is already significantly over-used and highly inefficient – endorsing use of this seems odd.	The view of the GDG was that this was a cost-efficient direct access test to identify testicular cancer as outlined in the Linking Evidence to Recommendations section.
514	NHS Gloucestershire CCG	14	Full	220	1.7.4 & 5	not sure what Dermatologists would feel about TWW referral for BCCs. Surely another pathway or system could be devised without imposing more targets particularly relating to non-fatal malignancy?	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they

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							have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
515	NHS Gloucestershire CCG	15	Full	240	1.9.1	would it not be better to say CT or MRI. The pick up rate for malignancy is already very low and CT is much more readily available and has far less likelihood of finding 'incidentilomas' that plague the whole issue of open access MRI scanning.	The recommendation has been changed to clarify that CT can be used when MRI is contraindicated.
516	NHS Gloucestershire CCG	16	Full	257		there is no mention of other diagnostic tests for Myeloma especially Bence Jones Proteins	We have included urine Bence Jones protein in the recommendation.
517	NHS Gloucestershire CCG	17	Full	279		here is no mention of size of lump – should this be considered – if not threshold will be very low. There also needs to be some consideration of availability of ultrasonagraphers – adding a large number of new scans to an already highly pressurised system may risk diverting activity away from high risk patients and towards very low risk patients.	There was insufficient primary care evidence to add qualifying terms to lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
518	NHS Gloucestershire CCG	18	Full	General	General	The impact of releasing these new lower thresholds and all the subsequent expectations, demands and pressures into the current struggling 'Cancer System' could well produce many unintended consequences with poorer outcomes for high risk patients. There seems a high risk of breaking the system and causing plummeting morale and soaring stress amongst clinicians who are already under enormous pressure. Disruptive	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.

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						innovation is all very well but there may be a lot of damage done in the short to medium term.	
519	NHS Gloucestershire CCG	19	Full	General	General	There is quite a lot of evidence that it is the quality of referral not the quantity that is important and that existing high referrers (who are likely to become even higher referrers) with a low conversion rate are unlikely to identify more cancers, other than by chance – many of the diagnoses may have been achieved by pure chance/random screening rather than presenting symptomatology. Rather than implementing wholesale untested and often, as is frequently admitted in the text, quite limited evidence, it might be better to consider how well adherence to the present guidance is monitored and evaluated and then to gradually introduce refinements, cancer site by cancer site, and monitor and evaluate their effect?	Given that this guideline is designed for use by primary care, it is important that it is derived from primary care evidence. CG27 was not. Therefore we do not think that monitoring adherence to the recommendations in CG27 is sensible. We consider that this updated guideline should improve the quality of referrals because it is based on the most relevant evidence.
520	NHS Gloucestershire CCG	20	General	General		The timing of the consultation over Christmas has also been less than ideal.	The standard consultation period for a guideline is 6 weeks. Due to the proximity to Christmas, the consultation period for this guideline was extended to 7 weeks.
521	NHS Gloucestershire CCG	21	Costings Report	2		Urology referrals up to 10% would also be a concern for us locally and nationally with our already stretched services but we would need to plan around this impact.	Thank you for comments, the costing tools are intended to help plan for implementation.
14	NHS Herefordshire CCG	1	NICE	General	General	Whilst the draft guideline states that it is not intended to be a medical textbook it is certainly looking bulky enough to be one, We do not take issue with the individual guidelines, most of which are obvious, but taken as a whole it seems to assume that primary care clinicians have very little knowledge or judgement. The length of the document at 133 pages makes it very unwieldy and we believe it is unlikely to be a useful working document in primary care (at which it is chiefly	This guideline covers 37 different cancers. As a consequence it contains a lot of information. By producing a section of the guideline focused on symptoms, the GDG have sought to make this information easier to navigate by primary care clinicians. In addition, NICE are exploring ways that we can improve usability of the document.

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						directed). We recognise the huge amount of work that has gone into this but wonder if the issue of improving early diagnosis is likely to be addressed by any guideline that is necessarily so complicated. Education lies at the heart of improvement in management of such a huge clinical field and we do not believe such a complex guideline will alone achieve this. It is, however, likely to be a helpful reference document and to inform education programs. A much shorter document, perhaps a simple list of red flag clinical features, would be a useful working document for busy clinicians. To improve the practical uptake of this guideline it might be helpful to consider reintroduction of slide packs, to consider the younger generation of clinicians by developing an app and to consider integrating the guideline into support tools already used by GPs.	We do not accept that the guideline 'assumes little knowledge or judgement' on the part of primary care clinicians. The recommendations made recognise that clinicians in primary care will need to use their clinical judgement in the interpretation of the recommendations. This was stated explicitly in the introduction. The continued professional development of GPs is covered by recommendation 1.16.1 We interpret this comment to request additional prominence to high risk presentations. The presentations for which we have made recommendations are the highest risk presentations. In addition, NICE are exploring ways that we can improve usability of the document.
428	NHS South Devon and Torbay	1	Full	147	1.4.16	Recommendation to refer people using a suspected cancer pathway referral (for an appointment with 2 weeks) for breast cancer if they are aged 30 and over and have an unexplained breast lump with or without pain.	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain.

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	CCG					We are extremely concerned that people under 30 are being excluded from this pathway referral and that this will encourage general practice to defer from referring women with symptoms under the age of 30 for further investigation leading to late diagnosis of breast cancer. The GDG notes that breast cancer in people under 30 is extremely rare – this does not mean that it does not occur and that those who do have cancer and present with early signs and symptoms of breast cancer to their GP will not be referred for the further investigations they require. We would like to see guidance given that includes people under 30 years of age. The GDG also note that they are making the recommendation to make the age 30 as a cut off in regard to 'an unexplained lump in the axilla' as a symptom of breast cancer to 'make this recommendation easier to implement' CoppaFeel! exists to encourage women – particularly those under 30 to know their own breasts, the signs and symptoms of breast cancer and to present early to their GP. This new guidance appears to counter act all this advice and will make it more difficult for those people with breast cancer under the age of 30 to benefit from an earlier diagnosis.	In addition, explicit cross reference has been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
37	NHS Stockport CCG	1	NICE	80 16	1.2.9 Top row	We are concerned about the short time scale of 2 weeks before recommending referral for urgent upper endoscopy is required for various combinations of symptoms and in potentially quite	The recommendations for upper GI cancers have been revised to make them simpler and easier to understand. As a result this symptom combination no

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						young patients ie upper abdo pain and weight loss. This feels v short, as many acute, self-limiting illnesses (eg. Gastro-enteritis) would last as long as this. I would worry, it will open the flood gates for lots of un-necessary investigations. A 3/52 cut off would seem more realistic, in line with other guidelines – ie cough persisting for 3/52. We can foresee the numbers of urgent endoscopies increasing dramatically so this would necessitate a complete redesign of the system in Stockport to facilitate this.	longer appears in the recommendations. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
38	NHS Stockport CCG	2	NICE	228 26	1.8.4 Bottom row	If patients need to be referred to a community dental service for assessment of lip or oral cavity lesions – how will this be managed - ?access to urgent dental care is difficult, what happens for those patients not registered with a dental service?	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'
39	NHS Stockport CCG	3	NICE	332 51	Top row	We would also have concerns around referring children down a suspected cancer route due to parental concerns – would this not increase parental and child anxiety? No specific symptoms are mentioned, this could refer to a significant number of inappropriate referrals and put GP's in a difficult position of feeling unable to refuse.	This recommendation was debated at length by the GDG. It was noted that the positive predictive value of parental concern had not been studied, but, based on their clinical experience, the GDG agreed it would be sufficiently high to warrant recommendations.
40	NHS Stockport CCG	4	NICE	51	General	Where weight loss is specified as a potential reason for referral – we think the degree of weight loss and over what kind of time period should be specified.	There was insufficient primary care evidence to add qualifying terms to weight loss. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
41	NHS Stockport CCG	5	NICE	169 59	1.6.3 4th row	With regard to referral for possible prostate cancer – urgent referral for all patients with psa outside age specific range also seems unrealistic. Again	The evidence for the performance of PSA is detailed on p168-9. It is clear that an abnormal PSA equates to a sufficiently

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						this is likely to massively increase referrals, anxiety and possibly unnecessary investigations in a huge proportion of men – we think the setting the target so low with no other qualifiers potentially will do more harm than good. Unless the urologists are going to take action with those patients with a psa of between 4-10, then we're not sure of the benefit of referring all of these patients.	high risk of prostate cancer to warrant investigation.
467	North and East London Commissioning Support Unit & London Cancer	1	Full	29 General	General	We are pleased to see the introduction of recommendations on safety netting of patients with 'grey area' symptoms not quite reaching 2WW referral criteria We are strongly supportive of the increased emphasis on increased GP-initiated diagnostic testing ('Straight to test') but emphasise that development of these services is best done in conjunction with local secondary care providers, to ensure seamless and timely onwards pathways for patients where the tests confirm or increase suspicion of a cancer diagnosis and to ensure efficient use of and planning for local diagnostic capacity.	Thank you for your support. We agree. Development of pathways will be a matter for implementation of this guideline.
468	North and East London Commissioning Support Unit & London Cancer	2	Full	General	General	It would be of greater value if NICE make it a specific point to support GPs in recognising that cancer diagnosis in primary care isn't always straight forward, and some patients present in convoluted way and only in hindsight does it fit together, therefore inevitably some cancers do take 3-4 consultations before the penny drops – it is too often stated that GPs are failing the patient in these cases and it isn't always so.	We agree. The difficulties in cancer diagnostics are covered in the introduction to the full guideline.

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						Denmark has a similar system of primary care /secondary care to UK Gate keepers' role of GP is the same. Same cancer issues as UK - outcomes/late presentation. Work in Denmark has demonstrated that only 40%of cancers are diagnosed using the tumour specific route. Led to a 3 legged diagnostic strategy. NICE is asked to consider recommendations for those who do not fit nicely in to a tumour specific route but suspicion exists.	The GDG discussed at length the difficulty of patients with unclear presentations. This is partly addressed by the symptoms based and the non-specific symptoms sections in the guideline. The configuration of cancer diagnostics in secondary care is beyond the scope of this guideline.
469	North and East London Commissioning Support Unit & London Cancer	3	NICE	General	General	Whilst the removal of the duration component is a welcome change so that patients do not have to wait to have 6 weeks of symptoms before referral, the introduction of several age limits make the guidelines complex and not easy to follow. All of this is likely to confuse general practitioners making the guidelines impractical and unusable or at least not used as intended. We would recommend using a one cut off age of 40 years instead of the 40, 50 and 60 age limits with some of the recommendations. The LCA working with Transforming Cancer Services in London and other stakeholders have obtained agreement on the introduction of guidance for referral of symptomatic patients in the Capital from the age of 40. Early diagnosis of cancer is the only way to improve outcomes and survival. We would wish to see this emulated nationally.	The ages included in the recommendations reflect the evidence that was available on the positive predictive value of symptoms. It would therefore not be appropriate to apply the same age group to all recommendations.
470	North and East London Commissioning Support Unit & London	4	Full	41	8	*(lines 8-10)* Included in the feedback of the NHSE lung CRG: It was noted that the statement that there is no primary care evidence about the accuracy of CXR or CT in the diagnosis of lung cancer is one that ignores a plethora of evidence in other setting that is easily and appropriately extrapolated. CT is a highly sensitive test, as shown in numerous	The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop

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	Cancer					screening studies and CXR far less so. These data are available for high risk populations. A suggestion for a recommendation was: Where a CXR in primary care is reported as suspicious of lung cancer that a direct access CT scan of the chest and upper abdomen is arranged simultaneously with a 2WW referral being made. This might be extended to: **Ensure all patients that fulfill criteria for urgent referral for suspected lung cancer have a CT of the lower neck, thorax and upper abdomen with the administration of intravenous contrast prior to attendance at the first outpatient appointment**. In reality, this is what many centres have been doing for years.	recommendations for a guideline targeted at a primary care population. In the absence of primary care evidence the GDG agreed by consensus that chest X-ray was a useful test, though the possibility of false negatives was a concern. The scope of the guideline was to identify those patients needing referral for suspected cancer. It was not within the scope to make recommendations on what tests may assist secondary care with their evaluation.
471	North and East London Commissioning Support Unit & London Cancer	5	Full	42		On the lung cancer section, there is mention of Cough and thrombocytosis – positive predictive value > 3% - unclear whether this guideline warrants a direct 2WW referral or not e.g. – are gps being advised that if a patient presents with a cough and their platelets are high – but the CXR is normal – would that qualify for a 2WW referral? (being clear will really help GPs)	The current recommendation is to perform an urgent chest X-ray on all patients with thrombocytosis. If the chest X-ray shows finding suggestive of lung cancer the guideline recommends a suspected cancer pathway referral. People with a normal CXR but persistent symptoms would be covered by the recommendations made on safety netting.
472	North and East London Commissioning Support	6	Full	46		On mesothelioma – it would be very useful if NICE can give clearer guidelines on what to do when pleural plaques are commented on in a chest x-ray report. Do they go for a CT chest next, chest clinic referral (routine /2WW) it's a grey area.	We have added a recommendation on what should happen if chest X-ray findings are suggestive of mesothelioma. Lesser abnormalities (including pleural plaques) will be a matter for clinical judgement.

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	Unit & London Cancer						
473	North and East London Commissioning Support Unit & London Cancer	7	Full	67	1.2.4	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for pancreatic cancer if they are aged 40 and over and have jaundice. [new 2015] (P67) - do they really mean this ?? there are differing types of jaundice – e.g. conjugated / unconjugated bilirubinaemia e.g. after acute hepatitis – do they really want 2WW to be triggered as over 40 years old gets viral hepatitis too	The PPV for jaundice in pancreatic cancer is one of the highest for any symptom in any cancer. If a GP has a clearly correct alternative diagnosis we would expect them to exercise their clinical judgement.
474	North and East London Commissioning Support Unit & London Cancer	8	Full	60	14	**OG cancers** open access investigations seems to be is a way of extending the 2WW process into primary care – e.g. the guidelines on upper GI/oesophageal cancers seems to suggest that patients presenting with dysphagia - GPs should use open access endoscopy –it specifically doesn't mention a cancer referral pathway as it does for other cancer elsewhere which makes me think they feel that endoscopy requests must go up in order to detect more upper GI cancers and to help off load 2WW clinics gps should first use open access (which in principal is fine except that most gps would ask for open access endoscopy in cases where they feel cancer is low risk not No risk, and the guideline is suggesting open access for the cohort that traditionally is being referred directly into 2WW upper GI clinics. There is little consideration that this will increase work load in primary care (except for one statement on page 30 saying it will lead to greater number of consultations (particularly gps).	The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG considered the issue of increased GP time in their deliberations on the resource requirements of the recommendations. This is documented in the Linking Evidence to Recommendations section that accompanies the recommendations in

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							section 4.1 of the full guideline.
475	North and East London Commissioning Support Unit & London Cancer	9	Full	240	1.9.1-2	**Brain and CNS cancers** Loss of central neurological function' is too vague a term. Clarify what constitutes 'abnormal cerebellar signs' Seizures (mentioned in 2005 version and NICE guidance CG37 on Epilepsy, January 2012) are not mentioned. Furthermore, headache and progressive sub-acute cognitive decline (both mentioned in 2005) have been dropped.	The GDG did not wish to try and describe loss of central neurological function or cerebellar signs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation. The PPV for seizures and headache were below the 3% threshold. Sub-acute cognitive decline is subsumed into the term 'progressive sub-acute loss of neurological function'.
476	North and East London Commissioning Support Unit & London Cancer	10	257	80	1.10.4	**Haematological cancers** The guidance around back pain is insufficiently detailed. Although 'persistent' pain is cited as a trigger for further investigation, the definition of persistence is not given. Other factors that might necessitate earlier investigation (e.g. thoracic site, presence of other warning symptoms) are not addressed comprehensively. Back pain is one of the most common complaints GPs deal with and it was our view that more information was required in this area. Myeloma accounts for about 10-15% of cases of malignant spinal cord compression and this is often a presenting feature. The presenting symptoms of impending cord compression were not included.	There was insufficient primary care evidence to add qualifying terms to persistent pain. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. None of the available evidence reported a PPV for this symptom that would warrant action. It should be noted that malignancy is not the commonest cause of cord compression.

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477	North and East London Commissioning Support Unit & London Cancer	11	NICE	130 70	1.3.2	Men at any age and post-menopausal women should be referred with iron deficiency anaemia. Cut offs for anaemia to be determined by testing laboratory There is a need to clarify if the Hb level for referral for women is irrespective of menstruation.	Menstruation was not examined in any of the anaemia studies used by the GDG. Therefore we could not make specific recommendations on this. However we would expect primary care clinicians to use their clinical judgement when using these recommendations. The haemoglobin levels have been removed from the recommendation because reference ranges vary from lab to lab and there was potential for confusion.
478	North and East London Commissioning Support Unit & London Cancer	12	NICE	130 70	1.3.4	Patients presenting with an abdominal or rectal mass must be referred for investigation. Object to the change from "should refer" to "consider a referral" as new version does not give clear guidance. This guideline would be improved if it started with the word refer.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
479	North and East London Commissioning Support Unit & London Cancer	13	NICE	130 70	1.3.6	Guaiac FOBT has false negative rates of 25-100% in the evidence in the full guidance. There is insufficient evidence to support the use of faecal immunological testing for symptomatic patients. Objection to recommending FOBT to patients presenting with new onset colorectal symptoms (change in bowel habit, abdominal pain, weight loss) with preference for an investigation that will give a definitive diagnosis e.g. colonoscopy. Objection to recommending FOBT to patients with iron deficiency anaemia urging proper and appropriate investigation to determine the aetiology.	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to

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						Concern that recommending introduction of FOBT complicates the colorectal diagnostic pathway and may negatively impact the implementation of Straight To Test diagnostic pathways.	recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
480	North and East London Commissioning Support Unit & London Cancer	14	Full	123	4	The 'full model structure' shown in the figure includes FOBT and Barium enema as guideline approved investigations for change in bowel habit. This very complex diagnostic pathway will result in unacceptable variation in patient care and time to definitive diagnosis: 'A false negative detected at 1 year' will be referred for a colonoscopy other patients would have had within weeks of referral. FOBT does not provide a definitive diagnosis. Barium enema has been widely removed from clinical guidelines and replaced by CT Colonography. Commissioners in London have stated that Barium Enema should not be used as a first line test for CRC within current commissioning intentions.	The full model structure is not intended to show the guideline approved investigations. It merely illustrates the structure of the economic model that was used to conduct the cost-effectiveness analysis. The recommendations made by the GDG show the 'guideline approved investigations' and it can be seen that barium enema was not recommended. Testing for occult blood in faeces was recommended but it should be noted that it was not used by itself to provide a definitive diagnosis. In the economic

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							analysis, patients with a positive FOBT result then go on to receive a colonoscopy where the patient would be diagnosed or identified as a false positive
481	North and East London Commissioning Support Unit & London Cancer	15	NICE	130 71	1.3.8	Strongly recommend consideration of referral of symptomatic patients under the age of 50 if they have a strong risk of colorectal cancer (IBD with extensive colitis for over 10 years, previous cancer or multiple polyps, known inherited syndrome or family history)	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG 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 IBD, previous cancer, multiple polyps, known inherited syndromes or family history affected the predictive power of symptoms for colorectal cancer.
482	North and East London Commissioning Support Unit & London Cancer	16	Full	85		Gall bladder cancer guidelines make no mention of surveillance of gallbladder polyps. It would be useful for NICE to comment on this. Gall bladder polyps may be premalignant. It is curious NICE guidance on gall bladder cancer fails to mention gall bladder polyps - perhaps there is no firm consensus. There is a useful article on this subject via this link http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3359430/r	Surveillance of non-cancerous lesions is outside the scope of this guideline
483	North and East London Commissioning Support Unit &	17	Full	147	1.4.1	**Breast Cancer:** Concern was expressed with the 30 years of age cut off. It avoids the young benign but could delay under 30's with a suspicious lump.	A new recommendation has been added to consider a non-urgent referral for breast opinion in people aged under 30 and with an unexplained breast lump with or without pain. In addition, explicit cross reference has

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	London Cancer						been made to recommendations in the diagnostic process section of the guideline, which detail discussions that should be had with specialists when a suspected cancer pathway referral has not been made.
484	North and East London Commissioning Support Unit & London Cancer	18	Full	155	1.5.13 11	Consider a direct access ultrasound scan to assess for endometrial cancer in women aged 55 and over with visible haematuria and any of the following: • low haemoglobin levels or • thrombocytosis or • high blood glucose levels. [new 2015] (would be good to have this explained)	The evidence on which this recommendation was based, was on the blood glucose level being above the local laboratory's normal range.
485	North and East London Commissioning Support Unit & London Cancer	19	Full	165		**Urological cancers** London Cancer: In general agreement with the proposed guidelines. However the guidance starts with suspected cancer rather than the symptoms; leading to several different possibilities for a GP to follow if a patient presents with visible hematuria. This should be clarified.	A symptom based section has also been included in the guideline which shows the range of recommendations that are appropriate for people with particular symptoms.
486	North and East London Commissioning Support Unit & London Cancer	20	Full	181	Para 5	The GDG acknowledged that the positive predictive values associated with urinary tract infections presenting in primary care were inconsistent for bladder cancer and that there was no evidence on recurrent (greater than two) urinary tract infections. However the GDG considered that this was a population in which cancer can be missed and therefore referral should be considered for people with this symptom. - be really useful if they can be specific – is this a 2WW referral or routine outpatients for cystoscopy	We have clarified that this is a non-urgent referral.
487	North	21	Full	220	15	Consider a suspected cancer pathway referral (for	The GDG did not include a list of potential

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	and East London Commissioning Support Unit & London Cancer					an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is concern that a delay may have an unfavourable impact, because of factors such as lesion site or size. [new 2015] - This guidance Is potentially confusing for gps as we have been traditionally taught not to use 2WW for BCCs – what do they mean by this – unfavourable impact of site of lesion???	sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs.
488	North and East London Commissioning Support Unit & London Cancer	22	Full	391		London Cancer supports the use of CA125 and USS simultaneously in cases of suspected ovarian cancer.	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.
825	Northern, Eastern and Western Devon CCG	1	Full	General		We welcome the guideline as an approach to improve cancer diagnosis in a timely fashion. We also welcome the publication of the positive predictive values which will support decision making at a local as well as national level.	Thank you
826	Northern, Eastern and Western Devon CCG	2	Full	General		In the context of an NHS with limited resources we have a number of concerns which we feel should be addressed before publication. In general, it takes the stance that all cancer diagnosis is more or less equivalent, does not address potential harms and does not adequately capture potential	When making recommendations, the GDG explicitly considered the cost consequences of these recommendations and the likely impact on service delivery. This has been documented in the Linking Evidence to Recommendations sections

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						costs and impact on existing services (including, and particularly, primary care).	in the full guideline.
827	Northern, Eastern and Western Devon CCG	3	Full	General		There are a large number of recommendations, some of which overlap, and it would be more helpful to present single recommendations or pathways for specific symptoms such as abdominal pain and haematuria, which feature in several cancers and are currently inconsistent. Patients present with symptoms, not as 'suspected gastric cancer' for example. As each cancer has been considered separately, several symptom combinations lead to different recommendations, depending on which cancer site is being considered. For example: the recommendation for abdominal pain and weight loss in those aged over 40 for colorectal cancer is for a 2ww referral. Similar symptoms in the Upper GI chapter lead to a recommendation to consider upper GI endoscopy in those aged over 55 (gastric cancer), offer upper GI endoscopy in those aged over 55 (oesophageal cancer) and to consider a CT scan for those aged over 60 and over (pancreatic cancer). It would be of practical use to general practitioners to indicate which investigation should be undertaken first in the absence of any other pointers; rationally this would favour lower GI investigations as colorectal cancer is more common than the other cancers and the benefit from early diagnosis is probably greater.	This guideline covers 37 different cancers. As a consequence it contains a lot of information. By producing a section of the guideline focused on symptoms, the GDG have sought to make this information more easy to navigate by primary care clinicians. . In addition, NICE are exploring ways that we can improve usability of the document. The GDG considered in detail, where there were multiple recommendations for similar symptom groups in different cancers. They discussed whether these could be combined into single recommendations on a case-by-case basis. Several factors were considered in this discussion: the specific findings in the evidence, transparency of process and the ease of use of the guideline. The GDG considered that the current presentation represented an optimal balance of all three factors.
828	Northern, Eastern and Western Devon CCG	4	Full	General		We support having a more clearly defined threshold for intervention but we are not sure that 3% is the right level. We note that cancer is common, and increasingly common in older people. Oudega et al, 2006, for instance showed that 2% of the normal (control) population developed cancer in a follow up period of 2 years.	The GDG considered this matter in depth and the rationale for the choice of 3% is detailed in the introduction to the full guideline.

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829	Northern, Eastern and Western Devon CCG	5	Full	General		There will be an increase in resources required to implement the changes and there is an uncertain impact on benefit, which is likely to vary between cancer sites.	Any increased rate of referral to secondary care and consequent resource issues will be addressed by the tariff from NHS England. Therefore there should be no adverse impact on the timeliness with which cancer diagnoses are made. When making recommendations, the GDG explicitly considered the cost consequences of these recommendations and the likely impact on service delivery. They also considered the balance between lowering the threshold for referral whilst providing more targeted referrals. This has been documented in the Linking Evidence to Recommendations sections in the full guideline.
830	Northern, Eastern and Western Devon CCG	6	Full	General		The stated threshold is 3% but we note the actual threshold used is variable, and in many cancers is lower than this, without evidence based justification of significant benefit.	The 3% threshold for referral for suspected cancer was universally applied when making recommendations for adults. A lower threshold was accepted for children and for recommendations for routine or simple tests. This has been documented in the introduction to the full guideline.
831	Northern, Eastern and Western Devon CCG	7	Full	General		The impact on primary care workload is not considered in any detail and many of the recommendations for primary care investigations are much lower than a PPV of 3%. The lowest is 0.8 which equates to 125 invasive investigations (upper GI endoscopy) to detect 1 cancer. This will have considerable implications for service delivery and resources.	The impact on primary care workload was specifically documented in the Linking Evidence to Recommendations in section 4.1. The threshold for urgent upper GI endoscopy for suspected cancer was 3%. We are not clear where the 0.8 figure you are quoting comes from.
832	Northern,	8	Full	General		The GDG acknowledges lack of service and	The GDG aspired to broaden

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	Eastern and Western Devon CCG					economic information but the conclusions drawn are "(we are) confident that the benefits outweighed the disadvantages" and "the GDG agreed this change (to a PPV of 3%) would not overwhelm clinical services". We are uncertain that either of these statements are justified.	recommendations to try and improve the timeliness and quality of cancer diagnosis. Patient viewpoints were central to the decision about where the risk threshold should be. The lower the threshold could reasonably be set, the more patients with cancer would have expedited diagnoses, with accompanying improvements in mortality and morbidity. The recommendations in previous NICE guidance equated to very different percentage risks of cancer. For instance in colorectal cancer, the estimated risk from diarrhoea in an adult is below 1%, and the risk from iron-deficiency anaemia in males in that guidance exceeded 10%. Across the whole guideline, few recommendations corresponded with a PPV below 5%. The GDG felt that, in order to improve diagnosis of cancer, a PPV threshold lower than 5% was preferable. Also germane to the selection of a risk threshold are the resource implications of change. At the time of setting the threshold figure, there were no strong quality health-economic reports which could help with the decision. Many reports described the costs involved in expanding cancer diagnostics. The benefits from expedited diagnosis were much less clear. It was, however, clear that broadening of recommendations would bring economic and clinical costs. The clinical costs include potential harms

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							to the patient through the side effects of investigations performed and also through increased anxiety. The lower a threshold is set, the more likely people are to be exposed to these potential harms. Taking all of this into account, the GDG agreed to use a threshold value of 3% PPV to underpin their recommendations. This value represented a considerable liberalisation of the estimated PPVs of previous recommendations, but the GDG agreed that this change would not overwhelm clinical services, nor greatly increase the possible harms to patients from over-investigation.
833	Northern, Eastern and Western Devon CCG	9	Full	General		We feel that insufficient note is made of potential complications and harms of additional investigations noting that most evidence suggests that patients and professionals overestimate benefits of interventions and underestimate harms. The guidance does not comment on the opportunity costs of resources diverted from other areas or the increased anxiety in those referred for additional investigation at a low probability of having cancer.	The balance between benefits and harms were considered for every recommendation made and are documented in the Linking Evidence to Recommendations sections in the full guideline. When making recommendations, the GDG explicitly considered the cost consequences of these recommendations and the likely impact on service delivery. Opportunity cost was part of this consideration. This has been documented in the Linking Evidence to Recommendations sections in the full guideline. Patients anxiety has been documented both in the introduction and the LETR

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							sections that accompany several of the recommendations.
834	Northern, Eastern and Western Devon CCG	10	Full	General		Potential survival benefits are stated as justifying potential increases in diagnostic investigations and costs, but for many of the cancers considered there is little evidence that there will be a survival benefit. We would find it more helpful to identify which cancer sites have the strongest evidence in this respect, to enable us to develop our implementation plan accordingly.	The GDG examined the evidence on the PPV of different symptoms for predicting cancer and different tests in primary care for identifying cancer. They did not examine evidence on survival benefit and therefore could not make the recommendations you have requested. Having said that, the GDG did not consider it equitable or appropriate to prioritise the implementation of recommendations according to potential survival benefit. The wording in the recommendations reflects the strength of the evidence. For more information on the wording of NICE recommendations please see pg 6 of the short version
835	Northern, Eastern and Western Devon CCG	11	Full	41 Chapter 7	Lung and pleural cancers	We consider that urgent CXR prior to urgent cancer referral would be a more cost effective option in people with a single episode of haemoptysis under the age of 55, as the PPVs are below 2%, and it would avoid large numbers of referrals to secondary care with the costs and harms as mentioned above. There is likely to be an increase in primary care workload, given the high frequency of many symptoms, such as unexplained chest pain, in primary care, and the low PPV (estimated from the data given to be about 1% for non-smokers and less than 2% in smokers) we feel that more emphasis should be given to investigation of persistent or recurrent symptoms, rather than simply unexplained symptoms.	The GDG agreed that haemoptysis is a serious symptom that would need a suspected cancer pathway referral, even with a negative chest X-ray. Given this, the GDG agreed not to make a recommendation for chest X-ray in the first instance as this could cause a delay in people being referred.

