1 2	NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
3	Guideline
4	Lung cancer: diagnosis and management
5	Draft for consultation, October 2018
6	

This guideline covers diagnosing and managing non-small-cell and small-cell lung cancer. The 2019 update makes recommendations on mediastinal lymph node assessment, brain imaging, prophylactic cranial irradiation, radical radiotherapy and combination therapy.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- People with suspected and diagnosed lung cancer, their families and carers

This guideline will update NICE clinical guideline CG121 (published April 2011).

We have reviewed the evidence on the use of:

- non-ultrasound-guided transbronchial needle aspiration (TBNA), endobronchial ultrasound-guided TBNA (EBUS-TBNA), or endoscopic ultrasound-guided fineneedle aspiration (EUS-FNA) for diagnosis
- routine use of MRI or CT of the brain before radical therapy with curative intent
- treatments for stage IIIA-N2 non-small-cell lung cancer (NSCLC)
- radiotherapy regimens with curative intent for NSCLC
- chemoradiotherapy for people with limited-stage small-cell lung cancer (SCLC)
- thoracic radiotherapy for people with extensive-stage SCLC
- prophylactic cranial irradiation in people with extensive-stage SCLC.

The guideline also provides <u>two new algorithms</u> and a series of contextual recommendations for systemic treatment options for people with advanced non-small-cell lung cancer. These are based on published NICE technology appraisal guidance, but no NICE technology appraisals have been updated.

You are invited to comment on the new and updated recommendations. These are marked as **[2019]**.

You are also invited to comment on recommendations that NICE proposes to delete from the 2011 guideline.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See <u>update information</u> for a full explanation of what is being updated.

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2019 recommendations and how they might affect practice
- the guideline context.

Full details of the evidence and the committee's discussion on the 2019 recommendations are in the <u>evidence reviews</u>. Evidence for the 2011 and 2005 recommendations is in the <u>full version</u> of the 2011 guideline.

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1 **Recommendations**

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

NHS England has produced guidance on <u>implementing a timed lung cancer</u> <u>diagnostic pathway</u>, to help organisations provide timely diagnosis and treatment.

2 1.1 Access to services and referral

3 The importance of early diagnosis

4 1.1.1 The public needs to be better informed of the symptoms and signs that
5 are characteristic of lung cancer, through coordinated campaigning to
6 raise awareness. [2005]

7 Referral and indications for chest radiography

- 8 1.1.2 For guidance on referral, see the recommendations on <u>referral for</u>
 9 <u>suspected lung cancer</u> in the NICE guideline on suspected cancer. [2019]
- 10 1.1.3 When a chest X-ray has been requested in primary or secondary care and
- 11 is incidentally suggestive of lung cancer, send a copy of the radiologist's
- 12 report to a designated member of the lung cancer multidisciplinary team
- (usually the chest physician). The multidisciplinary team should have a
 mechanism in place to follow up these reports, to enable the person's GP
- 15 to prepare a management plan. [2005]

16 **1.2** Communication

17 1.2.1 Find out what the person knows about their condition without assuming a
18 level of knowledge. Provide them with the opportunity to discuss tests and
19 treatment options in a private environment, with the support of family

1 2		members or carers (as appropriate), and give them time to make an informed choice. [2011]
3	1.2.2	Ensure that a lung cancer clinical nurse specialist is available at all stages
4	1.2.2	of care to support people and (as appropriate) their family members or
5		carers. [2011]
6	1.2.3	Offer accurate and easy-to-understand information to people and their
7		family members or carers (as appropriate). Explain the tests and
8		treatment options, including potential survival benefits, side effects and
9		effect on symptoms. [2011]
10	1.2.4	Consider tailor-made decision aids to help people to:
11		 understand the probable outcomes of treatment options
12		 think about the personal value they place on benefits versus harms of
13		treatment options
14		 feel supported in decision-making
15		 move through the steps towards making a decision
16		• take part in decisions about their healthcare. [2011]
17	1.2.5	Offer people a record of all discussions that have taken place with them
18		and a copy of any correspondence with other healthcare professionals.
19		Ensure all communications are worded in such a way to assist
20		understanding. [2011]
21	1.2.6	Respect the person's choice if they do not wish to confront future issues.
22		[2011]
23	1.2.7	Avoid giving people unexpected bad news in writing. Only give
24		unexpected bad news by phone in exceptional circumstances. [2011]
25	1.2.8	Offer to discuss end-of-life care with the person sensitively and when
26		appropriate. Wherever possible, avoid leaving this discussion until the
27		terminal stages of the illness. [2011]

