Suspected Cancer:

recognition and referral

NICE Guideline

Appendix H: Review protocols for Suspected Cancer update 2015

Developed for NICE by the National Collaborating Centre for Cancer

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This guideline updates and replaces NICE guideline CG27

These review protocols update and replace those in NICE guideline CG27 (published June 2005).

Evidence has been reviewed on the recognition and management of suspected cancer in children, young people and adults. New review protocols developed as part of this update are highlighted in peach.

PATIENT INFORMATION

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Patient information

Guideline subgroup members: Sue B, David, Susan H, Euan and Joan

Review question: What are the information needs of:

- Patients who are referred for suspected cancer and their carers/families, and

- Patients who are being monitored (for suspected cancer) in primary care and their carers/families?

Economic priority: Low

Population Situation	Timing	Outcomes	Study types
 Patients who are referred for suspected cancer and their Patients who are being Patients who are being Patients who are being Patients who are being monitored (for suspected cancer) in primary care and their carers/families 	n needs At the time of being referred for suspected cancer monitoring for suspected cancer in primary care.	Information or reported by er patients/carers to be useful/not useful or	Primarily Qualitative Also screen for quantitative studies and if enough time, include relevant quantitative studies

Question in PICO format

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library; Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED, google and charities for charity reports.
Can we apply date limits to the search	A date limit of 1980 was applied to the core databases. For additional searches on google and charities' websites no date limit was applied, as those databases are not structured in a way that allows date limits to be applied.
Are there any study design filters to be used (RCT, systematic review, diagnostic test)?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

What data will we extract (what	Demographic data describing the included
columns will be included in our	patients/participants (age, gender, suspected
evidence table) and how will we	cancer/referral type or reason for monitoring,
analyse the results?	relationship to referred/monitored patient, and setting
Which quality checklist will we use for	along with any other relevant patients/participant

appraisal? (Normally checklists from	details reported in the studies) will be extracted along
the NICE manual – but irrelevant items	with recruitment strategy including the inclusion and
could be omitted).	exclusion criteria. The included studies will be
List subgroups here and planned	appraised using the NICE checklist for qualitative
statistical analyses.(Recognised	studies (http://publications.nice.org.uk/the-guidelines-
approaches to meta-analysis should	manual-appendices-bi-pmg6b/appendix-h-
be used, as described in the manual	methodology-checklist-qualitative-studies). All the
from the NHS Centre for Reviews and	information reported by the study participants to have
Dissemination, and the Cochrane	been needed/not needed and wanted/not wanted will
Collaboration handbook).	be extracted for each study and the results will be
	summarised narratively, split by population
	(patient/carer/family) if the data allow it

(patient/carer/family) if the data allow it. Note any changes to the protocol or other considerations below

SAFETY NETTING

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Safety-netting

Guideline subgroup members: Yoryos, Lindsay, Susan, Joan

Review question: What safety-netting strategies are effective in primary care for patients being monitored for suspected cancer?

Economic priority: Low

Question in PICO format				
Patients/populat	Intervention	Comparison	Outcomes	
ion				
Patients with	Safety netting	No safety-netting	Cohort studies	
symptoms that		Other safety-netting	Proportion of patients with cancer in	
might indicate			the safety netted population	
cancer				
presenting in			Comparative studies	
primary care			Proportion of patients with cancer	
who have			Emergency presentation	
been			Stage at diagnosis	
investigated in			Survival	
primary care			Delayed diagnosis	
but the test is			Psychological morbidity	
negative/bord				
erline				
Patient with				
symptoms that				
might indicate				
cancer				
presenting in				
primary care who have not				
been				
 investigated Patients who 				
 Patients who have been 				
investigated in				
secondary				
care but with a				
negative				

investigation		
and persistent		
symptoms		

How the information will be searched

now the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library; Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review, diagnostic test). Primary care data only?	
List useful search terms.	Safety netting, Ongoing-care, Surveillance Watchful waiting, Watch and wait, Wait and see High risk patient, Diagnostic error, Monitoring Deferred referral, Unexplained persistent symptoms Timely re-appraisal, False negative, <u>Diagnostic error</u> High risk patient, False negative, Deferred referral, Unexplained persistent symptoms Timely re-appraisal

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

	The review endegy	
ſ	What data will we extract (what	For each included study the following characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting, patient
	evidence table) and how will we	characteristics (number, age, gender, country, any other relevant
	analyse the results?	characteristics reported such as relevant history or comorbidities),
	Which quality checklist will we use for	definition of symptom, safety-netting strategy, method of verification
	appraisal? (Normally checklists from	of diagnosis and any other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies will
	could be omitted).	be assessed using the QUADAS (II) tool for cohort studies and the
	List subgroups here and planned	Cochrane tool for intervention studies.
	statistical analyses.(Recognised	The proportion of patients with cancer will be extracted for all the
	approaches to meta-analysis should	study types and, if feasible, the results will be meta-analysed, to
	be used, as described in the manual	provide a summary estimate indicating the risk of cancer associated
	from the NHS Centre for Reviews and	with safety-netting. For comparative studies, the number of patients
	Dissemination, and the Cochrane	presenting as emergencies, the stage at diagnosis, survival, delayed
	Collaboration handbook).	diagnosis and psychological morbidity will also be extracted for each
		of the groups.

Note any changes to the protocol or other considerations below

LUNG

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Euan, Karen, Stuart

Review question: What is the risk of lung cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Cough		
suspected	(new cough / changed		
cancer*	cough)		
Calleer	Dysphoea (shortness of		
Subgroups:	breath)		
Age	Wheezing		
Sex	Haemoptysis		
Smoking	Fatigue		
Familial	Loss of weight		
syndromes	Loss of appetite		
Deprivation	Shoulder pain (Pancoast		
Obesity	tumour)		
Past history of	Chest/rib pain		
cancer	Pleuritic pain		
Ethnicity	Hoarseness (recurrent		
Alcohol exposure	laryngeal nerve palsy) Stridor		
Immuno-			
suppression	Facial swelling		
Occupational	Facial flushing		
history	Swelling of upper limb		
Asbestos	Distended veins upper limb		
Radon	Neck swelling		
Cannabis	Distended veins neck		
	Light headedness		
	Finger clubbing		
	Persistent or recurrent		
	chest infection		
	Pleural effusion		
	Radicular pain		
	Referred pain		
	Lower limb weakness		
	Impaired walking		
	Sensory impairment Bladder or bowel		
	incontinence Spinal tenderness		
	Muscle weakness /		
	swallowing problems /		
	coordination problems /		
	hyponatraemia		
	Abnormal spirometry		
	Abnormal chest x-ray		
	Fever		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		

	the second second self-second	
	thromboembolism	
	raised levels of	
	inflammatory	
	markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	symptoms of metastases	
C	hest	
	chest wall or rib pain	
	cough	
	dyspnoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
L	iver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	
B	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
B	Brain	
-	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	
	lethargy/hyper-	
	somnolence	
	visual disturbance	
	seizures	
	36120163	

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
What data will we extract (what	symptom X. For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the included studies.
List subgroups here and planned statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

LUNG

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for lung cancer

Guideline subgroup members: Euan, Karen, Stuart

Review question: Which investigations of symptoms of suspected lung cancer should be done with clinical responsibility retained by primary care?

Economic priority: Medium

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Chest x-ray	Histology/folLow up	Sensitivity
presenting to	СТ		Specificity
primary care with	Sputum cytology		Positive predictive value
symptoms of	Bronchoscopy		False negative rate
suspected lung			
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980

search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data only?	
,	
List useful search terms.	

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

MESOTHELIOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Euan, Karen, Stuart

Review question: What is the risk of mesothelioma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of suspected cancer*	Generic list fatigue appetite loss		
<u>Subgroups:</u> Age Sex Smoking Familial syndromes	weight loss thromboembolism raised levels of inflammatory markers anemia thrombocytosis		
Deprivation	thombocytosis		

Oh a a'tha		
Obesity	hypercalcemia	
Past history of	unexplained	
cancer	lymphadenopathy or	
Ethnicity	other mass	
Alcohol exposure		
Immuno-	Symptoms of metastases	
suppression	Chest	
Asbestos	chest wall or rib pain	
exposure	cough	
Occupational	dyspnoea/shortness of	
history	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	
	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
	Brain	
	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	
	somnolence	
	headache imbalance personality disturbance lethargy/hyper-	

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target

	cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items	For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

MESOTHELIOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for mesothelioma

Guideline subgroup members: Euan, Karen, Stuart

Review question: Which investigations of symptoms of suspected mesothelioma should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format			
Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Chest x-ray	Histology/folLow up	Sensitivity
presenting to	СТ		Specificity
primary care with	Abdominal x-ray		Positive predictive value
symptoms of	Ultrasound		False negative rate
suspected			
mesothelioma			
mesounelloma			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-	
	medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the	1980	
search		
Are there any study design filters to	Primary care data only	
be used (RCT, systematic review,		

diagnostic test). Primary care data only?	
List useful search terms.	

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

OESOPHAGEAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Sue B, Yoryos, Lindsay

Review question: What is the risk of oesophagael cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Epigastric pain		
suspected	Chest pain		
cancer*	Pain or discomfort in the		
	throat or back		
	Pain in the form of a		
Subgroups:	burning sensation when		
Age	swallowing food		
Sex	Pain or soreness behind		
Smoking	the breastbone, or		
Familial	between the shoulder		
syndromes	blades		
Deprivation	Reflux (acid regurgitation)		
Obesity	heartburn		
Past history of	Indigestion		

		1
cancer	Acid indigestion	
Ethnicity	Dyspepsia	
Alcohol exposure	persistent acid reflux	
Immuno-	persistent hiccups or	
	regurgitation of food,	
suppression		
Chronic iron	Dysphagia	
deficiency	Feeling that your food is	
anaemia	sticking in your throat	
History of	Hoarseness, or chronic	
Barretts	cough	
oesophagus	Coughing up blood	
Dietary history	Nausea	
Betel	vomiting	
HPV	Regurgitation	
	Constipation	
	Low cholesterol	
	Hypercalcemia	
	пурегсасенна	
	Generic list	
	fatigue	
	appetite loss	
	weight loss	
	thromboembolism	
	raised levels of	
	inflammatory markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	Symptoms of metastases	
	Chest	
	chest wall or rib pain	
	cough	
	dysphoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	
	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
	Brain	
	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	

lethargy/hyper-somnolence visual disturbance	
seizures	

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design) Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow u data is available detailing whether the symptom was of benig or malignant origin (prospective or retrospective), or diagnos case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patie groups. That is, in both these study types the patients will ha symptom X.	up gn tic t t
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results?For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any ot relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studi The risk of different biases associated with the included stud will be assessed using the QUADAS (I or II) tool for each of t included studies.List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).For each reported symptom the 2-by-2 table (consisting of th number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results w be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. positive predictive value will form the basis of the risk estimal	of es. ies he e rill e The
Note any changes to the protocol or other considerations holew	le.