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836	Northern, Eastern and Western Devon CCG	12	Full	50 Chapter 8	Upper gastro-intestinal cancers	The recommendations in this section are complex and confusing, and are likely to lead to a considerable increase in urgent referrals with potential unintended consequences for other patients and conditions. We note that there is considerable variation in the PPVs of the combination of symptoms chosen for recommendations for urgent direct access endoscopy – from 0.8 to 5.2 for stomach cancer and 1.9 to 4.2 for oesophageal cancer. Given that these cancers are relatively unamenable to curative treatment once symptomatic, and the intervention is invasive, we consider that simplification may be possible e.g. dysphagia, or weight loss plus abdominal pain plus another relevant symptom for a 2ww referral. No evidence was presented to support the guidance that urgent direct access endoscopy would be more cost-effective than the current 2ww system, and we feel this is an important area for further work before definitive guidance is issued.	The recommendations for upper GI cancers have been revised to make them simpler and easier to understand. The Methods section details the principles by which the GDG made recommendations for suspected cancer pathway referral and for testing. Additional text has been added to the Linking Evidence to Recommendation section to explain why certain symptom combinations have not been included in the recommendations. The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG also considered that cancer

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						The recommendations for CT for pancreatic cancer do not meet the 3% threshold and we are not clear why these have been made. Local experience of offering open access secondary care investigations in primary care has shown a twofold increase in numbers without a corresponding decrease in secondary care referrals. We are not sure that this will be cost effective given the small impact of treatment on pancreatic cancer.	tests directly available to GPs should be performed within the same time frame as tests which currently require referral. Exceptions to the 3% rule were where appropriate investigation using tests previously available to primary care could replace specialist referral. The GDG considered this was the case here. This has been documented in the methodology section of the guideline.
837	Northern, Eastern and Western Devon CCG	13	Full	147 Chapter 10	1.4.2 Breast cancer	The recommendations for a 2ww referral for those with unilateral nipple discharge or retraction in women over 50 do not meet the 3% threshold specified in the introduction. This is based on a supposition of benefit which is not supported by evidence.	We acknowledge your point. However the GDGs deliberations on this issue have been documented in the Linking Evidence to Recommendations section in the full guideline. The Walker paper did not distinguish between unilateral and bilateral changes. The GDG considered that a unilateral change would carry a higher PPV.
838	Northern, Eastern and Western Devon CCG	14	Full	169 Chapter 12	1.6.3 Urological cancer	Prostate cancer. The recommendation to refer all men for a 2ww with a PSA greater than the age specific range is based on small studies, one of which is unclear about the patient population, and hence the validity cannot be judged. The cost effectiveness of this recommendation is clearly dependent on the prevalence of prostate cancer in the population being tested, and we consider that economic evaluation should be performed here. Bladder cancer. The recommendation for 2ww referral in those with recurrent urinary tract	The evidence for the performance of PSA is detailed on p168-9. It is clear that an abnormal PSA equates to a sufficiently high risk of prostate cancer to warrant investigation. Our literature search did not identify any cost-effectiveness analyses in this area. In addition, a de novo economic analysis was not conducted as the topic was not prioritised by the GDG. The group considered that an analysis comparing

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						infection is not supported by evidence.	tests was not necessary as a PSA test is the only primary care investigation available. The GDG have acknowledged, in the Linking Evidence to Recommendation section, that the PPVs associated with urinary tract infections were not consistent. However the GDG agreed that this was a population in which cancer can be missed that, in their clinical judgement, the true PPV would exceed 3%. The GDG therefore considered it important to recommend that referral should be considered.
839	Northern, Eastern and Western Devon CCG	15	Full	203 Chapter 13	Skin cancer	Several references pertaining to diagnosis of skin cancer relating to a referral setting (Rosenthal 2010, 2011,2012) and hence are not directly applicable to usual general practice in this country. These PPVs are higher than would be found in UK primary care, given the high prevalence of cases in their study	These limitations are noted in the 'Risk of bias in the included studies' and 'Linking-Evidence-to-Recommendations' sections throughout the chapter, and (as outlined in the latter) have influenced the way the GDG used the evidence to develop the recommendations.
840	Northern, Eastern and Western Devon CCG	16	Full	228 Chapter 14	1.8.5 Head and neck cancer	Oral cancer. The recommendation to refer urgently with an ulcer that has lasted more than 14 days is not supported by evidence. Large aphthous ulcers may take more than 14 days to resolve and it may be helpful to mention exclusion of alternative diagnoses associated with prolonged ulceration such as inflammatory bowel disease.	We have changed the duration of oral ulceration to be 3 weeks, in line with recommendations made in the NICE guidance on 'Improving outcomes in head and neck cancers.' Non-malignant conditions are outside the scope of this guideline.
841	Northern, Eastern and Western Devon CCG	17	Full	332 Chapter 18	Children's cancer	There is no evidence base to support the recommendation that parental or carer anxiety is significantly associated with childhood cancer. Whilst we acknowledge that parents and carers are important sources of information, we have concerns that this recommendation will encourage unhelpful illness behaviour in some families and	This recommendation was debated at length by the GDG. It was noted that the positive predictive value of parental concern had not been studied, but, based on their clinical experience, the GDG agreed it would be sufficiently high to warrant recommendations.

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						that the harm from these adverse effects has not been taken into account. We would prefer this recommendation to be rephrased, omitting the second sentence.	
842	Northern, Eastern and Western Devon CCG	18	Full	366 Chapter 20	1.13.4 Non-specific symptoms and signs	We consider that the recommendation about urgent referral with DVT is not consistent with the evidence (Oudega, 2006) which shows that people in primary care with 'secondary DVT' had a cancer detection rate very little different to the control population. We think it would be more consistent to rephrase this recommendation to state 'unprovoked DVT '	The Oudega paper was the only paper that was included in the symptoms of concern summary evidence for DVT (cumulative PPV = 3.49%). In the paper the included patients were divided into idiopathic DVT (N = 162; PPV = 7.4%; 12/162) and secondary DVT (N = 268; PPV = 2.6%; 7/268). The GDG chose to retain 'all DVTs' irrespective of being idiopathic or secondary on the grounds of simplicity, as the secondary DVT figure was so close to 3%.
843	Northern, Eastern and Western Devon CCG	19	Costing template			We consider that referrals for lung and oral cancers are likely to increase greater than estimated, given the frequency of haemoptysis in primary care. I was unable to access the further information that was described as being in Appendix 1 so am unsure how the costs of direct access endoscopy have been calculated. Our local experience of allowing direct access investigations in primary care showed an 8 fold increase in the numbers of investigations with no corresponding decrease in secondary care referrals. It is not clear that, in general, earlier diagnosis of cancer is associated with lower costs. Costs may increase with increased treatment with surgery, radiotherapy or chemotherapy so it is important to be clear what the expectation of benefits are by cancer site.	Thank you for comments, the costing tools are intended to help plan for implementation. Further work to identify savings as result of this guideline is being undertaken.
42	Oesopha	1	Full	60		*(p50-63)* Oesophageal cancer is the sixth most	Thank you for this information.

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	geal Patients' Association					common cause of cancer death in the UK (2011). 70% of the cases relate to adenocarcinoma, the fastest growing tumour in the Western world. The UK has the highest incidence of oesophageal adenocarcinoma in the world. Unusually, oesophageal adenocarcinoma has a precursor condition, Barrett's Oesophagus. Dysplasia within Barrett's Oesophagus can be treated by radio frequency ablation, making opportunities for *preventing* cancer. 71% of oesophageal cancer diagnoses presenting from digestion symptoms (eg reflux/GORD) are treated with curative intent; contrasted with only 49% presenting with dysphagia, a classic symptom indicating later stages when the tumour may have grown two-thirds around the circumference of the oesophagus, penetrated the full thickness of the wall and spread to local lymph nodes.. Early diagnosis of oesophageal cancer makes a difference to outcomes (75-87% 1 –year survival at early stage; 20-21% at late stage). The Government are launching a *Be Clear on Cancer* campaign for OG cancer on 26 January 2015 based on persistent heartburn, a risk factor for Barrett's Oesophagus. Planning meetings involving surgeons and others involved in the campaign have been dismayed at the prospect of guidance conflicting with CG184 on Dyspepsia & Gastro Oesophageal Reflux Disease (GORD). The recently revised NICE guidelines CG184 on Dyspepsia and GORD deal with Barrett's Oesophagus and referral for endoscopy, have removed the age criterion and stated the	Thank you for this information. Thank you for this information. CG184 states that this guideline should be referred to when a person presents with symptoms that could be caused by cancer. Comparison of the

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						significance of unresolved Gastro Oesophageal Reflux Disease (GORD) so the two sets of NICE Guidelines need to be consistent to maintain credibility and reduce confusion. Therefore there should be more overt references to the significance of diagnosing, monitoring and treating Barrett's Oesophagus as a precursor condition in these guidelines. **Therefore the age and gender criterion for referral for endoscopy for unresolved persistent heartburn should be removed and a cross-reference inserted to Guidelines on CG184 Dyspepsia & GORD because of the relevance for cancer early diagnosis represented by Barrett's Oesophagus. This will ensure that two sets of NICE guidelines are not in conflict with each other.**	recommendations in the two documents, does not demonstrate any incompatibility. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
43	Oesophageal Patients' Association	2	Full	54	Table 10	Amongst others, the well-regarded Lagergren study pointed out the link between symptomatic gastro-oesophageal reflux and oesophageal adenocarcinoma. N Engl J Med. 1999 Mar 18;340(11):825-31. http://www.ncbi.nlm.nih.gov/pubmed/10080844 See also: *Guidelines on the Diagnosis and Management of Barrett's Oesophagus* Fitzgerald RC, di Pietro M, Ragunath K et al**.** http://www.bsg.org.uk/clinical-guidelines/oesophageal/guidelines-on-the-diagnosis-and-management-of-barrett-s-oesophagus.html Lagergren J, Lagergren P. *Oesophageal Cancer – Clinical Review*. BMJ. 2010; 341.	Thank you for providing these references. The suggested papers were not included as they did not meet our pre-specified inclusion criteria, that is, they were not conducted in an unselected population presenting to primary care with symptoms. Moreover, as we are developing an evidence-based guideline, we do not routinely use other guidelines unless they present original data that meets the inclusion criteria for consideration in this guideline.

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						O'Doherty MG, Freedman ND, Hollenbeck AR, Schatzkin A, Abnet CC. *A prospective cohort study of obesity and risk of oesophageal and gastric adenocarcinoma in the NIH–AARP Diet and Health Study*. *Gut* 2011;10:1136 A paper by Bhat SK and others concludes that prior identification of Barrett's Oesophagus is associated with an improvement in survival of patients with oesophageal adenocarcinoma . http://gut.bmj.com/content/early/2014/04/03/gutjnl-2013-305506.abstract	
44	Oesophageal Patients' Association	3	Full	60	14 Section 8.1	Oesophageal adenocarcinoma can affect people younger than 55 years. 18% of patients diagnosed with Barrett's Oesophagus were 50 years or younger in *Are newly diagnosed columnar-lined oesophagus patients getting younger?* Christine Wall et al *European Journal of Gastroenterology & Hepatology: October 2009 - Volume 21 - Issue 10 - pp 1127-1131* We therefore need to be able to refer patients with unresolved persistent heartburn for endoscopy regardless of age (but this may not be an immediate and urgent investigation for a tumour)	Thank you for providing these references. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
45	Oesophageal Patients' Association	4	NICE	2	Contents Page	The categories need to be extended to include a category for 'Heartburn and non-heartburn dyspepsia'	The recommendations made are only for dyspepsia with weight loss and make no reference to heartburn. Therefore we do not think this change would be helpful.
46	Oesophageal	5	NICE	61 67	1.2.1	The comments at point number 3 apply	Thank you for providing these references. Surveillance in Barrett's Oesophagus is

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	Patients' Association						outside the scope of this guideline
47	Oesophageal Patients' Association	6	NICE	61 68	1.2.3	The comments at point number 3 apply	Thank you for providing these references. Surveillance in Barrett's Oesophagus is outside the scope of this guideline
569	Pancreatic Cancer Action and Pancreatic Cancer UK	1	Full	General	General	We welcome the fact that this Draft Guideline includes separate guidance for pancreatic cancer.	Thank you
570	Pancreatic Cancer Action and Pancreatic Cancer UK	2	Full	General 10	General 8-12	We recognise that the guideline is not meant to be an exhaustive 'textbook' of symptoms for GPs to follow slavishly, and excludes making recommendations on 'topics where there is already agreed clinical practice.' (P10, Lines 8-12). However, where pancreatic cancer is concerned – with extremely low survival rates, based in no small part on low levels of early GP referral (*NCIN (2012) Routes to Diagnosis 2006-2008, England Information Supplement*) and diagnosis – we believe that the newly separated out pancreatic cancer section should be as extensive as possible, as it is clear GPs need as much assistance as possible in spotting signs and symptoms in patients. A 2012 report (Early Diagnosis Summit Report 2012, Pancreatic Cancer UK, http://www.pancreaticcancer.org.uk/media/86663/early-diagnosis-summit-report-final.pdf) showed that 'half of GPs surveyed…were not confident that they could identify the signs and symptoms of possible pancreatic cancer in a patient.'	Thank you for providing these references. The GDG considered it was equitable to choose a single threshold PPV for urgent assessment of possible adult cancers, but also considered the alternative – a variable threshold. If the GDG were to vary the PPV threshold for a suspected cancer referral across different cancers, an argument could be made that the PPV threshold should be lowered for those cancers for which we know effective treatments exist and for which we know that early diagnosis improves prognosis. For many of the cancers with poorer prognosis, though not for cancers in general, 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

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						This would imply that it would be prudent to use a lower PPV for pancreatic cancer than for some other cancers, or even using different forms of evidence – beyond PPV – to ensure a full range of pancreatic cancer signs and symptoms are included to aid GPs as much as possible. This is expanded on below.	in individual cases. For most cancers, the exact symptom timelines (when a patient with cancer actually starts to experience symptoms) and the cancer growth timelines (when a cancer grows to the extent it becomes incurable) are not well described in the research literature. However, the fact that these are two different timelines brings the possibility that these do not always overlap. It is possible that in some cancer sites with poor prognoses, the poor prognosis simply reflects that by the time patients experience symptoms from their cancer, the cancer has grown so much that it is incurable. Of course, there are still benefits from diagnosis in that tumour growth may be slowed, and symptom relief offered. But, in these groups, the GDG considered that the inherent poor prognosis cannot be avoided by improvements in symptomatic diagnosis. The GDG considered that lowering the PPV threshold for suspected cancer referral - however far - will not improve the cure rate. The GDG considered that this argument held for some poor prognosis cancers, however unfortunate this was. On this basis, to allocate resources preferentially to instances where there is less evidence of potential benefit, simply on the basis of current poor outcomes, would seem to be inequitable and

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							potentially less cost effective. Furthermore, it should be noted that referral and investigation are not without risk of harms. It is difficult to justify increasing the number of people potentially harmed, when it is not considered likely that there would be a concomitant increase in the persons who might benefit.
571	Pancreatic Cancer Action and Pancreatic Cancer UK	3	Full	26	21 onwards	*(p26-7)* We support the new additions to the section on Patient Information and Support, particularly providing 'information that is appropriate for the person in terms of language, ability and culture, recognizing the potential for different cultural meanings associated with the possibility of cancer.'	Thank you
572	Pancreatic Cancer Action and Pancreatic Cancer UK	4	General	General 19 24	General 32-36 22-27	We recognise that a standard risk system across all cancer types might be preferable, and that the GDG has chosen PPV. Indeed, the reason for adopting the risk threshold metric of PPV is given as 'to ensure internal consistency and equity within the guideline.' (P19, lines 32-36). However, we believe that there is not an equity diagnosis, treatment, research or care – and thus of survival - between all cancer types at the present time. As such, there is a need to depart from a uniform approach in developing the guidelines for cancers which have wildly varying survival rates, and which have also seen extremely low levels of research into symptoms over recent years. Therefore, we query an adherence to PPV measures only. As section 3.3 (P24, lines 22-27) discusses, pancreatic (and other forms of cancer) currently have a low evidence base for PPV for symptoms	The GDG considered it was equitable to choose a single threshold PPV for urgent assessment of possible adult cancers, but also considered the alternative – a variable threshold. If the GDG were to vary the PPV threshold for a suspected cancer referral across different cancers, an argument could be made that the PPV threshold should be lowered for those cancers for which we know effective treatments exist and for which we know that early diagnosis improves prognosis. For many of the cancers with poorer prognosis, though not for cancers in general, 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

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				24	29-30	and that 'the primary care evidence base on the predictive value of symptoms is thin or non-existent.' (P24, Lines 29-30). Whilst we agree that 'filling this gap should improve future clinical guidance' and would urge more research into this area, it does not solve the problem in the here and now, with an urgent need to increase earlier diagnosis of pancreatic cancer – a disease with 5 year survival rates of less than 4% that have not changed for nearly four decades. **Given this we urge you to consider including pancreatic cancer symptoms for referral where relevant and persuasive research evidence exists, even though it might not include data in the required PPV format.**	could be employed to improve prognosis in individual cases. For most cancers, the exact symptom timelines (when a patient with cancer actually starts to experience symptoms) and the cancer growth timelines (when a cancer grows to the extent it becomes incurable) are not well described in the research literature. However, the fact that these are two different timelines brings the possibility that these do not always overlap. It is possible that in some cancer sites with poor prognoses, the poor prognosis simply reflects that by the time patients experience symptoms from their cancer, the cancer has grown so much that it is incurable. Of course, there are still benefits from diagnosis in that tumour growth may be slowed, and symptom relief offered. But, in these groups, the GDG considered that the inherent poor prognosis cannot be avoided by improvements in symptomatic diagnosis. The GDG considered that lowering the PPV threshold for suspected cancer referral - however far - will not improve the cure rate. The GDG considered that this argument held for some poor prognosis cancers, however unfortunate this was. On this basis, to allocate resources preferentially to instances where there is less evidence of potential benefit, simply on the basis of current poor outcomes,

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							would seem to be inequitable and potentially less cost effective. Furthermore, it should be noted that referral and investigation are not without risk of harms. It is difficult to justify increasing the number of people potentially harmed, when it is not considered likely that there would be a concomitant increase in the persons who might benefit.
573	Pancreatic Cancer Action and Pancreatic Cancer UK	5	Full	67 13	1.2.4 – 1.2.5 46-50	We would also question the decision to adopt a PPV threshold of 3% for all cancer types. We certainly support the GDG's decision to adopt a PPV of less than 5% in order to 'improve the timeliness and quality of cancer diagnosis', but believe that in order to significantly improve the diagnosis for some cancer types, including pancreatic, it may be necessary to adopt a lower value than the standard. In fact, that principle has been recognized by the GDG itself in excepting recommendations for children and young people from the 3% threshold and adopting a level 'significantly below the 3% PPV threshold, although no explicit threshold value was set.' A PPV of 1% might be appropriate and help ensure more patients are diagnosed at an earlier stage. If you used an upper range score of PPV at 1%, Stapley et al's research would include an additional 6 symptoms/combinations to be included in the guideline: Nausea/vomitting and new onset diabetes 0.7 (0.5-1.0) coincidence interval Loss of weight 0.8 (0.7-1.0)	The GDG considered it was equitable to choose a single threshold PPV for urgent assessment of possible adult cancers, but also considered the alternative – a variable threshold. If the GDG were to vary the PPV threshold for a suspected cancer referral across different cancers, an argument could be made that the PPV threshold should be lowered for those cancers for which we know effective treatments exist and for which we know that early diagnosis improves prognosis. For many of the cancers with poorer prognosis, though not for cancers in general, 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. For most cancers, the exact symptom timelines (when a patient with cancer actually starts to experience symptoms)

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						Abdo pain/new onset diabetes 0.9(0.7-1.1) Abdo pain/nausea vomitting 0.9 (0.7-1.2) Abdo pain twice 1.0 (0.8-1.2) Loss wt/malaise 0.9 (0.4-2.1).	and the cancer growth timelines (when a cancer grows to the extent it becomes incurable) are not well described in the research literature. However, the fact that these are two different timelines brings the possibility that these do not always overlap. It is possible that in some cancer sites with poor prognoses, the poor prognosis simply reflects that by the time patients experience symptoms from their cancer, the cancer has grown so much that it is incurable. Of course, there are still benefits from diagnosis in that tumour growth may be slowed, and symptom relief offered. But, in these groups, the GDG considered that the inherent poor prognosis cannot be avoided by improvements in symptomatic diagnosis. The GDG considered that lowering the PPV threshold for suspected cancer referral - however far - will not improve the cure rate. The GDG considered that this argument held for some poor prognosis cancers, however unfortunate this was. On this basis, to allocate resources preferentially to instances where there is less evidence of potential benefit, simply on the basis of current poor outcomes, would seem to be inequitable and potentially less cost effective. Furthermore, it should be noted that referral and investigation are not without risk of harms. It is difficult to justify increasing the number of people

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							potentially harmed, when it is not considered likely that there would be a concomitant increase in the persons who might benefit.
574	Pancreatic Cancer Action and Pancreatic Cancer UK	6	Full	General 20	General 11-15	It is also worth noting that whilst the GDG believes that the lowering of the threshold, compared to estimates of previous recommendations (P20, Lines 11-15), represents a 'considerable liberalisation' this will only be the case on average and not for each cancer type. Indeed, when you read the accompanying paper Costing Report to support NICE Clinical Guideline on Suspected Cancer (Para 4), it becomes clear there will be no change in the number of referrals for some tumour types and that there will be a 40-80% drop in the number of referrals from Upper GI tumours. (We also recognise that the same paper indicates the number of referrals of patients with generic symptoms could increase, and that part of the predicted drop in UGI cancer referrals will be down to direct access endoscopy in primary care). However, this is still worrying and an estimate on the likely effect of the Draft Guidelines on the number of pancreatic cancer referrals is needed.	When direct access investigations are added into referrals, we anticipate an increase in urgent actions for suspected upper GI cancers. We also expect there to be an overall increase in urgent actions for suspected pancreatic cancer.
575	Pancreatic Cancer Action and Pancreatic Cancer UK	7	Full	General	General	If the GDG insists on restricting symptoms to those where strong research evidence with PPVs exist, and at a standard threshold of 3%, we would hope and expect that an early and rapid review of pancreatic cancer guidelines would take place if/when new evidence becomes available, as happened with the review of ovarian cancer guidelines in 2011.	NICE has a process for reviewing and updating guidelines. This can be found on the NICE web site.
576	Pancreatic Cancer	8	Full	General	General	Also, by restricting guidance to PPV there is a danger that other key indicators will be overlooked	The GDG discussed at length what approach should be taken to making

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	Action and Pancreatic Cancer UK					– e.g. frequency of visits to GP increasing in patients who had previously, if ever, visited their GP before, family history, lifestyle risk (smoking, obesity). Keane et al (2014), concluded that 'A change in attendance behaviour should therefore be considered as an alarm feature for cancer, particularly if patients re-attend with the same alarm symptom or a constellation of alarm symptoms.' (Keane et al A case–control study comparing the incidence of early symptoms in pancreatic and biliary tract cancer http://bmjopen.bmj.com/content/4/11/e005720.full?keytype=ref&ijkey=Of2zmYEB6srnZgd).	recommendations in this guideline, and determined that a PPV threshold was the most appropriate approach. We are aware of the Keane study, which unfortunately was published after the cut-off date for inclusion in the evidence review. It did not present data from which we could calculate PPVs and therefore has not been included.
577	Pancreatic Cancer Action and Pancreatic Cancer UK	9	Full	67	1.2.5 12	We support the proposal to 'consider an urgent direct access CT (within 2 weeks)' for patients presenting with certain symptoms. It should be noted that we have serious concerns over the age threshold introduced and also the combination of symptoms selected that would trigger those scans, which we discuss elsewhere.	The age thresholds and symptoms in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in other groups.
578	Pancreatic Cancer Action and Pancreatic Cancer UK	10	Full	67 General	1.2.5 General	We note and agree with the GDG's observation that 'a CT scan can image the whole pancreas, whilst ultrasound can only image the head.' In an ideal world CT scans should be routinely available and we hope that capacity issues will be addressed following the release of final Guidance. However, in the meantime, we agree with the GDG that patients should be sent for 'an urgent ultrasound scan if CT is not available' for patients presenting with certain symptoms. However, it is important to be aware that a normal ultrasound will often produce a false negative, which will not necessarily rule out pancreatic	Thank you, we agree. Thank you, we agree.

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						cancer. Sensitivity is compromised due to the location of the gland, in a larger patient and/or in the presence of gas and falls to about 30% for tumours <2cm in diameter. Multi-slice contrast enhanced CT scans, which have a sensitivity of 97% are therefore the most useful investigation to diagnose and stage pancreatic tumours and, where specific symptoms exist, referral for a CT scan should be the first action. (GP Online – Pancreatic Cancer http://www.gponline.com/Clinical/article/772932/Pancreatic-cancer/). It should be noted that we have serious concerns over the age threshold introduced and also the combination of symptoms selected, which we discuss elsewhere.	The age thresholds and symptoms in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in other groups.
579	Pancreatic Cancer Action and Pancreatic Cancer UK	11	Full	68-69 General	General	We agree with the GDG that it was 'important not to introduce further delay to the diagnostic process since this was a cancer that tends to present late' and 'that a quicker scan would also enable symptom relief and treatment to start sooner.' As such, we support the GDG's conclusion that any scan should be arranged as a matter or urgency.	Thank you
580	Pancreatic Cancer Action and Pancreatic Cancer UK	12	Full	67 General	1.2.4 General	We have serious concerns about the age-thresholds introduced in the Draft Guidance. Whilst it is clearly the case that incidence of pancreatic cancer increases with age, the fact remains that there were an average of 14%, or 1,236 cases per year , in patients under the age of 60 between the years 2009-2011 across the UK. (http://www.cancerresearchuk.org/cancer-info/cancerstats/types/pancreas/incidence/). Patients under the age of 69 make up 38% of all	The age thresholds in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the younger age groups you mention.

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						pancreatic cancer cases in England and Wales. (Office for National Statistics (2011), 'Cancer survival in England: patients diagnosed 2005–2009, followed up to 2010') While incidence is lower for those under the age of 60, they survive longer For example, on average, 51% of patients below the age of 60 survive I year whereas only 16% of patients over 60 survive 1 year. Those under 60 years of age have a 10% 5 year survival rate on average whereas those over 60 have a 3% 5-year survival see following graphs. (https://pancreaticcanceraction.org/pancreatic-cancer/stats-facts/incidence-mortality/#footnote_11_6941). Data from ONS Office for National Statistics (2011), 'Cancer survival in England: patients diagnosed 2005–2009, followed up to 2010	
581	Pancreatic Cancer Action and Pancreatic Cancer UK	13	Full	67 General	1.2.4 General	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 might deter or delay GPs from referring younger patients for diagnostic tests, particularly for the more comprehensive CT scans. We feel strongly that the age-thresholds should be removed, to fit in with those recently adopted by Health Improvement Scotland which have no such thresholds and to also reflect guidance by the London Cancer Alliance November 2014. (http://www.londoncanceralliance.nhs.uk/media/87762/lca-hpb-cancer-clinical-guidelines-november-2014.pdf). The LCA guidance in particular is clear and concise, and also includes prompts to question patients around family history and lifestyle.	The age thresholds in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the younger age groups you mention.

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						However, if thresholds are to remain, a lowering of the age 60 or above threshold would help reduce the number of 'missed' patients for other non-jaundice symptoms. On average, 887 new cases of pancreatic cancer are diagnosed each year in the UK in patients between the ages of 50 and 59. (Office for National Statistics (2011), 'Cancer survival in England: patients diagnosed 2005–2009, followed up to 2010'.)	
582	Pancreatic Cancer Action and Pancreatic Cancer UK	14	Full	67 General	1.2.4 General	The justification for a threshold of 40 at which jaundice triggers a cancer referral is particularly concerning. The Stapley et al study concludes that there is a PPV of 12.9 (7.89-27.1) **for all patients.** Jaundice is clearly abnormal in any patient so 'inappropriate' referral for CT is likely. If the patient is jaundiced they will have an important diagnostic outcome that will require appropriate treatment (differential diagnosis would include hepatitis, biliary blockage if not by PC tumour may be cholelithiasis or cholangiocarcinoma, range of liver diseases that cause hepatitis including alcoholic liver disease and the autoimmune diseases) so CT is not a wasted diagnostic tool for the jaundiced patient in any case.	There was no evidence that the PPV of jaundice in people younger than 40 was high enough to warrant action. It is not appropriate to estimate the likely PPV of jaundiced patients below the age of 40 from the available evidence.
583	Pancreatic Cancer Action and Pancreatic Cancer UK	15	Full	67 General	1.2.5 General	We support the inclusion of new onset diabetes in the list of presenting symptoms for the first time. However, the guidance looks to new-onset diabetes in the presence of unexplained weight loss. According to a recent study by Keane et al (2015) (Keane et al, (2014) A case-control study comparing the incidence of early symptoms in pancreatic and biliary tract cancer. BMJ Open 2014; 4: e005720 doi: 10.1136/bmjopen-2014-005720) weight loss is a symptom presenting in only 10% of pancreatic cancer patients and should	We are aware of the Keane study, which unfortunately was published after the cut-off date for inclusion in the evidence review. It did not present data from which we could calculate PPVs and therefore has not been included. The age thresholds and symptoms in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to

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						not therefore be the first reference symptom which triggers suspicion. New onset diabetes (either diagnosed concomitantly with the cancer or within 2 years of diagnosis) has recently been identified to occur in up to 30% of patients and is something that can be detected in the pre-symptomatic phase. (Ben et al., (2011) The relationship between new-onset diabetes mellitus and pancreatic cancer risk: A case-control study. European Journal of Cancer 47 pp 248-254 and Pannala et al., (2009) New-onset diabetes: a potential clue to the early diagnosis of pancreatic cancer. Lancet Oncology 10 pp 88-95). Particular attention should be made to a new-onset diabetic who doesn't conform to that of a patient with a typical metabolic syndrome (i.e. weight gain). This can occur up to 2 years before diagnosis **and in the absence of any other symptoms.**	warrant action in the absence of weight loss. The Ben et al. study was not included in the evidence review because it did not meet our inclusion criteria, that is, the patients were not primary care patients. Pannala et al. was not included because it was a narrative review and presented no original data.
584	Pancreatic Cancer Action and Pancreatic Cancer UK	16	Full	67 General	1.2.4 General	We are concerned that dyspepsia and reflux resistant to simple acid suppression (and after prescribed medication including PPIs) are not included in these guidelines. Both heartburn and indigestion are independently associated with risk of pancreatic cancer. (Hippesley-Cox Br J Gen Pract (March 2012) in Pancreatic Cancer Action/ BMJ Learning module "Diagnosing Pancreatic Cancer: a guide for hospital doctors (2014) available online: http://learning.bmj.com/learning/module-intro/.html?moduleId=10051332).	We assume that you are referring to the following paper: Hippisley-Cox, J., & Coupland, C. (2012). Predictive effect of heartburn and indigestion and risk of uppergastrointestinal malignancy. British Journal of General Practice, DOI: 10.3399/bjgp12X629991. This was not included in the evidence review because it did not present PPVs (our pre-specified outcome measure) nor did it present enough data to allow us to calculate the PPVs. Therefore this paper did not allow us to estimate the risk of these symptoms for malignancy in terms of PPVs. A BMJ learning module does not meet

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							our inclusion criteria. None of the available evidence reported PPVs for these symptoms that would warrant action.
585	Pancreatic Cancer Action and Pancreatic Cancer UK	17	Full	67 General	1.2.5 General	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 (symptoms with a presentation frequency greater than 5% of patients) should act as alarm symptoms. Weight loss (10.5% of patients, 6.6 OR) Abdominal pain (43.9%, 6.38) 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) Jaundice (30.8%, 246) Again, it is also worth highlighting their conclusion that 'A change in attendance behaviour should therefore be considered as an alarm feature for cancer, particularly if patients re-attend with the same alarm symptom or a constellation of alarm symptoms.' Moreover, and to reiterate, if a PPV threshold of 1% was introduced for pancreatic cancer, Stapley	The age thresholds and symptoms in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the absence of weight loss. We are aware of the Keane study, which unfortunately was published after the cut-off date for inclusion in the evidence review. It did not present data from which we could calculate PPVs and therefore has not been included. The GDG considered it was equitable to

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						et al's research would include an additional 6 symptoms/combinations to be included in the guideline: Nausea/vomitting and new onset diabetes 0.7 (0.5-1.0) coincidence interval Loss of weight 0.8 (0.7-1.0) Abdo pain/new onset diabetes 0.9(0.7-1.1) Abdo pain/nausea vomitting 0.9 (0.7-1.2) Abdo pain twice 1.0 (0.8-1.2) Loss wt/malaise 0.9 (0.4-2.1).	choose a single threshold PPV for urgent assessment of possible adult cancers, but also considered the alternative – a variable threshold. If the GDG were to vary the PPV threshold for a suspected cancer referral across different cancers, an argument could be made that the PPV threshold should be lowered for those cancers for which we know effective treatments exist and for which we know that early diagnosis improves prognosis. For many of the cancers with poorer prognosis, though not for cancers in general, 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. For most cancers, the exact symptom timelines (when a patient with cancer actually starts to experience symptoms) and the cancer growth timelines (when a cancer grows to the extent it becomes incurable) are not well described in the research literature. However, the fact that these are two different timelines brings the possibility that these do not always overlap. It is possible that in some cancer sites with poor prognoses, the poor prognosis simply reflects that by the time patients experience symptoms from their cancer, the cancer has grown so much that it is incurable. Of course, there are

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							still benefits from diagnosis in that tumour growth may be slowed, and symptom relief offered. But, in these groups, the GDG considered that the inherent poor prognosis cannot be avoided by improvements in symptomatic diagnosis. The GDG considered that lowering the PPV threshold for suspected cancer referral - however far - will not improve the cure rate. The GDG considered that this argument held for some poor prognosis cancers, however unfortunate this was. On this basis, to allocate resources preferentially to instances where there is less evidence of potential benefit, simply on the basis of current poor outcomes, would seem to be inequitable and potentially less cost effective. Furthermore, it should be noted that referral and investigation are not without risk of harms. It is difficult to justify increasing the number of people potentially harmed, when it is not considered likely that there would be a concomitant increase in the persons who might benefit.
586	Pancreatic Cancer Action and Pancreatic Cancer UK	18	Full	67 General	1.2.4 – 1.2.5 General	There is no mention of the presence of other risk factors associated with pancreatic cancer which, alongside presenting symptoms, could trigger suspicion of the disease. GPs should be aware that cigarette smoking is attributed to 29% of UK cases and obesity currently 12% (Parkin et al., (2011) The fraction of cancer attributable to lifestyle and environmental factors in the UK in	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking of sufficient impact on the predictive

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						2010. British Journal of Cancer 105, S77 – S81). Pancreatic cancer is, in 5-10% of cases, hereditary, so GPs need to take into account family history of patients when considering a referral/investigation. (Jacobs, E.J., et al. Family history of cancer and risk of pancreatic cancer: A pooled analysis from the pancreatic cancer cohort consortium (PANSCAN). Int J Cancer 2010) Again, the London Cancer Alliance HPB Cancer Clinical Guidelines include these important prompts. (http://www.londoncanceralliance.nhs.uk/media/87762/lca-hpb-cancer-clinical-guidelines-november-2014.pdf).	power of symptoms to require different recommendations. No evidence was found that cigarette smoking, family history or obesity affected the predictive power of symptoms for pancreatic cancer.
587	Pancreatic Cancer Action and Pancreatic Cancer UK	19	Full	29	21	*(p29-30; line 21 on, 29-30)* We support the addition of a new 'patient-initiated' safety netting procedure for reviewing patients presenting with symptoms that 'do not meet the criteria for referral or other investigative action', if their 'symptoms recur, persist or worsen, new symptoms develop or the person continues to be concerned.' We agree with the GDG that this recommendation is likely to result in an increase in number of consultations and length of consultations but also agree with the GDG that this will lead to a reduction in emergency presentations of cancer. If the symptoms for referral for pancreatic cancer contained in the current Draft Guidance are not changed from the age-limited and generally limited symptoms then the safety netting will become even more important. The vague nature of what constitutes a 'review' of a patient's case, and what actions should be taken as a result of that review, is therefore of concern. For those presenting with	Thank you for your support of the safety netting recommendations. The GDG considered whether separate safety netting recommendations could be made for different cancer sites. However they agreed that a single recommendation for all patients being safety netted was the best strategy, because low risk symptoms often span many cancers. It is not appropriate to recommend what should happen at the review because the review should be dependent on the needs, preferences and symptoms of the individual patient.