1	1.2.9	Document discussions with the person about end-of-life care. In particular,
2		document:
3		their specific concerns
4		 their understanding of their illness and its prognosis
5		 important values or personal goals for care
6		 their preferences for the types of care or treatment that may be
7		beneficial in the future and their availability. [2011]
8	1.2.10	Share information between healthcare professionals about:
9		 any problems the person has
10		 the management plan
11		 what the person has been told
12		 what the person has understood (if possible)
13		 the involvement of other agencies
14		 any advance decision made by the person. [2011]
15	1.3	Diagnosis and staging
16	Effective	eness of diagnostic and staging investigations
17	1.3.1	Sputum cytology is rarely indicated and should only be used for
18		investigation in people who have centrally placed nodules or masses and
19		who decline or cannot tolerate bronchoscopy or other invasive tests.
20		[2005]
21	1.3.2	Offer people with known or suspected lung cancer a contrast-enhanced
22		chest CT scan to further the diagnosis and stage the disease. Include the
23		liver, adrenals and lower neck in the scan ¹ . [2005, amended 2019]
24	1.3.3	When assessing mediastinal and chest wall invasion:
25		 be aware that CT alone may not be reliable
26		 consider other techniques such as ultrasound if there is doubt

¹ The guideline committee also recognised that contrast medium should only be given with caution to people with known renal impairment.

1 2		• be aware that surgical assessment may be necessary if there are no contraindications to resection. [2005]
3	1.3.4	Ensure that all people with lung cancer who could potentially have
4		treatment with curative intent are offered positron-emission tomography
5		CT (PET-CT) before treatment. [2011]
6	1.3.5	Every cancer alliance should have a system of rapid access to PET-CT
7		scanning for eligible people. [2005, amended 2019]
8	1.3.6	Do not routinely use MRI to assess the stage of the primary tumour
9		(T-stage) in non-small-cell lung cancer (NSCLC). [2005]
10	1.3.7	Use MRI when necessary to assess the extent of disease, for people with
11		superior sulcus tumours. [2005]
12	1.3.8	Offer endobronchial ultrasound-guided transbronchial needle aspiration
13		(EBUS-TBNA) for biopsy of paratracheal and peri-bronchial intra-
14		parenchymal lung lesions. [2011]
15	1.3.9	Every cancer alliance should have at least one centre with EBUS and/or
16		endoscopic ultrasound (EUS) to ensure timely access. [2011]
17	1.3.10	Audit the local test performance of EBUS-TBNA and endoscopic
18		ultrasound-guided fine-needle aspiration (EUS-FNA). [2011, amended
19		2019]
20	1.3.11	When taking samples, ensure they are adequate (without unacceptable
21		risk to the person) to permit pathological diagnosis, including tumour
22		subtyping and assessment of predictive markers. [2011, amended 2019]
23	1.3.12	For guidance on EGFR-TK mutation testing, see the <u>NICE diagnostics</u>
24		guidance on EGFR-TK mutation testing in adults with locally advanced or
25		metastatic non-small-cell lung cancer. [2019]
	To find (out why the committee made the 2019 recommendation on EBUS-TBNA

To find out why the committee made the 2019 recommendation on EBUS-TBNA and EUS-FNA audit and how it might affect practice, see <u>rationale and impact</u>.