Note any changes to the protocol or other considerations below

OESOPHAGEAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for oesophageal cancer

Guideline subgroup members: Sue B, Yoryos, Lindsay

Review question: Which investigations of symptoms of suspected oesophageal cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Upper GI endoscopy	Histology/folLow up	Sensitivity
presenting to	Ba swalLow		Specificity
primary care with	Chest X-Ray		Positive predictive value
symptoms of			False negative rate
suspected			
oesophageal			
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations beLow

PANCREAS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Sue B, Stuart, Lindsay, Euan

Review question: What is the risk of pancreatic cancer in patients presenting in primary care with symptom(s)?

Economic priority: Medium

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Abdominal mass		
suspected	Epigastric mass		
cancer*	Lumps		
	Abdominal distension		
	Unusual and sustained		
Subgroups:	bloating		
Age	Back pain		
Sex	Abdominal pain		
Smoking	Abdominal discomfort		
Familial	Colic		
syndromes	Epigastric pain		
Deprivation	Pain when eating		
Obesity	early satiety		
Past history of	Appetite loss		
cancer	Weight loss		
Ethnicity	Anorexia		
Alcohol exposure	Muscle weakness		
Immuno-	Cachexia		
suppression	Change in bowel habit		
BRCA1/BRCA2	Constipation		
Chronic	Diarrhoea		
pancreatitis	Pale coloured stools		
Diabetes	floating stools,		
High intake of	steatorrhoea, foul smelling,		
processed meat	difficult to flush		
Ulcerative colitis	Dark urine		
Gastric ulcer	Jaundice		
Lack of physical	Yellow skin		
activity	itching		
Cystic fibrosis	Unusual belching		
	Delayed gastric emptying		
	hiccups, flatulence, and		
	regurgitation		
	dyspepsia		
	indigestion		
	heartburn Diabatas		
	Diabetes		
	Dyspnoea		
	Breathlessness		
	Altered sleep patterns		
	Fatigue		
	Nausea		
	Vomiting		
	malaise		
	Thromboembolism		
	Unprovoked VTE		

migratory thrombophlebitis		
Trousseau's Syndrome		
DVT		
Dysgeusia		
Asthenia		
Pancreatitis		
Rectal bleeding		
Depression/low mood		
Fever		
Shivering (rigor)		
Night sweats		
Unusual naevi or moles		
(indicative of any familial		
cancer syndrome)		
· · ·		
Generic list		
fatigue		
appetite loss		
weight loss		
thromboembolism		
raised levels of		
inflammatory		
markers		
anemia		
thrombocytosis		
hypercalcemia		
unexplained		
lymphadenopathy or other mass		
other mass		
Sumptomo of motostopoo		
Symptoms of metastases		
Chest		
chest wall or rib pain		
cough		
dyspnoea/shortness of		
breath		
haemoptysis		
hoarseness		
Liver		
abdominal distension		
abdominal pain		
Hepatomegaly		
jaundice		
abnormal liver function		
tests		
vomiting		
bowel obstruction		
Bone		
bone or skeletal pain		
pathological fracture		
pain at multiple sites		
Brain		
confusion		
focal neurological signs		
headache		
imbalance		
personality disturbance		
lethargy/hyper-		
somnolence		
visual disturbance	1	

seizures	
How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what columns will we included in our	For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and Dissemination, and the Cochrane	be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or (

Note any changes to the protocol or other considerations below

PANCREAS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for pancreatic cancer

Guideline subgroup members: Sue Ballard, Lindsay, Stuart, Euan

Review question: Which investigations of symptoms of suspected pancreatic cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format			
Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Ultrasound	Histology/folLow up	Sensitivity
presenting to	СТ		Specificity
primary care with	MRI?		Positive predictive value
symptoms of	CEA		False negative rate
suspected	CA19-9		
pancreatic cancer	Beta hCG		
paricieatic cancer	CA72-4		

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

The review strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	
Note any changes to the protocol or a	ther considerations below

Note any changes to the protocol or other considerations below

<u>STOMACH</u> GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Lindsay, Sue B, Liliana

Review question: What is the risk of cancer of the stomach in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Persistent (every day)		
suspected	heartburn (acid reflux)		
cancer*	'Silent reflux'		
	Sleep apnoea,		
	Sleep disorders,		
Subgroups:	Chronic cough		
Age	Hoarseness		
Sex	Chest pain (non-heartburn)		
Smoking	Dyspepsia		
Familial	Persistent hiccups or		
syndromes	regurgitation of food		
Deprivation	Difficulty or pain in		
Obesity	swallowing food		
Past history of	Food sticking in the throat		
cancer	Dysphagia		
Ethnicity	Short of breath		
Alcohol exposure	Vomiting,		
Immuno-	Nausea,		
suppression	Sickness		
Salt intake	Anorexia		
Dietary history	Feeling full very early		
H pylori	when eating meals		
Pernicious	Persistent indigestion,		
anaemia	acidity, burping and		
HIV/AIDS	vomiting		
Reflux	trapped wind and frequent		
Occupational history	burping Water brash		
history	Bloating		
	Pain/discomfort in the		
	upper abdomen		
	Pain just under your		
	breastbone (sternum) or		
	slightly lower down.		
	Metallic taste		
	Bleeding		
	Feeling breathless		
	Blood clots		
	Fluid in the abdomen		
	Blood in your stool		
	Black stools		
	Vomit streaked with blood		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	thromboembolism		

raised levels of	
inflammatory markers	
anemia	
thrombocytosis	
hypercalcemia	
unexplained	
lymphadenopathy or	
other mass	
Symptoms of metastases	
Chest	
chest wall or rib pain	
cough	
dyspnoea/shortness of	
breath	
haemoptysis	
hoarseness	
Liver	
abdominal distension	
abdominal pain	
Hepatomegaly	
jaundice	
abnormal liver function	
tests	
vomiting	
bowel obstruction	
Bone	
bone or skeletal pain	
pathological fracture	
pain at multiple sites Brain	
confusion	
focal neurological signs	
headache	
imbalance	
personality disturbance	
lethargy/hyper-somnolence	
visual disturbance	
seizures	

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be used (RCT, systematic review, diagnostic	Primary care data only
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

STOMACH

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for stomach cancer

Guideline subgroup members: Lindsay, Sue B, Liliana

Review question: Which investigations of symptoms of suspected stomach cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat ion	Test	Comparison	Outcomes
Patients presenting to primary care with symptoms of suspected stomach cancer	Upper GI endoscopy Barium meal Abdo USS	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.

	Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

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ſ	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
I	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	

Note any changes to the protocol or other considerations below

SMALL INTESTINE

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Lindsay, Joan, Sue B

Review question: What is the risk of small intestine cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
Subgroups:			
Age			
Sex			
Smoking			
Familial			
syndromes			

Deprivation		
Obesity		
Past history of		
cancer		
Ethnicity		
Alcohol exposure		
Immuno-		
suppression		

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

The review strategy

The review Strategy	
Criteria for considering studies (e.g., study design)Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.	
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results?For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies.List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.	
Note any changes to the protocol or other considerations below	

Note any changes to the protocol or other considerations below

SMALL INTESTINE

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for small intestine cancer

Guideline subgroup members: Lindsay, Joan, Sue B

Review question: Which investigations of symptoms of suspected **small intestine/gall bladder cancer** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Capsule endoscopy	Histology/folLow up	Sensitivity
presenting to	Barium folLow through		Specificity
primary care with	СТ		Positive predictive value
symptoms of			False negative rate
suspected small			
· · · · · · · · · · · · · · · · · · ·			
intestine cancer			
	1	1	l

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

-	The review strategy	
ſ	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	
	Note any changes to the protocol or o	other considerations below

lote any changes to the protocol or other considerations below

GALL BLADDER

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Sue B, Stuart, David

Review question: What is the risk of gall bladder cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
.			
Subgroups:			
Age			
Sex			
Smoking			
Familial			
syndromes			
Deprivation			
Obesity			
Past history of			
cancer			
Ethnicity			
Alcohol exposure			
Immuno-			
suppression			

Question in PICO format

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate?

The review strategy

· · · · · · · · · · · · · · · · · · ·	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient

	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our evidence table) and how will we	extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from the NICE manual – but irrelevant items	diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

GALL BLADDER

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for gall bladder cancer

Guideline subgroup members: Sue B, Stuart, David

Review question: Which investigations of symptoms of suspected **gall bladder cancer** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format				
Patients/populat	Test	Comparison	Outcomes	
ion				
Patients	Ultrasound	Histology/folLow up	Sensitivity	
presenting to	LFT		Specificity	
primary care with	СТ		Positive predictive value	
symptoms of	CA19-9		False negative rate	
suspected cancer				
of the gall bladder				

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
Sources to be searched	
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	

diagnostic test). Primary care data only?	
List useful search terms.	

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

LIVER

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Sue B, Stuart, David

Review question: What is the risk of liver cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Abdominal mass		
suspected	Enlarged tender liver		
cancer*	Distinct sound in the liver		
	(hepatic bruit)		
Subgroups:	Abdominal distension		
Age	Swollen abdomen		
Sex	Ascites – excess		
Smoking	fluid/swelling in abdomen		
Familial	and/or legs		
syndromes	Abdominal		
Deprivation	pain/tenderness		
Obesity	Discomfort or pain in		
Past history of	abdomen		
cancer	Epigastric/hypochondrial		