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						recurring and persistent vague symptoms, such as dyspepsia and change in bowel habit, we would urge a set of diagnostic tests.	
588	Pancreatic Cancer Action and Pancreatic Cancer UK	20	Full	27		The recommendation on Patient Information and Support to do with safety netting to 'explain to people who are being offered safety netting…which symptoms to look out for and when they should return for re-evaluation. It may be appropriate to provide written information about this.' This is potentially extremely important but relies upon the GP being confident of the symptoms to look out for themselves. We know this is not always the case - Pancreatic Cancer UK's Early Diagnosis Summit 2012 Report (http://www.pancreaticcancer.org.uk/media/86663/early-diagnosis-summit-report-final.pdf) showed that '**half of GPs surveyed were not confident that they could identify the signs and symptoms of pancreatic cancer.'** This is yet another reason why we need a comprehensive list of symptoms in the referral guidelines.	Recommendation 1.16.1 covers the need for GPs to keep up to date. The guideline already contains those symptoms, which the evidence and clinical opinion of the GDG, find to be sufficiently predictive of cancer.
589	Pancreatic Cancer Action and Pancreatic Cancer UK	21	Full	372	All	*(p372-40)* The section on Recommendations for Specific Symptoms and Signs, rather than by cancer type, is an important inclusion, especially for pancreatic cancer where we know GP knowledge is less than for other cancer types. This may prompt clinicians to consider pancreatic cancer when they might not otherwise have done so. In line with previous comments, we believe that Dyspepsia needs to prompt consideration of pancreatic cancer (Keane et al 2014).	Thank you, we agree. We are aware of the Keane study, which unfortunately was published after the cut-off date for inclusion in the evidence review.. It did not present data from which we could calculate PPVs and therefore has not been included.
162	Plymouth Hospitals NHS	1	NICE	240 79	1.9.1	I think this is a very reasonable guideline, However, the description 'progressive, sub-acute loss of central neurological function' is vague and	We note your concern but disagree about how often GPs see such patients.

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	Trust					would encompass almost any presentation to general practice, A&E and clinic. Therefore a substantial increase in demand for urgent MRI which may have not been considered.	The GDG did not wish to try and describe progressive, sub-acute loss of central neurological function because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation.
163	Plymouth Hospitals NHS Trust	2	NICE	240 79	1.9.2	Once the possibility of a brain tumour has been raised it will be hard not to offer an MRI, a significant proportion of which will be under GA. Cost /impact needs to be included	Thank you for this comment. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
164	Plymouth Hospitals NHS Trust	3	NICE	General	General	The impact on MRI may be underestimated. other sections that may have significant implications for the MRI service are the sections on, Breast Cancer, Urological Cancers, Head and Neck Cancers, Sarcomas and Neuroblastoma / childhood cancers. The implications will depend on the specifics of the 'cancer referral pathways' alluded to in the document but not fully specified.	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral.

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165	Plymouth Hospitals NHS Trust	4	NICE	General	General	The document refers to more Direct Access to investigations for suspected cancer by GPs, However this may cause confusion as if a GP suspects cancer they have previously been advised to refer via the 2WW system. If they use direct access for tests the GP retains responsibility for the patient . It would be helpful to have more clarity.	In the guideline we have defined 'direct access' as 'where a test is performed with primary care retaining clinical responsibility throughout, including acting upon the result.' We have also now made this explicit in recommendation 1.15.1 in the short version.
388	Prostate Cancer UK	1	Full	19	8	A timeframe should be added to the statement that, '...a quarter of all people will die of cancer' (eg 'a quarter of all people alive now').	We have made this change.
389	Prostate Cancer UK	2	Full	26	General	*(page 26-28)* The Patient Information and Support section of Chapter 4 focusses on information to support patient choice in referral. This is important; however the guideline should explain how the patient's wellbeing and levels of anxiety whilst they await a diagnosis can also be addressed with information and support.	We consider these issues are already covered by recommendation 1.14.10 and 1.14.11.
390	Prostate Cancer UK	4	Full	26	General	The Scottish referral guidelines for suspected cancer state that: 'It is good practice for the referrer to consider ways of supporting the patient [such as text message reminders] to attend investigations or reviews and addressing any concerns the patient may have about their referral.' The NICE guideline should also encourage GPs to think about how they can support patients to attend future appointments.	We consider this issue is in part covered by recommendations 1.14.10 and 1.16.5. However the guideline did not investigate a review question on the best methods to prevent non-attendance. Therefore the evidence on this has not been examined and we are unable to make recommendations.
391	Prostate Cancer UK	5	Full	26	21	The guideline states 'Discuss with people with suspected cancer (and their carers as appropriate, taking account of the need for confidentiality) their preferences for being involved in decision-making about referral options and further investigations including their potential risks and benefits'. We support this recommendation as there is a	We agree. This is the purpose of recommendations 1.14.1, 1.14.5 and 1.14.7.

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						need to ensure that men with prostate cancer are more routinely involved in referral discussions. Almost half (46%) of men diagnosed with prostate cancer who responded to a survey conducted by Prostate Cancer UK were not told what they could expect to happen at their referral by their GP (1). However, we believe that this recommendation should go further to include the need for informed decision making about any tests conducted in the primary care setting. In the same survey, 51% of respondents who approached their GP because they had symptoms told us that they had not had a discussion about the pros and cons of the PSA test with their GP before they had one (1). Furthermore, almost a quarter (24%) of respondents who were referred for suspected prostate cancer by their GP were not told, or do not remember being told, what their PSA test results meant (1). The guideline should also give some examples of the way in which preferences may vary. For example, whether the patient would prefer to be contacted by telephone or email; who will call them with the results (if applicable); and whether they are given a value for test results, such as the PSA test. Prostate Cancer UK's specialist nurses often hear from men who are confused about the meaning of results from a PSA test. A discussion about information preferences before administering any test may help to mitigate this by establishing the most accessible way to share information about results in advance. Finally, the guidance should explain the benefits of	This issue was not investigated in the guideline so the evidence on it has not been appraised and we are unable to make any recommendations.

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						an informed patient and shared decision-making prior to diagnosis. Men with prostate cancer tell us that this is important in minimising later decision regret related to their treatments.	
392	Prostate Cancer UK	6	Full	26	21	The guideline states 'Explain to people who are being referred with suspected cancer that they are being referred to a cancer service, but when appropriate reassure them that most people referred will not have a diagnosis of cancer, and discuss alternative diagnoses with them.' We are concerned that the words 'when appropriate', could create a false reassurance for the patient. To address this, tumour-specific information demonstrating the proportion of referrals and/or associated symptoms that result in a diagnosis should be provided to GPs and used to underpin this recommendation.	The use of the term 'when appropriate' was done specifically to prevent false reassurance being given to people who have a high risk of cancer. We would expect primary care clinicians to exercise their clinical judgement when applying the recommendations.
393	Prostate Cancer UK	7	Full	26	21	*(page 26-27)* The guideline states 'Give the person information on the possible diagnosis (both benign and malignant) in accordance with their wishes for information (see also the NICE guideline on patient experience in adult NHS services). [2015]' This should specify that both verbal and written information should be provided. The guideline should signpost clinicians towards the information prescriptions section of NHS choices: http://www.nhs.uk/ipg/Pages/IPStart.aspx.	Given that patient preference will vary, the GDG did not consider it appropriate to specify the format. We consider that the phrase 'in accordance with their wishes for information' would include the format in which patients wish to receive the information. NICE guidelines do not signpost to external information sources.

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						The guideline goes on to state that: 'The information given to people with suspected cancer and their families and/or carers should cover, among other issues: • 'where the person is being referred to' We welcome the inclusion of this recommendation in the guideline - 86% of the men in our survey who had been referred for suspected prostate cancer said that they had received information on where their referral appointment was and 94% of men stated that they thought this information was 'moderately important' or 'very important' (1). • 'how long they will have to wait for the appointment' We welcome this recommendation as our survey showed only 50% of the men referred for suspected prostate cancer were told when their referral appointment would be by their GP, yet 92% think this is 'very important' (1). • 'how to obtain further information about the type of cancer suspected or help before the specialist appointment' We welcome this recommendation as our survey showed that 56% of men referred for suspected prostate cancer were not given the option to contact their GP for support, yet 91% of men think it is 'moderately important' or 'very important' for	Thank you Thank you Thank you

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						men to be able to contact their GP (1). • 'what to expect from the service the person will be attending' We welcome this recommendation as our survey results showed that only 47% of men referred for suspected prostate cancer were told what to expect at the referral appointment by their GP yet 80% think that this is 'very important' (1). • 'what type of tests may be carried out, and what will happen during diagnostic procedures' We appreciate the inclusion of this recommendation as only 54% of the men referred for suspected cancer in our survey were given information about the type of tests that would be carried out, yet 85% of men stated that this was 'very important' (1). • 'how long it will take to get a diagnosis or test results' We welcome the addition of this recommendation to the guideline as 60% of men referred for suspected prostate cancer in our survey did not receive information on how long it would take to get their diagnosis, yet 91% of men stated that this was 'very important' (1). We recommend that the following is added to the recommendation: '…and who they should contact if they do not receive confirmation of an appointment'. It is important to clarify where responsibility for the appointment lies in this	Thank you Thank you Thank you We have made this suggested change.

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						interim period, as Prostate Cancer UK's Specialist Nurses often hear from men who are waiting for an appointment and do not know who to contact about it in the meantime.	
394	Prostate Cancer UK	8	Full	27	21	The guideline states 'Have information available in a variety of formats on both local and national sources of additional support for people who are being referred with suspected cancer'. We welcome the inclusion of this statement in the guideline, but want it to apply to all kinds of information provided, not just information on sources of support. It would also be helpful to provide examples of different information formats. Our survey results showed that men prefer to receive information about their prostate health in a variety of formats including verbally, written and online (1). Almost 9 in 10 (89%) men would prefer to receive information about prostate health from their GP or nurse. A third of men (33%) would prefer to receive information in written and 31% from online sources. A third of respondents (33%) would prefer to receive information in two or more different formats.	We have made this change. The format that information is provided will vary considerably between different individuals. Therefore we do not think it is appropriate to include examples.
395	Prostate Cancer UK	9	Full	28	4	The first recommendation in this box should specify that continuing support should be physical and/or emotional. Qualitative research that we have conducted with men with prostate cancer has shown that there are often unmet emotional needs throughout diagnosis, treatment and follow up (2).	This recommendation is from the 2005 guideline. This was not part of the update process, so the evidence on this issue has not been examined and we are not able to make any changes to the recommendation.
396	Prostate Cancer	10	Full	29	9	For prostate cancer, 'watchful waiting' is a specific term used to describe a management strategy for	We understand the issue you are raising. The text you are citing is background

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	UK					cancers that may have been investigated, but where a decision has been made not to pursue treatments with curative intent. Our understanding is that this definition of 'watchful waiting' falls outside the scope of 'safety netting' as described in the guideline, and it would be helpful to state this and clarify the difference.	information not recommendations. Since watchful waiting is sometimes used as a synonym for safety netting the GDG considered it was important that this was highlighted in the background. However in the recommendations the GDG have used the term 'safety netting'.
397	Prostate Cancer UK	11	Full	165	General	*(p165-171)* While the provision of patient information is covered generically in an earlier chapter, the specific section on prostate cancer should stress the need to provide information and counselling before a PSA test or biopsy. The guideline should recommend that GPs discuss the benefits and risks of these tests in advance of their being conducted.	We consider these issues are adequately covered by the recommendations in section 1.14 in the short version of the guideline/chapter 4 in the full guideline.
398	Prostate Cancer UK	12	Full	165	6	The statement that 'Prostate cancer usually presents with lower urinary tract symptoms' is incorrect, as most men with early stage prostate cancer do not have any symptoms and prostate cancer is unlikely to lead to symptoms until it has reached an advanced stage (3,4). We recognise that this guidance is for symptomatic men. However, as currently written the guideline implies the investigations listed should not be pursued for asymptomatic men. This contradicts the guidance in the Prostate Cancer Risk Management Programme (PCRMP). We therefore strongly recommend that reference is made to the PCRMP (5) for guidance on the management of asymptomatic men.	We disagree. The word 'presents' represents a symptomatic person. We agree a significant proportion of prostate cancers are diagnosed by a screening or targeted case-finding process. But once symptomatic, the majority have LUTS. This guideline covers people presenting to primary care with symptoms. It does not cover asymptomatic people and we do not make any recommendations on this group. We do not consider that the recommendations made in this guideline imply that investigation should not be pursued in asymptomatic patients. In such situations we would expect primary care clinicians to use their clinical judgement.
399	Prostate Cancer	13	Full	165	10	We suggest replacing 'Examination of the prostate gland' with 'Digital rectal examination (DRE)' as	We have made this change.

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	UK					this will provide more clarity and consistency with the terminology used in the PCRMP.	
400	Prostate Cancer UK	14	Full	165	13	We understand that the PSA test is routinely available in primary care. We recommend removing the word 'generally'.	We agree. Our concern is that there are thousands of general practices, some with atypical populations and laboratory arrangements. We therefore consider it is wiser to allow for there being exceptions to routine access in some instances. Therefore, we have not changed the text.
401	Prostate Cancer UK	15	Full	165	14	Reference is made to age specific raised [PSA] values suggestive of cancer, but these are not provided in the guidance. The guidance should include or signpost towards a table of values that should trigger a referral for biopsy, such as those included in the PCRMP.	The GDG did not have sufficient primary care evidence to produce a table of values such as you suggest. It is not part of NICE methodology to cross reference guidance from other organisations.
402	Prostate Cancer UK	16	Full	169	1.6.29	It is not clear from this table what factors a should consider before conducting a DRE. We suggest re-ordering the first and second paragraphs in the 'recommendations' box. As above, it would be helpful to provide, or signpost towards, the relevant age-specific PSA reference ranges.	We state in the introduction that there is an expectation that 'the clinician will have taken an appropriate history and performed an appropriate physical examination'. We consider this adequately covers the situation you describe. The recommendations have been ordered according to the urgency of action. Therefore our recommendation to refer for suspected cancer needs to come first, to be consistent with the rest of the guideline. It is not part of NICE methodology to reference information from other organisations into their guidelines.
403	Prostate Cancer	17	Full	171	9	Under 'other considerations', the document states that risk factors such as ethnicity might warrant	We have documented in the introduction, there are very few instances where risk

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	UK					testing at a lower age. However, no reference is made to this in the recommendations. The guidelines should make GPs aware of the following, and discuss these risk factors with patients where relevant: • Black men have a higher risk of developing prostate cancer. 1 in 4 Black men are diagnosed with prostate cancer (6), compared to 1 in 8 of all men (7); • Men are two and a half times more likely to get prostate cancer if their father or brother has been diagnosed with it, compared to a man who has no relatives with prostate cancer (8–10).	factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. No evidence was found that ethnicity or family history affected the predictive power of symptoms for prostate cancer.
404	Prostate Cancer UK	18	Full	General		References 1. Prostate Cancer UK. Total sample size was 569 UK men, of which 480 had had a PSA test and 431 had been referred for suspected prostate cancer following a PSA test. Fieldwork was undertaken between October and November 2014. The survey was carried out online. 2014. [a summary of the survey data and analysis is provided in Appendix 1 below] 2. BritainThinks for Prostate Cancer UK. Findings from qualitative research carried out by BritainThinks. Total sample size was 53 adults affected by prostate cancer across the UK (including 8 partners of men with prostate cancer). Fieldwork was undertaken between 5th February and 13th March 2014, comprising telephone interviews, focus groups and online qualitative research. 2014. 3. Burford D, Kirby M, Austoker J. Advising men about the PSA test for prostate cancer [Internet]. 2009. Available from:	Thank you for providing these references to support the points you make in your previous comments.

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						http://www.cancerscreening.nhs.uk/prostate/prostate-summary-sheet.pdf 4. Collin SM, Metcalfe C, Donovan J, Lane JA, Davis M, Neal D, et al. Associations of lower urinary tract symptoms with prostate-specific antigen levels, and screen-detected localized and advanced prostate cancer: a case-control study nested within the UK population-based ProtecT (Prostate testing for cancer and Treatment) study. BJU Int. 2008 Nov;102(10):1400–6. 5. NHS Cancer Screening Programmes. Prostate Cancer Risk Management Programme [Internet]. [cited 2014 Aug 11]. Available from: http://www.cancerscreening.nhs.uk/prostate/ 6. Prostate Cancer UK. Working out the risk of prostate cancer in Black men [Internet]. 2013 [cited 2013 Oct 30]. Available from: http://prostatecanceruk.org/we-can-help/african-caribbean-communities/1-in-4-stat-explained 7. Cancer Research UK. Prostate cancer incidence statistics: Lifetime risk. [Internet]. 2010 [cited 2013 Aug 22]. Available from: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/prostate/incidence/#Lifetime 8. Johns L, Houlston R. A systematic review and meta-analysis of familial prostate cancer risk. BJU Int. 2003;91(9):789–94. 9. Bruner DW, Moore D, Parlanti A, Dorgan J, Engstrom P. Relative risk of prostate cancer for men with affected relatives: systematic review and meta-analysis. Int J Cancer J Int Cancer. 2003 Dec 10;107(5):797–803. 10. Kiciński M, Vangronsveld J, Nawrot TS. An epidemiological reappraisal of the familial aggregation of prostate cancer: a meta-analysis. PloS One. 2011;6(10):e27130.	

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30	Public Health England	1	Full	42	1.1.2 – 1.1.5 Line 1 (table)	The age sub-categorisations in this section are over-complex and based on very limited evidence. They are likely to make decision-making in primary care more difficult than it is at present. In particular the use of a Full Blood Count (looking for thrombocytosis in lung cancer) adds another period of potential delay for a test that no-one believes is of major relevance in this situation. The evidence for the use of this test comes from a single paper (Hamilton 2005) which retrospectively studied only 247 lung cancer patients which, from their characteristics, are not (in the view of the NCIN's Lung Cancer Site-Specific Clinical Reference Group) representative of a population-based group of lung cancer patients. In addition, but only 34 of these 247 patients had thrombocytosis. So is the GDG really suggesting we add another 'diagnostic' layer onto the process on the evidence of one study in which only 34 patients had that feature? We know of no other study or expert group which supports the routine use of a FBC in the early diagnosis of lung cancer. We suggest this is removed.	The recommendations for lung cancer have been revised to make them simpler and easier to understand. The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended.
31	Public Health England	2	Full	46	Line 1 (table)	The table on this page refers, in part, to the diagnosis of mesothelioma. We know of no study (and none are quoted) in which the FBC is in any way diagnostic of this disease which is based entirely on imaging and biopsy investigations. As with the comments on lung cancer above, we strongly suggest that recommending a FBC adds potential delay and complexity to an already complex issue with no obvious benefit.	The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended.
32	Public	3	Appendix	42		It seems difficult to understand why there were no	This guideline is targeted at primary care

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	Health England		A			site-specific experts on any of the cancers included in any way as part of the development of these guidelines. Whilst we accept that these are guidelines for primary care one would have thought that seeking expert clinical advice for each tumour studies was essential.	where patients suspected of having cancer are identified. Therefore it was appropriate to have a majority of primary care clinicians on the GDG. Given there were 37 separate cancer sites to be investigated, it was unrealistic to have representation from each specialty on the group. When the GDG needed further specialist input to make their recommendation, they called on expert advice.
128	Roy Castle Lung Cancer Foundation	1	Full	26	21	There is value in highlighting the need to support patients either being referred to cancer services or monitored. Identifying the patient's and carers information and support preferences are vital to maintaining confidence in the diagnostic and treatment pathways. Diagnostic information may be difficult to provide depending on likelihood and sub-type of lung cancer.	Thank you We appreciate your concern, however we consider that where possible, diagnostic information should still be provided.
129	Roy Castle Lung Cancer Foundation	2	Full	27	21	Providing accurate timeframe for test results may not be feasible at time of referral for suspected lung cancer. This may depend on local service agreements and also fitness of patient for invasive diagnostic testing.	We appreciate there may be difficulties in doing this in some instances, but nevertheless the GDG consider it was important to make a recommendation on this matter.
130	Roy Castle Lung Cancer Foundation	3	Full	29	21	The value of providing an agreed timeframe for follow up to safety netting will provide reassurance for patients of active monitoring. It is useful to identify patient symptom concerns as a trigger for review. To make this an effective safety net it is essential that patient monitoring systems identify and link multiple presentations with linked symptoms/concerns to primary care.	We agree and this is implicit within the recommendation.

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131	Roy Castle Lung Cancer Foundation	4	Full	General	General	We are concerned that this guidance will not lend itself to implementation in practice. The current formatting results in a complex document, with many evidence tables that require sifting. Whilst the document offers risk stratification guidance it does not suggest proactive management of patients who may be reticent in presenting symptoms and anxious about likelihood of smoking behaviour increasing their cancer risk. An at a glance tool for primary care may be required, and/or education sessions to engage non-specialists in raising their threshold for suspicion amongst higher risk patient groups.	The short version of this guideline presents only the recommendations – both in a symptom-based section and according to cancer site. You may find this presentation easier to read. There are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking (in lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations. NICE are exploring ways that we can improve usability of the document.
132	Roy Castle Lung Cancer Foundation	5	Full	General	General	We do not feel the current document has a function in offering guidance and support to patients/carers with a concern about cancer referral. The language, context and formatting are unlikely to be accessible to those with limited knowledge of clinical terminology. There may be a value in sign posting to relevant diagnostic patient information sources, including voluntary sector groups working through the NHS Information Standard.	A patient version of this guideline will be produced and published at the same time as the other guideline documentation.
133	Roy Castle Lung Cancer Foundati	6	Full	41-42 32	General	The non-specific range of lung cancer symptoms is recognised in this document. However the distinction of symptoms from primary and metastatic cancer are not differentiated.	The GDG did not expect the presentation of metastatic cancer in the lung to be materially different from primary lung cancer.

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134	Roy Castle Lung Cancer Foundation	7	Full	34	general	It is not clear how a physician considering referral would make use of the data in tables 6 and 7. If the intention is to assist in risk stratification the format seems quite complex and unwieldy.	Tables 6 & 7 display the evidence upon which the recommendations were made. In clinical practice we would expect clinicians to focus on using the recommendations.
135	Roy Castle Lung Cancer Foundation	8	Full	42	general	The guidance places emphasis on the use of blood count as part of the diagnostic process. From the thousands of contacts we have each year from people with a diagnosis we are not aware of this as standard practice. Is there clear evidence it would enhance the diagnostic pathway?	The evidence reviewed for signs and symptoms found that a raised platelet count was predictive of lung cancer. Platelet count is normally assessed through a full blood count, therefore the GDG recommended its use. This is documented in the Linking Evidence to Recommendations section in the full guideline.
136	Roy Castle Lung Cancer Foundation	9	Full	44	general	There is very little in the guideline that identifies what to do with an atypical patient (under 40 and/or non-smoker). Whilst risk stratification is useful non-inclusion can potentially be misinterpreted as no risk and therefore no monitoring required.	The GDG did not find any evidence suggesting high PPVs for lung cancer in people under 40. We agree that GPs should use their clinical judgement when assessing patients and have mentioned this in the introduction to the full guideline.
137	Roy Castle Lung Cancer Foundation	10	Full	44	General	Given the benefits measured from the Be Clear on Cancer lung focused campaign there is very limited reference in the guidelines to the benefits identifying early stage lung cancers.	In the introduction we clearly state that early diagnosis is beneficial. We do not think it is necessary to re-state this for each cancer site.
279	Royal College of General Practitioners	1	Full	63	8	Dyspepsia and associated symptoms are very common. Where does HP testing fit in? Likely that there are increased referrals for upper GI endoscopy.	HP testing was not included in the review question for this cancer site and therefore no recommendations have been made on it. Our recommendations are for direct access tests, not suspected cancer

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							pathway referrals. We agree that more patients will be investigated by direct access tests if our recommendations are followed. However this should reduce the number of suspected cancer referrals, so the overall cost-consequences should be somewhat improved.
280	Royal College of General Practitioners	2	Full	83	8	As above.	Thank you
281	Royal College of General Practitioners	3	Full	149	32	"whomen" instead of women	Change made
282	Royal College of General Practitioners	4	Full	157	11.2	Where endometrial cancer is suspected the GP should arrange for an ultrasound examination.	The course of action included in the recommendations was based on the primary care evidence of the PPVs of diverse symptoms. Some symptoms had a PPV high enough to warrant a suspected cancer referral, others to warrant investigation with direct access ultrasound.
283	Royal College of General Practitioners	5	Full	397	11	The recommendation for an ultrasound is omitted in error?	The recommendations for ultrasound do not relate to post menopausal bleeding and therefore have not been included here.
284	Royal College of	6	Full	218	13.3	"raises the suspicion of squamous cell ca is likely to be SCC" is unclear. Would be improved by describing the lesions.	The GDG did not wish to try and describe SCCs because there is considerable variability and considered that there was

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	General Practitioners						a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation.
285	Royal College of General Practitioners	7	Full	332	18.5	*(p323-331)* Clusters of symptoms rather than single symptoms are more common which is what alerts the concerned parent. In areas where there are high levels of anxiety or parents are used to different health systems there is frequently pressure for scans for minor symptoms. A scan is not always the best way to resolve the anxiety or the symptom. An open relationship with the clinician who can order a scan is to be preferred.	This recommendation was debated at length by the GDG. It was noted that the positive predictive value of parental concern had not been studied, but, based on their clinical experience, the GDG agreed it would be sufficiently high to warrant recommendations.
286	Royal College of General Practitioners	8	Full	General	General	Under **every** section bullet points of red flags.	We interpret this comment to request additional prominence to high risk presentations. The presentations for which we have made recommendations are the highest risk presentations.
287	Royal College of General Practitioners	10	Full	210	1.7.11	I am commenting as one of the Clinical Advisors for the RCGP, I am also a GP and a GPSI in Dermatology. I am the GP member of the NICE Melanoma GDG. I would welcome some more clarification on the use of Dermoscopy in your recommendation. Dermoscopy is used in primary care by some trained GPs but I think it should be highlighted that the training and keeping up to date in this skill is essential. Dermoscopy in primary care can be a very useful tool in diagnosing benign lesions but in terms of diagnosing Melanoma this is more specialised and may be used by GPSI's or by GP's that are trained in the use of Dermoscopy. We are making a recommendation on Dermoscopy in the Melanoma Guideline and it would make	Thank you for this comment. Recommendation 1.7.1. does not recommend dermoscopy, but acknowledges that some primary care clinicians use it. The recommendation covers what to do when dermoscopy suggests malignant melanoma.

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						sense that the recommendations agree with each other.	
288	Royal College of General Practitioners	11	Full	98	General	*(p96-140)* I would applaud the group's attempts to derive clear and unequivocal guidance from the considerable range of literature summarised in the tables. On p98 for each individual symptom a summary positive predictive value is given that doesn't reflect the very wide range of figures for PPV given in the tables. This in turn gives what appears to be spurious precision to the recommendations on p130-131….	While the meta-analyses were considered by the GDG, some important limitations with them were also identified (e.g, they were performed across all ages) and, as outlined in the 'Linking-Evidence-to-Recommendation' table these limitations were taken into account when the GDG developed the recommendations.
289	Royal College of General Practitioners	12	Full	130	1.3.1 & 1.3.3 general	*(p130-131)* In particular, while the group regrets the lack of different PPVs stratified by age, they nevertheless make a very sharp distinction between the age at which referral should take place on the basis of rectal bleeding (50) and change in bowel habit or anaemia (60). Again looking at the PPVs given in table 27, it is not possible to see precisely how that distinction has been made. For instance Lawrenson (2006) would suggest that the PPV does not reach 3% in men until the age of 60; in the same paper a change in bowel habit is quoted as 4.07 for men aged 50-59. The group recommend referral for women with Hb<11, but Hamilton (2008) is quoted as giving a PPV of 2.4 for women aged 60-69 with Hb values of 10-10.9. The recommendations are justified in several places (p133) with the phrase 'based on their clinical experience' which should have no place in such a document. If there is uncertainty around the figures the recommendations should reflect that, and not offer false certainty.	This is an evidence based guideline. The GDG considered whether it was appropriate to make recommendations on areas where there was no or insufficient evidence. In order to provide the best guidance for primary care, it was decided that it was appropriate to use the clinical experience of the GDG to make recommendations when there was no or insufficient evidence. This is explicitly documented in the Linking Evidence to Recommendations sections. The symptoms in recommendation 1.3.1 were based on evidence. The age cut-offs were extrapolated from evidence using clinical experience. The symptoms in recommendation 1.3.2 were based on clinical experience. Recommendation 1.3.3 was based on both evidence and clinical experience. In recommendation 1.3.4 the symptoms were based on clinical evidence, the choice of test was

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							based on clinical and health economic evidence and the age cut-offs were extrapolated from evidence using clinical experience
290	Royal College of General Practitioners	13	Full	96	4	'A full time GP'. Very odd phrase in these days. What does NICE understand by this term? More helpful perhaps to relate it to a population denominator of 1000 or 2000.	We consider most readers would understand this term, and would actually find it easier to visualise. Your alternative would be much more difficult to apply to non-principals and people who work part-time, whose list size responsibility may be unclear.
291	Royal College of General Practitioners	14	Full	122	4	Cost-effectiveness evidence. My expertise with health economic models is poor so I was unable to appraise this study. As far as I could understand it (and I may be wrong) it compares faecal occult blood testing with barium enema, colonoscopy etc as methods to *diagnose* colonic carcinoma. This feels like a very false comparison. While it is possible to diagnose cancer on ba enema, colonoscopy etc, it would never be possible to arrive at a diagnosis on the basis of a positive faecal occult blood test. One would use the test to increase or decrease the probability of a cancer diagnosis, and then continue with a more invasive tests. Have I completely missed the point?	In the analysis, the diagnosis would not be based upon faecal occult blood tests alone (nor barium enema). These tests would be used as the first test. If the patient was found to be positive then the patient would go on to have a colonoscopy where the patient would be diagnosed or identified as a false positive. This process is illustrated in the model structure figure in the report.
292	Royal College of General Practitioners	15	Full	131	1.3.6 1.3.7	*(p119 and 131)* I was pleased to see advice given to use fob testing (in my own area the test has been discontinued by the local laboratory). The advice when to use it seems sensible. Separating the two paragraphs (Offer testing… and 'Refer people …') is odd. The second one only makes sense if linked to the first.	Thank you The recommendations for colorectal cancer have been revised to make them simpler and easier to understand.