1	Sequenc	e of investigations
2	1.3.13	Choose investigations that give the most information about diagnosis and
3		staging with the least risk to the person. Think carefully before performing
4		a test that gives only diagnostic pathology when information on staging is
5		also needed to guide treatment. [2011]
6	1.3.14	Perform CT of the chest, liver adrenals and lower neck ² before:
7		 an intended bronchoscopy or EBUS
8		 any other biopsy procedure. [2005, amended 2019]
9	Peripher	al primary tumour
10	1.3.15	Offer <mark>image-guided biopsy</mark> to people with peripheral lung lesions when
11		treatment can be planned on the basis of this test. [2011, amended 2019]
12	1.3.16	Biopsy any enlarged mediastinal nodes (10 mm or larger maximum short
13		axis on CT) or other lesions in preference to the primary lesion if
14		determination of stage affects treatment ³ . [2011]
15	Central p	primary tumour
16	1.3.17	Offer <mark>flexible</mark> bronchoscopy to people with central lesions on CT if nodal
17		staging does not influence treatment. [2011, amended 2019]
18	Mediasti	nal lymph node assessment
19	1.3.18	Offer PET-CT as the preferred first test after CT with a low probability of
20		mediastinal malignancy (lymph nodes below 10 mm maximum short axis
21		on CT), for people with lung cancer who could potentially have treatment
22		with curative intent. [2011]
23	1.3.19	Offer PET-CT (if not already done), and one or both of EBUS-TBNA and
24		EUS-FNA, as the initial investigations for people with lung cancer who
25		have an intermediate probability of mediastinal malignancy (lymph nodes

² The guideline committee also recognised that contrast medium should only be given with caution to

people with known renal impairment. ³ Some people with lung cancer will not be well enough for treatment with curative intent. This needs to be taken into account when choosing diagnostic and staging investigations

1		between 10 and 20 mm maximum short axis on CT) and who could
2		potentially have treatment with curative intent. [2019]
3	1.3.20	Offer neck ultrasound with sampling of visible lymph nodes to people with
4		a high probability of mediastinal malignancy (lymph nodes over 20 mm
5		maximum short axis on CT). If neck ultrasound is negative, follow with
6		PET-CT (if not already done), EBUS-TBNA and/or EUS-FNA. [2019]
7	1.3.21	Evaluate PET-CT-positive mediastinal nodes with EBUS-TBNA and/or
8		EUS-FNA if nodal status would affect the treatment plan. [2019]
9	1.3.22	Consider surgical mediastinal staging for people with a negative
10		EBUS-TBNA or EUS-FNA if clinical suspicion of mediastinal malignancy is
11		high and nodal status would affect their treatment plan. [2019]
	To find	out why the committee made the 2010 recommendations on medicating

To find out why the committee made the 2019 recommendations on mediastinal lymph node assessment and how they might affect practice, see <u>rationale and impact</u>.

12 Further staging

13	1.3.23	Confirm the presence of isolated distant metastases/synchronous tumours
14		by biopsy or further imaging (for example, MRI or PET-CT) in people
15		being considered for treatment with curative intent. [2011]
16	1.3.24	Do not offer dedicated brain imaging to people with stage I NSCLC who
17		have no neurological symptoms and are having treatment with curative
18		intent. [2019]
19	1.3.25	Offer contrast-enhanced brain CT to people with stage II NSCLC who are
20		having treatment with curative intent. If CT shows suspected brain
21		metastases, offer contrast-enhanced brain MRI. [2019]
22	1.3.26	Offer contrast-enhanced brain MRI for people with stage IIIA NSCLC who
23		are having treatment with curative intent. [2019]
24	1.3.27	Offer people with clinical features suggestive of intracranial pathology CT
25		of the head followed by MRI if normal, or MRI as an initial test. [2011]

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- 1.3.28 Perform an X-ray as the first test for people with localised signs or
 symptoms of bone metastasis. If the results are negative or inconclusive,
 offer bone scintigraphy or an MRI scan. [2005]
- 4 1.3.29 Avoid bone scintigraphy when PET-CT has not shown bone metastases.
 5 [2011]

To find out why the committee made the 2019 recommendations on brain imaging and how they might affect practice, see <u>rationale and impact</u>.