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Ethnicity	pain		
Alcohol exposure	Right shoulder tip pain		
Immuno-	Pain in right shoulder –		
suppression	referred pain		
Chronic hepatitis	Gastrointestinal bleeding		
Cirrhosis	Abnormal bleeding		
Aflatoxin	(gastrointestinal)		
exposure	dilated (widened) veins		
Occupation	called esophageal varices		
Diabetes	Fine blood vessels visible		
HIV	on the skin in a radial		
Betel quid	pattern resembling the legs		
Anabolic steroids	of a spider (known as		
Liver infection			
Liver intection	spider naevi)		
	Vomiting blood		
	Dark black tarry stools		
	Feeling full or bloated after		
	eating, even after a small		
	meal		
	Confusion		
	Diarrhoea		
	Jaundice		
	Dark coloured urine and		
	pale coloured stools		
	Jaundice		
	Itching		
	Cachexia		
	Muscle wasting		
	Hypercalcaemia		
	(Erythrocytosis)		
	Fever		
	Sweats		
	A high temperature and		
	sweating		
	fever with high		
	temperatures and shivers		
	Being sick		
	Nausea/feeling sick		
	-		
	Vomiting		
	A sudden worsening of		
	health in somebody with		
	known chronic hepatitis or		
	cirrhosis		
	Weakness and tiredness		
	Lethargy		
	Loss of libido		
	Erectile dysfunction		
	Swollen testicles		
	Blood in urine		
	Breast development in		
	men		
	Gynaecomastia		
	Stomach pain and cramps		
	mistaken for period pains		
	Flushing		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	weight loss		

	the second second self-second		
	thromboembolism		
	raised levels of		
	inflammatory		
	markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
_	other mass		
	Symptoms of metastases		
C	Chest		
	chest wall or rib pain		
	cough		
	dyspnoea/shortness of		
	breath		
	haemoptysis		
	hoarseness		
L	iver		
	abdominal distension		
	abdominal pain		
	Hepatomegaly		
	jaundice		
	abnormal liver function		
	tests		
	vomiting		
	bowel obstruction		
E	Bone		
	bone or skeletal pain		
	pathological fracture		
	pain at multiple sites		
E	Brain		
	confusion		
	focal neurological signs		
	headache		
	imbalance		
	personality disturbance		
	lethargy/hyper-		
	somnolence		
	visual disturbance		
	seizures		
	36120163	l]	

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we analyse the results?	patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for liver cancer

Guideline subgroup members: Sue B, Stuart, David

Review question: Which investigations of symptoms of suspected liver cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Ultrasound	Histology/folLow up	Sensitivity
presenting to	СТ		Specificity
primary care with	MRI		Positive predictive value
symptoms of	Alpha Feta Protein		False negative rate
suspected liver			
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:

	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

-		
	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
l	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
l	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	

Note any changes to the protocol or other considerations below

COLORECTAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Liliana, Jeanne, Joan

Review question: What is the risk of colorectal cancer in patients presenting in primary care with symptom(s)?

Economic priority: High

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Rectal bleeding		
suspected	Abdominal mass		
cancer*	Rectal mass		
	Tenesmus		
Subgroups:	Abdominal distension		
Age	Abdominal pain		
Sex	Appetite loss		
Smoking	Constipation		
Familial	Diarrhoea		

	— • • • •		
syndromes	Epigastric pain		
Deprivation	Dyspepsia		
Obesity	Colic		
Past history of	Dyspnoea		
cancer	Fatigue		
Ethnicity	Jaundice		
Alcohol exposure	Lower urinary tract		
Immuno-	symptoms		
suppression	Lumps		
IBD	Pelvic mass		
Sexual practices	Pelvic pain		
Polyps	Thromboembolism		
	Vomiting		
Occupational	0		
history	Weight loss		
	Change in bowel habit		
	Anaemia		
	Raised levels of		
	inflammatory markers		
	Thrombocytosis		
	Hepatomegaly		
	Night sweats		
	Abnormal Ift		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	thromboembolism		
	raised levels of		
	inflammatory		
	markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
	other mass		
	other mass		
	Symptome of motostagoe		
	Symptoms of metastases		
	Chest		
	chest wall or rib pain		
	cough		
	dyspnoea/shortness of		
	breath		
	haemoptysis		
	hoarseness		
	Liver		
	abdominal distension		
	abdominal pain		
	Hepatomegaly		
	jaundice		
	abnormal liver function		
	tests		
	vomiting		
	bowel obstruction		
	Bone		
	bone or skeletal pain		
	pathological fracture		
	pain at multiple sites		
	Brain		
		1	

confusion
focal neurological signs
headache
imbalance
personality disturbance
lethargy/hyper-
somnolence
visual disturbance
seizures

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
study design)	
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant item	s The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol of	r other considerations helps:

Note any changes to the protocol or other considerations below

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for colorectal cancer

Guideline subgroup members: Liliana, Jeanne, Joan

Review question: Which investigations of symptoms of suspected colorectal cancer should be done with clinical responsibility retained by primary care?

Economic priority: High

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients presenting to primary care with symptoms of suspected colorectal cancer	Colonoscopy Sigmoidoscopy CT colonoscopy/ colonography CT CEA FOB Barium enema	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

The review Shalegy		
What data will we extract (what	For each included study the folLowing characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any	
appraisal? (Normally checklists from	other relevant details reported in the studies.	
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report on the index test, the results will be	
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the	
Dissemination, and the Cochrane	sensitivity and specificity of the index test.	
Collaboration handbook).		
Note any changes to the protocol or other considerations helew		

Note any changes to the protocol or other considerations below

ANAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Liliana, Jeanne, Joan

Review question: What is the risk of anal cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

The review Strategy		
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients	
	presenting to primary care with symptom X for whom follow up	
	data is available detailing whether the symptom was of benign	
	or malignant origin (prospective or retrospective), or diagnostic	
	case-control studies where cases are patients with the target	
	cancer and controls are (matched) patients without the target	
	cancer that report the prevalence of symptom X in both patient	
	groups. That is, in both these study types the patients will have	
	symptom X.	
What data will we extract (what	For each included study the following characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of	
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.	
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the	

approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook). number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

ANAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for anal cancer

Guideline subgroup members: Lilliana, Jeanne, Joan

Review question: Which investigations of symptoms of suspected **anal** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format				
Patients/populat	Test	Comparison	Outcomes	
ion				
Patients	Proctoscopy	Histology/folLow up	Sensitivity	
presenting to	Sigmoidoscopy		Specificity	
primary care with			Positive predictive value	
symptoms of			False negative rate	
suspected anal				
cancer				

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.

the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should	The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted.
be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane	If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.
Collaboration handbook).	

BREAST

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Joan, Nicki, Jeanne

Review question: What is the risk of breast cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive
symptoms of	Breast lump		value
suspected	Breast pain		
cancer*	Nipple bleeding		
	Nipple inversion		
Subgroups:	Skin change (on breast)		
Age	Unilateral 'eczema' around		
Sex	nipple (Paget's disease)		
Smoking	[searching on 'nipple may be		
Familial	simplest for the three nipple		
syndromes	symptoms]		
Deprivation	Skin changes – dimpling,		
Obesity Deet history of	peau d'orange, ulceration		
Past history of	Nipple discharge		
cancer Ethnicity	Generic list		
Alcohol exposure	fatigue		
Immuno-	appetite loss		
suppression	weight loss		
BRCA1/BRCA2	thromboembolism		
HRT	raised levels of		
Combined	inflammatory markers		
hormonal	anemia		
contraceptive	thrombocytosis		
(CHC) use	hypercalcemia		
Lack of physical	unexplained		
activity	lymphadenopathy or		
Reproductive	other mass		
history			
Lack of breast	Symptoms of metastases		

feeding	Chest	
Ŭ	chest wall or rib pain	
	cough	
	dysphoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	
	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
	Brain	
	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	
	lethargy/hyper- somnolence	
	visual disturbance	
	seizures	

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target
case-control studies where cases are patients with the target
cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient
groups. That is, in both these study types the patients will have symptom X.

What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or	other considerations below

BREAST

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for breast cancer

Guideline subgroup members: Joan, Nicki, Jeanne

Review question: Which investigations of symptoms of suspected breast cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

	Patients/populat	Test	Comparison	Outcomes
	ion			
ſ	Patients	Ultrasound	Histology/folLow up	Sensitivity
	presenting to	Mammography		Specificity
	primary care with	FNA		Positive predictive value
	symptoms of			False negative rate
	suspected breast			-
	cancer			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

_	The review strategy			
ſ	What data will we extract (what	For each included study the folLowing characteristics will be		
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,		
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other		
	analyse the results?	relevant characteristics reported such as relevant history or		
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any		
	appraisal? (Normally checklists from	other relevant details reported in the studies.		
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies		
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the		
	List subgroups here and planned	included studies.		
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the		
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.		
	be used, as described in the manual	If more than one study report on the index test, the results will be		
I	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the		
I	Dissemination, and the Cochrane	sensitivity and specificity of the index test.		
L	Collaboration handbook).			
	Note any abay was to the waste callengether considerations below			

ENDOMETRIAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Joan, Nicki, Richard

Review question: What is the risk of endometrial cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Post menopausal vaginal		
suspected	bleeding		
cancer*	Abnormal/change in pre-		
	menopausal vaginal		
Subgroups:	bleeding (heavy/heavier		
Age	periods,menorrhagia, long		
Sex	periods, inter-menstrual		
Smoking	bleeding, more frequent		
Familial	periods, irregular bleeding)		
syndromes	Vaginal discharge		
Deprivation	Lower abdominal pain		
Obesity	Lower abdominal pressure		
Past history of	Pelvic pain		
cancer	Pelvic pressure		
Ethnicity	Pain on sexual intercourse		
Alcohol exposure	Abdominal swelling		
Immuno-	Lump in abdomen		
suppression	Increased Urinary		
Diabetes	frequency		
Lack of physical	Polyuria		
activity	Dysuria		
Reproductive	Constipation		

		1 1
history	Leg swelling	
HRT use	Abdominal mass	
Previous complex	Abdominal tenderness	
atypical	Enlarged/or irregular	
hyperplasia of	uterus on PV examination	
endometrium	Dysmenorrhoea	
	Polymenorrhoea	
	Dyspareunia	
	Generic list	
	fatigue	
	appetite loss	
	weight loss	
	thromboembolism	
	raised levels of	
	inflammatory	
	markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	Symptoms of metastases	
	Chest	
	chest wall or rib pain	
	cough	
	dyspnoea/shortness of	
	breath	
	haemoptysis	
	hoarseness Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice abnormal liver function	
	tests	
	vomiting bowel obstruction	
	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
	Brain	
	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	
	lethargy/hyper-	
	somnolence	
	visual disturbance	
L	seizures	
How the informati	on will be searched	
Sources to be sea		Core databases to be searched: EMBASE, medline,
		pre-medline, web of science, Cochrane library.
		Specialist databases to be searched if appropriate:

	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).	symptom X. For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

ENDOMETRIAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for endometrial cancer

Guideline subgroup members: Joan, Nicki, Richard

Review question: Which investigations of symptoms of suspected endometrial cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
Patients presenting to	Ultrasound Pipelle sampling CA125	Histology/folLow up	Sensitivity Specificity Positive predictive value

primary care with symptoms of suspected endometrial cancer	Hysteroscopy NB ultrasound may be trans-abdominal or trans- vaginal		False negative rate
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How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

CERVICAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Joan, Nicki, Richard

Review question: What is the risk of cervical cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Unusual vaginal bleeding		
suspected	(Intermenstrual bleeding,		
cancer*	postcoital		
	bleeding,irregular vaginal		
Subgroups:	bleeding, any vaginal		
Age	bleeding in woman past		
Smoking	the menopause- better to		
Familial	use PMB post menopausal		
syndromes	bleeding)		
Deprivation	Pain when having sex-		
Obesity	dyspareunia		
Past history of	Unpleasant smelling		
cancer	vaginal discharge- blood		
Ethnicity	stained vaginal discharge		
Alcohol exposure	Pain when passing		
Immuno-	urinedysuria		
suppression	Increased frequency		
HPV	passing urine		
HIV	Constipation		
COC pill use	Haematuria		
Sexual history	Urinary Incontinence		
	should this be in the		
	secondaries category		
	Swelling in leg		
	Pelvic pain		
	Abnormal looking cervix		
	Abnormal smear-various		
	grades CIN		
	Enlarged/craggy/firm cervix on vaginal		
	examination		
	Contact bleeding when		
	smear taken		
	Sincartaken		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	thromboembolism		
	raised levels of		
	inflammatory		
	markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
	other mass		
	Symptoms of metastases		
	Chest		
	chest wall or rib pain		
	cough		
	dysphoea/shortness of		
	breath		
	haemoptysis		l

	hoarseness
	Liver
	abdominal distension
	abdominal pain
	Hepatomegaly
	jaundice
	abnormal liver function
	tests
	vomiting
	bowel obstruction
1	Bone
	bone or skeletal pain
	pathological fracture
	pain at multiple sites
	Brain
	confusion
	focal neurological signs
	headache
	imbalance
	personality disturbance
	lethargy/hyper-
	somnolence
	visual disturbance
	seizures

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.

statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook). For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

CERVICAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for cervical cancer

Guideline subgroup members: Joan, Nicki, Richard

Review question: Which investigations of symptoms of suspected cervical cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO	Question in PICO format			
Patients/populat	Test	Comparison	Outcomes	
ion				
Patients presenting to primary care with symptoms of suspected cervical cancer	Cervical smear	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate	

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980	
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only	
List useful search terms.		

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.

the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should	The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

VULVA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Karen, Jeanne, Sue B

Review question: What is the risk of cancer of the vulva in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes	
ion				
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value	
symptoms of	suspected cancer			
suspected cancer				
Subgroups:				
Age				
Smoking				
Familial				
syndromes				
Deprivation				
Obesity				
Past history of				
cancer				
Ethnicity				
Alcohol exposure				
Immuno-				
suppression				

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from the NICE manual – but irrelevant items	diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

VULVA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for vulval cancer

Guideline subgroup members: Karen, Jeanne, Sue B

Review question: Which investigations of symptoms of suspected **cancer of the vulva** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Biopsy	Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected cancer			
of the vulva			

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980	
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only	
List useful search terms.		

_	The review strategy	
	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	

Note any changes to the protocol or other considerations below

VAGINAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Joan, Richard, Nicki

Review question: What is the risk of vaginal cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with symptoms of suspected cancer	Signs and symptoms of suspected cancer	Cancer diagnosis	Positive predictive value
Subgroups:			

Age		
Smoking		
Familial		
syndromes		
Deprivation		
Obesity		
Past history of		
cancer		
Ethnicity		
Alcohol exposure		
Immuno-		
suppression		

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review	strategy
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_	The review Shalegy	
	Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.
	What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).	For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The
	Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

VAGINAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for vaginal cancer

Guideline subgroup members: Joan, Richard, Nicki

Review question: Which investigations of symptoms of suspected **vaginal cancer** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format					
ſ	Patients/populat	Test	Comparison	Outcomes	
	ion				
	Patients		Histology/folLow up	Sensitivity	
	presenting to			Specificity	
	primary care with			Positive predictive value	
	symptoms of			False negative rate	
	suspected				
	vaginal cancer				

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The forfield strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

PROSTATE

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: David, Euan, Yoryos

Review question: What is the risk of prostate cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO		Companie ou	Outcomes
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion Detients with	la alcolla ac	Oomeen die eeste	Desitive and listics of
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Nocturia		
suspected	Urinary frequency		
cancer*	Urinary urgency		
Out many a	poor flow		
Subgroups:	Hesitation Incontinence		
Age Sex			
Smoking	Urinary retention Feeling of incomplete		
Familial	bladder emptying		
syndromes	Dysuria		
Deprivation	Impotence		
Obesity	Erectile dysfunction		
Past history of	Loss of libido		
cancer	Pain on ejaculation		
Ethnicity	Haematospermia		
Alcohol exposure	Haematuria		
Immuno-	Pelvic discomfort / pain		
suppression	Abnormal rectal		
Occupational	examination (prostate		
history	enlargement, nodule, hard		
	craggy prostate)		
	Abnormal renal function		
	(raised urea or creatinine)		
	Raised PSA		
	Back pain		
	Swelling in legs		
	Radicular pain		
	Referred pain		
	Lower limb weakness		
	Impaired walking		
	Sensory impairment Bladder or bowel		
	incontinence		
	Spinal tenderness		
	opinal tendemess		
	Generic list		
	fatigue		
	appetite loss		

weight loss	
thromboembolism	
raised levels of	
inflammatory	
markers	
anemia	
thrombocytosis	
hypercalcemia	
unexplained	
lymphadenopathy of	r
other mass	
Symptoms of metastases	
Chest	
chest wall or rib pain	
cough	
dyspnoea/shortness of breath	
haemoptysis	
hoarseness	
Liver	
abdominal distension	
abdominal pain	
Hepatomegaly	
jaundice	
abnormal liver function	
tests	
vomiting	
bowel obstruction	
Bone	
bone or skeletal pain	
pathological fracture	
pain at multiple sites	
Brain	
confusion	
focal neurological sign	S
headache	
imbalance	
personality disturbance	
lethargy/hyper-	
somnolence	
visual disturbance	
seizures	
30120103	

How the information will be searched Sources to be searched Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED. Can we apply date limits to the search 1980 onwards Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only? Primary care data only

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
What data will we avtract (what	symptom X. For each included study the following characteristics will be
What data will we extract (what columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

PROSTATE

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for prostate cancer

Guideline subgroup members: David, Euan, Yoryos

Review question: Which investigations of symptoms of suspected prostate cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
Patients presenting to primary care with symptoms of suspected prostate cancer	PSA MRI for detection	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.

	Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

	0,	
ſ	What data will we extract (what	For each included study the folLowing characteristics will be
l	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
l	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
l	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
l	List subgroups here and planned	included studies.
l	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
l	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
l	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	

Note any changes to the protocol or other considerations below

BLADDER

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: David, Yoryos, Karen

Review question: What is the risk of bladder cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Abdominal pain		
suspected	Haematuria		
cancer*	Vaginal bleeding		
	Appetite loss		
	Bone or skeletal pain		
Subgroups:	Confusion		
Age	Recurring urinary infection		
Sex	Fatigue		

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imbalance personality disturbance lethargy/hyper- somnolence			
personality disturbance lethargy/hyper- somnolence			
lethargy/hyper- somnolence			
somnolence			
		somnolence	
		visual disturbance	

seizures	
How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for appraisal? (Normally checklists from	comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies.
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	other considerations below

Note any changes to the protocol or other considerations below

BLADDER

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for bladder cancer

Guideline subgroup members: David, Yoryos, Karen

Review question: Which investigations of symptoms of suspected bladder cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format			
Patients/populat ion	Test	Comparison	Outcomes
Patients presenting to primary care with symptoms of suspected bladder cancer	Urine cytology Ultrasound Cystoscopy Blood HCG Urine marker NMP22 Urine marker MCM5	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

<u>RENAL</u> (8)

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: David, Richard, Yoryos, Karen

Review question: What is the risk of renal cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Abdominal mass		
suspected	abdominal distension,		
cancer*	abdominal pain,		
	haematuria,		
	appetite loss,		
Subgroups:	constipation,		
Age	lower urinary tract		
Sex	symptoms including UTI,		
Smoking	vomiting,		
Familial	weight loss,		
syndromes	fever including night		
Deprivation	sweats		
Obesity	pelvic mass		
Past history of	flank / loin pain		
cancer	scrotal / groin pain		
Ethnicity	varicocoele		
Alcohol exposure			
Immuno-	Generic list		
suppression	fatigue		
Occupation	appetite loss		
Personal history	weight loss		
of hypertension	thromboembolism		
	raised levels of		
	inflammatory		
	markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
	other mass		
	Symptoms of metastases		
	Chest		
	chest wall or rib pain		
	cough		
	dyspnoea/shortness of		
	breath		
	haemoptysis		
	hoarseness		
	Liver		
	abdominal distension		
	abdominal pain		
	Hepatomegaly		
	jaundice		
	abnormal liver function		
	tests		
	vomiting	1	

	bowel obstruction
B	one
	bone or skeletal pain
	pathological fracture
	pain at multiple sites
B	rain
	confusion
	focal neurological signs
	headache
	imbalance
	personality disturbance
	lethargy/hyper-
	somnolence
	visual disturbance
	seizures

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy			
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive		
study design)	test. These studies will either be of a series of patients		
	presenting to primary care with symptom X for whom follow up		
	data is available detailing whether the symptom was of benign		
	or malignant origin (prospective or retrospective), or diagnostic		
	case-control studies where cases are patients with the target		
	cancer and controls are (matched) patients without the target		
	cancer that report the prevalence of symptom X in both patient		
	groups. That is, in both these study types the patients will have		
	symptom X.		
What data will we extract (what	For each included study the following characteristics will be		
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,		
evidence table) and how will we	patient characteristics (number, age, gender, country, any other		
analyse the results?	relevant characteristics reported such as relevant history or		
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of		
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.		
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies		
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the		
List subgroups here and planned	included studies.		
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the		
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.		
be used, as described in the manual	If more than one study report a given symptom, the results will		
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate		
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The		
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.		
Note any changes to the protocol or other considerations below			

Note any changes to the protocol or other considerations below

RENAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for renal cancer

Guideline subgroup members: David, Richard, Yoryos, Karen

Review question: Which investigations of symptoms of suspected renal cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Abdominal ultrasound	Histology/folLow up	Sensitivity
presenting to	Urine cytology		Specificity
primary care with	X-ray		Positive predictive value
symptoms of	IVP		False negative rate
suspected renal	CT scan of abdomen and		
	pelvis		
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

 ine retrett en alogy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

TESTICULAR

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Yoryos, Karen, David

Review question: What is the risk of testicular cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
Subgroups:			
Age			
Smoking			
Familial			
syndromes			
Deprivation			
Obesity			
Past history of			
cancer			
Ethnicity			
Alcohol exposure			
Immuno-			
suppression			

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
, , ,	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic

	and a sector lateralized where a sector and setting to with the terms t
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or	

TESTICULAR

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for testicular cancer

Guideline subgroup members: Yoryos, Karen, David

Review question: Which investigations of symptoms of suspected **testicular cancer** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes	
ion				
Patients	Ultrasound	Histology/folLow up	Sensitivity	
presenting to			Specificity	
primary care with			Positive predictive value	
symptoms of			False negative rate	
suspected				
testicular cancer				