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						On p119 a potentially high false negative rate is quoted for fob testing. It should be pointed out somewhere that the advice to refer on the grounds of a positive fob test, a negative one does not completely rule out cancer.	People with a negative FOB but persistent symptoms would be covered by the recommendations made on safety netting. These recommendations now explicitly state that people should be aware of the possibility of false negatives with this test.
293	Royal College of General Practitioners	16	Full	130	1.3.4 1.3.9 General	*(p130-131)* Recommendations: There are some odd things here. Is it really necessary to include the following: Cancer pathway referral for people with a rectal or abdominal mass. There were papers that quoted PPVs in the event of a rectal tumour, but no papers that I could see giving data for abdominal mass. In any case it's hard to see that any doctor needs prompting in this case. This is insulting to doctors, and makes the group look slightly ridiculous. Similarly 'offer a digital rectal examination … lower gastrointestinal tract'. It's hard to imagine this altering any clinical behaviour. I was also surprised that family history is not given any attention in the recommendations. The papers on p109 that consider family history give divergent PPVs, which may have led the GDG to disregard the importance. However thinking in Bayesian terms might correctly prompt a referral in someone who didn't quite reach the threshold if there were a positive family history.	This guideline is for all primary care professionals, not just GPs. Therefore it is important that it is sufficiently comprehensive for all users. The recommendation on digital rectal examination for colorectal cancer has been deleted. We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG 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. We did not find sufficient evidence across all studies whereby a family history would warrant

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							differential recommendations. No evidence was found that family history affected the predictive power of symptoms for colorectal cancer.
294	Royal College of General Practitioners	17	Full	108	General	Some papers appeared to indicate that the presence of haemorrhoids had no effect on the PPV of rectal bleeding for cancer. This is helpful, but again didn't invite a comment in the recommendations.	The symptoms in the recommendations were derived from the evidence on PPVs. There was not evidence of a PPV high enough to warrant action in other groups.
295	Royal College of General Practitioners	18	Full	137	General	'Despite the lack of evidence …' This is the kind of sentence that infuriates me. If there isn't any evidence the guideline should say just that. Is any clinician going to be helped by being told to refer patients with an unexplained anal mass or ulceration? There is also the statement that 'diagnosis at an early stage improves the outcome.' Is there any evidence for that statement? No paper is quoted, and while it may be true, NICE guidelines should take care to distinguish between the two.	This guideline is for all primary care professionals, not just GPs. Therefore it is important that it is sufficiently comprehensive for all users. The lack of evidence in this area has been discussed in the introduction to the full guideline. It is also known that early diagnosis improves cancer survival, and there is no reason to expect that this would be different in colorectal cancer.
296	Royal College of General Practitioners	19	Full	180	1.6.56	These changes in practice are based on the finding of one research team (one of the co-authors is a lead for NICE guideline revision). The study is case/control which has limitations and there are twice as many cases as controls. Furthermore the authors state that the coding of non visible haematuria in controls was insufficient to use these data. In a study published by Wallace 2002 (BJUI 89,868-878) 6% of newly diagnosed bladder cancer patients presented with NVH but more (7%) had had no haematuria. To our knowledge no case control studies have	The quality of all studies was assessed by the NCC-C technical team, not the GDG. That some of the research used in the guidance has the clinical lead as a co-author is to be expected – clinical leads are appointed to be an expert in the topic area. All GDG members are required to declare any conflicts of interest in line with NICE policy. A complete record of all interests declared and the action taken as a result is included in the guideline.

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						been commissioned to compare the risk of bladder cancer in age/sex matched groups with or without NVH. The National Screening Committee in 2009 stated that screening for bladder cancer should not be offered based on dipstick urine test. Therefore we feel a further case control study needs to be conducted. For example: If one recruited roughly equal numbers of NVH and non-NVH subjects, and assume that cancer is found in 2% of NVH subjects, to detect a RR of 2.00 (i.e. cancer present in 1% of non-NVH subjects) for a power of 80% and significance level of 5% the study would need to recruit 3960 individuals.	The NVH recommendations are based on the Price paper, not the Shephard paper you are alluding to. The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop recommendations for a guideline targeted at a primary care population.
297	Royal College of General Practitioners	20	Full	165	6	Only advanced prostate cancer causes LUTS therefore if early disease is diagnosed it is as result of screening.	We agree. This guideline relates to diagnosis of cancer in a symptomatic population and not screening.
298	Royal College of General Practitioners	21	Full	165	11	Loss of central sulcus is a sign of significant BPH not cancer.	Thank you. This finding has also been reported with cancer, but for simplicity, we have removed it from the background section.
299	Royal College of General Practitioners	22	Full	165	16	The wrong clinical questions are being asked and should be: a) What is the risk of advanced prostate cancer in men with LUTS and a normal DRE; b) Is early organ confined prostate cancer more common in men with LUTS than in age matched asymptomatic men.	Our task was to update CG27. Consequently we had to investigate the same issues that were covered in that guideline. This led to the clinical questions on p 165 being investigated.

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300	Royal College of General Practitioners	22	Full	166	2	*(line 2-3*) This sentence on the PPV of "symptoms" includes "malignant feeling" prostate which is of course a SIGN.	We have made this change.
302	Royal College of General Practitioners	25	Full	41-42 33	General	*(p33-42)* Evidence refers to increased PPV if thrombocytosis and additional symptom (weight loss, cough). Guideline says 'offer fbc' but does not state what the action should be if FBC demonstrates thrombocytosis in these circumstances.	This recommendation has now been removed from the guideline.
303	Royal College of General Practitioners	26	Full	42	General	Term 'unexplained symptoms' is used in reference to the list of symptoms that includes cough. Should this also refer to 'persistent', as current practice is to investigate persistent and unexplained cough.	The GDG discussed both these qualifying adjectives at length. They decided to use 'unexplained' because many conditions (such asthma) can lead to a 'persistent cough, that is unlikely to be cancer.
304	Royal College of General Practitioners	27	Full	42	General	Consider clarification of recommendation that individuals with more than one general symptom (eg weight and fatigue) should have CXR – as this seems to overlap considerably with other recommendations.	The symptom-based section of the guideline should help with clarity of the appropriate action where people have several general symptoms.
305	Royal College of General Practitioners	28	Full	General	General	Would it be possible to give some "take home messages"? Such as in upper GI cancers, five year survival is 15% and this may be increased to 30% if time to diagnosis is reduced by x months, and the delay mainly occurs at yyy Common missed diagnoses are zzz. (I'm aware they also say *"It is generally believed that early diagnosis of cancer is beneficial. However, this is quite difficult to prove scientifically, in part because the natural course of*	The guideline investigated which symptoms predict which cancers in primary care. It did not look at evidence on the impact of earlier diagnosis on survival. Therefore we cannot make recommendations on this. The background information to each cancer does contain some data on incidence and survival.

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						cancer, and of its 11 symptoms, is imperfectly understood.")	
306	Royal College of General Practitioners	29	Full	62 General	But the first example is page 62	Page 62 I can see no evidence for – "*The GDG noted that the recommendation for urgent direct access upper gastrointestinal endoscopy is likely to result in a cost increase due to an increase number of endoscopies performed. However, this cost increase is likely to be counteracted to some extent by a cost saving from an optimised diagnostic process that will see an increase in the proportion of patients being referred on a suspected cancer pathway who have oesophageal cancer and a decrease in the number of patients without oesophageal cancer being referred."* especially when they go on to say – "*Other considerations: The GDG recognised that to implement these recommendations, there may initially be some capacity issues in some localities as urgent endoscopies are harder to accommodate than non-urgent endoscopies."* If we reduce the threshold at which we refer, we will refer more people. Since the plot of "hardness of symptoms" against prevalence of that level of symptomatology in a population will be a curve, this will disproportionately increase the number of people we refer. I see nothing persuasive in this document that will, by refining my diagnostic skills, reduce my referral rate.	This sentence describes the GDGs deliberations on the potential cost consequences of the recommendations made. Our recommendations are for direct access tests, not suspected cancer pathway referrals. We agree that more patients will be investigated by direct access tests if our recommendations are followed. However this should reduce the number of suspected cancer referrals, so the overall cost-consequences should be somewhat improved.
307	Royal College of	30	Full	67 General	1.2.5 General	Pancreatic Cancer There is no standard pathway for all features of possible pancreatic cancer. CT provides 10 more	The GDG did not find any NPV evidence for ultrasound for pancreatic cancer in primary care. As you quote, the

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	General Practitioners					complete assessment for pancreatic cancer although ultrasound may also be of some 11 use. What do they mean by this? – my impression is that U/S is used by many of my colleagues to investigate "vague" abdominal pain. They partly answer this later, by saying "*The GDG acknowledged that CT scans are not as widely available in primary care as ultrasound and more expensive. However a CT scan can image the whole pancreas, whilst ultrasound can only image the head. The GDG therefore considered that a CT scan would be the most appropriate investigation in primary care. However, since it was not possible to do an analysis of the cost-effectiveness of these different investigations, due to a lack of directly relevant data, the GDG agreed to include ultrasound as an option where CT scans were not available."* But it does not answer the NPV of a US test.	recommendations were based on the GDGs clinical opinion and experience.
308	Royal College of General Practitioners	31	Full	73	General	Absolute risk for cancer with Dyspepsia = 2.28 (paper is from Hallissey 1990, NICE says "all patients" but Hallissey says over 40)	"All patients" was used in the guideline to mean all included patients. We have reviewed the text and now used "All patients" and "All included patients" more consistently. The evidence tables in Appendix F present detailed inclusion and exclusion criteria for all the included papers.
309	Royal College of General Practitioners	32	Full	74	List of studies and PPVs	Hippersley-Cox 2011 ie I'm not sure where they get their Dysphagia = 7.8 in "all patients", because the papers figures are very much more nuanced than that eg "•A 50-year-old female who is a heavy smoker with dysphagia has an estimated risk of gastro-oesophageal cancer of 3%. If she has also had anaemia in the last year, her estimated risk is 7%, and if she also has abdominal pain, the	We agree, especially as it is in patients aged 30-84 years. However, the PPV of 7.8% is reported in the paper for dysphagia for this patient group and we have therefore used it in our evidence review.

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						estimated risk of gastro-oesophageal cancer is 29%."	
310	Royal College of General Practitioners	33	Full	75	List of studies and PPVs	Similarly with Stapley - However, Stapley et al in a big English study say (BJC 2013) "In contrast, no symptom in patients <55 years had a risk >1%, even dysphagia." – (and this is for stomach and oesophageal cancer combined)	The risk of 4.8% reported by Stapley is in patients aged 55 years and above and therefore does take account of age being a risk factor too.
311	Royal College of General Practitioners	34	Full	41	17	The guidelines for use of a suspected cancer pathway for patients with haemoptysis seems to imply that GPs should not bother trying to "exclude" lung cancer with a Chest X Ray. This will be a significant change in practice for many – presumably this is because of false negative Chest Xray results. It is a change worth highlighting, perhaps with brief additional information about why the change has been made. 2 week wait referrals are likely to increase significantly with this change.	The GDG agreed that haemoptysis is a serious symptom that would need a suspected cancer pathway referral, even with a negative chest X-ray. Given this, the GDG agreed not to make a recommendation for chest X-ray in the first instance as this could cause a delay in people being referred.
312	Royal College of General Practitioners	35	Full	42	1.1.6 Table	The role of checking for thrombocytosis in diagnosing lung cancer will be new to many GPs. Could some practical parameters be presented around upper limits of normal and predictive value?	The evidence on which this recommendation was based, was on the platelet count being above the local laboratory's normal range.
313	Royal College of General Practitioners	36	Full	80	1.2.109	The recommendation to consider Upper GI endoscopy in people with reflux and nausea/vomiting: Reflux + nausea is a quite common presentation – it would be useful to have some further information here about predictive value if available to assist the process of consideration.	Further information about the PPVs is available in the evidence tables in the full guideline.
314	Royal	37	Full	210	1.7.2	The weighted checklist score for melanoma may	Thank you

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	College of General Practitioners				1	be different to other systems in use. It is simple and helpful and would be worth highlighting as a resource.	
315	Royal College of General Practitioners	38	Full	220	15	The advice to consider a 2 week wait referral for a possible BCC if concern about site or size may raise some eyebrows in Dermatology departments. My local experience is that this has been discouraged so far.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
316	Royal College of General Practitioners	39	Full	228	1.8.5 17	Unexplained oral ulceration > 14 days is fairly common in primary care and much of it is clearly non malignant (eg typical apthous ulcers). Could there be further detail here about suspicious features which have a significant predictive value so as to avoid over referral of non malignant ulceration?	We have changed the duration of oral ulceration to be 3 weeks, in line with recommendations made in the NICE guidance on 'Improving outcomes in head and neck cancers.'
317	Royal College of General Practitioners	40	Full	240	1.9.1 12	I note the difficulty in finding evidence about neurological symptoms and brain tumours. Headache as a symptom suggestive of a tumour is of course a source of much concern for patients and doctors - it may be helpful to have a clear statement in the guideline regarding this symptom, if only to comment on the lack of evidence. GPs do think in terms of "red flags" for brain tumours and it's surprising not to find them here. Also the recommendation to use MRI rather than	The PPV of 'headache' for brain cancer was considerably below 3% in the evidence.

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						CT is important to highlight if this is indeed the better investigation. Of course MRI is a scarcer resource.	The recommendation has been changed to clarify that CT can be used when MRI is contraindicated.
318	Royal College of General Practitioners	41	Full	257	14	The recommendation of what one might call a "2step" approach to a myeloma screen is useful. Not needing urinary BJ protein or electrophoresis as part of an initial screen makes things simpler (and perhaps therefore more likely to get done) and reduces cost. This might be a practice change for many and is worth highlighting.	Thank you for this information.
319	Royal College of General Practitioners	42	Full	366	1.13.2	Unexplained weight loss: This is a not uncommon presentation, particularly in the elderly and it is interesting that on the whole it seems to have quite a low PPV for cancer. Is it a correct interpretation of the recommendation that investigation is only needed if there are localising symptoms or signs present? OR if the recommendation is to investigate anyway, then a "minimum necessary" batch of investigations would need to be recommended. NOT investigating weight loss as an isolated symptom in the elderly has potential to reduce harm from waste and distressing investigation and if this were the recommendation it would be worth highlighting very clearly. Deep Vein Thrombosis : The PPV of >3% for DVTs in primary care is a useful figure. Again, it's not clear if this is recommending a minimum diagnostic set to hunt for malignancy – how far should we go post DVT looking for cancers?	Weight loss only has a low PPV when single cancers are considered. Cumulatively, the PPV for cancer as a whole exceeds 3%. The expectation of the GDG was that most patients with unexplained loss of weight would have other clues in their history and examination would guide investigation strategy. The expectation of the GDG was that most patients with DVT would have other clues in their history and examination would guide investigation strategy.
320	Royal College	43	Full	372	And onward	These summary tables are useful to condense what is a huge and complex guideline. It would be	Meta-analysis was undertaken for symptoms where possible. However this

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	of General Practitioners				s	very useful to have an additional column with approximate PPVs of these symptoms accompanied by brief practical comments on the nature of the evidence. This is especially important when thinking about the "consider" recommendations where this information would help GPs make balanced judgements about how and when to investigate. Providing this kind of information in other easily accessible formats would be very valuable – something that is searchable in a very brief time frame.	was only possible for a limited number of symptoms and therefore adding a summary PPV to each recommendation would not be possible.
321	Royal College of General Practitioners	44	Full	General	General	There is a vast amount of information in this guideline and tools and resources to go with it would be valuable to aid in its dissemination eg Powerpoint presentations, Summary highlights etc	We will pass this information on to the Implementation team at NICE who will be working on assisting people to implement the recommendations in the guideline.
322	Royal College of General Practitioners	45	Full	General	General	There is a feeling that symptom pathways may be a more intuitive way of managing patients – on the rather obvious reality that patients present with symptoms, and not a specific suspected cancer. One of the issues that GPs face, is, for example, which pathway to enter someone with abdominal pain – for example, it could be upper GI, lower GI, renal, gynae etc. as is intimated later in the document. Would it not be better to have the symptom section first, and the site specific sections later – this may also have more impact as it would be very different to how things have been done to date.	The symptom based section was included in order to make the guideline easier to use for this purpose in a primary care setting. Given that primary care is the target audience for this guideline, it was placed first in the short version.
323	Royal College of General	46	Full	19	6	The lifetime risk of cancer is now over 40% : http://www.cancerresearchuk.org/cancer-info/cancerstats/incidence/risk/	We have amended the text to 'More than one third...' in accordance with the reference you have supplied.

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324	Royal College of General Practitioners	47	Full	19	8	In 2011, 29% of deaths were from cancer: http://publications.cancerresearchuk.org/downloads/Product/CS_REPORT_MORTALITY.pdf	We have changed the text to '....more than a quarter...'
325	Royal College of General Practitioners	48	Full	21	42	It is felt that most cases of mesothelioma (97% of cases in men and 83% in women) are related to asbestos exposure: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/Mesothelioma/risk-factors/	Thank you for this information. Recommendation 1.1.5 has been amended to include asbestos exposure.
326	Royal College of General Practitioners	49	Full	32	8	*(lines 8/9)* Non-traumatic shoulder pain is an important symptom. (5-12% of cases): http://fampra.oxfordjournals.org/content/21/6/605/T3.expansion.html This symptom is mentioned in tables on P36	The symptoms listed in the background are examples and not intended to be exhaustive or to pre-empt the recommendations. The GDG did not find any evidence suggesting that non-traumatic shoulder pain had a PPV high enough to warrant referral.
327	Royal College of General Practitioners	50	Full	45	General	Mesothelioma: It is worth stating that there is very wide geographical variation of incidence: http://www.hse.gov.uk/statistics/pdf/area8100.pdf - a fifteen-fold variation between Barrow-in-Furness and Barnsley http://www.hse.gov.uk/statistics/tables/mesoarea.xls	Thank you for this information.
328	Royal College of General Practitioners	51	Full	88	3	Should be 3-4 cases in an average full time career.	We have changed this to 2-4.
329	Royal	52	Full	366	7	*(box)* Does not mention gynae cancer – can	The list of cancer sites in our

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	College of General Practitioners					present with any one of combination of weight loss, appetite loss and DVT.	recommendation was determined by the cancers in which a PPV was reported. In recognition of the fact that other cancers can cause weight loss, we specifically used the term 'including' before the list.
330	Royal College of General Practitioners	53	Full	386	General	See comment above re: page 32	The symptoms listed in the background are examples and not intended to be exhaustive or to pre-empt the recommendations. The GDG did not find any evidence suggesting that non-traumatic should pain had a PPV high enough to warrant referral.
331	Royal College of General Practitioners	54	Full	399	General	Potential for a section of shoulder pain (non-traumatic) – should have CXR	There was no specific evidence to support including shoulder pain in a recommendation.
64	Royal College of General Practitioners	55	Full	General		I like the guidance for non-specific symptoms, feels helpful. Childrens guidance raises profile well Not sure why we are distinguishing between Hodgkins and Non-Hodgkins lymphoma as it's a pathology distinction-symptoms and signs will be the same.	Thank you At the time of constructing the review questions for this guideline, the GDG did not know if the two main types of lymphoma would have separate symptom profiles. Therefore we set two separate review questions and have maintained this separation in the guideline to ensure transparency of process. Where possible, recommendations have been combined in the symptom-based section of the guideline. In the case of NHL and Hodgkin's lymphoma, the subtle differences between the recommendations meant that this could

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						Colorectal feels very complicated with 3 different age –related criteria . Confusing for doctors and patients. I understand the varying levels of evidence and PPV but less age distinction would be more manageable.	not be done. The recommendations for colorectal cancer have been revised to make them simpler and easier to understand.
15	Royal College of Paediatrics and Child Health	1	Full	151 General	General	We think the Ovarian Cancer guidance was >18 yrs old, and therefore need to consider how to incorporate this into the all-age guideline as some of the items (e.g. bloating on/off in a 6 month old) would NOT be appropriate to send CA125 on.	We have clarified that the ovarian cancer recommendations relate to women who are 18 or older.
16	Royal College of Paediatrics and Child Health	2	NICE	General	General	Some of the guideline statements in the symptoms section are given ages and other not. This would be best done if all had an age statement with numbers (i.e. '18 and over' not just 'adult' and 'all ages' where appropriate).	We have included a definitions section in the guideline so that it is clear what the terms used in the recommendations mean, including those relating to age. Where there is evidence for specific age groups these have been included in the recommendations.
17	Royal College of Paediatrics and Child Health	3	NICE	80	1.10.2	Surely unexplained fever alone doesn't get an FBC -- presumed viral == explained perhaps.	A fever presumed to result from a virus would not be considered 'unexplained'.
18	Royal College of Paediatrics and Child Health	4	NICE	263 268 81	1.10.8 & 9	If short of breath and splenomegally/other symptoms of lymphoma (more quickly than 2 wks) we would suggest immediate investigation.	The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
19	Royal	5	NICE	42	1.1.6	This needs an age on it, as children often have an	Thank you. We have amended the

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	College of Paediatrics and Child Health			59	Thrombocytosis	enthusiastic platelet response and don't often have lung cancer.	recommendation to clarify it only relates to adults
20	Royal College of Paediatrics and Child Health	6	NICE	29 86	1.15	Safety netting with TYA - should this be different - not just 'come back' but make it much clearer; perhaps keeping the ball and arranging a review appointment and chasing up that review to make sure it's improved if they DNA (experience only & work on cancer-cases without any 'control' to balance this).	We agree with this point and consider that the issue of DNA is covered by 1.16.5.
21	Royal College of Paediatrics and Child Health	7	Full	235	Table 73	Some marked with % some not - consistency please (we are in favour of percentages it as it hammers home how small these numbers are). Why have NICE placed all of the childhood cancer tables and the bland evidence statement in every childhood cancer question bit - especially in the retino & wilms sections where there are NO data at all...?	The data presented include both the positive predictive values (in % as denoted in the column heading) and the raw numbers (denoted with "Frequency" in the column heading) that form the basis of the positive predictive values, in order to be transparent about the size of the evidence base. The childhood cancer tables are included because they show the PPVs of symptoms of any childhood cancer, of which a proportion would be expected to be Wilm's, neuroblastoma and retinoblastoma. As such they constitute the best available primary care evidence on the PPVs of symptoms in children. This was the evidence that was presented to the GDG when they agreed their recommendations and so it is included here for transparency of process. We have however removed the

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							duplication so that the evidence is only presented once.
22	Royal College of Paediatrics and Child Health	8	Full	General	General	Having discussed the guidance document with the Oncology CSAC, we believe there is a need for a separate paediatric referral guideline document. The specific comments raised by colleagues include the following: 1. The diagnoses specifically included are Wilm's (this is mis-spelled - it should be Wilms or possibly Wilms'), Retinoblastoma and neuroblastoma. Whilst it is not unreasonable to include these, it is not adequate and gives an impression that these are the only concerns. A far greater concern is the delay of diagnosis for primary CNS tumours (30% of all tumours), and other sarcomas. 2. Referral guidelines which include the two-week wait process are not useful. There is good evidence that this pathway does not work for paediatric patients. Referral of a child for suspected cancer needs to involve a telephone call today to a local paediatrician or paediatric oncologist. 3. There is no recommendation for spinal cord compression in children, as a presenting feature of spinal tumours. This is specifically excluded from the adult guideline document, and so there is a gap.	We have corrected the spelling of Wilms'. The GDG have made a separate recommendation for children for primary CNS tumours in chapter 15. We have amended chapter 18 to make it clearer where children-specific recommendations for cancers that affect both adults and children appear in the guideline. The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'. There was no evidence on spinal presentation of malignant CNS tumours in adults or children. It should be noted that benign spinal tumours are outside the scope of this guideline. Recommendation 1.10.2 is for immediate specialist assessment for unexplained petechiae. A full blood count within 48

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						4. 48 hour referral for unexplained bleeding or petechiae is inappropriately slow, although this is referred to as "Very Urgent". If a blood count is indicated, it should happen today. 5. 2 week wait for a suspected Non-Hodgkin Lymphoma is much too slow. Same day referral. 6. 2 week wait for new abnormal cerebellar or other central neurological function deficit is much too slow. Same day referral. 7. There is no clarity around ages – for example does "below 50" with PR bleeding include children?	hours has been recommended for unexplained bleeding. The recommendations have been amended to clarify that the action for children should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'. This recommendation is for adults not children. There is a separate recommendation for children to be seen within 48 hours. For all recommendations, we would expect the GP to use their clinical judgement in determine the appropriate action for a specific patient.
23	Royal College of Paediatrics and Child Health	9	Full	240 General	1.9.2 General	The Oncology CSAC have concerns about the GDGs recommendations for referral for brain tumours, which relate to the threshold for referral according to particular symptoms or signs. There is considerable discussion about the likelihood of particular signs being associated with cancer, which rather misses the point. For example, a patient with definite new cerebellar symptoms has a significant neurological abnormality, which needs to be investigated promptly. One cause is a primary CNS tumour, and if the cause is indeed a tumour, the patient is at risk of acute severe deterioration. Such a patient needs to be seen	We have documented the GDG's deliberations when agreeing the timescale for this recommendation in the Linking Evidence to Recommendations section. We would expect primary care clinicians to use their clinical judgement when applying this recommendation.

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						immediately, and probably will require an MRI within 24 hours. A second concern, which is not addressed, is the frequent difficulties of establishing whether a patient does indeed have a particular sign. Fundoscopy can be impossible in children. Recognition of a specific neurological deficit may require specific paediatric examination skills, which are not universally present. The perception that inappropriate referral casues undue stress for parents is not that seen in clinical practice. Whenever I see parents whose child has been referred to exclude a diagnosis of cancer, there is general appreciation of the GP's concerns. In contrast, on the numerous occasions when patients are seen who have been seen repeatedly without being referred, there is anger and distrust.	We accept that examination of a sick child can be difficult. We would expect primary care clinicians to use their clinical judgement in such situations. Thank you for this information.
263	Royal College of Physicians	1	General	General	General	The RCP is grateful for the opportunity to respond to the draft Suspected Cancer guideline consultation. In doing so, we wish to fully endorse the submission of the British Society of Gastroenterology (BSG). In particular, we wish to express the greatest concern regarding: • the decision to use FOBt in the decision-making algorithm. There is no evidence to justify this, and it may actually cause patient harm by providing false re-assurance due to the poor sensitivity of the test.	The evidence for the clinical and cost-effectiveness of FOB test is detailed in the guideline. Your comment does not take account of the different patient group in which FOB is being recommended. This group

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							receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations.
						• the recommendations for referral to open-access endoscopy services will require a major reconfiguration of UK endoscopy services which are currently over-subscribed and being put under increasing pressures of demand. As they stand, the recommendations on upper GI cancer will not be practical to implement given this.	All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral. The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly

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							increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral.
264	Royal College of Physicians	2	General	General	General	The RCP has also liaised with our GP Steering Group which has returned the following comments. Although the aim to diagnose cancer in an earlier stage in primary care is, of course, highly desirable we are uncertain, as presented, how these guidelines are going to be used by practising GPs. • The guideline is clearly far more complex than the previous one. There are approximately 180 symptom complexes each with variable actions that a GP using the guideline will have to be able to access and use either with the patient present or immediately afterwards. Currently, there is no tool or algorithm presented to allow this to happen. There is also no mention of the development of GP software that might prompt a GP that a threshold for appropriately urgent referral has been met. Without these, we have serious concerns regarding implementation	Thank you for this information. NICE are exploring ways that we can improve usability of the document. The creation of clinical decision support software based on these recommendations is outside the scope of this guideline.
595	Royal		NICE	41	1.1.4	Chest x-ray would be a useful test to consider in	The recommendations for lung cancer

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	College of Radiologists			65		some of these patients (non-smokers with a single unexplained chest symptom). Obviously it is a very diverse group and an 80 year old would have a much higher risk of lung cancer than a 41 year old. The RCR is doubtful as to the benefit of performing a FBC alone in the investigation of lung cancer (although it is understood that thrombocytosis may prompt further investigation, it is not spelt out in the guideline NICE version that this is the reason for performing FBC).	have been revised to make them simpler and easier to understand. The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended.
590	Royal College of Radiologists	1	NICE	General	General	Thank you to the Guideline Group for their hard work in addressing this challenging topic. A general concern is that in attempting to organise the document in terms of symptoms and signs (for understandable reasons) this has led to a great deal of repetition and has greatly reduced the readability and usefulness of the document. The second section of the document which retains the original format of organisation of recommendations by tumour site is much easier to read and is more likely to be referred to by clinicians. This section should be given priority within the document (perhaps the signs and symptoms could then be cross referenced to the relevant tumour types).	The symptom based section was included in order to make the guideline easier to use in a primary care setting. Given that primary care is the target audience for this guideline, it was placed first. However, a site-based section has also been included.
591	Royal College of Radiologists	2	Full	General	General	The RCR supports the principle of direct access to radiologists and radiological investigations by GPs. However, this is inhibited by the chronic shortage of radiologists in the UK. We have around 48 trained radiologists, whereas the equivalent figures are 92 in Germany, 112 in Spain and 130 in France. This has implications across the breadth of healthcare but one of which is that patients, including cancer patients, are waiting too long for	Thank you for your comments. We understand your concerns about capacity but implementation in secondary care and making recommendations on service provision are outside the scope of this guideline.