6 Organisational factors relevant to diagnosis and staging

- 7 1.3.30 Provide treatment without undue delay for people who have lung cancer
- 8 that is suitable for radical treatment or chemotherapy, or who need
- 9 radiotherapy or ablative treatment for relief of symptoms. [2005, amended
 10 2019]

11 Multidisciplinary teams

- 12 1.3.31 Refer all people with a suspected diagnosis of lung cancer to a member of
 13 a lung cancer multidisciplinary team (usually a chest physician). [2005]
- 14 1.3.32 The care of all people with known or suspected lung cancer should be
 15 discussed at a lung cancer multidisciplinary team meeting. [2005]

16 Fast track lung clinics

17 1.3.33 Provide fast track lung cancer clinics⁴ for investigating suspected lung
18 cancer, because they are associated with faster diagnosis and less
19 anxiety. [2005]

20 Cancer clinical nurse specialists

- 21 1.3.34 All cancer units/centres should have one or more trained lung cancer22 clinical nurse specialists to:
- see people before, at the time of and after diagnosis
- 24
- provide continuing support

⁴ These were previously known as early diagnosis clinics and rapid access clinics.

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1		 facilitate communication between the secondary care team (including
2		the multidisciplinary team), the person's GP, the community team and
3		the <mark>person with lung cancer</mark>
4		 help people access advice and support whenever they need it. [2005,
5		amended 2019]
6	1.3.35	For standards on lung cancer clinical nurse specialists, see quality
7		statement 4 in the NICE quality standard on lung cancer. [2019]
8	1.4	Treatment
9	Stop sm	oking interventions and services
10	1.4.1	Inform people that smoking increases the risk of pulmonary complications
11		after lung cancer surgery. [2011]
12	1.4.2	Advise people to stop smoking as soon as the diagnosis of lung cancer is
13		suspected and tell them why this is important. [2011]
14	1.4.3	Offer nicotine replacement therapy and other therapies to help people to
15		stop smoking in line the NICE guideline on stop smoking interventions and
16		services and the NICE technology appraisal guidance on varenicline for
17		smoking cessation. [2011]
18	1.4.4	Do not postpone surgery for lung cancer to allow people to stop smoking.
19		[2011]
20	Assessii	ng people with non-small-cell lung cancer for treatment with curative
21	intent	
22	Perioper	rative mortality
23	1.4.5	When evaluating surgery as an option for people with non-small-cell lung
24		cancer (NSCLC), consider using a global risk score such as Thoracoscore
25		to estimate the risk of death. Ensure the person is aware of the risk before
26		they give consent for surgery. [2011]
27	Cardiova	ascular function
28	1.4.6	Avoid surgery within 30 days of myocardial infarction. [2011]

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1	1.4.7	Seek a cardiology review in people with an active cardiac condition, or
2		3 or more risk factors, or poor cardiac functional capacity. [2011]
3	1.4.8	Offer surgery without further investigations to people with 2 or fewer risk
4		factors and good cardiac functional capacity. [2011]
5	1.4.9	Optimise any primary cardiac treatment and begin secondary prophylaxis
6		for coronary disease as soon as possible. [2011]
7	1.4.10	Continue anti-ischaemic treatment in the perioperative period, including
8		aspirin, statins and beta-blockers. [2011]
9	1.4.11	For people with coronary stents, discuss perioperative anti-platelet
10		treatment with a cardiologist. [2011]
11	1.4.12	Consider revascularisation (percutaneous intervention or coronary artery
12		bypass grafting) before surgery for people with chronic stable angina and
13		conventional indications for revascularisation. [2011]
14	Lung fun	ction
14 15	<i>Lung fun</i> 1.4.13	ction Perform spirometry <mark>and transfer factor (TLCO)</mark> in all <mark>people</mark> being
	•	
15	•	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second
15 16	1.4.13	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019]
15 16 17	1.4.13	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second
15 16 17 18	1.4.13 1.4.14	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011]
15 16 17 18 19	1.4.13 1.4.14	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict
15 16 17 18 19 20	1.4.13 1.4.14 1.4.15	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict postoperative lung function. [2011]
15 16 17 18 19 20 21	1.4.13 1.4.14 1.4.15	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict postoperative lung function. [2011] Offer people with predicted postoperative FEV1 or TLCO below the
15 16 17 18 19 20 21 22	1.4.13 1.4.14 1.4.15	 Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict postoperative lung function. [2011] Offer people with predicted postoperative FEV1 or TLCO below the recommended limit of 30% the option of treatment with curative intent if
15 16 17 18 19 20 21 22 23	1.4.13 1.4.14 1.4.15	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict postoperative lung function. [2011] Offer people with predicted postoperative FEV1 or TLCO below the recommended limit of 30% the option of treatment with curative intent if they accept the risks of dyspnoea and associated complications. [2011,
15 16 17 18 19 20 21 22 23 24	1.4.13 1.4.14 1.4.15 1.4.16	Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019] Offer people surgery if they have a forced expiratory volume in 1 second (FEV1) within normal limits and good exercise tolerance. [2011] When considering surgery perform a functional segment count to predict postoperative lung function. [2011] Offer people with predicted postoperative FEV1 or TLCO below the recommended limit of 30% the option of treatment with curative intent if they accept the risks of dyspnoea and associated complications. [2011, amended 2019]