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	

Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

The review strategy

The review Strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

PENIS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: David, Yoryos, Karen

Review question: What is the risk of penile cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
	orginosymptom	Companson	outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
Subgroups:			
Age			
Smoking			
Familial			
syndromes			
Deprivation			
Obesity			
Past history of			
cancer			
Ethnicity			
Alcohol exposure			

Immuno- suppression		
How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

The review strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	

Note any changes to the protocol or other considerations below

PENIS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for penile cancer

Guideline subgroup members: David, Yoryos, Karen

Review question: Which investigations of symptoms of suspected **cancer of the penis** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
on			
Patients		Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected penile			
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

	The	review	strategy	
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The review strategy				
What data will we extract (what	For each included study the folLowing characteristics will be			
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,			
evidence table) and how will we	patient characteristics (number, age, gender, country, any			
analyse the results?	other relevant characteristics reported such as relevant			
Which quality checklist will we use for	history or comorbidities), index and reference test			
appraisal? (Normally checklists from	characteristics and any other relevant details reported in the			
the NICE manual - but irrelevant items	studies.			
could be omitted).	The risk of different biases associated with the included			
List subgroups here and planned	studies will be assessed using the QUADAS (I or II) tool for			
statistical analyses.(Recognised	each of the included studies.			
approaches to meta-analysis should	For each included study the 2-by-2 table (consisting of the			
be used, as described in the manual	number of true/false positives/negatives) will be extracted.			
from the NHS Centre for Reviews and	If more than one study report on the index test, the results			
Dissemination, and the Cochrane	will be meta-analysed, if feasible, to provide a summary			
Collaboration handbook).	estimate of the sensitivity and specificity of the index test.			
Note any changes to the protocol of	Note any changes to the protocol or other considerations helow			

Note any changes to the protocol or other considerations below

MELANOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Richard, Euan, Nicki

Review question: What is the risk of melanoma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Change in appearance of		
suspected	skin lesion (see classic		
cancer*	complex):		
	Asymmetry		
Subgroups:	• Borders (irregular)		
Age	• Color (variegated),		
Sex	and		
Smoking	• D iameter > 6mm		
Familial	Evolving over time		
syndromes	Elevated above		
Deprivation	the skin surface		
Obesity	• F irm to the touch		
Past history of	Growing		
cancer	New pigmented skin lesion		
Ethnicity	Bleeding or ulcerated skin		
Alcohol exposure	lesion		
Immuno-	Itching		
suppression	Painful		
Sun exposure	Redness		
Sunbed exposure	Tingling		
Occupation	Burning		
	Friability (pieces that break		
	off		
	Change in size		
	Irregular shape		
	Inflammation		
	Change in sensation)		
	Abnormality under finger or		
	toe nail		
	Decreased visual acuity		
	Visual field loss		
	Flashing lights		
	Floaters		
	Ocular pain		
	Choroidal melanoma on		
	ophthalmoscopy		
	O an a via liat		
	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	thromboembolism		
	raised levels of		
	inflammatory markers		
	anemia		
	thrombocytosis		
	hypercalcemia		

unexplained	
lymphadenopathy or	
other mass	
Symptoms of metastases	
Chest	
chest wall or rib pain	
cough	
dyspnoea/shortness of	
breath	
haemoptysis	
hoarseness	
Liver	
abdominal distension	
abdominal pain	
Hepatomegaly	
jaundice	
abnormal liver function	
tests	
vomiting	
bowel obstruction	
Bone	
bone or skeletal pain	
pathological fracture	
pain at multiple sites	
Brain	
confusion	
focal neurological signs	
headache	
imbalance	
personality disturbance	
lethargy/hyper-	
somnolence	
visual disturbance	
seizures	
30120103	

Sources to be searched Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED. Can we apply date limits to the search 1980 onwards Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only? Primary care data only List useful search terms. Image: Core databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.	How the information will be searched	
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?Primary care data only		pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate:
used (RCT, systematic review, diagnostic test). Primary care data only?	Can we apply date limits to the search	1980 onwards
test). Primary care data only?	Are there any study design filters to be	Primary care data only
	used (RCT, systematic review, diagnostic	
List useful search terms.	test). Primary care data only?	
	List useful search terms.	

Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient

	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our evidence table) and how will we	extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other
analyse the results? Which quality checklist will we use for	relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted). List subgroups here and planned	will be assessed using the QUADAS (I or II) tool for each of the included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual from the NHS Centre for Reviews and	If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

MELANOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for melanoma

Guideline subgroup members: Richard, Euan, Nicki

Review question: Which investigations of symptoms of suspected melanoma cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO			
Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Mole mate dermatoscopy	Histology/folLow up	Sensitivity
presenting to	Biopsy		Specificity
primary care with	Ophthalmoscopy		Positive predictive value
symptoms of			False negative rate
suspected			
melanoma			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-	
	medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the	1980	
search		
Are there any study design filters to	Primary care data only	
be used (RCT, systematic review,		

diagnostic test). Primary care data only?	
List useful search terms.	

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any	
analyse the results?	other relevant characteristics reported such as relevant history	
Which quality checklist will we use for	or comorbidities), index and reference test characteristics and	
appraisal? (Normally checklists from	any other relevant details reported in the studies.	
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report on the index test, the results will	
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate	
Dissemination, and the Cochrane	of the sensitivity and specificity of the index test.	
Collaboration handbook).		

Note any changes to the protocol or other considerations below

SQUAMOUS CELL CARCINOMA OF THE SKIN

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Richard, Euan, Nicki

Review question: What is the risk of SCC in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Rough patch on skin		
suspected	Raised lump on skin		
cancer*	Reddish, enlarging flat		
	patch of skin		
Subgroups:	Scaly patch		
Age	Irritated patch of skin		
Sex	Crusted patch		
Smoking	Non-healing patch of skin		
Familial	Ulcerated patch of skin		
syndromes	Bleeding from skin lesion		
Deprivation	Growing bump		
Obesity	Changed mole		
Past history of	Changed wart		
cancer	Changed skin lesion		
Ethnicity			

Alcohol exposure		
Immuno-		
suppression	Generic list	
Sun exposure	fatigue	
Solar keratosis	appetite loss	
	weight loss	
Sunbed exposure	thromboembolism	
Occupation	raised levels of	
Immunosuppressi	inflammatory	
on	markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	Symptoms of metastases	
	Chest	
	chest wall or rib pain	
	cough	
	dyspnoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	
	Bone	
	bone or skeletal pain	
	pathological fracture	
	pain at multiple sites	
	Brain	
	confusion	
	focal neurological signs	
	headache	
	imbalance	
	personality disturbance	
	lethargy/hyper-	
	somnolence	
	visual disturbance	
	seizures	

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

The review strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

SQUAMOUS CELL CARCINOMA OF THE SKIN

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for squamous cell carcinoma of the skin

Guideline subgroup members: Richard, Euan, Nicki

Review question: Which investigations of symptoms of suspected SCC should be done with clinical responsibility retained by primary care?

Economic priority: low

Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Dermatoscopy	Histology/folLow up	Sensitivity
presenting to	Excision / Biopsy		Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected SCC			

How the information will be searched			
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.		
Can we apply date limits to the search	1980		
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only		
List useful search terms.			

The review strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

BASAL CELL CARCINOMA OF THE SKIN

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Richard, Euan, Nicki

Review question: What is the risk of BCC in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Ulcer with raised rolled		
suspected	edge		
cancer*	Prominent fine blood		
	vessels around lesion		
Subgroups:	Nodule on skin		

Age	Pearly / waxy nodule on
Sex	skin
Smoking	Red patch of skin
Familial	Patch of skin that looks like
syndromes	a scar
Deprivation	Bleeding skin lesion
Obesity	Non-healing skin lesion
Past history of	Ulcerated patch of skin
cancer	Bleeding from skin lesion
Ethnicity	Growing bump
Alcohol exposure	Changed mole
Immuno-	Changed wart
suppression	Changed skin lesion
Sun exposure	
Solar keratosis	Conoria list
Sunbed exposure	<u>Generic list</u>
Occupation	fatigue
Immunosuppressi	appetite loss
on	weight loss
	thromboembolism
	raised levels of
	inflammatory
	markers
	anemia
	thrombocytosis
	hypercalcemia
	unexplained
	lymphadenopathy or
	other mass

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

Diagnostic accuracy studies treating a symptom as a positive
test. These studies will either be of a series of patients
presenting to primary care with symptom X for whom follow up
data is available detailing whether the symptom was of benign
or malignant origin (prospective or retrospective), or diagnostic
case-control studies where cases are patients with the target
cancer and controls are (matched) patients without the target
cancer that report the prevalence of symptom X in both patient
groups. That is, in both these study types the patients will have
symptom X.

What data will we extract (what	For each included study the following characteristics will be		
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,		
evidence table) and how will we	patient characteristics (number, age, gender, country, any other		
analyse the results?	relevant characteristics reported such as relevant history or		
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of		
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.		
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies		
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the		
List subgroups here and planned	included studies.		
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the		
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.		
be used, as described in the manual	If more than one study report a given symptom, the results will		
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate		
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The		
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.		
Note any changes to the protocol or other considerations below			

BASAL CELL CARCINOMA OF THE SKIN

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for basal cell carcinoma of the skin

Guideline subgroup members: Richard, Euan, Nicki

Review question: Which investigations of symptoms of suspected **BCC** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes	
ion				
Patients	Dermatoscopy	Histology/folLow up	Sensitivity	
presenting to	excision biopsy of lesion		Specificity	
primary care with			Positive predictive value	
symptoms of			False negative rate	
suspected BCC				
Suspected DOO				

How the information will be searched

now the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-	
	medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the	1980	
search		
Are there any study design filters to	Primary care data only	
be used (RCT, systematic review,		
diagnostic test). Primary care data		
only?		
List useful search terms.		

The review strategy

What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook). For each included study the folLowing characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), index and reference test characteristics and any other relevant details reported in the studies.

The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies.

For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.