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						test results. On 13 November 2014, the RCR released the results of a snapshot survey it had undertaken, which showed that it is likely that about 300,000 patients are currently waiting more than a month for their x-rays to be analysed. More details can be found here: http://www.rcr.ac.uk/docs/newsroom/pdf/Backlog_survey_press_release_FINAL.pdf In addition, there is intrinsic diagnostic difficulty in the diagnosis of cancer in many patients. Most patients with cancer present to primary care with symptoms that have low or very low predictive values. Even red flag symptoms (such as rectal bleeding, dysphagia, haemoptysis and haematuria) have positive predictive values for cancer of <10% in men, and typically up to twofold lower for women and even lower for young adults and children (1%). This means that the great majority of patients with such symptoms will not have cancer. Despite the low specificity of cancer symptoms, about 80% of patients subsequently diagnosed with cancer are referred to a hospital specialist after 1 (50%) or 2 (30%) consultations. http://www.bmj.com/content/349/bmj.g7400.full.pdf+html Radiologists are always mindful of the need to balance the demand for early diagnosis with the potential harmful consequences of false positive findings which may themselves generate real harm as well as anxiety. The more tests we do, the more we will find and the greater the potential for causing harm as well as benefit.	
592	Royal	3	NICE	275	General	Whilst it is recognised that the guideline group are	The use of the term 'consider' reflects the

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	College of Radiologists			General		constrained by NICE conditions on the use of the words 'refer', 'offer' and 'consider' dependent on the strength of available evidence, there is concern that 'consider' is used inappropriately in several situations where a stronger recommendation of action is needed. The most obvious example of this is in section 1.11.2, bone sarcoma (see below).	strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
593	Royal College of Radiologists	4	NICE	41 General	General	It is concerning that the well recognised issue of limited sensitivity of chest x-ray in detection of lung cancer has not been addressed. The primary care clinician should be advised that non-specific x-ray findings or a normal chest x-ray report do not exclude lung cancer. Patients with symptoms suspicious of lung cancer should be referred on a suspected cancer pathway even if they have a normal chest x-ray (particularly those with the higher suspicion signs in section 1.1.5).	The GDG considered that if someone has persistent symptoms but a negative chest X-ray, the PPV of those symptoms would be well below the 3% threshold for a suspected cancer pathway referral. Therefore they have not recommended this. The GDG expect that such people would be covered by the recommendations on safety-netting.
594	Royal College of Radiologists	5	NICE	General	General	The RCR publishes regularly updated radiology referral guidelines – *iRefer* – which is the RCR's radiological investigations guidelines tool - http://www.rcr.ac.uk/content.aspx?PageID=995 Much of the draft NICE guidelines are in line with the RCR guidelines but there were a few areas we wished to comment on – see below.	Thank you for this information.
596	Royal College of Radiologists	6	NICE	46 66	1.1.7 1.1.10	*(p66-67)* It seems strange that exposure to asbestos has not been included in the section on mesothelioma. Surely a history of exposure should be sought and if present should trigger referral.	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking of sufficient impact on the predictive power of symptoms to require different

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							recommendations. However, it was agreed that given the high relative risk of mesothelioma in people exposed to asbestos, a known history of exposure to asbestos was likely to increase the predictive value of symptoms for mesothelioma and therefore needed to be included in the recommendation.
597	Royal College of Radiologists	7	NICE	46 67	1.1.9	Similarly to FBC in lung cancer, the reason for doing this should be spelt out, there is no mention that thrombocytosis should trigger referral (suggest adding this to section 1.1.10)	The use of a full blood count has been removed from the recommendations because it was considered superfluous given that a chest X-ray was also being recommended.
598	Royal College of Radiologists	8	NICE	67 68	1.2.5	Direct GP access to CT is not widely available and ultrasound has a very limited sensitivity for detection of pancreatic cancer in the absence of jaundice, therefore the RCR does not feel that a direct to test approach is appropriate in this group. Also, it could be argued that these symptoms are not specific for any particular abdominal cancer and referral for a specialist assessment on the suspected cancer pathway would be more appropriate.	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable. The symptom based section shows the range of recommendations that are appropriate for people with particular symptoms. GPs will need to use their clinical judgement to decide which is the most appropriate cancer to exclude first.
599	Royal College of Radiologists	9	NICE	86 & 89	1.2.12 1.2.13	These groups of patients with possible gallbladder or liver masses are diverse in their clinical characteristics and a divert referral for urgent ultrasound will not be appropriate in all. For instance a patient with a hard craggy mass would more appropriately be referred on the direct suspected cancer pathway. The RCR would suggest that both urgent ultrasound and referral on	We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. In your example, it is considered that a GP would recognise the probability of cancer and take appropriate action.

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						the suspected cancer pathway be given as options for consideration.	
600	Royal College of Radiologists	10	NICE	1599 74	1.5.14	Suggest stronger wording for this recommendation, surely a 'refer' recommendation is justified.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
601	Royal College of Radiologists	11	NICE	231 79	1.8.7	This recommendation regarding unexplained thyroid lumps is too general to be useful, new or enlarging lumps should be treated with a higher degree of suspicion.	There was insufficient primary care evidence to add qualifying terms to unexplained lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
602	Royal College of Radiologists	12	NICE	275 81	1.11.2	A stronger wording is required for this recommendation. Surely referral on the suspected cancer pathway is mandatory in this situation.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
603	Royal College of Radiologists	13	NICE	279 82	1.11.4	Again, a stronger wording is required. Referral would be mandatory if ultrasound suggests a soft tissue sarcoma.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
604	Royal College of Radiologists	14	NICE	366 83	1.13.4	Whilst DVT is associated with all malignancies, it would be a very unusual presenting feature for breast and lung cancer (unless very advanced). However, no specific consideration is given to the possibility of a pelvic mass in this group. As a minimum, the primary care clinician should be prompted to consider this and examine for a pelvic mass. Further investigation with ultrasound or referral should be considered if there are clinical	DVT only has a low PPV when single cancers are considered. Cumulatively, the PPV for cancer as a whole exceeds 3%. Whilst DVT can be a feature of gynaecological cancers, our primary care evidence did not give a PPV for this association. The list of cancer sites in our

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						features concerning for a mass.	recommendation was determined by the cancers in which a PPV was reported. In recognition of the fact that other cancers can cause DVT, we specifically used the term 'including' before the list.
605	Royal College of Radiologists	15	NICE	131	1.14.28	For suspected bone tumours, NICE recommends XR in 1.14.28 . Although this is concordant with the *iRefer* guideline for bone pain in children, P36 Imaging expert panels have, for suspected musculoskeletal tumours, recommended as indicated the use of not just XR but also MRI, US, NM and CT contained within Ca 53. A reasonable suggestion to harmonise guidance and not to miss radiolucent tumours eg telangiectatic osteosarcoma, would be for NICE to consider US and/or MRI when clinical suspicion is high but XR non-contributory.	Recommendation 1.14.28 comes from CG27. We are proposing to delete this recommendation and replace them with the new recommendations made (labelled 2015). This is the purpose of including this table in the consultation document.
606	Royal College of Radiologists	16	NICE	279 63	1.11.4 1.11.13	*(p63, 120)* For suspected soft tissue sarcoma NICE recommends US in 1.11.4 and 1.11.13 . This is at slight variance with RCR Guidance for a soft tissue mass, M10 which recommends US, MRI and XR as indicated. The difference probably lies in the definition of the lesion size, growth characteristic and deep relationships. Perhaps NICE could clarify which lumps rather than just "unexplained lumps increasing in size" (http://www.clinicalradiologyonline.net/article/S0009-9260(14)00410-3/pdf http://www.ncbi.nlm.nih.gov/pubmed/19864525 http://www.ncbi.nlm.nih.gov/pubmed/19448123 http://www.bcmj.org/article/soft-tissue-sarcomas-extremities-how-stay-out-trouble) MRI will still be the best modality for large or deep seated masses. A suggestion to harmonise guidance would be for NICE to advocate considering MRI for large or	We would expect that the clinician ordering imaging would take into account any features such as extreme size, which would warrant different action. We do not consider this needs to be specified in the recommendation.

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						deep seated masses or when US is equivocal.	
607	Royal College of Radiologists	17	NICE	130	1.14.22 1.14.24	Although the NICE and RCR recommendations (P30) are concordant for suspected neuroblastoma (1.14.22) and Wilm's tumours (1.14..24) ie US as first investigation, the comment on p130 is somewhat curious "If the child or young person is uncooperative and abdominal examination is not possible, referral for an urgent abdominal ultrasound should be considered". Perhaps this may be amended to "If abdominal examination is equivocal, referral for an urgent abdominal ultrasound should be considered."	The text that you quote comes from recommendations in CG27. We are proposing to delete these recommendations and replace them with the new recommendations made (labelled 2015).. This is the purpose of including this table in the consultation document.
608	Royal College of Radiologists	18	NICE	240 29	1.9.1	For brain cancer NICE 1.9.1, CT must be given as an alternative to MRI as in *iRefer* Ca01 as 10% of patients cannot undergo MRI.	Thank you for your comment. We have amended the recommendation.
609	Royal College of Radiologists	19	NICE	41 22		*(p22-23)* For Lung cancer, CT needed for diagnosis of early cancer- (see p11) http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/PCCL/Rapidreferralguidelines.pdf	Thank you for this information. It was not within the scope to make recommendations on what tests may assist secondary care with their evaluation.
356	Royal College of Surgeons & The Association for Cancer Surgery	1	NICE	General	General	We would recommend that the revised version is offered out for further consultation given the short consultation timeline	The standard consultation period for a guideline is 6 weeks. Due to the proximity to Christmas, the consultation period for this guideline was extended to 7 weeks. NICE does not plan to run a second consultation on this guideline.
357	Royal	2	NICE	General	General	There is already a noticeable impact on access to	The GDG considered the balance

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	College of Surgeons & The Association for Cancer Surgery					NHS services for non-cancer patients, as result of waiting time targets for cancer. The proposed changes within this guideline, more referrals to secondary care can be expected, a proportion of whom will later be found not to have cancer. Whilst agreeing that it is vital to identify cancer earlier, current care models may not efficiently fulfil the aim of this guideline and the effort to meet these targets may negatively impact on other patient groups. It is essential that resource is allocated for this "early referral" from primary care, which will result in the displacement of workload to secondary care.	between lowering the threshold for referral whilst providing more targeted referrals when forming their recommendations. The impact of this guideline on non-cancer services will be a matter for implementation. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
358	Royal College of Surgeons & The Association for Cancer Surgery	3	NICE	General	General	The current guidance has a 'one size fits all' approach to referral (except for a few rare childhood cancers), that fits with the current national cancer waiting time targets. No differentiation is made for timing of referrals for different suspected cancers. NICE should take into consideration individual cancers' behaviour and the ability to provide person centred care, when considering referral pathways, to ensure that cancers with the worst outcomes are not negatively impacted by the overall impact on the services from the quantity of referrals.	Although the behaviour of different cancers was not investigated by the guideline, the GDG were not aware of sufficient evidence to support prioritisation of one cancer over another. Any increased rate of referral to secondary care and consequent resource issues will be addressed by the tariff from NHS England. Therefore there should be no adverse impact on the timeliness with which cancer diagnoses are made.
359	Royal College of Surgeons & The Association for Cancer Surgery	4	NICE	General	General	The disease processes and service issues for children, young people and adults are different and are not easily identifiable within the current layout of this document.	Whilst we agree that the disease processes and service configuration will be different between children, young people and adults, these issues are outside the scope of this guideline.
360	Royal College	5	NICE	General	General	Identification of potential cancer remains mostly the remit of primary care services. Diagnosis,	The continued professional development of GPs is covered by recommendation

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	of Surgeons & The Association for Cancer Surgery					especially of rarer cancers, can be very difficult and lengthy as a result. There is no inclusion of any guidance on the type of training and competencies that GPs should maintain in order to achieve these goals. To avoid multiple consultations and delayed referrals, much greater flexibility in targets for harder to diagnose cancers and perhaps earlier access to either investigation or specialist clinical opinion would augment that.	1.16.1. NICE will also develop a Quality Standard following publication of this guideline. National cancer targets are outside the remit of this guideline.
361	Royal College of Surgeons & The Association for Cancer Surgery	6	NICE	General	General	Rare tumours represent a serious problem, affecting 20-30% of the whole cancer population and require treatment at specialised centres to be seen by those with the skill to manage their care. There is no differentiation within this guideline between the management of more common and rarer cancers, this is not achievable within primary care for the GP, rather for surgeons who treat them – it can only be solved by creating awareness and vigilance among Surgical Oncologists who should be updated and ready to suspect an unusual cancer.	The scope of the guideline is the referral of people suspected of having cancer. The management of cancer is beyond our scope. The continued professional development of GPs is covered by recommendation 1.16.1
362	Royal College of Surgeons & The Association for Cancer Surgery	7	NICE	240 29	1.9.1 18	Considering an urgent direct access MRI scan of the brain (within 2 weeks) to assess for brain or central nervous system cancer in adults with progressive, sub-acute loss of central neurological function, opens the doors to an inundation of inappropriate primary care referrals for MRI imaging of the CNS and both the imaging time and the facilities for reporting will have to be funded. Repeated audits across the UK have previously shown the 'hit rate' of referrals by primary care for CNS tumours is very low; 50% of referrals turn out to be migraine headache. With even fewer	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer

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						tumours. Only 40% of patients with brain and CNS tumours have a headache as part of their presentation. With current diagnostic rates through A&E running at >70% for Brain and CNS tumour vs >50% for most other cancers there does clearly need to be improvement in early diagnosis, but the implied load on both imaging and current clinics will be heavy and will need support.	out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
363	Royal College of Surgeons & The Association for Cancer Surgery	8	NICE	240 29	1.9.1 18	It is the 'consider' element in the text that is the weakest element and hence the referrals will flounder on this. In addition to the acute obvious symptoms of seizure hemiplegia, aphasia etc. we would favour a more specific set of statements along the lines 1. All patients with new headache symptoms lasting longer than 10/7 should have an MRI. 2. All patients with existing headache symptoms with new features lasting more than two weeks should have an MRI. 3 All patients with more than one progressive neurological symptom attributable to the CNS should have an MRI. This would ensure that the intent of the revision of these guidelines moves from the hopeful to the deliverable earlier diagnoses. Although this gives a more specific framework for GP's to work on, there may be training issues with regards to method and frequency of examining patients neurologically in primary care.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. The continued professional development of GPs is covered by recommendation 1.16.1 in the short version.

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364	Royal College of Surgeons & The Association for Cancer Surgery	9	NICE	240 29	1.9.1 18	The adult recommendation may stretch some radiology services initially but investment in increasing numbers of MRIs done sooner rather than later may provide more cost effective and productive in terms of picking up tumour patients earlier than the sudden expansion in the number of neurologists doing "two week wait headache clinics" that the last IOG brought (and which from our network's point of view has not been a source of newly diagnosed tumour patients).	Thank you
365	Royal College of Surgeons & The Association for Cancer Surgery	10	NICE	224 26	1.8.2 26	*(lines 26-31)* Metastatic neck nodes are not a common sole presenting sign of laryngeal cancer and so any unexplained neck node at any age should be considered potentially malignant although it is more likely to represent a haematological malignancy or an oropharyngeal cancer. With the rise in HPV driven tumours in H&N an age cut off of 45 years or over seems inappropriate.	As documented in the Linking Evidence to Recommendations section that accompanies the recommendations on laryngeal cancer, the GDG considered that laryngeal cancer is extremely rare in people below 45. Consequently they agreed that the PPV of unexplained lump in the neck in those under 45 were likely to be below 3% and therefore did not warrant a suspected cancer referral.
366	Royal College of Surgeons & The Association for Cancer Surgery	11	NICE	228 26	1.8.4 32	*(lines 32-38)* This recommendation seems to advocate a further step in the diagnostic pathway. Presumably a dental surgeon who has assessed a lesion as likely to be a cancer will already have referred the patient through a 2 week wait system rather than referring the patient to their GP for onward referral.	Whilst we acknowledge this may introduce some delay, the GDG agreed that reduction in unnecessary referrals to cancer services resulting from lesions being seen by a more expert clinician, outweighed any risks associated with a short delay.
367	Royal College of Surgeons & The Association for	12	NICE	228 26	1.8.3 39	*(lines 39-46)* This appears to suggest that the initial referral for a lesion that the GP feels is suspicious, should be to the community dental service for assessment. This seems to me to be an unnecessary step which will lead to diagnostic delays. The community dental service will not treat any of the cancers that are identified and so this	Whilst we acknowledge this may introduce some delay, the GDG agreed that reduction in unnecessary referrals to cancer services resulting from lesions being seen by a more expert clinician, outweighed any risks associated with a short delay.

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	Cancer Surgery					will cause treatment delays. It would be more appropriate for the GP to refer direct to a 2 week wait clinic. If an oral head and neck cancer is suspected then the patient should be referred as per 2 week wait criteria to a head and neck oncology service rather than to a community dentist.	
368	Royal College of Surgeons & The Association for Cancer Surgery	13	NICE	147 71	1.4.1 20	*(lines 20-23)* "unexplained breast lump" is an inappropriate term, as the lobular structure of the mammary gland physiologically presents with lumps – it should be rephrased as "unexplained and suspicious breast lump"	We would expect primary care professionals to exercise their clinical judgement in applying these recommendations
369	Royal College of Surgeons & The Association for Cancer Surgery	14	NICE	147 71	1.4.1 20	*(lines 20-23)* Would strongly encourage deleting ""with or without pain" – this is because 80% referrals to the breast clinic are due to pain – pain is not a specific sign of breast cancer – the misleading association of pain and breast cancer should be cleared out of the referral guidelines	We did not wish to discourage the referral of painful breast lumps. We do not have a recommendation for referral solely on the basis of breast pain.
370	Royal College of Surgeons & The Association for Cancer Surgery	15	NICE	275 63	1	*(lines 1-5)* Would strongly advise rewording of this paragraph, which advises the use of further imaging when a patient suspected of a bone sarcoma has already been sent for an x-ray which confirms the suspect – this is for tertiary centres to take action.	We have swapped the order of the recommendations on bone sarcoma to avoid any misunderstanding.
371	Royal College	16	NICE	37		*(p37, 38, 40)* Specifying that penile (page 37) and testicular cancers (page 40) affect men, as well as	This is the terminology used by NICE to ensure a consistent approach across the

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	of Surgeons & The Association for Cancer Surgery					erectile dysfunctions (page 39) does not seem necessary.	guideline.
372	Royal College of Surgeons & The Association for Cancer Surgery	17	NICE	220 38	7	*(lines 7-18)* Basal Cell Carcinoma. A 2-week referral for all potential basal cell carcinomas may overwhelm the secondary care facilities currently available but it is important that suspected basal cell carcinoma are seen in a timely manner, as the waiting lists for routine referrals are often so long that the lesion has enlarged so much by the time the patient is seen in the clinic that a considerably larger operation is necessary than if the patient had been seen within 4 - 6 weeks. Also, squamous cell carcinomas can mimic basal cell carcinomas in appearance, with potentially serious results if a squamous cell carcinoma is not diagnosed early.	The guideline does not recommend a suspected cancer pathway referral for all basal cell carcinomas. We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
373	Royal College of Surgeons & The Association for Cancer Surgery	18	NICE	210 & 216 115		*(p115-118)* A lot of the previous document's advice on skin cancer is to be deleted (pages 115 - 118 of the new document) which is appropriate but it should still be emphasised that that GPs should refer patients with suspected malignant melanoma or squamous cell carcinoma and not undertake incisional or excisional biopsy.	The recommendations in this guideline for malignant melanoma and SCC are to refer. We would expect GPs to follow these recommendations and not to take an alternative course of action, such as biopsy.
110	Royal College of Surgeon	1	Full	General	General	RCSEd believes that cost implications should be included for all recommendations, along with an analysis of the impact of increased referrals on secondary care.	Formally assessing the cost implications of all recommendations was not feasible due to time and data constraints.

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	s of Edinburgh						However, a cost impact analysis was conducted that aimed to assess the costs associated with the increased referrals expected as a result of the recommendations.
111	Royal College of Surgeons of Edinburgh	2	Full	General	General	RCSEd believes that the referral system should be according to broad groupings [UGI, HPB, LGI, etc] as this would allow efficiency in the presentation of evidence and the provision of advice. We would also recommend that, rather than linking symptoms to specific cancers, a list of symptoms which warrant referral that can then be triaged in secondary care be produced.	Organisational arrangements in secondary care vary around the country. Making recommendations for the suspected cancer that is the subject of the referral, allows GPs to send the person to the right place. A section of the guideline has already been produced that focuses on symptoms. This is available in both the NICE and full versions of the guideline.
112	Royal College of Surgeons of Edinburgh	3	Full	General	General	RCSEd believes that further analysis should be done to map the impact on the diagnosing and treatment of other conditions if cancer referrals are increased. A number of investigations outlined in this document will help identify the 5% of patients with cancer, but will offer little information to those whose symptoms have another cause.	This would be outside the scope of this guideline.
113	Royal College of Surgeons of Edinburgh	4	Full	41-42 32	12	*(lines 12-13)* RCSEd believes that the recommendation that patients with a persistent cough and a normal x-ray should undergo a CT scan should be reconsidered as it will have significant cost implications, generate longer waiting times and increase the chances of unnecessary exposure to radiation for many patients.	The consultation version of the guideline did not make a recommendation for patients with persistent cough and normal X-ray to have a CT. The GDG considered that someone with persistent symptoms but a negative chest X-ray would be covered by the recommendations on safety-netting.
114	Royal College of	5	Full	96	Whole page	RCSEd believes that wet wind should be included as this is often an important symptom in the diagnosing of rectal cancer or proctitis.	The symptoms in the recommendations were derived from the evidence on PPVs. There was not evidence of a PPV high

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	Surgeons of Edinburgh						enough to warrant action in other groups.
115	Royal College of Surgeons of Edinburgh	6	Full	122	Cost-effectiveness evidence section	RCSEd believes that this section should be removed as it offers little, particularly as a barium enema is no longer advocated for investigation.	The reporting of the de novo economic analysis that was conducted for the guideline will not be removed from the report. The analysis was utilised by the GDG when making recommendations for patients with suspected colorectal cancer. The GDG were aware that the use of barium enema is being phased out. However they agreed it was important not to exclude any test that might be cost effective from the economic modelling.
116	Royal College of Surgeons of Edinburgh	7	Full	130	Colorectal cancer recommendations	*(p130-131)* RCSEd believes that these recommendations should be reconsidered as the guidance remains unclear.	We have responded to your detailed comments below.
117	Royal College of Surgeons of Edinburgh	8	Full	147	Breast Cancer	*(p141-10)* RCSEd welcomes all of the recommendations in this section.	Thank you
118	Royal College of Surgeons of Edinburg	9	Full	General	General	RCSEd welcomes all of the other recommendations not discussed above.	Thank you

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844	Royal College of Surgeons of England	1	General	General	General	1) Primary care referrals for suspected cancer are to be routed through the Community Dental Service and not through Oral Medicine or Oral Surgery tier 2 practitioners or secondary care. Apparently there has been no consultation with the Community Dental Service and additional resources would be needed if this was to be implemented 2) Medical practitioners will not be able to send in a 2 week cancer referral unless the patient has seen a dentist but the idea is that the dentist will see them at no cost! 3) Referral criteria are not good – red & white patches and speckled lesion would be a much better referral criterion than lumps	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...' We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation.
181	Royal Surrey County Hospital Foundation Trust	1	Full	General	General	A few comments regarding the 2WR/suspected cancer consultation. - In general the pick-up rate of malignancy for patients referred on the 2WR in haematology is low. There is almost an attitude of 'it's a 2WR, it won't be a cancer'... I think that is because the system is used incorrectly. Patients should only be referred if clinical suspicion is high (so it seems likely there is a malignancy), hence the request to inform the patient of the referral. It should not be used as 'screening' tool or a referral of exclusion. For patients where clinical suspicion is low, they can still be referred of course but not on the 2WR. I think this is not always understood. The system seems to frequently be used to get people seen quickly without great clinical	The remit of this guideline is to advise primary care about which patients warrant referral for suspected cancer. The arrangements used by secondary care to manage these referrals are outside the scope of this guideline. Section 1.16 in the short version makes recommendations about primary care's obligations during the referral process. We recognise that there will be challenges in implementing this guideline

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						suspicion. Part of that is the box-ticking side of the form. 'Fatigue' for instance is a box easily ticked and can make people 'qualify' for a 2WR referral, though isn't always appropriate. In my opinion screening of referrals is by far the best method of picking of 'suspected cancer referrals'. We screen all our referrals and if suspicion is high (and it's not a 2WR) we still treat it as such and get the patient up the same day. - Very frequently the box 'patient informed of referral' is not ticked. A 2WR referral is only appropriate if the patient is aware. Understandably people are concerned to not 'worry patients unnecessarily', but this referral system is designed for patients where the referrer is worried, and the patient should be too. - Finally, frequently all we receive is the standard tick box form with no accompanying letter. I feel an accompanying letter is required as the standard form does not put symptoms/findings in context (speed of onset, social factors, comorbidities).	but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. We consider that this issue is covered in recommendation 1.14.3 in the short version. We consider that this issue is covered in section 1.16 of the short version.
182	Royal Surrey County Hospital Foundation Trust	2	Full	240 General	1.9.1 General	I have looked at the relevant NICE documentation for TWR for brain SOLs in adults. No criteria reach the 3% threshold.	We acknowledge that none of the symptoms in the evidence had a PPV that met the 3% threshold. For this reason the GDG did not make any recommendations on these symptoms. The evidence available did not contain PPV values for the symptoms in recommendation 1.9.1. The GDG agree that these symptoms were likely to have had a PPV of 3% or above, on the basis of their clinical judgement.

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						One's conclusion would be TWR for this should no longer exist. There is a recommendation for direct access to MRI by GPs for progressive sub-acute loss of central neurological function. CCG need to purchase MRI wherein would have access in case the patient was referred in. The REPORTING must be very careful indeed to avoid a no. of socio-clinical pitfalls.	Thank you for your comment
183	Royal Surrey County Hospital Foundation Trust	3	Full	General	General	A referral letter with clinical history and medicines should be mandatory for a TWR referral	We consider that this issue is covered in section 1.16 of the short version.
232	Sarcoma UK	1	Full	272 General	General	Failure to refer patients with suspected sarcoma promptly for diagnosis is a well-recognised problem within the sarcoma world. It is a key factor hindering the improvement of outcomes for sarcoma patients. Sarcoma UK's evidence base of patient experiences clearly indicates that diagnostic delay is a common occurrence, combined with failure to access sarcoma specialist services. This leads to poor patient experience and poor outcomes overall for all types of sarcoma – bone and soft tissue. The sarcoma community of patients and specialists work closely together to try to improve diagnosis of suspected sarcoma. This includes the development of NICE Improving Outcomes Guidance for People with Sarcoma (2006); development of management guidelines by the British Sarcoma Group; education events for sharing best practice; published papers; national	Thank you for this information.

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						awareness campaigns; patient surveys; and through the Sarcoma Clinical Reference Group's work on service specifications for the assessment and treatment of sarcoma patients. Sarcoma UK has some significant concerns about the sarcoma content of this NICE draft guideline and the process of producing this draft guideline: 1. Failure to reference the NICE Improving Outcomes for People with Sarcoma (2006) and other relevant publications/papers in the literature search, leading to questions about the quality of the search. We question why NICE was unaware of its own previous (and extensive) work on the Sarcoma IOG, and why other established published papers were not identified through the literature search. New guidance should not be developed based on a sub-standard literature search, with no input or consultation from the sarcoma specialist community (see 2). 2. Failure to seek specialist advice from the sarcoma world – both clinicians and patients. There is excellent sarcoma clinical expertise available in specialist centres, and a professional organisation that represents sarcoma clinicians (British Sarcoma Group). In addition, a Clinical Reference Group for Sarcoma was established by NHS England, acknowledging the specific problems that exist with sarcoma patients' experience of diagnosis and accessing specialist care, and working to address these. Sarcoma UK is the main sarcoma patient organisation and has access to a wide range of patient experiences through	The description of soft tissue sarcomas in the IOG were taken from CG27. This guideline is updating CG27. No primary care evidence was found on symptoms with a PPV consistent with referral. The GDG agreed, on the basis of their clinical judgement, that it was appropriate to make the recommendations they did. The prior recommendations in CG27 were explicitly reviewed by the GDG and the new recommendations were agreed to be more appropriate. This guideline is targeted at primary care where patients suspected of having cancer are identified. Therefore it was appropriate to have a majority of primary care clinicians on the GDG. Given there were 37 separate cancer groupings to be investigated, it was unrealistic to have representation from each specialty on the group. When the GDG needed further specialist input to make their recommendation, they called on expert advice.

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						surveys, support groups and day-to-day contact with patients. We question why this wealth of sarcoma expertise was not involved in the early stages of the draft, whilst evidence was clearly sought and considered from GPs who only see a limited number of sarcoma cases. 3. Failure to reference current examples of best practice that is occurring locally in relation to sarcoma diagnostic centres. The NICE IOG recommends the establishment of local diagnostic services (under the guidance of a sarcoma MDT) that refer any confirmed diagnoses to a specialist treatment centre. Whilst this is not in place everywhere, where they do exist, they provide a cost-effective way of reducing the referral burden and improving patient experience. The experiences of these diagnostic clinics should be fully considered as part of this consultation.	Our recommendations do not specify to whom referral should be made, so we do not consider that they are inconsistent with the IOG.
233	Sarcoma UK	2	Full	275	1.11.2 11	The first recommendation should include adults. Any person with unexplained bone swelling or pain, **whatever their age**, should be referred for an x-ray. Sarcoma UK has contact with adults in the 25-30 year age group diagnosed with osteosarcoma and Ewing's sarcoma, and also older people which reflects the peak in osteosarcoma incidence in the age 75+ group. Our case studies indicate they experience the same problems with delayed diagnosis as younger patients. It is not sufficient to simply note that "it does not preclude clinicians following the same instructions for adults". Evidence from patients points to GP's lack of understanding of the symptoms of bone sarcoma.	The reason the recommendation specifies children and young people, and excludes adults, is that the anticipated PPV of this clinical presentation in adults being a bone sarcoma would be extremely low. We have amended the LETR to make this more explicit.

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						It is unlikely in practice that GP's will refer adults based on guidelines citing children only.	We would expect that primary care clinicians would use their clinical judgement in such situations
234	Sarcoma UK	3	Full	275	11	"Recommending symptoms of bone sarcoma". Much work has already been undertaken around the red flag symptoms of bone sarcoma including a consensus in the sarcoma world about the key symptoms that should trigger suspicion. Sarcoma UK's 'On the Ball' national awareness campaign, launched in 2014, provided GPs with resources, based on published evidence, to inform them about these symptoms and to help them refer appropriately.	Thank you for this information
235	Sarcoma UK	4	Full	275	1.11.2 11	Patient feedback and clinical experience indicates that levels of suspicion in general practice are not as high as the GDG seems to suggest. The second recommendation uses vague words: "consider", "if", and "suggests". This leaves it open to misinterpretation. We recommend replacing the word "consider" with "Make".	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
236	Sarcoma UK	5	Full	275	11	Bone sarcomas are rare. Therefore, it is important that the professional carrying out the x-ray is trained to recognise indications of bone sarcoma. Sarcoma UK is aware of patients who have returned to their GP multiple times following initial investigations that have overlooked clinical indications, leading to diagnosis in A & E following acute problems such as fracture.	Training in secondary care is outside the scope of this guideline.
237	Sarcoma UK	6	Full	275	11	Sarcoma UK's proposes these alternative recommendations: 1. Consider an urgent direct access x-ray (within 2 weeks) to assess for bone sarcoma in anyone with unexplained bone swelling or pain.	Thank you for your suggestions. The reason the recommendation specifies children and young people, and excludes adults, is that the anticipated PPV of this clinical presentation in adults being a bone sarcoma would be extremely low. We have amended the

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						2. Make a suspected cancer pathway referral (for an appointment within 2 weeks) for people if an x-ray suggests the possibility of bone sarcoma. 3. Where symptoms of bone pain and/or swelling persist following an x-ray, an urgent referral should be made.	LETR to make this more explicit. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
238	Sarcoma UK	7	Full	279	11	The proposed guidelines are a radical change from the current NICE IOG for People with Sarcoma which is well-established. It recommends that an urgent referral for suspicion of soft tissue sarcoma should be made if the lump is: • Greater than 5cm in diameter • Deep to fascia • Increasing in size • A recurrence after previous excision We question the evidence for making this proposed change and are concerned that this proposed guideline will undermine existing work to improve diagnosis of sarcoma for patients.	The description of soft tissue sarcomas in the IOG were taken from CG27. This guideline is updating CG27. No primary care evidence was found on symptoms with a PPV consistent with referral. The GDG agreed, on the basis of their clinical judgement, that it was appropriate to make the recommendations they did. The prior recommendations in CG27 were explicitly reviewed by the GDG and the new recommendations were agreed to be more appropriate.
239	Sarcoma UK	8	Full	279	1.11.311	The reference to an "Unexplained lump" is open to misinterpretation. Patient experiences tell us that the GP will attempt to explain away the lump (eg haematoma, cyst, or lipoma), partly because patients themselves demand an explanation. This makes it an 'explained lump' and therefore outside the remit of this guidance.	We appreciate your concern of a potential misdiagnosis delaying investigation. However it would be inappropriate to recommend an ultrasound for all lumps that are increasing in size, so the word 'unexplained' is a sensible qualifier.
240	Sarcoma UK	9	Full	279	1.11.311	We are unaware of the extent to which the two-week access to ultra-sound diagnostics is available to general practitioners in England and Wales. For this recommendation to be viable, there must be availability to every GP practice and	Availability of ultrasound will be a matter for implementation.