Note any changes to the protocol or other considerations below

LARYNX

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Euan, Karen, Stuart

Review question: What is the risk of cancer of the larynx in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion		•	
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
O 1			
Subgroups:			
Age			
Sex			
Smoking			
Familial			
syndromes			
Deprivation			
Obesity			
Past history of			
cancer			
Ethnicity			
Alcohol exposure			
Immuno-			
suppression			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy

	The review strategy	
	Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
	study design)	test. These studies will either be of a series of patients
		presenting to primary care with symptom X for whom follow up
		data is available detailing whether the symptom was of benign
		or malignant origin (prospective or retrospective), or diagnostic
		case-control studies where cases are patients with the target
		cancer and controls are (matched) patients without the target
		cancer that report the prevalence of symptom X in both patient
		groups. That is, in both these study types the patients will have
		symptom X.
	What data will we extract (what	For each included study the following characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
	appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report a given symptom, the results will
	from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
	Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
L	Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
	Note any changes to the protocol of a	NTHAT CONSIDERATIONS HOLOW

Note any changes to the protocol or other considerations below

LARYNX

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for laryngeal cancer

Guideline subgroup members: Euan, Karen, Stuart

Review question: Which investigations of symptoms of suspected **cancer of the larynx** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat ion	Test	Comparison	Outcomes
Patients presenting to primary care with symptoms of suspected cancer of the larynx	Chest x-ray	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

_	The review strategy		
ſ	What data will we extract (what	For each included study the folLowing characteristics will be	
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
	analyse the results?	relevant characteristics reported such as relevant history or	
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any	
	appraisal? (Normally checklists from	other relevant details reported in the studies.	
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies	
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
	List subgroups here and planned	included studies.	
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the	
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
	be used, as described in the manual	If more than one study report on the index test, the results will be	
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the	
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.	
	Collaboration handbook).		
	Note any changes to the protocol or other considerations helpy		

Note any changes to the protocol or other considerations below

ORAL GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Jeanne, Stuart, Richard

Review question: What is the risk of oral cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

•

Question in PICO format			
Patients/population	Sign/symptom*	Comparison	Outcomes
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Ulcers on tongue		
suspected cancer*	Ulcers on lip		
	Ulcers in mouth		
Subgroups:	Plaques		
Age	Bleeding gums		
Sex	Lichen planus		
Smoking	Sore throat		
Familial syndromes	Dysphagia		
Deprivation	Pain		
Obesity	Pain on chewing		
Past history of	Pain on swallowing		
cancer	Earache		
Ethnicity	Toothache		
Alcohol exposure	Loose teeth		
Immuno-	Speech impediment		
suppression	Halitosis		
Chewing betel	Swollen lymph glands		
HPV	(under chin, in neck)		
Dietary history	Bony lumps (on palpate)		
Syphilis	Pain wearing dentures		
Cannabis	i an wearing demarco		
Carinabis	Generic list		
	fatigue		
	appetite loss		
	weight loss		
	thromboembolism		
	raised levels of		
	inflammatory markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
	other mass		
	Symptoms of metastases		
	Chest		
	chest wall or rib pain		
	cough		
	dyspnoea/shortness of		
	breath		
	haemoptysis		
	hoarseness		
	Liver		
	abdominal distension		
	abdominal distension abdominal pain		
	•		
	Hepatomegaly		
	jaundice		

abnormal liver function	
tests	
vomiting	
bowel obstruction	
Bone	
bone or skeletal pain	
pathological fracture	
pain at multiple sites	
Brain	
confusion	
focal neurological signs	
headache	
imbalance	
personality disturbance	
lethargy/hyper-	
somnolence	
visual disturbance	
seizures	

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review Strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	· · · ·
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The

Collaboration handbook).

positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

ORAL

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for oral cancer

Guideline subgroup members: Jeanne, Stuart, Richard

Review question: Which investigations of symptoms of suspected oral cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

_	Question in PICO format				
	Patients/populat	Test	Comparison	Outcomes	
	ion				
	Patients	Biopsy	Histology/folLow up	Sensitivity	
	presenting to			Specificity	
	primary care with			Positive predictive value	
	symptoms of			False negative rate	
	suspected oral				
	cancer				

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any
analyse the results?	other relevant characteristics reported such as relevant history
Which quality checklist will we use for	or comorbidities), index and reference test characteristics and
appraisal? (Normally checklists from	any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies

could be omitted).	
List subgroups here and planned	
statistical analyses.(Recognised	
approaches to meta-analysis should	
be used, as described in the manual	
from the NHS Centre for Reviews and	
Dissemination, and the Cochrane	
Collaboration handbook).	

will be assessed using the QUADAS (I or II) tool for each of the included studies. For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.

Note any changes to the protocol or other considerations below

THYROID

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Lindsay, Joan, Karen

Review question: What is the risk of thyroid cancer in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes	
ion				
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value	
symptoms of	suspected cancer			
suspected cancer				
Subgroups:				
Age				
Sex				
Smoking				
Familial				
syndromes				
Deprivation				
Obesity				
Past history of				
cancer				
Ethnicity				
Alcohol exposure				
Immuno-				
suppression				

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Disparing the Cashrapa	For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane Collaboration handbook).	indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

THYROID

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for thyroid cancer

Guideline subgroup members: Lindsay, Joan, Karen

Review question: Which investigations of symptoms of suspected **thyroid cancer** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients Ultrasound Hist	
presenting to primary care with symptoms of suspected thyroid cancer	blogy/folLow up Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

The review strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any
analyse the results?	other relevant characteristics reported such as relevant history
Which quality checklist will we use for	or comorbidities), index and reference test characteristics and
appraisal? (Normally checklists from	any other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	of the sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

BRAIN & CNS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Lindsay, Jeanne, Susan H

Review question: What is the risk of brain-central nervous system cancer in patients presenting in primary care with symptom(s)?

Economic priority: Medium

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Headache		
suspected	Nausea and vomiting		
cancer*	Abnormal gait		
	Squint		

Subgroups:	Visual disturbance	
Age	Seizures	
Sex	Growth failure (failure to	
Smoking	thrive)	
Familial	Precocious puberty	
syndromes	Personality change	
Deprivation	Imbalance	
Obesity	Polyuria	
Past history of	Delayed puberty	
cancer	Fatigue	
Ethnicity	Impaired higher	
Alcohol exposure	functioning: (concentration,	
Immuno-	memory loss, distraction,	
suppression	behavioural change, co-	
HIV/AIDS	ordination, speech	
	difficulty)	
Children and	Parental concern	
young people	Sleep disturbance	
young people	Hearing loss	
	pallor	
	Confusion	
	Pupil irregularity	
	Bulging fontanelle	
	No red reflex	
	Weakness	
	Abnormal neurological examination	
	examination	
	Generic list	
	fatigue	
	appetite loss	
	weight loss thromboembolism	
	raised levels of	
	inflammatory	
	markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	Symptoms of metastases	
	Chest	
	chest wall or rib pain	
	cough	
	dysphoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
	jaundice	
	abnormal liver function	
	tests	
	vomiting	
	bowel obstruction	

Bone
bone or skeletal pain
pathological fracture
pain at multiple sites
Brain
confusion
focal neurological signs
headache
imbalance
personality disturbance
lethargy/hyper-
somnolence
visual disturbance
seizures

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).	symptom X. For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

BRAIN & CNS

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for brain & CNS cancer

Guideline subgroup members: Lindsay, Jeanne, Susan H

Review question: Which investigations of symptoms of suspected brain and CNS should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Question in 1100	Torritat		
Patients/populat	Test	Comparison	Outcomes
ion			
Patients	СТ	Histology/folLow up	Sensitivity
presenting to	MRI		Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected brain			
and CNS			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

_	The review strategy	
	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.

Collaboration handbook).

Note any changes to the protocol or other considerations below

LEUKAEMIA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Liliana, Jeanne, Susan H

Review question: What is the risk of leukaemia in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion		-	
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Fever,		
suspected	tiredness,		
cancer*	weight loss,		
	dizzy,		
Subgroups:	non-specific aches, bone		
Age	tenderness,		
Sex	joint pain,		
Smoking	muscle pain,		
Familial	lymphadenopathy,		
syndromes	bruising,		
Deprivation	bleeding,		
Obesity	nausea,		
Past history of	vomiting,		
cancer	diffuse abdominal pain,		
Ethnicity	hepatosplenomegaly,		
Alcohol exposure	headache,		
Immuno-	isolated cranial nerve		
suppression	palsies,		
Occupation	skin rash,		
Genetic	non-blanching		
conditions	erythematous papules,		
(Down's	stridor,		
syndrome)	wheezing,		
Autoimmune	pericardial effusions,		
conditions such	superior vena cava		
as rheumatoid	syndrome,		
arthritis,	anaemia,		
autoimmune	fatigue,		
haemolytic	dyspnoea (exertional),		
anaemia and	palpitations,		
ulcerative colitis,	angina,		
HIV/AIDS may be	claudication		

due to actual	thrombocytopenia,	
condition or the	epistaxis,	
medicines taken	gingival haemorrhage,	
for the condition	menorrhagia,	
that increases	cutaneous petechiae,	
risk	haemorrhage	
	(gastrointestinal ,urinary,	
Children and	intracranial retinal),	
young people	hyperviscosity,	
)	hypoxia,	
	respiratory failure,	
	seizures,	
	confusion,	
	coma,	
	visual disturbances,	
	priapism,	
	hyperleukocytosis,	
	convulsion,	
	fits,	
	focal neurology	
	gum hypertrophy,	
	stomatitis,	
	soft tissue masses,	
	testicular involvement	
	(include painless,	
	asymmetric enlargement)	
	neutropaenia,	
	infections (bacterial or	
	fungal of teeth and	
	oropharynx, sinuses, lung,	
	skin, perineum and bowel)	
	· · · · · · · · · · · · · · · · · · ·	
	Generic list	
	fatigue	
	appetite loss	
	weight loss	
	thromboembolism	
	raised levels of	
	inflammatory	
	markers	
	anemia	
	thrombocytosis	
	hypercalcemia	
	unexplained	
	lymphadenopathy or	
	other mass	
	Symptoms of metastases	
	Chest	
	chest wall or rib pain	
	cough	
	dyspnoea/shortness of	
	breath	
	haemoptysis	
	hoarseness	
	Liver	
	abdominal distension	
	abdominal pain	
	Hepatomegaly	
L		

	jaundice
	abnormal liver function
	tests
	vomiting
	bowel obstruction
E	Bone
	bone or skeletal pain
	pathological fracture
	pain at multiple sites
E	Brain
	confusion
	focal neurological signs
	headache
	imbalance
	personality disturbance
	lethargy/hyper-
	somnolence
	visual disturbance
	seizures

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The

Collaboration handbook).

positive predictive value will form the basis of the risk estimate.

Note any changes to the protocol or other considerations below

LEUKAEMIA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for leukaemia

Guideline subgroup members: Liliana, Jeanne, Susan H

Review question: Which investigations of symptoms of suspected leukaemia should be done with clinical responsibility retained by primary care?