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						access under two-week wait rules would need to be guaranteed by providers. All this must be explicitly understood by all practitioners.	
241	Sarcoma UK	10	Full	279	1.11.3 11	The clinical technicians undertaking ultra-sound examinations rarely see sarcomas. This is increasingly a contracted-out service which mainly focuses on obstetrics. Therefore, it is important that all technicians are receive (ongoing) training to recognise indications of soft tissue sarcoma. If this recommendation is accepted Commissioners should be required to ensure training is in place from a sarcoma MDT and that technicians are working in association with a sarcoma MDT.	Making recommendations on training for people who perform ultrasounds is outside the scope of this guideline.
242	Sarcoma UK	11	Full	279	1.11.4 11	Re recommendation 2 (suspected cancer pathway referral), the word "consider" is too vague. We believe that a suspected cancer pathway referral to a sarcoma specialist centre should always be made for ultrasound findings that suggest soft tissue sarcoma.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
243	Sarcoma UK	12	Full	279	11	Sarcoma UK proposes the following statement to replace both recommendations: "Make a suspected cancer referral (within 2 weeks) to assess for soft tissue sarcoma in people with an unexplained lump that is increasing in size or is greater than 4cm in adults or 2cm in children." **Note:** there has been a collective effort within the sarcoma world to improve the referral standards of primary care, including the establishment of a guiding principle that a lump the size of a golf ball (approx. 4cm) needs a referral. This message has been well received by GPs via Sarcoma UK's national and regional campaigns. This draft guideline should complement the current work that is taking place around this issue rather than taking an alternative approach.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version. As we have detailed in the introduction, we have used primary care evidence to formulate our recommendations. The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that because of the highly selected populations in secondary care diagnostic

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							studies, it was not appropriate to extrapolate from them to develop recommendations for a guideline targeted at a primary care population. There was insufficient primary care evidence to add qualifying terms to lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
244	Sarcoma UK	13	Full	General	General	**In summary**, Sarcoma UK's view is that the GDG's draft guideline (for sarcoma) will not improve outcomes for sarcoma patients, and will only increase the poor level of experience of sarcoma patients (as indicated in the National Cancer Patient Experience Survey 2014 where sarcoma patient experience is one of the worst of all cancer types).	We disagree and have responded to your detailed comments above.
245	Sarcoma UK	14	Full	General	General	This draft guideline has failed to take into account: • Published evidence on diagnostic experience • NICE IOG for People with Sarcoma which has an extensive section on diagnosis • The experience of existing regional diagnostic centres • The experience of the sarcoma specialist community • The experience of the sarcoma patient community	The function of this guideline is to identify which patients require referral for suspected cancer on the basis of their symptoms and other findings. Evidence that is not from primary care and not concerned with the predictive power of symptoms or findings is unhelpful.
246	Sarcoma UK	15	General			Sarcoma UK believes that the poor standard of this work and any implementation of its recommendations is likely to put patients at risk.	NICE guidelines are developed in accordance with a robust methodology to ensure they are of a sufficiently high standard. This guideline has been developed in line with this methodology so we disagree with your assertion that it is of a 'poor standard' and is likely to put patients at risk.

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122	Scibase	1	Full	203	13, particularly 13.1	§13.1 summarises the clinical literature on malignant melanoma of the skin in respect of two clinical questions: 1. what is the risk of MM in patients presenting in primary care with symptom(s)? 2. which investigations of symptoms of suspected malignant melanoma should be done with clinical responsibility retained by primary care? With respect to the first question, the evidence review refers to the following papers: • Emery, J.D., Hunter, J., Hall, P.N., Watson, A.J., Moncrieff, M., Walter, F.M. (2010). Accuracy of SlAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. BMJ Dermatology, 10:9. • Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C, Norris, P., Walls, J., Johnson, M., Kinmonth, AL, Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in pnmary care: randomised controlled trial. BMJ, 345:e4110. • Walter, F.M., Prevost, A.T., Vasconcelos, J., Hall, P.N., Burrows, N., Morris, H.C., Kinmonth, Ai., Emery, J.D. (2013). Using the 7-point checklist as a diagnostic aid for pigmented skin lesions in general practice: A diagnostic validation study. British Journal of General Practice, DOl: 10.33991bjgp13X667213.	Thank you for this summary of the evidence presented in the guideline

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						With respect to the second question, the evidence review refers to the following papers: • Emery, J.D., Hunter, J., Hall, P.N., Watson, A.J., Moncrieff, M., Walter, F.M. (2010). Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. BMJ Dermatology, 10:9. • Menzies. S. W., Emery, J., Staples, M., Davies, S., McAvoy, B., Fletcher, J., Shahid, K. R., Reid, G., Avramidis, M., Ward, A. M., Burton, R. C. & Elwood, J. M. (2009) Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. British Journal of Dermatoloqy, 161:1270-1277. • Rosendahl, C., Tschandl, P., Cameron, A. & Kittler, H. (2011) Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. Journal of the American Academy of Dermatology, 64:1068-1073. • Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C, Norris, P., Walls, J., Johnson, M., Kinmonth, AL, Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in pnmary care: randomised controlled trial. BMJ, 345:e4110. Emery (2010) and Walter (2012) report the results of SIAscan/MoleMate. Menzies (2009) and	

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						Rosendahl (2011) report the results of using dermoscopy.	
123	Scibase	2	Full	203	13, particularly 13.1	We were surprised that there is no reference in §13 to the use of electrical impedance spectroscopy (EIS) using Nevisense in the diagnosis of suspected skin cancers. The key relevant papers are: • Aberg P, Birgersson U, Elsner P, Mohr P, Ollmar S. (2011). Electrical impedance spectroscopy and the diagnostic accuracy for malignant melanoma. Experimental dermatology, 20(8):648-52. PubMed PMID: 21539620. • Mohr P, Birgersson U, Berking C, Henderson C, Trefzer U, Kemeny L, et al. (2013). Electrical impedance spectroscopy as a potential adjunct diagnostic tool for cutaneous melanoma. Skin research and technology : official journal of International Society for Bioengineering and the Skin, 19(2):75-83. PubMed PMID: 23350668. • Malvehy J, Hauschild A, Curiel-Lewandrowski C, Mohr P, Hofmann-Wellenhof R, Motley R, et al. (2014). Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multicentre, prospective and blinded clinical trial on efficacy and safety. The British journal of dermatology, 171(5):1099-107. PubMed PMID: 24841846	Thank you for providing these references. Electrical impedance spectroscopy was not included in this review question. Therefore the evidence on it has not been appraised and we are not able to make any recommendations.
124	Scibase	3	Full	203	13, particularly 13.1	The clinical performance of EIS is good. • In an initial training study with a prototype device (n = 495 lesions), Aberg et al reported a sensitivity to MM of 95% and a specificity to MM of 49%.	Thank you for providing these references. Electrical impedance spectroscopy was not included in this review question. Therefore the evidence on it has not been appraised and we are not able to make any recommendations.

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						• In a subsequent training study with the current device (n = 1300 lesions), Mohr reported for one algorithm a sensitivity for MM of 98.1%, for non-melanoma skin cancer 100%, and for dysplastic nevus with severe atypia 84.2%. Overall specificity for clinically significant lesions was 23.6%. For another algorithm, Mohr reported a sensitivity for MM of 99.4%, for non-melanoma skin cancer 98.0%, and for dysplastic nevus with severe atypia 93.8% (60/64). Overall specificity for clinical significant lesions was 24.5%. • In the pivotal study (n = 2416 lesions), Malvehy et al. report a sensitivity of 96.6% and specificity of 34.4% for MM, and a sensitivity of 100% for nonmelanoma skin cancer. Note that the lesions included in the study were all atypical lesions excised due to a clinical suspicion of melanoma. The study physicians has – per definition and study design – specificity of 0% on the same lesions. Thus Nevisense specificity of 34.4% refers to lesions that are selected for excision (or similar) and thus represents the potential reduction of unnecessary excisions.	
125	Scibase	4	Full	203	13, particularly 13.1	Although the three studies listed above (Aberg (2011), Mohr (2013), and Malvehy (2014)) report the results of EIS (using Nevisense) in a dermatological clinic setting rather than a primary care setting, note that the participating clinicians in the study were blinded to any device output: the study results are therefore a reflection of the performance of the device itself, irrespective of the physician speciality performing the measurement.. The GDG should note that in some countries dermatologists work in both primary and secondary settings.	Electrical impedance spectroscopy was not included in this review question. Therefore the evidence on it has not been appraised and we are not able to make any recommendations.

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						Use of the device requires a three-hour training session. The device can be used by a trained nurse. At a capital cost of €3,500 and a disposable cost of €35 per patient (up to 10 lesions), Nevisense is potentially appropriate for use in general practice. NeviSense is designed to be used where the clinical diagnosis of MM is uncertain. The results are available immediately allowing the GP to make a decision to excise the tumour or refer the patient. With an NPV of 98%, Nevisense provides valuable guidance that a lesion does not need to be excised or referred for a dermatologist opinion. Based on reported study results, the use of Nevisense is expected to improve the appropriateness of GP referrals, decreasing the number of referrals while referring all patients who need the clinical expertise of a dermatologist. The use of Nevisense is also expected to improve the appropriateness of excision in general practice. Reducing pressure on dermatology outpatients, increasing efficiency, decreasing costs, and providing services in primary care when possible are widely recognised policy objectives and managerial concerns and is consistent with NICE guidance.	
126	Scibase	5	Full	203	13, particularly 13.1	We suggest that it would be helpful to include the literature on EIS in the brief evidence review, and the listed references, in §13. On this basis, the GDG may wish to review the recommendations about suspected melanoma on page 400 of the consultation draft.	Electrical impedance spectroscopy was not included in this review question. Therefore the evidence on it has not been appraised and we are not able to make any recommendations.

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53	Sheffield Teaching Hospitals NHS Foundation Trust	1	NICE	210 37	1.7.1 15	The reference to referral for melanoma being indicated if dermatoscopy suggests melanoma is very vague and takes no account of diverse opinions about the use of dermatoscopy as it makes no reference to what features should be regarded as suggestive of melanoma. Dermatoscopy is a technique requiring considerable training and experience for reliable use. In addition to the high probability of many inappropriate referrals resulting from inexpertly performed dermatoscopy, such a recommendation from NICE could very well have the effect of encouraging people with little knowledge or experience of dermatoscopy to place undue reliance on it and consequently failing to refer appropriate melanoma cases.	Thank you for this comment. Recommendation 1.7.1. does not recommend dermatoscopy, but acknowledges that some primary care clinicians use it. The recommendation covers what to do when dermatoscopy suggests malignant melanoma.
54	Sheffield Teaching Hospitals NHS Foundation Trust	2	NICE	198 37	1.6.11 38	The description of symptoms of the foreskin or glans penis that might be associated with cancer is hopelessly vague, making no distinction between itch or redness which, alone, are low risk symptoms and lump, ulceration or persistent bleeding which are higher risk symptoms.	We would expect primary care clinicians to use their clinical judgement when applying these recommendations.
55	Sheffield Teaching Hospitals NHS Foundation Trust	3	NICE	220 38	9	The suggestion that suspected basal cell carcinoma should be eligible for 2 week wait referral with such a vague statement about concern that a delay may have an unfavourable impact is inadequate because already, far too many cases of basal cell carcinoma which do not need urgent treatment are being referred inappropriately as 2 week wait cases. If such a modification is to be introduced, it should at least be qualified by reference to mention of potentially relevant lesions being situated in close proximity to vital structures such as the eye or nose.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not

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						The two week wait system was intended to reduce cancer mortality which is not a significant consideration for BCC. However, increased numbers of unnecessary 2ww referrals for BCC will prejudice the timely treatment of patients with severe inflammatory skin diseases by concentrating clinical resources on this perversely prioritised activity.	included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.
56	Sheffield Teaching Hospitals NHS Foundation Trust	4	NICE	217 38	21	A guideline that gives no more than the 'advice' proposed in this section represents a total failure to address the principal objective of the document as it gives the absurd impression that no clinical features can be identified that are indicative of squamous cell carcinoma of the skin. It is unclear what is the point of the proposed statement made and is quite unhelpful to anyone seeking information about which cases to refer.	The GDG did not wish to try and describe SCCs because there is considerable variability and considered that there was a risk of false reassurance. We would expect primary care clinicians to use their clinical judgement when applying this recommendation.
57	Sheffield Teaching Hospitals NHS Foundation Trust	5	NICE	38	26	The heading 'vulval ulceration' clearly needs to be reworded or reconsidered if this category is also to include lump or bleeding as mentioned in the detail.	Thank you. We have changed the heading to 'vulval symptoms'
231	Society of British	1	Full	240	1.9.1 12	In principle the SBNS agrees with the recommendations. On page 240, line 12 the	The GDG considered that the majority of people referred urgently for certain

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	Neurological Surgeons					recommendation regarding referral of adults for a direct access MR Brain scan within 2 weeks will impose a huge burden on existing radiology capacity for imaging. Therefore, financial resources will be required to provide this additional service. We agree with the recommendation regarding the 48 hour appointment for children and young adults.	cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
24	Target Ovarian Cancer	1	Full	151	7	Listed symptoms should also include urinary symptoms i.e. increased urinary urgency and/or frequency; this would better reflect the guidance in this document and CG122.	The symptoms listed in the background are examples and not intended to be exhaustive or to pre-empt the recommendations.
25	Target Ovarian Cancer	2	Full	151	7	Abnormal vaginal bleeding is listed as a possible ovarian cancer symptom, however, there is no guidance given in the document on appropriately managing women presenting with this symptom.	The symptoms listed in the background are examples and not intended to be exhaustive or to pre-empt the recommendations. The recommendations on ovarian cancer

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							have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes.
26	Target Ovarian Cancer	3	Full	151	15	The final bullet point in the recommendations section offers safety netting advice, however, the information is vague and would benefit from being enhanced with the information from the Ovarian Cancer Quality Standard, QS18, specifically Quality Statement 3 *"Women with normal CA125, or raised CA125 but normal ultrasound, but no confirmed diagnosis but continuing symptoms, are reassessed by their GP within one month"*	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes.
27	Target Ovarian Cancer	4	Full	390	3	Recommendations are made for abnormal blood test results pertaining to a possible ovarian cancer, however, the safety netting advice could be further enhanced with the information from the Ovarian Cancer Quality Standard, QS18, specifically Quality Statement 3 *"Women with normal CA125, or raised CA125 but normal ultrasound, but no confirmed diagnosis but continuing symptoms, are reassessed by their GP within one month"*	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.
28	Target Ovarian Cancer	5	Full	General	General	We welcome the updates to this guideline, in particular the recommendations regarding suspected ovarian cancer. We feel the updated guidance will give primary care clinicians clearer information helping them better recognising and managing suspected ovarian cancers. Clearer guidance will give women with ovarian cancer a much better chance of obtaining an appropriate diagnosis in a timely fashion.	Thank you
29	Target	6	Full	General	General	We feel that the approach taken in this guideline to	Thank you

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	Ovarian Cancer					organising recommendations by symptom as well as cancer site will help clinician in their day-to-day practice by making information and guidance more accessible to them, and perhaps prompting them to consider a diagnosis they may not have otherwise contemplated.	
624	Taunton & Somerset NHS Foundation Trust	1	Full	General	General	The recommendations frequently are worded 'consider a suspected cancer referral', rather than providing a clear directive to refer under specific criteria. This puts GPs in a difficult situation and poses the risk of secondary care being inundated with suspected cancer referrals if GPs are not provided with more specific guidance. If a GP is being asked to 'consider' a suspected cancer referral, they will need to be provided with clear guidelines regarding what additional investigations or treatments should be carried out in primary care before referring to secondary care under a suspected cancer pathway. The term 'consider' is too open and likely to have a detrimental impact on the ability of hospital providers to see and treat cancer patients promptly.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
625	Taunton & Somerset NHS Foundation Trust	2	Full	General	General	Many of the recommendations suggest direct GP access to ultrasound; this is already in place in our Trust but recognised that it is a modality already under pressure. If volume increases this would put the service under extreme pressure so GPs would need clear guidelines on when this is appropriate if not to swamp the system and delay ultrasounds for the patients that really need them quickly	We anticipate that this guideline will clarify which patients should be referred for open access ultrasound. Implementation in secondary care is outside the scope of this guideline.
626	Taunton & Somerset NHS Foundati	3	Full	26	Recom m-endatio ns (patient	The recommendation to explain to people that they are being referred to a cancer service is felt to be crucial; if this is not explained patients are less likely to commit to an appointment within 2 weeks (both putting themselves at risk and putting	Thank you for your support of recommendation 1.14.3.

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	on Trust				Info & support)	additional pressure on hospital Trusts trying to meet their targets). Also it is poor experience for a patient to be informed over the telephone by a scheduler or by a receptionist on arrival that they are booked into a suspected cancer clinic. This should be mandatory information that a GP is expected to provide.	
627	Taunton & Somerset NHS Foundation Trust	4	Full	41-42 33	16	Definitive diagnosis requirement should also include radiologically guided biopsy	Thank you for this information. This guideline is about the referral of people with suspected cancer from primary care. Definitive diagnosis in secondary care is outside the scope of this guideline.
628	Taunton & Somerset NHS Foundation Trust	5	Full	33	17	Sputum cytology is rarely used due to low sensitivity and specificity	Thank you. We consider that our current text reflects this.
629	Taunton & Somerset NHS Foundation Trust	6	Full	42	1.1.4 Recom m-endatio ns (lung)	There is felt to be little value in a full blood count alone for evaluating non-smokers with unexplained symptoms such as cough or breathlessness. A chest X-ray should also be considered	The PPVs of these single symptoms in non-smokers are very low. The purpose of the FBC is to identify any thrombocytosis. These symptoms in combination with thrombocytosis have PPVs that would warrant further investigation.
630	Taunton & Somerset NHS Foundation Trust	7	Full	45	16	Definitive diagnosis requirement should also include radiologically guided biopsy	Thank you for this information. This guideline is about the referral of people with suspected cancer from primary care. Definitive diagnosis in secondary care is outside the scope of this guideline.
631	Taunton & Somerset NHS	8	Full	46	Recom mendati ons (mesoth	There is no advice provided about asbestos exposure which should also be taken into consideration when assessing patients' symptoms	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same

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	Foundation Trust				el-ioma)		symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking of sufficient impact on the predictive power of symptoms to require different recommendations. However, it was agreed that given the high relative risk of mesothelioma in people exposed to asbestos, a known history of exposure to asbestos was likely to increase the predictive value of symptoms for mesothelioma and therefore needed to be included in the recommendation.
632	Taunton & Somerset NHS Foundation Trust	9	Full	60	Recom-endations (oesoph & stomach)	*(p60, 80)* Direct GP access to endoscopy carries significant risks and would need careful planning and strict control. Currently at our Trust GPs have indirect but nevertheless fast-track access to endoscopy via the fast-track referral route, which means that patients are properly triaged before proceeding. Any increased access would need to be properly governed and tracked with very strict guidelines for GPs on when (if ever) this would be appropriate.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. We consider that the recommendations in this guideline provide clear guidance on when direct access endoscopy is appropriate.
633	Taunton & Somerset NHS Foundation Trust	10	Full	60	1.2.1 Recom-endations (oesoph)	Age restriction for referring patients with weight loss and pain, reflux or dyspepsia (aged 55 & over) may exclude some cases that should be referred	The age threshold was supported by the primary care evidence that was available.
634	Taunton & Somerset NHS	11	Full	67	1.2.4 Recom-endatio	Age restriction for referring patients with jaundice (aged 40 & over) may exclude some cases that should be referred	There was no evidence that the PPV of jaundice in people younger than 40 was high enough to warrant action. It is not appropriate to estimate the likely PPV of

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	Foundation Trust				ns (pancreatic)		jaundiced patients below the age of 40 from the available evidence.
635	Taunton & Somerset NHS Foundation Trust	12	Full	67	1.2.5 Recommendations (pancreatic)	Suggesting direct access to CT for very general symptoms of diarrhoea, back pain & constipation would certainly increase the demand for direct-access CT which would need to be very strictly controlled in order not to swamp the system. Again GPs would need clear guidelines on when direct access is appropriate	We consider that our recommendations provide clear guidance on when direct access CT is appropriate. Dealing with any increased demand resulting from these recommendations will be a matter for implementation.
636	Taunton & Somerset NHS Foundation Trust	13	Full	80	Recommendations (stomach)	Age restriction on all of the recommendations under stomach cancer may exclude some cases that should be referred	The age threshold was supported by the primary care evidence that was available.
637	Taunton & Somerset NHS Foundation Trust	14	Full	130	1.3.1 1.3.3 Recommendations (colorectal)	Advice to refer patients with 'unexplained rectal bleeding' or 'unexplained changes in bowel habit' is not felt to be specific enough. GPs will need guidance on what should be considered 'unexplained' & what other investigations should be carried out prior to referring to secondary care	There was insufficient primary care evidence to add qualifying terms to rectal bleeding or change in bowel habit. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
638	Taunton & Somerset NHS Foundation Trust	15	Full	131	1.3.5 Recommendations (colorectal)	New recommendation to refer people with unexplained weight loss and abdominal pain is likely to have a large impact on referral rates to secondary care (increased numbers) and (again) GPs will need guidance on what should be considered 'unexplained' & what other investigations should be carried out prior to referring to secondary care	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. We would expect primary care clinicians to exercise clinical judgement when applying these recommendations.
639	Taunton & Somerse	16	Full	131	1.3.6 Recomm-	Testing for occult blood in faeces is not felt to be helpful or necessary	The evidence for the clinical and cost-effectiveness of FOB testing is detailed in the guideline.

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	t NHS Foundation Trust				endations (colorectal)		Your comment does not take account of the different patient group in which FOB is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
640	Taunton & Somerse	17	Full	131	1.3.9 Recom m-	Advice to 'offer' a digital rectal examination is not specific or sufficiently directive. GPs should be routinely digitally examining patients if referring on	The recommendation on digital rectal examination for colorectal cancer has been deleted.

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	t NHS Foundation Trust				endations (colorectal)	a suspected colorectal cancer pathway	
641	Taunton & Somerset NHS Foundation Trust	18	Full	147	1.4.2 Recom-endations (breast)	Age restriction for referring patients with nipple retraction (i.e. 50 & over) may exclude some cases that should be referred	The age threshold for nipple changes was based on the evidence in Walker et al. and the clinical experience of the GDG (as documented in the Linking Evidence to Recommendations section) If someone presented with these symptoms under 50, we would expect the GP to use their clinical judgement.
642	Taunton & Somerset NHS Foundation Trust	19	Full	147	Recom-endations (breast)	There is no advice in the guidance regarding breast pain. As breast clinics are currently inundated with benign breast pain, suggestion that women with breast pain under 30 with no other breast symptoms and signs should **not** be referred to breast clinics, or at least be excluded from 2 week wait for clinic appt.	In order to make a recommendation not to do something, the GDG would have needed strong evidence that this would not result in harm. Such evidence was not available.
643	Taunton & Somerset NHS Foundation Trust	20	Full	180	1.6.4 Recom-endations (bladder)	Age restriction for referring patients with visible haematuria (i.e. 45 & over) may exclude some cases that should be referred – suggestion that visible haematuria at any age should be referred if infection has been excluded	The age thresholds in the recommendations were derived from the evidence on PPVs. There was no evidence of a PPV high enough to warrant action in the younger age groups you mention. In the case of a patient with visible haematuria who was under 45 we would expect primary care clinicians to use their clinical judgement when applying this recommendation.
644	Taunton & Somerset NHS Foundation Trust	21	Full	220	1.7.5 Recom-endations	GPs should be given more guidance on what are the high-risk areas whereby a delay 'may have an unfavourable impact' i.e. ears, noses and eyes	The GDG did not include a list of potential sites in this recommendation as they were concerned that any such list could not be exhaustive. Consequently there was a risk that potentially relevant sites could be missed because they were not

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					(BCCs)		included in the recommendation. Recommendations in the NICE guidance on improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) provide greater clarity on the definition of a low-risk BCCs.
645	Taunton & Somerset NHS Foundation Trust	22	Full	224	1.8.1 Recom-endations (laryngeal)	Definition of 'persistent' hoarseness needs to be given e.g. suggest a timescale of 6 weeks	There was insufficient primary care evidence to add qualifying terms to hoarseness in this instance. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations. A definition of persistent is included in the guideline.
646	Taunton & Somerset NHS Foundation Trust	23	Full	224	1.8.2 Recom-endations (laryngeal)	For patients with unexplained lumps in the neck, an idea of time frame would be helpful e.g. an unexplained lump that has not resolved within 3 weeks	There was insufficient primary care evidence to add qualifying terms to neck lump. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.
647	Taunton & Somerset NHS Foundation Trust	24	Full	240	1.9.1 Recom-endations (brain)	Although numbers are likely to be small, direct GP access to MRIs for suspected brain or central nervous system cancers could put this service under pressure and again would need to be strictly controlled	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer

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							out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
648	Taunton & Somerset NHS Foundation Trust	25	Full	245	1.10.1 Recom-endations (leukaemia)	Advice to 'consider a very urgent full blood count' to assess for leukaemia is not felt to be strong enough. This should be routine for patients with the outlined symptoms regardless of age	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
649	Taunton & Somerset NHS Foundation Trust	26	Full	247	1.10.1 Recom-endations (myeloma)	Plasma viscosity tests are not considered to be helpful or necessary	We are surprised at this comment, as there is supporting evidence in the cited paper, and viscosity is generally accepted to be very abnormal in myeloma.
650	Taunton & Somerset NHS Foundation Trust	27	Full	263	Recom-endations (lymphomas)	*(p263, 268)* Age of patient should also be taken into account – with adolescents with unexplained neck lumps being a particular high risk area that should be referred to secondary care as a suspected cancer referral	The GDG has made recommendation for young people with unexplained lymphadenopathy (which would include cervical lymphadenopathy) to be referred on a suspected cancer pathway. For children, more urgent action is

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							recommended.
651	Taunton & Somerset NHS Foundation Trust	28	Full	306	Recom-endations (paeds)	It is suggested that urgent ophthalmological assessments should be requested via paediatric cancer teams rather than straight to ophthalmology if retinoblastoma is suspected in children	This was specifically debated, and was thought to be an unnecessary step, as an ophthalmological opinion would usually be necessary. The recommendation, however, does not specify to whom the referral is made, merely the nature of the assessment. Local pathways are a matter for implementation.
652	Taunton & Somerset NHS Foundation Trust	29	Full	334	Recom-endations (paeds)	The recommendation to take account of the insight and knowledge of parents is felt to be important but the last part of the statement 'even if the symptoms are most likely to have a benign cause' should be removed as it would be impractical to advise GPs to refer children in under a suspected cancer pathway if they do not suspect cancer.	This recommendation was debated at length by the GDG. It was noted that the positive predictive value of parental concern had not been studied, but, based on their clinical experience, the GDG agreed it would be sufficiently high to warrant recommendations.
653	Taunton & Somerset NHS Foundation Trust	30	Full	366	1.13.2 Recom-endations (non site specific)	The general symptoms of unexplained weight loss, unexplained appetite loss and deep vein thrombosis should be excluded unless specific guidelines can be provided for GPs on the assessments that need to be carried out before determining which cancer is most likely. Otherwise there is a risk of GPs referring patients into secondary care (potentially to inappropriate teams) before thorough investigations that can be carried out in primary care have taken place. This would have a detrimental impact on the ability of hospital providers to see and treat cancer patients promptly.	We disagree and made a deliberate choice to include symptoms of this nature, to avoid patients with such symptoms being disadvantaged. GPs will have the experience to make investigation decisions appropriately.
405	The Brain Tumour Charity	1	General	General		In general we welcome the comprehensive approach of the guidance which addresses all age groups. In respect of brain tumours we have some concerns around the methodology (use of PPV research) used in the guidance which we are	Thank you There was no realistic alternative to the use of a risk threshold – and implicitly that was part of all previous guidance.

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						concerned may disadvantage cancers with smaller patient populations.	We have been explicit about the decisions made – and have sought to maximise equity.
						Although it can be said of several cancers the symptoms of brain tumour are diverse and in isolation can often indicate/mimic other conditions. We hear anecdotally from adult patients who have been diagnosed with a brain tumour that they often visit the GP a number of times before there is a referral , research we conducted shows that 38% of people visited their GP more than five times before being diagnosed (1) and in many cases there is no referral instead patients end up being diagnosed following an emergency presentation at A&E. Statistically we know that emergency presentations are very high in this disease group at 62% in adults (2) and 55% of children and young people are diagnosed as an emergency (3).	We consider that the recommendation for direct access imaging and the broader criteria for action should help reduce the number of people whose brain tumour diagnosis is delayed.
						We hear anecdotally that many families present repeatedly to healthcare professionals before receiving a diagnosis. We believe that raising awareness of the common signs and symptoms of brain tumour amongst the public and healthcare professionals will result in earlier presentation to GP's and quicker referral.	A lay version of the recommendations called 'Information for the public' is produced alongside the guideline.
						In children a delay in diagnosis can have significant effect on survivorship and outcomes. Delayed diagnosis of childhood brain tumours often results in an emergency presentation when children are extremely unwell. The risk of peri-operative morbidity is increased in children who present as an emergency. In the longer term, a prolonged symptom interval is associated with increased cognitive deficits, endocrinopathies and	Thank you for this information about the potential benefits of early diagnosis of brain tumours in children and young people. We consider that our recommendations will improve on the current situation. NICE has received a request to develop a clinical guideline for primary and metastatic brain tumours.

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						visual loss. Children and young people with brain tumours develop increasing numbers of symptoms and signs during the interval from symptom onset to diagnosis. The development of additional symptoms and signs during the symptom interval reflects progressive neurological damage due to either the direct effects of the tumour on the brain or raised intracranial pressure. Many children with brain tumours have life-long visual impairment, cognitive deficits and endocrinopathies (due to hypothalamic and pituitary damage), 62% of children who survive a brain tumour will be left with a life-altering, long-term disability (4). Brain tumours are the biggest cause of preventable or treatable blindness in children. (5) Childhood brain tumour survivors are 10 times more likely to suffer long term disability than well children (6). Reducing the symptom interval experienced by children diagnosed with a brain tumour should reduce the long term disability they experience. (7) The Brain Tumour Charity funded research into this issue. This underpins the award winning awareness raising campaign 'HeadSmart – Be brain tumour aware'. http://www.headsmart.org.uk/home/ The research which looks at symptom onset and routes to diagnosis has not been considered for the Suspected Cancer Guideline and we would strongly suggest that the findings of this research are included. In particular we would refer you to two published research papers looking at the presentations of childhood CNS tumours (8) and progression from first symptom to diagnosis. (8) The campaign aims to raise awareness of the signs and symptoms of brain tumour both amongst	The cited references have been checked and do not meet the inclusion criteria because they are not a primary care population.

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						the public and healthcare professionals. With the sole aim of reducing diagnosis times in children. Since the campaign launched in 2011 there has been a reduction in the diagnosis times of children from 9.3 weeks to 6.7 weeks.	
406	The Brain Tumour Charity	2	Full	233	5	*(lines 5-7)* The guideline states that brain cancer is one of the more common forms of childhood cancer (9); brain tumour is in fact accountable for 26% of all childhood cancer so although brain tumour is rare overall across all patient age groups there needs to be a balance between epidemiological evidence and a fair and appropriate resource for paediatric referral as detailed above in point 1. The HeadSmart campaign is based on the diagnosis of brain tumour in children guideline (10) which has received NICE NHS evidence accreditation. We would like to see this and the HeadSmart quick reference guide for clinicians added as an appendix to this guideline or otherwise incorporated. The quick guide can be found here on the HeadSmart website (11)	Thank you for this information. It is not part of NICE methodology to cross reference information from other organisations in their guidelines.
407	The Brain Tumour Charity	3	Full	240	1.9.2 12	In respect of the recommendations for referral we agree with the recommendation of urgent referral where brain and CNS cancer is suspected, within 2 weeks for adults and a very urgent referral within 2 days for children and young people. We are, however concerned about the sole use of the term 'loss of central neurological function' and would ask that the HeadSmart guidance for clinicians be included as an appendix here. Additionally in respect of urgent referral for Paediatric patients suspected to have Brain or	It is not part of NICE methodology to cross reference guidance from other organisations in their guidelines. We consider this is already covered by recommendation 1.16.6.

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						CNS cancer, the GP should be encouraged to state in referral that the child should receive an MRI scan, as GP likely knows family history and will have seen the progression of symptoms and the legitimate concerns of parents whereas hospital clinician will not. An MRI remains best option for diagnosis.	
408	The Brain Tumour Charity	4	NICE	29		The use of the term 'Neurological symptoms – loss of central neurological function' is not comprehensive enough. The symptoms of brain tumour are varied and often indicative of other conditions, as such we would urge the inclusion of HeadSmart Guide for clinicians as an appendix to this section.	The GDG did not wish to try and describe progressive, sub-acute loss of central neurological function because there is considerable variability and considered that there was a risk of false reassurance. NICE guidelines do not signpost to external guidance.
409	The Brain Tumour Charity	5	NICE	332 82	1.13.1	We welcome this comment as we know from our research many families present repeatedly to healthcare professionals and feel that they have had to insist that something was wrong with their child / young person for a diagnosis to be made. Families find this extremely distressing, and often say that they felt regarded as "time wasters" and "neurotic parents". (12)	Thank you for your support
410	The Brain Tumour Charity	6	General	General		References: 1. The Brain Tumour Charity - Finding a better way? Improving the quality of life for people affected by brain tumours Report of a survey of people affected by brain tumours and their carers - http://www.thebraintumourcharity.org/Resources/SDBTT/news/documents/the-brain-tumour-charity-report-on-improving-quality-of-life-final-report-dec2013.pdf 2. http://www.ncin.org.uk/publications/routes_to_diagnosis 3. The Brain Pathways Guideline: A guideline to	Thank you for providing these references. They have been checked and do not meet the inclusion criteria for the following reasons: 1) No original data presented in detail (for the patient information question) 2) Not directly relevant to any of the clinical questions in terms of outcomes. 3) Different guideline, includes no relevant unidentified or new evidence. 4) See 2)

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						assist healthcare professionals in the assessment of children who may have a brain tumour. - http://www.rcpch.ac.uk/sites/default/files/Diagnosis%20of%20Brain%20Tumours%20in%20Children%20Guideline%20-%20Full%20report.pdf 4. NCIN Routes to Diagnosis 2006-2010 Workbook, "Percentage of diagnoses by route – Children (0-14 yrs) and Teenagers and Young Adults (TYA, 15-24 yrs). Accessed at: http://www.ncin.org.uk/view?rid=2645 5. Durnian JM, Cheeseman R, Kumar A, Raja V, Newman W, Chandna A. Childhood sight impairment: a 10-year picture. Eye (2009); 24: 112-117. 5. Rahi JS, Cable N; British Childhood Visual Impairment Study Group. Severe visual impairment and blindness in children in the UK. Lancet. (2003) 362:1359-65. 6. The Brain Pathways Guideline: A guideline to assist healthcare professionals in the assessment of children who may have a brain tumour. 7. Wilne SC, Kennedy C, Jenkins A,.Grout J,.Mackie S,Koller K, Grundy R, Walker D Progression from first symptom to diagnosis in childhood brain tumours: a multicentre study (Abstract). Archives of Disease in Childhood. 2007;92 (Supp 1):A69 8. Wilne SC, Collier J, Kennedy C, Koller K, Grundy R, Walker D. Presentation of childhood CNS tumours: a systematic review and meta-analysis Lancet Oncol. 2007	5) Both 5) entries: Not a primary care population. 6) See 3) 7) Not a primary care population 8) Both 8) entries: Not a primary care population 9) We are not sure what this reference relates to 10) See 3) 11) Different guideline, includes no relevant unidentified or new evidence. 12) This paper does not meet the inclusion criteria for any of our questions either (i.e., not in an unselected, symptomatic primary care population; does not present data directly relevant the patient information or safety-netting questions either)

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						Aug;8(8):685-95. 8. Wilne SC, Kennedy C, Jenkins A,.Grout J,.Mackie S,Koller K, Grundy R, Walker D Progression from first symptom to diagnosis in childhood brain tumours: a multicentre study (Abstract). Archives of Disease in Childhood. 2007;92 (Supp 1):A69 9. 2006-2008. National Registry of Childhood Tumours/Childhood Cancer Research Group. 10. Wilne SC, Koller K, Collier J, Kennedy C, Grundy R, Walker D. The diagnosis of brain tumours in children: a guideline to assist healthcare professionals in the assessment of children who may have a brain tumour. Arch Dis Child. 2010 Jul;95(7):534-9. Epub 2010 Apr 6. - http://www.rcpch.ac.uk/sites/default/files/Diagnosis%20of%20Brain%20Tumours%20in%20Children%20Guideline%20-%20Full%20report.pdf 11. http://www.rcpch.ac.uk/sites/default/files/Diagnosing%20Brain%20Tumours%20in%20Children-%20Quick%20Reference%20Guide.pdf 12. Dixon-Woods M, Findlay M, Young B, Cox H, Heney D. "Parents' accounts of obtaining a diagnosis of childhood cancer."Lancet. 2001;357(9257):670-4	
415	University Hospital 29Birmingham NHS	5	NICE	40	General	Haematuria – visible with low haemoglobin or thrombocytosis or high blood glucose (women 55 and over)" should be referred for USS for suspected Endometrial cancer, but two paragraphs earlier (if the blood glucose) is normal, they should be reffered for suspected urological cancers.	Haematuria can be a manifestation of both endometrial and urological cancers. Therefore the indexing must reflect this.

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	Foundation Trust						
411	University Hospital Birmingham NHS Foundation Trust	1	NICE	18	General	implication of the GPs taking responsibility for getting the endoscopies is worrying	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable. The issue you describe is covered by recommendations 1.15.1 and 1.16.5 (in the short version).
412	University Hospital Birmingham NHS Foundation Trust	2	NICE	80 18	1.2.8 General	New or changed dyspepsia in over 55 yr olds seemed to have been removed (now only when associated with weight loss. This will reduce early diagnosis of UGI cancer.	This recommendation was based on primary care evidence. Meta-analysis of dyspepsia alone gave an estimated PPV of 0.65%. Consequently no recommendation for referral for this symptom alone was made.
413	University Hospital Birmingham NHS Foundation Trust	3	NICE	58	General	iron deficiency anaemia, UGI cancers seem to have been excluded. This will reduce early diagnosis of UGI cancer.	None of the six studies in our evidence review specified iron-deficiency anaemia, reporting instead 'anaemia' per se. The PPV of this symptom did not meet the threshold for a suspected cancer pathway referral.
414	University Hospital Birmingham NHS Foundation Trust	4	NICE	130 59	1.3.2	Fe deficient anaemia in under 60s (where if this is combined with weight loss a FOB is recommended)	Recommendation 1.3.2 covers patients who are over 60, not under 60 as in your comment
416	University Hospital Birmingham NHS	6	NICE	240 29	1.9.1	Considering an urgent direct access MRI scan of the brain (within 2 weeks) to assess for brain or central nervous system cancer in adults with progressive, sub-acute loss of central neurological function, opens the doors to an inundation of	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that

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	Foundation Trust					inappropriate primary care referrals for MRI imaging of the CNS and both the imaging time and the facilities for reporting will have to be funded. Repeated audits across the UK have previously shown the 'hit rate' of referrals by primary care for CNS tumours is very low; 50% of referrals turn out to be migraine headache. With even fewer tumours. However only 40% of patients with brain and CNS tumours have a headache as part of their presentation. With current diagnostic rates through A&E running at >70% for Brain and CNS tumour vs >50% for most other cancers we clearly need to do something but the implied load on both imaging and current clinics will be heavy and will need support	making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
417	University Hospital Birmingham NHS Foundation Trust	7	NICE	240 29	1.9.2	It is the 'consider' element that is the weakest element and hence the referrals will founder on this. In addition to the acute obvious symptoms of seizure hemiplegia, aphasia etc I would favour a more specific set of statements along the lines 1. All patients with new headache symptoms lasting longer than 10/7 should have an MRI. 2. All patients with existing headache symptoms with new features lasting more than two weeks should have an MRI. 3 All patients with more than one progressive neurological symptom attributable to the CNS should have an MRI. This would ensure that the intent of the revision of these guidelines	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						moves from the hopeful to the deliverable earlier diagnoses	
418	University Hospital Birmingham NHS Foundation Trust	8	NICE	29	General	6 and 7 are not mutually antagonistic as they give a very specific framework for GP's etc to work rather than leaving them to lurch between the extremes of what they interpret 'consider' to mean. But they may have to *consider* examining patients neurologically better and more frequently.	The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.
419	University Hospital Birmingham NHS Foundation Trust	9	NICE	275 279 282 General	General	Basically great that it mentions young people, but that the issues around delays in diagnosis could be beefed up. The sarcoma sections don't have enough urgency about them either in this age group.	The recommendations have been amended to clarify that the action for children (and young people where appropriate) should be 'very urgent referral (for an appointment within 48 hours) for specialist assessment'.
420	University Hospital Birmingham NHS Foundation Trust	10	NICE	General	General	Concerned that the recommendations will open the floodgates for direct access referral for scanning (CT, MRI and US) over and above what is already agreed as appropriate for direct access Imaging (which is very limited). In addition, interpretation and understanding of the reports following, for instance, brain MRI is not always straightforward.	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be

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							performed within the same time frame as tests which currently require referral. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
421	University Hospital Birmingham NHS Foundation Trust	11	NICE	General	General	Will this prompt the development of access to imaging in the primary care sector as opposed to referral in to acute Trusts?	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
422	University Hospital Birmingham NHS Foundation Trust	12	NICE	General	General	Concerns relating to the additional unmet demand crammed into a service with limited current capacity (MRI has no capacity) combined with an expectation of scan and report within two weeks.	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
423	University Hospital Birmingham NHS Foundation Trust	13	NICE	220 77	1.7.5	Concerns that allowing primary care to book BCCs as a 2ww would effectively cause a crisis and use up all of our existing capacity. It is difficult for us to distinguish how many might be referred via this pathway so if the data could be clarified that would be helpful.	We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact. We have also put the recommendation to 'consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma' as the first recommendation in this section to highlight that in most cases, only routine referral is needed.

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424	University Hospital Birmingham NHS Foundation Trust	14	NICE	220 77	General	Concern that BCCs after being seen via the proposed 2ww referral pathway are then subject to being treated in 31 days? This would also have massive implications for surgical capacity.	This guideline is about the referral of people with suspected cancer from primary care. Treatment in secondary care is outside the scope of this guideline. We have amended the recommendation to make it clearer that a suspected cancer referral should only be done if there is a particular concern that a delay in referral may have a significant impact.
425	University Hospital Birmingham NHS Foundation Trust	15	NICE	General	General	Imaging criteria - if you look at the criteria for an "urgent CT scan" there has to be a huge population within GP practices who would meet criteria such as "abdo pain with weight loss (60 and over)". It effectively is using CT abdominal scanning as a screening tool. What radiation does to the population as a whole should be taken into account. Similar applies to urgent MRI for adult head scanning as above there will be a significant population of patients meeting the criteria of "adult with progressive or sub acute loss of central neurological function" page 79.	We disagree that there would be a huge population meeting these criteria as both of the clinical presentations that you describe are relatively rare in primary care. We are recommending a CT scan in people with symptoms, therefore this is not a screening tool. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
426	University Hospital Birmingham NHS Foundation Trust	16	NICE	General	General	Imaging capacity - To meet the requirements of "urgent" requests, capacity would have to be protected within the scanner schedules in order to meet turnaround times. Likewise, in order to meet reporting turnaround time, there will need to be radiologists with job planned capacity – it should be noted that not all radiologists can report all radiology ie they are individually sub specialised – this may cause a logistical problem in allocating the appropriate expertise. It should be noted that this is set against a backdrop of a short of radiologist nationally. Without significant	We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis. National targets are outside the remit of this guideline.

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						investment, this demand will jeopardise our ability to meet the 6 and 18 week targets. Radiological reports for the more complex scanning include very detailed anatomical and physiological description and interpretation. This is particularly true for neurological scanning. Will GPs be appropriately skilled to interpret such reports and determine the most appropriate subsequent treatment pathway?	It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these reporting challenges are not insurmountable.
160	University Hospitals Bristol NHS Foundation Trust	1	Full	General	General	Where GPs are being encouraged to refer patients to providers for direct access tests such as endoscopy or radiology rather than via a conventional generic 'suspected cancer' referral, it would be helpful to have a clear indication of the timescale expectation on these and where the responsibility lies for handling any findings of the tests. Direct access systems are the right way to go but do circumvent the current two week wait referral systems which are robust in terms of safety and helping people get timely care. There is a risk of everyone thinking someone else is acting on the test results and patients getting lost if we do not have it explicitly stated. The guidance should be clear on what timescales should be adhered to for such direct access referrals (e.g. the standard 6 weeks for diagnostics or the 2 weeks for suspected cancer). There should be clear guidance for GPs on what to do if the test does indicate possibility of cancer – which would ideally be a two week wait fast track referral at that point to an appropriate service. This is the main	We have clarified in the recommendations that urgent direct access gastrointestinal endoscopy should be performed within 2 weeks. Defintions for all timescales included in the recommendations are already included in the guideline. A recommendation has been added to clarify that GPs retain responsibility for reviewing and acting up the results of the tests they have ordered. It was deemed unnecessary to make recommendations on what GPs should do if a test clearly diagnoses cancer. Where a test is suggestive but not diagnostic of cancer, we have made recommendations for further action where appropriate.

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						feasibility problem with direct access that has come up when we've locally tried to bring in more direct access, so a clear national steer from NICE would be very welcome. It is important to encourage GPs to make a 'two week wait' suspected cancer referral once they have noted an abnormal result as this is the most reliable way to get patients onto 'cancer tracking'. It also means services get the right information to assess the patient – the information needed for a full cancer assessment tends to be different from that needed for a radiology test request.	
161	University Hospitals Bristol NHS Foundation Trust	2	Full	General	General	There needs to be more consideration for where patients with symptoms that relate to more than one cancer site should be referred (several of these throughout the guidance, e.g. 'non specific symptoms', 'weight loss' etc. There is a need within cancer services nationally to consider how best to provide services for patients with vague symptoms that give rise to a suspicion of cancer – what is the optimum service for these patients to be referred to? We are doing some work with the ACE programme on this but it is challenging as the vague symptoms may well indicate a non-cancer pathology which means it is a broader issue than just cancer and we cancer specialists are not necessarily the best people to suggest a solution. We need to be clearer where patients with vague symptoms should be referred to by GPs, and national guidance on how such patients would be best served would be very helpful.	The GDG recognised the problem of symptoms potentially representing a number of possible cancer sites. The GDG considered in addition to symptoms suggestive of a particular cancer, symptoms that were suggestive of more than one cancer and symptoms that were predictive of cancer as a whole. In each instance the GDG made appropriate recommendations for symptom combinations where this was possible. The configuration of local services to manage these patients is outside the scope of this guideline.
65	University of Nottingh	1	NICE	3	45	We support the increased emphasis on a symptoms based approach to early diagnosis of cancer as opposed to an individual tumour based	We are aware of the two papers mentioned. These papers presented calculations on the risk of cancer as a

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	am					approach. However the GDG appears to have overlooked two key papers which provide a detailed analysis based on very large UK populations. These papers present prediction models for the absolute risks of cancer associated with a range of different symptoms and risk factors (such as smoking and family history) in both men and women for 12 of the commonest cancers[1 2]. The omission is a surprise since I attended the GDG meeting in Cardiff in Dec 2012 & circulated the published papers to the committee shortly after and received an acknowledgment. The algorithms are presented in these two papers (QCancer algorithms) and the accompanying web tables for men http://qcancer.org/male/QCancer-2013-Men-Tables.pdf and women http://qcancer.org/female/QCancer-2013-Women-Tables.pdf The QCancer algorithms are important since they are now integrated into EMIS Web which is the clinical computer system used by the majority of GPs. These tools readily provide absolute risks (equivalent to positive predictive values) of having any cancer as well as the risks of different cancers for patients aged 25-89, and can account for multiple symptoms, as well as important established risk factors for cancer such as age, smoking and family history. They include smooth functions of age which gives a more consistent approach rather than the absolute age thresholds given in the guideline.	whole and describe an algorithm which predicts 'cancer' and then tests the algorithm. However we were unable to use this information because our guideline was investigating the risk of symptoms for specific cancers. Where these papers did provide data for specific cancers, they were described as relative risks. We needed the data presented as either 2x2 tables for the symptoms or absolute risks for symptom/specific cancer dyads to be able to use them in this guideline. As such we were not able to use the data and these two papers were not included in the evidence base. However, a large part of the data included in these papers was included in the guideline through a series of related papers that presented the data for specific cancers. The decision not to cover the use of clinical decision support tools for the assessment of cancer risk in the guideline is documented in the Methodology section of the full guideline.

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66	University of Nottingham	2	NICE	11	5	In the draft guideline abdominal distension is listed as a possible symptom only for ovarian cancer. However the evidence from our research based on over 2 million men and women shows that abdominal distension is also associated with an increased risk of colorectal cancer in both men[1] (see Table 5[1]: adjusted hazard ratio 3.89, 95% CI 2.77 to 5.45) and women[2] (Table 5 adjusted hazard ratio 1.94, 95% CI 1.28 to 2.93) and haematological cancers in men[1] (Table 5 adjusted hazard ratio 2.32, 95% 1.31 to 4.13).	We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. The two papers you cite presented calculations on the risk of cancer as a whole and describe an algorithm which predicts 'cancer' and then tests the algorithm. However we were unable to use this information because our guideline was investigating the risk of symptoms for specific cancers. Where these papers did provide data for specific cancers, they were described as relative risks. We needed the data presented as either 2x2 tables for the symptoms or absolute risks for symptom/specific cancer dyads to be able to use them in this guideline. As such we were not able to use the data and these two papers were not included in the evidence base. However, a large part of the data included in these papers was included in the guideline through a series of related papers that presented the data for specific cancers. We note that in the companion paper on colorectal cancer (Hippisley-Cox & Coupland (2012) BJGP; DOI:10.3399/bjgp12X616346), the PPV for abdominal distension is not presented, although the symptom clearly was considered.

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67	University of Nottingham	3	NICE	13	20	Our research found that abdominal pain is also associated other cancers. For example, it is associated with an increased risk of renal cancer in men and women[1 2], cervical and uterine cancers in women[2] and prostate cancer in men[1]	We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. According to these papers (and where there was no primary care evidence, the consensus of the GDG), the risk of the cancers mentioned is below 3% for abdominal pain.
68	University of Nottingham	4	NICE	18	1	Our research found that dyspepsia is also associated with other cancers such as pancreatic cancer in both men and women where there is more than a three-fold increased risk [1 2]. This is important especially as pancreatic cancer is so difficult to spot early.	We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. We note that in the companion paper on pancreatic cancer (Hippisley-Cox & Coupland (2012) BJGP; DOI:10.3399/bjgp12X616355), the PPV for dyspepsia is not presented.
69	University of Nottingham	5	NICE	22	1	Our research found that haematemesis is also associated with other cancers such as pancreatic cancer in both men and women [1 2]. This is important especially as pancreatic cancer is so difficult to spot early.	We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. We note that in the companion paper on pancreatic cancer (Hippisley-Cox & Coupland (2012) BJGP; DOI:10.3399/bjgp12X616355), the PPV for haematemesis is not presented.
70	University of	6	NICE	23	Last section	Post-menopausal bleeding is associated with an increased risk of a range of cancers in women	We only included papers that either presented PPVs or sufficient data (i.e.,

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	Nottingham					including ovarian, cervix and breast cancer[2].	true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. None of the included papers reported the PPV of post-menopausal bleeding for the mentioned cancers and the GDG did not consider the risk to be above 3%.
71	University of Nottingham	7	NICE	24	Middle section	Rectal bleeding is also associated with an increased risk of prostate cancer[1]	We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. None of the included papers reported the PPV of rectal bleeding for prostate cancer and the GDG did not consider the risk to be above 3%.
72	University of Nottingham	8	NICE	42	Whole page	Appetite loss is also associated with ovarian cancer, this is important to highlight given the challenges around early diagnosis of ovarian cancer[2]	The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.
73	University of Nottingham	9	NICE	36644	1.13.4 Bottom section	DVT is associated with an increased risk of the cancers mentioned but also pancreatic cancer in both men and women. Please include this given the challenges around early diagnosis of pancreatic cancer[1 2].	Whilst DVT can be a feature of pancreatic cancer, our primary care evidence did not give a PPV for this association. The list of cancer sites in our recommendation was determined by the cancers in which a PPV was reported. In recognition of the fact that other cancers can cause DVT, we specifically used the term 'including' before the list.
74	Universit	10	NICE	58	middle	Anaemia is also associated with additional cancers	We only included papers that either

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	y of Nottingham					to CRC. For example, it is associated with oesophageal gastric, lung ovary, blood cancers[1 2]	presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. The majority of the included studies reported that the risk associated with anaemia was low for oesophageal-gastric and myeloma; and none of the included papers reported the PPV of anaemia for lung, leukaemia, Non-Hodgkin's lymphoma or Hodgkin's lymphoma and the GDG did not consider the risk to be above 3%. The recommendations on ovarian cancer have been incorporated into this guideline in line with NICE processes. The evidence has not been updated and we are therefore not able to make any changes to the recommendations.
75	University of Nottingham	11	NICE	24 88	3-5 2.1	Please note that the QCancer cohorts included patients aged 25-89 years. Age was included in the algorithms so the absolute risks for each cancer account for patient's age.	The GDG, having considered the available evidence, agreed that there is a need for a broader evidence base on this matter and therefore recommended further research.
76	University of Nottingham	12	NICE	24 88	12-17 2.2	Some of this information on sensitivity, specificity etc is presented in the papers which the GDG has overlooked [2]	Having considered the available evidence on the diagnostic accuracy of tests in primary care, the GDG agreed that there was a need for a broader evidence base on this matter and therefore recommended further research.
77	University of Nottingham	13	NICE	24 89	23-27 2.3	Sensitivity is also clearly important as this will help assess how many people with specific types of cancer might be picked up by an approach. Symptoms with high PPVs may detect a lower	We have amended this research recommendation to include 'other performance metrics'.

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						proportion of cancer cases than more common symptoms with lower PPVs, so consideration of both values is important.	
78	University of Nottingham	14	Full	10	15	The QCancer tools have been validated by an external team in an independent population[3-7]. The implementation of the tools has been trialled in > 500 general practices by Macmillan http://www.macmillan.org.uk/Aboutus/Healthandsocialcareprofessionals/Macmillansprogrammesandservices/Earlydiagnosisprogramme.aspx and evaluated by CRUK. The QCancer tools are now integrated into EMIS Web which is the GP computer system used by the majority of GPs.	Thank you for this information.
79	University of Nottingham	15	Full	13	15	Whilst the PPV is important, so are other measures such as sensitivity and the % of the total population likely to be identified as at high risk. We think this information should be included. We are disappointed that there appears to be no clear evidence base for choosing a 3% PPV. Please include references to analyses conducted using this threshold if available	The GDG agree that sensitivity is important. By lowering the PPV threshold, this guideline will capture a greater proportion of cancers early. So the 'sensitivity' of this guideline will be considerably higher compared to previous guidance. As we have documented in the introduction, in the absence of evidence identifying a universally agreed PPV, the decision to use 3% was based on the consensus of the GDG.
80	University of Nottingham	16	Full	22	5	The guidance states that of the possible risk factors that were reported in the literature, only age and smoking were found to significantly influence the chance of cancer in a patient with symptoms". This is incorrect and should be updated. The appendices for the NICE guideline include multiple references to papers on this topic where risk factors such as family history, alcohol,	We have clarified in the text that ...'only age and smoking were found to significantly influence the chance of symptoms being predictive of cancer.'

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						diagnosis of COPD, diagnosis of chronic pancreatitis, type 2 diabetes and body mass index have been shown to be significant risk factors for cancer in patients with symptoms[1 2 8-13].	
81	University of Nottingham	17	Full	24	3.3	Other measures of performance are also important such as the total % of patents likely to identified as "at risk" and the sensitivity of symptom- based approaches.	We have amended this research recommendation to include 'other performance metrics'.
82	University of Nottingham	18	Full	51	table	We wonder if you have misread the paper by Hippisley-Cox (2011) which is included in the table. The paper clearly states that table 4 is restricted to patients who developed the outcome or who had at least 2 years of follow up. This is appropriate for these tests of performance given the study design and nature of the follow up of the cohort study. Please correct this	While we do not dispute the appropriateness of the analyses, data are missing. This, in turn, leaves the estimates open to some risk of attrition bias given that we do not know if these data are missing at random or selectively.
83	University of Nottingham	19	Full	64	table	We wonder if you have misread the paper by Hippisley-Cox (2012) which is included in the table. The paper clearly states that table 4 is restricted to patients who developed the outcome or who had at least 2 years of follow up. This is appropriate for these tests of performance given the study design and nature of the follow up of the cohort study. Can you correct this please in the full guidance and also the appendices	While we do not dispute the appropriateness of the analyses, data are missing. This, in turn, leaves the estimates open to some risk of attrition bias given that we do not know if these data are missing at random or selectively.
84	University of Nottingham	20	Full	64	Table12	The paper (Hippisley-Cox ,2012) clearly shows that a risk-based assessment based on a multivariate model combining symptoms and risk factors is superior to an approach based on single symptoms (table 4), with higher PPV and also higher sensitivity. This appears to have been overlooked.	We have documented in the introduction, there are very few instances where risk factors allow different recommendations to be made for people with the same symptoms. The GDG actively sought exceptions to this in the evidence searches, finding only age and smoking

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							(lung cancer) of sufficient impact on the predictive power of symptoms to require different recommendations.
85	University of Nottingham	21	Full	71	table	You have misread the paper by Hippisley-Cox (2011) which is included in the table. The paper clearly states that the results in table 4 are restricted to patients who developed the outcome or who had at least 2 years of follow up. This is appropriate for these tests of performance given the study design and nature of the follow up of the cohort study. Can you correct this please in the full guidance and also the appendices etc?	While we do not dispute the appropriateness of the analyses, data are missing. This, in turn, leaves the estimates open to some risk of attrition bias given that we do not know if these data are missing at random or selectively.
86	University of Nottingham	22	General	General		1. Hippisley-Cox J, Coupland C. Symptoms and risk factors to identify men with suspected cancer in primary care: derivation and validation of an algorithm. Br J Gen Pract 2013;**63**(606):1-10. 2. Hippisley-Cox J, Coupland C. Symptoms and risk factors to identify women with suspected cancer in primary care: derivation and validation of an algorithm. Br J Gen Pract 2013;**63**(606):11-21. 3. Collins GS, Altman DG. Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of QCancer® (Pancreas). British Journal of General Practice 2013;**63**(614):636-42. 4. Collins GS, Altman DG. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer((R)) (Renal) prediction model. Cancer epidemiology 2012. 5. Collins GS, Altman DG. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer® (Gastro-Oesophageal). European journal of cancer (Oxford, England : 1990) 2012.	Thank you for providing these references. Regarding papers 1 and 2 - they presented calculations on the risk of cancer as a whole and describe an algorithm which predicts 'cancer' and then tests the algorithm. However we were unable to use this information because our guideline was investigating the risk of symptoms for specific cancers. Where these papers did provide data for specific cancers, they were described as relative risks. We needed the data presented as either 2x2 tables for the symptoms or absolute risks for symptom/specific cancer dyads to be able to use them in this guideline. As such we were not able to use the data and these two papers were not included in the evidence base. However, a large part of the data included in these papers was included in the guideline through a series of related papers that presented the data for specific cancers. .

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						6. Collins GS, Altman DG. Identifying women with undetected ovarian cancer: independent and external validation of QCancer((R)) (Ovarian) prediction model. European journal of cancer care 2012. 7. Collins GS, Altman DG. Identifying patients with undetected colorectal cancer: an independent validation of QCancer (Colorectal). Br J Cancer 2012. 8. Hippisley-Cox J, Coupland C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. Br J Gen Pract 2012;**62**(597):e251-60. 9. Hippisley-Cox J, Coupland C. Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. British Journal of General Practice 2012;**62**(594):e38-e45. 10. Hippisley-Cox J, Coupland C. Identifying patients with suspected colorectal cancer in primary care: derivation and validation of an algorithm. British Journal of General Practice 2012;**62**(594):e29-e37. 11. Hippisley-Cox J, Coupland C. Identifying women with suspected ovarian cancer in primary care: derivation and validation of algorithm. BMJ 2012;**344**. 12. Hippisley-Cox J, Coupland C. Identifying patients with suspected lung cancer in primary care: derivation and validation of an algorithm. British Journal of General Practice 2011;**61**(592):e715-23. 13. Hippisley-Cox J, Coupland C. Identifying patients with suspected gastro-oesophageal cancer in primary care: derivation and validation of an algorithm. British Journal of General Practice	The remaining papers were all included, apart from 6 and 11 which were outside the scope of this guideline.

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						2011;**61**(592):e707-14.	
223	Welsh Association for Gastroenterology and Endoscopy	1	NICE	50 General		The use of the term "urgent suspected cancer" in gastrointestinal practice is often unhelpful. Dysphagia is thought to be the GI symptom with the highest positive predictive value, but less than 5% turn out to have cancer. Therefore referring patients as USC and informing them they are being referred as a suspected cancer will be unhelpful in over 95%. Perhaps "urgent need to exclude cancer" and "exclude cancer pathway" would be more helpful and less anxiety provoking terms.	We understand your point, however it would be impossible to change the terminology across the guideline to reflect the likelihood of cancer for each cancer type.
224	Welsh Association for Gastroenterology and Endoscopy	2	NICE	130 16	1st & 6th rec 1.3.1 and 1.3.6	*(p16, 70)* There is duplication here. Under pancreatic cancer it advises urgent direct access CT scan in people aged >60 with wt loss and diarrhoea, back pain, abdo pain, nausea/vomiting/constipation or new-onset diabetes. Those with upper abdominal pain might also end up being referred for direct access gastroscopy, whereas those with altered bowel habit might also end up being referred for exclusion of colorectal cancer. Surely the guidelines should make it easier for GPs to make a "forced choice" for the optimal route of referral. A case can be made for CT in all those with unexplained weight loss associated with abdominal symptoms, but GPs should be advised to first ensure renal function is reasonable as intravenous contrast is normally given.	The symptom based section shows the range of recommendations that are appropriate for people with particular symptoms. GPs will need to use their clinical judgement to decide which is the most appropriate cancer to exclude first. The introduction to the full version clarifies the need for a history, examination and routine investigations as part of general patient management. This would cover the testing of kidney function in such an instance.
225	Welsh Association for Gastroenterology and	3	NICE	130 16	1st & 6th rec 1.3.1 and 1.3.6	*(p16, 52, 70)* Faecal occult blood testing is now recommended, but this has only been validated in the context of screening for bowel cancer and not in the symptomatic population. The suggested indications for FOB testing are very wide: abdo pain and/or wt loss and/or aged <60 with altered	The evidence for the clinical and cost-effectiveness of FOB testing as a diagnostic test is detailed in the guideline. Your comment does not take account of the different patient group in which FOB

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	Endoscopy					bowel habit or iron deficiency anaemia. The latter is in its own right normally an indication for gastrointestinal evaluation in males and post-menopausal women, and national guidelines do not recommend FOB testing in this context. FOB testing for the symptomatic population is not practical, does not normally alter management and should be removed altogether.	is being recommended. This group receives no diagnostic activity at all under CG27 (2005).The GDG believed this group should be offered FOB testing since they have a risk of colon cancer between 1-3 %, with 3% being the threshold for urgent referral. There is evidence in this low risk group to suggest testing for occult blood. This is documented in the Linking evidence to recommendations section in the full guideline. This evidence was used alongside the economic analysis to form the recommendations. All tests may have false negatives, including that for occult blood in faeces. The true positive group, are the real beneficiaries as their diagnosis would be expedited. The false negative group are covered by the recommendation made on safety netting, which now explicitly states in recommendation 1.15.1 that people should be aware of the possibility of false negatives with the FOB test. Depending on their clinical course, they may become candidates for an urgent referral under the updated guideline, or their GP may decide that they warrant a routine referral.
226	Welsh Association for Gastroenterology and	4	NICE	130 32	1.3.1	*(p32, 70)* "Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if they are aged over 50 and have unexplained rectal bleeding". Rectal bleeding occurs in 30% of the population, and is usually longstanding and intermittent. It would	There was insufficient primary care evidence to add qualifying terms to rectal bleeding. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations.