Economic priority: Low

 Question in PICO	format			
Patients/populat	Test	Comparison	Outcomes	
ion				
Patients	White blood cell count	Histology/folLow up	Sensitivity	
presenting to			Specificity	
primary care with			Positive predictive value	
symptoms of			False negative rate	
suspected				
leukaemia				

How the information will be searched Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED. Can we apply date limits to the search 1980 Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only Primary care data only List useful search terms. Image: Search database databas

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any

appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations beLow

LIVER

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for liver cancer

Guideline subgroup members: Sue B, Stuart, David

Review question: Which investigations of symptoms of suspected liver cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients presenting to primary care with symptoms of suspected liver	Ultrasound CT MRI Alpha Feta Protein	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate
cancer			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre- medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980
Are there any study design filters to be used (RCT, systematic review, diagnostic test). Primary care data only?	Primary care data only
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

_	The review strategy	
	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
	Collaboration handbook).	
	Note and the second of the second second second	

Note any changes to the protocol or other considerations below

MYELOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Liliana, Yoryos, Lindsay

Review question: What is the risk of myeloma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Including:	Cancer diagnosis	Positive predictive value
symptoms of	Abnormal bleeding		
suspected	(including, haemoptysis,		
cancer*	haematuria,		
	gastrointestinal and		
Subgroups:	vaginal bleeding)		
Age	Appetite loss		
Sex	Bruising		
Smoking	Ankle swelling		
Familial	Malaise		
syndromes	Polyuria		
Deprivation	Thirst		
Obesity	Bone or skeletal pain		
Past history of	Chest wall or rib pain		
cancer	Confusion		
Ethnicity	Constipation		
Alcohol exposure	Dyspnoea		
Immuno-	Epigastric pain (including		
suppression	dyspepsia)		
Race	Fatigue		
Radiation	Focal neurological signs		
exposure	Spinal cord compression		
	Infections suggesting		

Immunocompromise	
Lower urinary tract	
symptoms	
Lumps (including breast,	
neck, abdominal, bony	
and soft-tissue masses,	
unexplained	
lymphadenopathy)	
Pain at multiple sites	
Pathological fracture	
Shortness of breath	
Thromboembolism	
Vomiting	
Weight loss	
Anaemia	
Abnormal	
liver function tests	
Hypercalcaemia	
Raised levels of	
inflammatory markers	
Thrombocytosis.	
Back pain	
Generic list	
fatigue	
appetite loss	
weight loss	
thromboembolism	
raised levels of	
inflammatory	
markers	
anemia	
thrombocytosis	
hypercalcemia	
unexplained	
lymphadenopathy or	
other mass	
00101 11000	
Symptoms of metastases	
Chest	
chest wall or rib pain	
cough	
dyspnoea/shortness of	
breath	
haemoptysis	
hoarseness	
Liver	
abdominal distension	
abdominal pain	
Hepatomegaly	
jaundice	
abnormal liver function	
tests	
vomiting	
bowel obstruction	
Bone	
bone or skeletal pain	
pathological fracture	
pain at multiple sites	
Brain	

confusion
focal neurological signs
headache
imbalance
personality disturbance
lethargy/hyper-
somnolence
visual disturbance
seizures

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline,	
	pre-medline, web of science, Cochrane library.	
	Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

The review Strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up data is available detailing whether the symptom was of benign or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).	For each included study the following characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), definition of symptom, method of verification of diagnosis and any other relevant details reported in the studies. The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies. For each reported symptom the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate indicating the risk of cancer associated with each symptom. The positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	

Note any changes to the protocol or other considerations below

MYELOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for myeloma

Guideline subgroup members: Liliana, Yoryos, Lindsay

Review question: Which investigations of symptoms of suspected myeloma should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients presenting to primary care with symptoms of suspected myeloma	Paraprotein/serum Electrophoresis / Bence-Jones protein (urine test) ESR Viscosity Calcium X-ray	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched

	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
liagnostic test). Primary care data	
only?	
ist useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

_	The review strategy	
	What data will we extract (what	For each included study the folLowing characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
	appraisal? (Normally checklists from	other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report on the index test, the results will be
	from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
	Dissemination, and the Cochrane	sensitivity and specificity of the index test.
L	Collaboration handbook).	
	Note any changes to the protocol or o	other considerations below

Note any changes to the protocol or other considerations below

NON-HODGKIN LYMPHOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Stuart, Liliana, Lindsay

Review question: What is the risk of lymphoma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO		Comparison	Outcomos
Patients/populat	Sign/Symptom	Companson	Outcomes
ion Patients with	Including	Concer discressio	Desitive predictive value
symptoms of	Including: Lumps	Cancer diagnosis	Positive predictive value
	Swollen glands		
suspected	U		
cancer*	Sweats Breathlessness		
Subgroupor			
Subgroups:	Cough		
Age Sex	Weight loss Itch		
Smoking	Fatigue		
Familial	Skin rash		
syndromes Deprivation	Alcohol induced pain		
	Feeling of weakness		
Obesity Dest bistory of	Abnormal bruising Anaemia		
Past history of cancer	Fever		
Ethnicity			
Alcohol exposure	Abdominal pain Appetite loss		
Immuno-			
	Infection suggesting		
suppression	immunocompromise		
Treatment, Race	Pathological fracture Abnormal Ift		
HIV/AIDS	Raised levels of		
Rheumatoid			
arthritis	inflammatory markers Pallor		
arunnus	FallOI		
Children and	Generic list		
young people	fatigue		
young people	appetite loss		
	weight loss		
	thromboembolism		
	raised levels of		
	inflammatory		
	markers		
	anemia		
	thrombocytosis		
	hypercalcemia		
	unexplained		
	lymphadenopathy or		
	other mass		
	00101 11035		
	Symptoms of metastases		
	Chest		
L	UNUU		1

	also a formall an allow of the
	chest wall or rib pain
	cough
	dyspnoea/shortness of
	breath
	haemoptysis
	hoarseness
Li	ver
	abdominal distension
	abdominal pain
	Hepatomegaly
	jaundice
	abnormal liver function
	tests
	vomiting
	bowel obstruction
Bo	one
	bone or skeletal pain
	pathological fracture
	pain at multiple sites
Br	ain
	confusion
	focal neurological signs
	headache
	imbalance
	personality disturbance
	lethargy/hyper-
	somnolence
	visual disturbance
L _.	seizures

How the information will be searched			
Sources to be searched	Core databases to be searched: EMBASE, medline,		
	pre-medline, web of science, Cochrane library.		
	Specialist databases to be searched if appropriate:		
	CINAHL, BNI, psychinfo, AMED.		
Can we apply date limits to the search	1980 onwards		
Are there any study design filters to be	Primary care data only		
used (RCT, systematic review, diagnostic			
test). Primary care data only?			
List useful search terms.			

The review strategy		
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow u data is available detailing whether the symptom was of benigr	p n
	or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target cancer and controls are (matched) patients without the target cancer that report the prevalence of symptom X in both patient groups. That is, in both these study types the patients will have symptom X.	nt

What data will we extract (what	For each included study the following characteristics will be			
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,			
evidence table) and how will we	patient characteristics (number, age, gender, country, any other			
analyse the results?	relevant characteristics reported such as relevant history or			
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of			
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.			
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies			
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the			
List subgroups here and planned	included studies.			
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the			
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.			
be used, as described in the manual	If more than one study report a given symptom, the results will			
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate			
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The			
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.			
Note any changes to the protocol or other considerations below				

NON-HODGKINS LYMPHOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for non-Hodgkin's lymphoma

Guideline subgroup members: Stuart, Liliana, Lindsay

Review question: Which investigations of symptoms of suspected Non Hodgkins lymphoma cancer should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion		-	
Patients	Chest X-Ray	Histology/folLow up	Sensitivity
presenting to	CT scan		Specificity
primary care with	ultrasound		Positive predictive value
symptoms of	LDH		False negative rate
suspected non-			
hodgkins			
lymphoma			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook). For each included study the folLowing characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), index and reference test characteristics and any other relevant details reported in the studies.

The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies.

For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.

Note any changes to the protocol or other considerations below

HODGKIN'S LYMPHOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Stuart, Liliana, Lindsay

Review question: What is the risk of Hodgkin's lymphoma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patient	s/populat	Sign/symptom*	Comparison	Outcomes
ion				
Patients symptor	ms of ted cancer	Signs and symptoms of suspected cancer	Cancer diagnosis	Positive predictive value
Sex Smokin Familial syndron Depriva Obesity	nes ution			
Past his cancer Ethnicity Alcohol Immunc suppres	y exposure >-			

Children and young people	
How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy	
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	other considerations below

Note any changes to the protocol or other considerations below

HODGKIN'S LYMPHOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for Hodgkin's lymphoma

Guideline subgroup members: Stuart, Liliana, Lindsay

Review question: Which investigations of symptoms of suspected **Hodgkins lymphoma** should be done with clinical responsibility retained by primary care?

Economic priority: Low

	Question in PICO format				
Γ	Patients/populat	Test	Comparison	Outcomes	
	ion				
	Patients	Chest X-Ray	Histology/folLow up	Sensitivity	
	presenting to	CT scan		Specificity	
	primary care with	ultrasound		Positive predictive value	
	symptoms of	LDH		False negative rate	
	suspected				
	hodgkins				
	U U				
	lymphoa				

How the information will be searchedSources to be searchedCore databases to be searched: EMBASE, medline, pre-
medline, web of science, Cochrane library.
Specialist databases to be searched if appropriate:
CINAHL, BNI, psychinfo, AMED.Can we apply date limits to the
search1980Are there any study design filters to
be used (RCT, systematic review,
diagnostic test). Primary care data
only?Primary care data onlyList useful search terms.Image: Constant of the search terms.

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy

What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any
appraisal? (Normally checklists from	other relevant details reported in the studies.
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will be
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the
Dissemination, and the Cochrane	sensitivity and specificity of the index test.
Collaboration handbook).	

Note any changes to the protocol or other considerations below

BONE SARCOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Susan H, Euan, Nicki

Review question: What is the risk of bone sarcoma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format

Patients/populat	Sign/symptom*	Comparison	Outcomes	
ion				
Patients with	Signs and symptoms	Cancer diagnosis	Positive predictive value	
symptoms of				
suspected				
cancer*				
Subgroups:				
Age				
Sex				
Smoking				
Familial				
syndromes				
Deprivation				
Obesity				
Past history of				
cancer				
Ethnicity				
Alcohol exposure				
Immuno-				
suppression				

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate:	
	CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.

What data will we extract (what	For each included study the following characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of	
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.	
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report a given symptom, the results will	
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate	
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The	
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.	
Note any changes to the protocol or other considerations below		

BONE SARCOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for bone sarcoma

Guideline subgroup members: Susan Hay, Euan, Nicki

Review question: Which investigations of symptoms of suspected **bone sarcoma** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
ion			
Patients presenting to primary care with symptoms of suspected bone sarcoma	X-ray Calcium Alkaline phosphatase	Histology/folLow up	Sensitivity Specificity Positive predictive value False negative rate

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook).

For each included study the folLowing characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), index and reference test characteristics and any other relevant details reported in the studies.

The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies.

For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.

Note any changes to the protocol or other considerations below

SOFT TISSUE SARCOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Susan H, Euan, Nicki

Review question: What is the risk of soft tissue sarcoma in patients presenting in primary care with symptom(s)?

Economic priority: LOW

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Patients with	Signs and symptoms of	Cancer diagnosis	Positive predictive value
symptoms of	suspected cancer		
suspected cancer			
. .			
Subgroups:			
Age			
Sex			
Smoking			
Familial			
syndromes			
Deprivation			
Obesity			
Past history of			
cancer			
Ethnicity			
Alcohol exposure			
Immuno-			
suppression			

How the information will be searched		
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-medline, web of science, Cochrane library. Specialist databases to be searched if appropriate: CINAHL, BNI, psychinfo, AMED.	
Can we apply date limits to the search	1980 onwards	
Are there any study design filters to be	Primary care data only	
used (RCT, systematic review, diagnostic		
test). Primary care data only?		
List useful search terms.		

The review strategy

_	The review strategy	
	Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
	study design)	test. These studies will either be of a series of patients
		presenting to primary care with symptom X for whom follow up
		data is available detailing whether the symptom was of benign
		or malignant origin (prospective or retrospective), or diagnostic
		case-control studies where cases are patients with the target
		cancer and controls are (matched) patients without the target
		cancer that report the prevalence of symptom X in both patient
		groups. That is, in both these study types the patients will have
L		symptom X.
	What data will we extract (what	For each included study the following characteristics will be
	columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
	evidence table) and how will we	patient characteristics (number, age, gender, country, any other
	analyse the results?	relevant characteristics reported such as relevant history or
	Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
	appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
	the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
	could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
	List subgroups here and planned	included studies.
	statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
	approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
	be used, as described in the manual	If more than one study report a given symptom, the results will
	from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
	Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
L	Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
	Note any changes to the protocol or c	

Note any changes to the protocol or other considerations below

SOFT TISSUE SARCOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for soft tissue sarcoma

Guideline subgroup members: Susan H, Euan, Nicki

Review question: Which investigations of symptoms of suspected **soft tissue sarcoma** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format			
Patients/populat	Test	Comparison	Outcomes
ion			
Patients	Ultrasound	Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected soft			
tissue sarcoma			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The	review	strategy
-		

What data will we extract (what	For each included study the folLowing characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use fo	comorbidities), index and reference test characteristics and any	
appraisal? (Normally checklists from	other relevant details reported in the studies.	
the NICE manual - but irrelevant iten	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report on the index test, the results will be	
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the	
Dissemination, and the Cochrane	sensitivity and specificity of the index test.	
Collaboration handbook).		

Note any changes to the protocol or other considerations below

NEUROBLASTOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Susan H, Jeanne

Review question: What is the risk of neuroblastoma in child patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format

Question in PICO format			
Patients/popula	t Sign/symptom*	Comparison	Outcomes
ion			
Child patients with symptoms of suspected cance Any subgroups reported		Cancer diagnosis	Positive predictive value

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
Criteria for considering studies (e.g., study design)	Diagnostic accuracy studies treating a symptom as a positive test. These studies will either be of a series of patients presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have symptom X.
What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual from the NHS Centre for Reviews and	If more than one study report a given symptom, the results will be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	

Note any changes to the protocol or other considerations below

NEUROBLASTOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for neuroblastoma

Guideline subgroup members: Susan H, Jeanne

Review question: Which investigations of symptoms of suspected **neuroblastoma** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Question in 100	Tormat		
Patients/populat	Test	Comparison	Outcomes
ion			
Patients		Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected			
neuroblastoma			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

The review strategy	
What data will we extract (what	For each included study the folLowing characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any
analyse the results?	other relevant characteristics reported such as relevant history
Which quality checklist will we use for	or comorbidities), index and reference test characteristics and
appraisal? (Normally checklists from	any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report on the index test, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	of the sensitivity and specificity of the index test.

Collaboration handbook).

Note any changes to the protocol or other considerations below

RETINOBLASTOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Susan H, Jeanne

Review question: What is the risk of retinoblastoma in child patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format			
Patients/populat	Sign/symptom*	Comparison	Outcomes
ion			
Child patients with symptoms of suspected cancer	Signs and symptoms of suspected cancer	Cancer diagnosis	Positive predictive value
Any subgroups reported			

How the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

If we know before the literature search there is unlikely to be any evidence for the population or intervention is there a similar population or intervention (with high quality evidence) from which we could extrapolate? No

Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive
study design)	test. These studies will either be of a series of patients
	presenting to primary care with symptom X for whom follow up
	data is available detailing whether the symptom was of benign
	or malignant origin (prospective or retrospective), or diagnostic
	case-control studies where cases are patients with the target
	cancer and controls are (matched) patients without the target
	cancer that report the prevalence of symptom X in both patient
	groups. That is, in both these study types the patients will have
	symptom X.

What data will we extract (what	For each included study the following characteristics will be
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,
evidence table) and how will we	patient characteristics (number, age, gender, country, any other
analyse the results?	relevant characteristics reported such as relevant history or
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the
List subgroups here and planned	included studies.
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.
be used, as described in the manual	If more than one study report a given symptom, the results will
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.
Note any changes to the protocol or o	other considerations below

RETINOBLASTOMA

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for retinoblastoma

Guideline subgroup members: Susan H, Jeanne

Review question: Which investigations of symptoms of suspected **retinoblastoma** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Question in PICO format

Patients/populat	Test	Comparison	Outcomes
ion			
Patients		Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected			
retinoblastoma			

How the information will be searched

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy

What data will we extract (what columns will we included in our evidence table) and how will we analyse the results? Which quality checklist will we use for appraisal? (Normally checklists from the NICE manual – but irrelevant items could be omitted). List subgroups here and planned statistical analyses.(Recognised approaches to meta-analysis should be used, as described in the manual from the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook). For each included study the folLowing characteristics will be extracted: Study design, inclusion/exclusion criteria, setting, patient characteristics (number, age, gender, country, any other relevant characteristics reported such as relevant history or comorbidities), index and reference test characteristics and any other relevant details reported in the studies.

The risk of different biases associated with the included studies will be assessed using the QUADAS (I or II) tool for each of the included studies.

For each included study the 2-by-2 table (consisting of the number of true/false positives/negatives) will be extracted. If more than one study report on the index test, the results will be meta-analysed, if feasible, to provide a summary estimate of the sensitivity and specificity of the index test.

Note any changes to the protocol or other considerations below

WILM'S TUMOUR

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: What is the risk of cancer in patients presenting in primary care with symptom(s)?

Guideline subgroup members: Susan H, Liliana

Review question: What is the risk of neuroblastoma in child patients presenting in primary care with symptom(s)?

Economic priority: LOW

Question in PICO format

Patients/populat	Sign/symptom*	Comparison	Outcomes
ion	olghioymptom	Companoon	Cateonics
Child patients with symptoms of suspected cancer	Signs and symptoms of suspected cancer	Cancer diagnosis	Positive predictive value
Any subgroups reported			

How the information will be searched

now the information will be searched	
Sources to be searched	Core databases to be searched: EMBASE, medline,
	pre-medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the search	1980 onwards
Are there any study design filters to be	Primary care data only
used (RCT, systematic review, diagnostic	
test). Primary care data only?	
List useful search terms.	

The review strategy		
Criteria for considering studies (e.g.,	Diagnostic accuracy studies treating a symptom as a positive	
study design)	test. These studies will either be of a series of patients	
	presenting to primary care with symptom X for whom follow up	
	data is available detailing whether the symptom was of benign	
	or malignant origin (prospective or retrospective), or diagnostic	
	case-control studies where cases are patients with the target	
	cancer and controls are (matched) patients without the target	
	cancer that report the prevalence of symptom X in both patient	
	groups. That is, in both these study types the patients will have	
	symptom X.	
What data will we extract (what	For each included study the following characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use for	comorbidities), definition of symptom, method of verification of	
appraisal? (Normally checklists from	diagnosis and any other relevant details reported in the studies.	
the NICE manual – but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each reported symptom the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report a given symptom, the results will	
from the NHS Centre for Reviews and	be meta-analysed, if feasible, to provide a summary estimate	
Dissemination, and the Cochrane	indicating the risk of cancer associated with each symptom. The	
Collaboration handbook).	positive predictive value will form the basis of the risk estimate.	

Note any changes to the protocol or other considerations below

WILM'S TUMOUR

GDG subgroup lead fills in highlighted areas, NCCC staff all other area.

Guideline Title GP referral for suspected cancer

Review Protocol for: Primary care tests for Wilm's tumour

Guideline subgroup members: Susan H, Liliana

Review question: Which investigations of symptoms of suspected **Wilm's tumour** should be done with clinical responsibility retained by primary care?

Economic priority: Low

Patients/populat	Test	Comparison	Outcomes
ion			
Patients		Histology/folLow up	Sensitivity
presenting to			Specificity
primary care with			Positive predictive value
symptoms of			False negative rate
suspected Wilms			

ſ	tumour		

Sources to be searched	Core databases to be searched: EMBASE, medline, pre-
	medline, web of science, Cochrane library.
	Specialist databases to be searched if appropriate:
	CINAHL, BNI, psychinfo, AMED.
Can we apply date limits to the	1980
search	
Are there any study design filters to	Primary care data only
be used (RCT, systematic review,	
diagnostic test). Primary care data	
only?	
List useful search terms.	

The review strategy		
What data will we extract (what	For each included study the folLowing characteristics will be	
columns will we included in our	extracted: Study design, inclusion/exclusion criteria, setting,	
evidence table) and how will we	patient characteristics (number, age, gender, country, any other	
analyse the results?	relevant characteristics reported such as relevant history or	
Which quality checklist will we use for	comorbidities), index and reference test characteristics and any	
appraisal? (Normally checklists from	other relevant details reported in the studies.	
the NICE manual - but irrelevant items	The risk of different biases associated with the included studies	
could be omitted).	will be assessed using the QUADAS (I or II) tool for each of the	
List subgroups here and planned	included studies.	
statistical analyses.(Recognised	For each included study the 2-by-2 table (consisting of the	
approaches to meta-analysis should	number of true/false positives/negatives) will be extracted.	
be used, as described in the manual	If more than one study report on the index test, the results will be	
from the NHS Centre for Reviews and	meta-analysed, if feasible, to provide a summary estimate of the	
Dissemination, and the Cochrane	sensitivity and specificity of the index test.	
Collaboration handbook).		
Note any changes to the protocol or other considerations below		