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	Endoscopy					reduce unnecessary referrals to specify "new onset unexplained rectal bleeding" and/or "blood mixed with the stool in the absence of anal symptoms". Lower GI clinics are already inundated with requests for sigmoidoscopy/colonoscopy. Commonly patients have already undergone previous investigation for the same symptoms.	Of the 30% in the population who experience rectal bleeding, only a small proportion attend general practice. We recognise that there will be challenges in implementing this guideline but consider that the more targeted referrals resulting from the recommendations will improve the timeliness and quality of cancer diagnosis.
227	Welsh Association for Gastroenterology and Endoscopy	5	NICE	130 71	1.3.8	Suggest "Consider a referral (for an appointment within 2 weeks) in people aged under 50 with ***new onset unexplained*** rectal bleeding and any of the following: □ abdominal pain or □ change in bowel habit or □ weight loss or □ iron-deficiency anaemia (haemoglobin levels 12 g/dl or below for men and 11 g/dl or below for women). [new 2015]" Rectal bleeding and abdominal pain are very common symptoms in the general population	There was insufficient primary care evidence to add qualifying terms to rectal bleeding. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
228	Welsh Association for Gastroenterology and Endoscopy	6	NICE	130 16	1.3.3	Referring those aged ≥ 60 as urgent suspected cancer for any changes in bowel habit. Transient changes in bowel habit are very common (e.g with antibiotics or infection). Should state "for 6 weeks or more" and or "persistent and progressive".	There was insufficient primary care evidence to add qualifying terms to change in bowel habit. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
229	Welsh Association for Gastroen	7	NICE	18		Dysphagia has not been defined, as it was in the previous guidance. The Edinburgh group investigated a scoring system (Br J Surg 2010; 97: 1831-7). This suggested that symptoms for more	There was insufficient primary care evidence to add qualifying terms to dysphagia. We would expect primary care clinicians to exercise their clinical

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	terology and Endoscopy					than 6 months, co-existing reflux and localisation to neck were negative predictors for malignancy. Nearly all patients with reflux admit to occasional sensations of food sticking. Suggest "persistent progressive" or at least "some limitation of diet"	judgement when using the recommendations
230	Welsh Association for Gastroenterology and Endoscopy	8	NICE	80 20	1.2.9	Reflux with nausea/vomiting aged >55: Should read: consider direct access upper GI endoscopy in those aged >55 with ***recent onset persistent*** reflux with nausea and vomiting	There was insufficient primary care evidence to add qualifying terms to reflux with nausea and vomiting. We would expect primary care clinicians to exercise their clinical judgement when using the recommendations
121	West Cheshire CCG	1	Full	General	General	Concerns around rapid access to diagnostics, this in relation to the increased emphasis on access to diagnostics in the draft guideline.	The GDG considered that the majority of people referred urgently for certain cancers would be having urgent imaging after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for imaging first would not significantly increase the number of urgent requests, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with these cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral. All of the direct access tests

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							recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
138	WHO Collaborating Centre for Oral Cancer	1	Full	228	14.2 Oral cancer Recommendations	**RESPONSE**: This recommendation should include a "red patch" or a "mixed red and white patch" of the oral mucosa persisting for more than 2 weeks after being seen by a dental surgeon. There were few other previous recommendations in NICE (2005) that are missed out in this review. Eg. non- healing socket for more than 2 weeks Excessive mobility of a tooth / teeth when other teeth are sound **IN GENERAL , THESE NEW RECOMMENDATIONS ARE WEAKER AND INCOMPLETE COMPARED TO 2000 / 2005 NICE GUIDELINES FOR HEAD AND NECK CANCERS**	We have included 'red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia' in the recommendation. We did not find any primary care evidence to support retaining these recommendations as part of the update.
139	WHO Collaborating Centre for Oral Cancer	2	Full	226	12	*(lines 12-13, 14.2)* **GDG REPORTED**: No primary care evidence was identified pertaining to the risk of oral cancer in patients presenting with symptoms in primary care. **RESPONSE:** One study in the UK did examine what factors or cues primary care dentists (PCDs) take into account when diagnosing and referring Potentially Malignant Disorders. This study confirmed that risk factors were statistically significant in their ability to predict a referral decision. The study was on Potentially Malignant Disorders but would reflect on their decision for cancer referrals too. Brocklehurst PR, Baker SR, **Speight PM**. Factors which determine the referral of potentially	Thank you for providing this reference. We only included papers that either presented PPVs or sufficient data (i.e., true and false positives) to allow us to calculate them. In other words, for questions that looked at the cancer risk of symptoms, the only outcome we considered was PPVs. The proposed paper did not report such data and was therefore not included.

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						malignant disorders by primary care dentists. J Dent. 2010 Jul;38(7):569-78.	
140	WHO Collaborating Centre for Oral Cancer	3	Full	227	14.2 Oral Cancer Evidence statement	**GDG QUOTED** Trans-epithelial oral brush biopsy study from USA. **RESPONSE**: This is not relevant for the UK as the method is not recommended by UK Pathologists	The GDG considered the evidence on a range of possible investigations. No recommendation was made on brush biopsy.
141	WHO Collaborating Centre for Oral Cancer	4	Full	228	14.2 Oral Cancer Quality of the evidence	**Signs and symptoms of oral cancer** **GDG statement**; No evidence was found pertaining to the positive predictive values of different symptoms of oral cancer in primary care. **A recently published Cochrane review** gives sensitivity and specificity of dental practitioners finding suspected new oral cancers in primary care: REF : Walsh T, Liu JL, Brocklehurst P, Glenny AM, Lingen M, Kerr AR, Ogden G, **Warnakulasuriya S**, Scully C. Clinical assessment to screen for the detection of oral cavity cancer and potentially malignant disorders in apparently healthy adults. Cochrane Database Syst Rev. 2013 Nov 21;11:CD010173. doi:10.1002/14651858	Thank you for providing this reference. The Cochrane review was not included because the included studies were all screening studies, which are outside of the scope of this guideline.
142	WHO Collaborating Centre for Oral	5	Full	228	14.2 Oral Cancer Quality of the	**GDG STATEMENT:** No evidence was found for this outcome **RESPONSE:** : There is one study in the UK (not quoted in the GDG) that has assessed the predictive value of the two week wait Head and	Thank you for providing this reference. The GDG considered the issue of whether to use evidence from primary or secondary care, early in the development of the guideline. They agreed that

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	Cancer				evidence	neck (oral cancer) initiative using existing NICE guidelines for referrals received from primary care to a hospital consultant; Ref: Singh and Warnakulasuriya 2006: Citation: Singh P, **Warnakulasuriya S**. The two-week wait cancer initiative on oral cancer; the **predictive value of urgent referrals** to an oral medicine unit. Br Dent J. 2006;201 :717- 20. With reference to current NICE Guidelines, this study found 6/76 referrals from primary care with an urgent referral (7.9%) and 6/25 (24%) of suspected malignancy referrals had cancer diagnosed by biopsy, following referral. Predictive values are given.	because of the highly selected populations in secondary care diagnostic studies, it was not appropriate to extrapolate from them to develop recommendations for a guideline targeted at a primary care population.
143	WHO Collaborating Centre for Oral Cancer	6	Full	230	14.2 Oral Cancer Other considerations	**GDG statement**: Noted that the Community Dental Service is free, available in all areas, and provides more standardised care than individual dental practitioners, but the GDG recognised that it is currently only set up to treat children and people with special needs and not people with suspected cancer **RESPONSE** : This is exactly why the Community Dental Service (CDC) is **unsafe** to handle this urgent need. CDS is the **most difficult** service **to access** in the country, though it is free. To qualify to attend CDS it may take months, not days as the appointments beyond children, and special needs people have to be approved by their managers. There appears to be a lack of rigour among many CDS practitioners when screening for oral cancer or potentially malignant disorders as very few	In light of concerns raised by stakeholders we have amended the recommendation to read 'Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist...'

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						cases arrive in secondary care from CDS. **The recommendation to the public** should be to seek the opinion of a dental practitioner, but if that is considered costly for the patient to seek help from their GP. **Triage through CDS is unsafe, will cause further delays to a patient's cancer journey. A GDP or GP should refer suspected cases direct to a hospital. As CDC does not provide a routine dental service to ordinary individuals in the society they do not provide opportunistic screening to find new cancers!**	
144	WHO Collaborating Centre for Oral Cancer	7	Full **14.2 Oral cancer**	228	Trade-off between clinical benefits and harms	**GDG** set a positive predictive value of 3% **Response:** This recommended PPV is too low, and should be set at 5%. Otherwise too many benign mucosal disorders will be referred to secondary care facilities. For this reason signs and symptoms in the referral guideline should be evidence-based,	The decision on what PPV threshold to use was extensively documented in the introduction to the full guideline.
145	WHO Collaborating Centre for Oral Cancer	8	Full	226	2	**GDG stated: Mos**t oral cancers are diagnosed by dental surgeons. **RESPONS**E: This is not so. In our experience in South East England (perhaps elsewhere as well) equal numbers do come from GPs. This is important to recognize in generating proposals for referrals, as **patient choice** is still to see their GP for any non dental symptom (such as ulcers and lumps) in their mouths.	We have changed this to 'many'.
146	WHO Collaborating	9	Full	226	6	**GDG stated**; Oral cancer **can** present as advanced disease with regional lymphadenopathy.	We have deleted the term 'rarely'.

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	Centre for Oral Cancer					**RESPONSE**: In secondary care we still encounter many (close to 50%) with regional (neck) lymphadenopathy in stages 3 or 4. Wording should be changed to **do often present.**	
499	Womb Cancer Alliance	1	Full	155	Recommendation for referral for suspected uterine cancer	We are extremely concerned about the proposed deletion from the NICE guideline CG27 (2005) of **"An urgent referral should be considered in a patient with persistent inter-menstrual bleeding and a negative pelvic examination. [1.7.9.]"** The deletion of "persistent inter-menstrual bleeding" would fail to protect the 496 menstruating women each year who develop endometrial cancer. **(Evidence: Office for National Statistics Cancer Statistics Registrations, England (Series MB1), No. 43, 2012:** Total of 496 patients under 50 were diagnosed with malignant neoplasm of corpus uteri in 2012. Total of 1,058 patients under 55 were diagnosed with same.**)** It would also reinforce the unscientific and outdated stereotype of endometrial cancer as a disease of exclusively postmenopausal women. (**Evidence: Ibid.** 7% womb cancer is diagnosed in pts < 50 yrs; 14% womb cancer is diagnosed in pts < 55 yrs.) **In our own series of 145 patients diagnosed with endometrial cancer at St Mary's Hospital in Manchester (one of the 2 gynae cancer centres in Greater Manchester) in 2014, 20 (14%) were under the age of 50 years. We saw 5 women who were diagnosed with endometrial cancer in their 30's.**	The primary care evidence did not support the retention of this recommendation from CG27. Thank you for this information.

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						The decision to remove persistent intermenstrual bleeding from the recommendation is based on the data from a single publication (Walker et al 2013) which in turn is based on a retrospective analysis of GP records. Persistent intermenstrual bleeding was not specifically recorded in this study. Comments from survivors indicate that persistent inter-menstrual bleeding is not well recognised by GPs as an endometrial cancer symptom: "The GP said it was just the menopause'; 'The GP ignored it for months and I was only referred when a locum noticed the awful smell'; 'I kept going to the GP but the cancer was detected when I passed a tumour in A&E'. Data taken retrospectively from GP records is inherently biased due to problems related to accuracy and missing data.	All symptoms reported in the primary and secondary care literature were studied in the Walker paper. Symptoms that did not meet statistical significance, or which were excessively rare amongst cases, were not reported in the results (negative findings rarely are). Whilst individual narrative is important in many situations, the GDG consider that clinical guidelines are better based upon peer-reviewed scientific papers alongside clinical judgement and experience.
						Endometrial cancer should be suspected in the presence of persistent intermenstrual bleeding, new onset menorrhagia or irregular bleeding, particularly if the woman has additional risk factors, most notably obesity and diabetes. Whilst high blood sugar features in this new guidance there is no mention of BMI, despite the fact that endometrial cancer ranks highest amongst all cancers in its association with obesity [Crosbie et al Cancer Epidemiol Biomarkers Prev (2010)]. It is our opinion that morbidly obese (BMI >40) women over the age of 40 and obese (BMI >30) women over the age of 45 with **any abnormal bleeding** should be investigated urgently for suspected endometrial cancer.	We have documented in the introduction, there are very few instances where risk factors impact sufficiently on the predictive power of symptoms to allow different recommendations to be made for people with the same symptoms. The GDG 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 obesity or diabetes affected the predictive power of symptoms for endometrial cancer.
						Obesity is not mentioned in the draft guidance	We have documented in the introduction,

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						because the recommendations are based on data from Walker et al (2013), which did not look at BMI. This is a fundamental omission similar to ignoring smoking history when suspecting lung cancer. Other important risk factors such as PCOS are also not mentioned. This further calls into doubt the validity of their findings. **We believe that prospective data is essential to inform a change in recommendation of this nature. In the absence of prospective data, we believe the guideline should NOT be changed to exclude persistent intermenstrual bleeding as a red flag symptom.**	there are very few instances where risk factors impact sufficiently on the predictive power of symptoms to allow different recommendations to be made for people with the same symptoms. The GDG 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 obesity or diabetes affected the predictive power of symptoms for endometrial cancer. No primary care evidence was identified that persistent intermenstrual bleeding was a symptom of endometrial cancer requiring a suspected cancer pathway referral.
500	Womb Cancer Alliance	2	Full	155	1.5.10 Recommendation for referral for suspected uterine cancer	We are extremely concerned about the proposed decision to only refer urgently women **over the age of 55 years** with postmenopausal bleeding. We believe that it discriminates against women under the age of 55 years. We do not believe that such a policy is in line with the Department of Health's report "Equal and inclusive: Government policy aimed at reducing health inequalities" which tackles 'Cancer inequalities' with "A range of policy documents focused upon reducing the gap between those with the poorest health outcomes and those with the best." http://www.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@pol/documents/generalcontent/crukmig_1000ast-3345.pdf	There are two recommendations for post-menopausal bleeding; the former for women aged 55 and over are for referral using a suspected cancer pathway. The latter – for women under 55, is a 'consider' recommendation, also for referral under the same pathway. The use of the term 'consider' reflects the strength of the evidence base upon which the recommendation was made. For more information on the wording of NICE recommendations please see p 6 of the short version.

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						In our own series of 145 patients diagnosed with endometrial cancer at St Mary's Hospital in Manchester in 2014, 32 (22%) were under the age of 55 years at diagnosis, and 12 (8%) were aged between 50 and 55 years. Postmenopausal bleeding is abnormal whatever age the woman is and should be investigated urgently. It is not only a symptom of endometrial cancer but also of cervical, vaginal and vulval cancers. The combination of postmenopausal bleeding at any age plus additional risk factors, notably obesity and diabetes, are particularly alarming for endometrial cancer. If guidance is changed in line with the new recommendations and an urgent referral is indicated only for women over the age of 55 years with postmenopausal bleeding, 22% of our patients last year would have been denied the opportunity for early diagnosis and prompt treatment. This is particularly important for endometrial cancer which has excellent survival rates for women diagnosed with early stage disease, but very poor survival rates indeed with advanced disease. We do not believe that the evidence that supports the change in guidance is robust or reliable and urge NICE to take the age limit out of this recommendation.	We have documented in the introduction, there are very few instances where risk factors impact sufficiently on the predictive power of symptoms to allow different recommendations to be made for people with the same symptoms. The GDG 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 obesity and diabetes affected the predictive power of symptoms for endometrial cancer.
768	Yeovil District Hospital NHS	1	Full	130 Colorectal	6th rec General	Where is the evidence of ANY benefit from FOB testing except in population based screening	The evidence for the clinical and cost-effectiveness of FOB diagnostic testing is detailed in the section 9.1 of the full guideline.

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	Foundation Trust						
769	Yeovil District Hospital NHS Foundation Trust	2	Full	17	1.2.1	Should this not read **NEW** dyspepsia for >55yrs and reflux/dyspepsia symptoms	The available evidence did not generally use the term 'new' to qualify dyspepsia. We would expect the primary care clinician to use their clinical judgement when applying this recommendation.
770	Yeovil District Hospital NHS Foundation Trust	3	Full	Upper GI	1.2.4 General	Do we need to see ALL jaundiced patients >40yrs on a cancer pathway; ie painful jaundice more likely to be gallstones and lots of medical reasons for jaundice, not least Acute Hepatitis?	The PPV for jaundice in pancreatic cancer is one of the highest for any symptom in any cancer. If a GP has a clearly correct alternative diagnosis we would expect them to exercise their clinical judgement.
771	Yeovil District Hospital NHS Foundation Trust	4	Full	68	1.2.5	For ? pancreas they suggest direct access to CT within 2 weeks for a lot of possible indications. However if you can't get CT go for U/S – our preference would be for the U/S than direct access CT	The GDG considered this issue and agreed that CT was the preferred imaging modality because of anticipated superior performance characteristics. This was documented in the Linking Evidence to Recommendations section in the full guideline.
772	Yeovil District Hospital NHS Foundation Trust	5	Full	240 29	1.9.1	For "loss of central neurology function or progressive/subacute loss" they suggest direct access to MRI (p 29). This should be via a clinician. If the MRI doesn't show a cancer then the patient still needs investigating	We agree that the patient would still need investigating but it is outside the scope of this guideline and we therefore cannot make any recommendations. It is worth noting that all of the direct access tests recommended in the guideline are currently available in parts of the UK, suggesting that these operational challenges are not insurmountable.
773	Yeovil District Hospital NHS	6	Full	155	1.5.13	Visible haematuria over 40 should be referred to urology. But visible haematuria in an over 55 yr old woman with a discharge should have an U/S of her uterus (p 74). These suggestions **are at odds** with	Several symptoms may have a number of possible underlying malignant causes (as well as benign ones). Haematuria is a good example of this. Therefore we do

ID	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Foundation Trust					each other.	not think that these recommendations are contradictory. We would expect primary care clinicians to use their clinical judgement which cancer site to investigate first. This would usually be urological cancer, but it is important to recommend possible investigation for uterine cancer, as the evidence suggested it had a PPV worthy of testing.
774	Yeovil District Hospital NHS Foundation Trust	7	Full	366	1.13.4	The more worrying elements are the nonspecific symptoms ie Wt loss, appetite and a DVT. These should be assessed for possible primary symptoms AND referred (p 83). The loss of weight and appetite needs to be "unexplained" but maybe that should have some clarification. Do they really mean that all DVTs should be assessed? And by whom if there are no clues as to a primary tumour?	The rationale for including these symptoms is that they equate to an overall risk of cancer greater than 3%. We think the precise referral route is best left the clinical judgement of the primary care clinician.
775	Yeovil District Hospital NHS Foundation Trust	8	Full	130 General	6th rec General	One of the comments that came up and is not recorded on the next document was that the FOB test which NICE guidance is recommending GPs do is a one off. In bowel screening they have a series of 3. With one test it was felt there may be a number of false positives	The GDG chose not to stipulate the specifics for administering the test in the recommendation. They would expect people to refer to the manufactures instructions for its use as a diagnostic test. The specific details of each of the relevant papers are documented in Appendix F.
776	Yeovil District Hospital NHS Foundation Trust	9	Full	General	General	There are some serious concerns about the recommendation to treat urgent as 2ww and the effect this would have on a number of services – especially endoscopy.	When we use the term urgent in this guideline we define it as within 2 weeks. However, this does not mean that our definition should be applied to the term urgent when it is used outside the recommendations in this guideline. The GDG considered that the large majority of people referred urgently for upper GI cancers would be having urgent

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							endoscopies after the suspected cancer out-patient appointment. They therefore agreed that making an urgent referral for endoscopy first would not significantly increase the number of urgent endoscopies, or the timeframe in which they need to be performed (from the point of the test being ordered). In addition, it would reduce the number of suspected cancer out-patient appointments that are needed and would accelerate the diagnosis of people with upper GI cancers and improve patient experience. The GDG also considered that cancer tests directly available to GPs should be performed within the same time frame as tests which currently require referral.

These organisations were approached but did not respond:

A Little Wish
Abbott GmbH & Co KG
Abbott Molecular UK
Action Cancer - NI
Airedale NHS Trust
Alder Hey Children's NHS Foundation Trust
All Wales Dietetic Advisory Committee

Allocate Software PLC
AMMF - TheCholangiocarcinoma Charity
Aneurin Bevan Health Board
AngioDynamics
Archimedes Pharma Ltd
Association for Clinical Biochemistry and Laboratory Medicine
Association of Anaesthetists of Great Britain and Ireland
Association of British Insurers
Association of Chartered Physiotherapists in Oncology and Palliative Care
Association of Clinical Pathologists
Association of Surgeons of Great Britain and Ireland
Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
Astrazeneca UK Ltd
Bard Limited
Barnsley Hospital NHS Foundation Trust
Barrett's Oesophagus Campaign
Baxter Healthcare
Bayer HealthCare
Beating Bowel Cancer
Becton Dickinson
Belfast Health and Social Care Trust
Biohit Healthcare Ltd
BME cancer.communities
Boehringer Ingelheim
Bolton Hospitals NHS Trust
Boots
Bradford District Care Trust

Brain Tumour Research
Bristol and Avon Chinese Women's Group
British and Irish Orthoptic Society
British Association for Cytopathology
British Association of Oral Surgeons
British Association of Otorhinolaryngologists, Head and Neck Surgeons
British Association of Spinal Surgeons
British Committee for Standards in Haematology
British Dermatological Nursing Group
British Dietetic Association
British Heart Foundation
British HIV Association
British Liver Trust
British Lung Foundation
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Nuclear Medicine Society
British Paediatric Neurology Association
British Psychological Society
British Psychosocial Oncology Society
British Red Cross
British Society for Colposcopy and Cervical Pathology
British Society of Paediatric Radiology
British Society of Gastrointestinal and Abdominal Radiology

British Thyroid Foundation
BUPA Foundation
C. R. Bard, Inc.
Calderstones Partnerships NHS Foundation Trust
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Cancer Black Care
Cancer of Unknown Primary Foundation
Cancer Services Collaborative Primary Care Lead
Cancer Services Co-ordinating Group
Cancer Voices
Cancer52
Caper Research Unit
Caplond Services
Capsulation PPS
Capsulation PPS
Cardiff and Vale University Health Board
Care Not Killing Alliance
Care Quality Commission
Central & North West London NHS Foundation Trust
Central London Community Health Care NHS Trust
Central Manchester and Manchester Children's Hospital NHS Trust
Chartered Society of Physiotherapy
Cheshire and Merseyside SCN
Childhood Cancer Parents Alliance
Children's Brain Tumour Research Centre
Chronic Lymphocytic Leukaemia Support Association

City Hospitals Sunderland NHS Foundation Trust
Clarity Informatics Ltd
CLIC Sargent
Cochrane Oral Health Group
Colchester Hospital University NHS Foundation Trust
Community District Nurses Association
ConvaTec Ltd
Countess of Chester Hospital NHS Foundation Trust
Covidien Ltd.
Croydon Council
Croydon Health Services NHS Trust
Croydon University Hospital
Cumbria Partnership NHS Foundation Trust
CWHHE Collaborative CCGs
Cwm Taf Health Board
Department for Communities and Local Government
Department of Health, Social Services and Public Safety - Northern Ireland
Doncaster Council
Dudley PACT Patient Advisory Cancer Team
East and North Hertfordshire NHS Trust
East Kent Hospitals University NHS Foundation Trust
East of England Strategic Clinical Network
Eisai Ltd
Eli Lilly and Company
Equalities National Council
Ethical Medicines Industry Group
Faculty of Dental Surgery

Faculty of General Dental Practice
Faculty of Public Health
False Allegations Support Organisation
Ferring Pharmaceuticals
Fibroid Network Charity
Fight Bladder Cancer
Five Boroughs Partnership NHS Trust
Frimley Park NHS Foundation Trust
Galderma
GE Healthcare
General Practice and Primary Care
George Eliot Hospital NHS Trust
Gilead Sciences Ltd
GIST Support UK
GlaxoSmithKline
Globe Microsystems Ltd
Gloucestershire LINk
Gorlin Syndrome Group
GP update / Red Whale
Great Ormond Street Hospital
Great Western Hospitals NHS Foundation Trust
Greater Manchester, Lancashire and South Cumbria Strategic Clinical Network
Guerbet Laboratories Ltd
Guy Francis Bone Cancer Research Fund
Guy's and St Thomas' NHS Foundation Trust
Health and Care Professions Council
Health and Social Care Information Centre

Healthcare Improvement Scotland
Healthcare Infection Society
Healthcare Quality Improvement Partnership
Healthwatch East Sussex
Help Adolescents With Cancer
Hertfordshire Partnership NHS Trust
Herts Valleys Clinical Commissioning Group
Hindu Council UK
Hiraeth Services Ltd
Hockley Medical Practice
HQT Diagnostics
Hull and East Yorkshire Hospitals NHS Trust
Humber NHS Foundation Trust
Humberside Oesophageal Support Group
Imaging Equipment Ltd
Impact of Neutropenia in Chemotherapy European study group
Imperial College Healthcare NHS Trust
Independent Healthcare Advisory Services
InferMed
Institute of Biomedical Science
International Brain Tumour Alliance
Intuitive Surgical
IOTA - International Ovarian Tumor Analysis group
James Whale Fund for Kidney Cancer
JETDoc
Jo's Trust
KCARE

Kidney Cancer Support Network
Kidney Cancer UK
Kings College Hospital
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds Teaching Hospitals NHS Trust
Leo Pharma
Leukaemia & Lymphoma Research
Leukaemia Cancer Society
Leukaemia CARE
Lilly UK
Link Pharmaceuticals
Local Government Association
Luton and Dunstable Hospital NHS Trust
Lymphoma Association
Maidstone and Tunbridge Wells NHS Trust
mBriefs Limited
MDS UK Patient Support Group
Medical Directorate Services
Medicines and Healthcare Products Regulatory Agency
Medway NHS Foundation Trust
Mencap
Mid Staffordshire NHS Foundation Trust
Milton Keynes Hospital NHS Foundation Trust
Ministry of Defence
Mole Clinic Ltd, The
Mouth Cancer Foundation

Musculoskeletal Association of Chartered Physiotherapists
Muslim Doctors and Dentists Association
Myeloma UK
National Association of Primary Care
National Cancer Action Team
National Cancer Intelligence Network
National Cancer Research Institute
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Deaf Children's Society
National Institute for Health Research Health Technology Assessment Programme
National Institute for Health Research
National Kidney Federation
National Kidney Research Foundation
National Patient Safety Agency
National Public Health Service for Wales
National Radiotherapy Implementation Group
NB Medical Education
NET Patient Foundation
NHS Barnsley Clinical Commissioning Group
NHS Bowel Cancer Screening Programme Southern Hub
NHS Brighton & Hove CCG
NHS Chorley and South Ribble CCG
NHS Clinical Knowledge Summaries
NHS Connecting for Health

NHS County Durham and Darlington
NHS Crawley CCG
NHS Cumbria Clinical Commissioning Group
NHS Doncaster CCG
NHS Halton CCG
NHS Hardwick CCG
NHS Health at Work
NHS Horsham and Mid Sussex CCG
NHS Improvement
NHS Knowsley CCG
NHS Leeds West CCG
NHS Liverpool CCG
NHS Medway Clinical Commissioning Group
NHS Milton Keynes
NHS National Cancer Screening Programmes
NHS North Derbyshire CCG
NHS North East Hampshire and Farnham CCG
NHS North Somerset CCG
NHS Oldham CCG
NHS Pathways
NHS Plus
NHS Sheffield
NHS Somerset CCG
NHS South Cheshire CCG
NHS South Gloucestershire CCG
NHS South Manchester CCG
NHS South Sefton CCG

NHS St Helens CCG
NHS Vale Royal CCG
NHS Wakefield CCG
NHS Wandsworth
NHS Warrington CCG
NHS Warwickshire North CCG
NIHR CCRN ENT Specialty Group
Norfolk and Suffolk Palliative Care Academy
North and East London Commissioning Support Unit
North East Lincolnshire Care Trust Plus
North of England Commissioning Support
North Staffordshire Cancer Service User Forum
North West London Hospitals NHS Trust
Northern Health and Social Care Trust
Northern Region Endoscopy Group
Northern, Eastern, Western Devon CCG
Nottingham City Council
Nottingham City Hospital
Nottingham University Hospitals NHS Trust
Nottinghamshire Healthcare NHS Trust
Novartis Pharmaceuticals
NS Technomed
Nursing and Midwifery Council
Nutricia Advanced Medical Nutrition
Older People's Advocacy Alliance
Ovacome
Ovarian Cancer Action

Oxford Health NHS Foundation Trust
Oxfordshire Clinical Commissioning Group
Pancreas Society of Great Britain and Ireland
PERIGON Healthcare Ltd
Peterborough and Stamford Hospitals NHS Foundation Trust
Pfizer
Pharmametrics GmbH
POhWER
Primary Care Pharmacists Association
Primary Care Respiratory Society UK
Primrose Bank Medical Centre
Pseudomyxoma Survivor
Public Health Wales NHS Trust
QResearch
Queen Elizabeth Hospital
Queen Elizabeth Hospital King's Lynn NHS Trust
Queen's Medical Centre Nottingham University Hospitals NHS Trust
Rarer Cancers Foundation
Robert Jones & Agnes Hunt Orthopaedic & District Hospital NHS Trust
Roche Diagnostics
Roche Products
Royal Berkshire NHS Foundation Trust
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Nursing

Royal College of Obstetricians and Gynaecologists
Royal College of Ophthalmologists
Royal College of Pathologists
Royal College of Physicians and Surgeons of Glasgow
Royal College of Speech and Language Therapists
Royal Cornwall Hospitals NHS Trust
Royal Devon and Exeter NHS Foundation Trust
Royal National Institute of Blind People
Royal National Orthopaedic Hospital NHS Trust
Royal Pharmaceutical Society
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust
Sandoz Ltd
Sanofi
Sarcoma Information Services Ltd.
Schering Health Care Ltd
School of Health and Population Sciences
Scottish Intercollegiate Guidelines Network

SNDRi
Social Care Institute for Excellence
Society and College of Radiographers
Society for Cardiothoracic Surgery of Great Britain and Ireland
Somerset, Wiltshire, Avon and Gloucestershire Cancer Services Operational Group
South Asian Health Foundation
South Devon Healthcare NHS Trust
South Eastern Health and Social Care Trust

South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
Southern Health & Social Care Trust
Southport and Ormskirk Hospital NHS Trust
St Helens and Knowsley Teaching Hospitals NHS Trust
St Mary's Hospital
Staffordshire and Stoke on Trent Partnership NHS Trust
Step4Ward Adult Mental Health
Stockport Clinical Commissioning Pathfinder
Sue Ryder
Surrey and Sussex Healthcare NHS Trust
Swindon and Marlborough NHS Trust
Tackle Prostate Cancer
Tameside Hospital NHS Foundation Trust
Teenage Cancer Trust
Teenagers and Young Adults with Cancer
Tenovus Cancer Information Centre
Tenovus The Cancer Charity
The Anthony Pilcher Bone Cancer Trust

The British In Vitro Diagnostics Association
The British Society for Haematology
The Eve Appeal
The Hepatitis C Trust
The Institute of Cancer Research
The National LGB&T Partnership
The Neuro Foundation

The Neuroblastoma Society
The Patients Association
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust
The University of Birmingham
The Walton Centre for Neurology and Neurosurgery
Throat Cancer Foundation
UCL Partners
UK Clinical Pharmacy Association
UK Liver Alliance
UK National Screening Committee
United Response
University College London Hospital NHS Foundation Trust
Velindre NHS Trust
Walsall Local Involvement Network
Welsh Cancer Services Coordinating Group
Welsh Government
Welsh Scientific Advisory Committee
West Suffolk Hospital NHS Trust
Western Health and Social Care Trust
Western Sussex Hospitals NHS Trust
Westminster Local Involvement Network
Whitehouse Consultancy
Wicked Minds
Wigan Borough Clinical Commissioning Group
Wilmslow Health Centre
Wirral University Teaching Hospital NHS Foundation Trust

York Hospitals NHS Foundation Trust