1	1.4.18	Consider cardiopulmonary exercise testing to measure oxygen uptake
2		(VO2 max) and assess lung function in people with moderate to high risk
3		of postoperative dyspnoea, using more than 15 ml/kg/minute as a cut-off
4		for good function. [2011]
5	Assessn	nent before radiotherapy with curative intent
6	1.4.19	A clinical oncologist specialising in thoracic oncology should determine
7		suitability for radiotherapy with curative intent, taking into account
8		performance status and comorbidities. [2011]
9	Surgery	and radiotherapy with curative intent for non-small-cell lung cancer
10	Surgery	
11	1.4.20	For people with NSCLC who are well enough and for whom treatment with
12		curative intent is suitable, offer lobectomy (either open or thoracoscopic).
13		[2019]
14	1.4.21	Offer more extensive surgery (bronchoangioplastic surgery, bilobectomy,
15		pneumonectomy) only when needed to obtain clear margins. [2011]
16	1.4.22	Perform hilar and mediastinal lymph node sampling or en bloc resection
17		for all people having surgery with curative intent. [2011]
18	1.4.23	For people with T3 NSCLC with chest wall involvement who are having
19		surgery, aim for complete resection of the tumour using either extrapleural
20		or en bloc chest wall resection. [2005]
21	Surgery	or radiotherapy for people not having lobectomy
22	1.4.24	For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline
23		lobectomy or in whom it is contraindicated, offer radical radiotherapy with
24		stereotactic ablative radiotherapy (SABR) or sublobar resection. [2019]
25	Radical ı	radiotherapy for people not having surgery
26	1.4.25	For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline
27		surgery or in whom any surgery is contraindicated, offer SABR. If SABR is
28		contraindicated, offer alternative radical radiotherapy. [2019]

1 2 3	1.4.26	For eligible people with stage IIIA NSCLC who cannot tolerate or who decline chemoradiotherapy (with or without surgery), consider radical radiotherapy (either conventional or hyperfractionated). [2019]	
4 5 6	1.4.27	For eligible people with stage IIIB NSCLC who cannot tolerate or who decline chemoradiotherapy, consider radical radiotherapy (either conventional or hyperfractionated). [2019]	
7	1.4.28	If conventionally fractionated radical radiotherapy is used, offer either:	
8		• 55 Gy in 20 fractions over 4 weeks or	
9		 60–66 Gy in 30–33 fractions over 6–6½ weeks. [2019] 	
10 11	1.4.29	All people should have pulmonary function tests (including lung volumes and transfer factor) before radical radiotherapy for NSCLC. [2005]	
12 13 14	1.4.30	People who have poor lung function but for whom radical radiotherapy is otherwise suitable should still be offered radiotherapy, provided the volume of irradiated lung is small. [2005]	
15 16	1.4.31	People receiving radiotherapy with curative intent should be part of a national quality assurance programme. [2011]	
	To find out why the committee made the 2019 recommendations on surgery and radiotherapy with curative intent, and how they might affect practice, see <u>rationale</u> and <u>impact</u> .		
17	Combina	ation treatment for non-small-cell lung cancer	

- 18 1.4.32 Consider chemoradiotherapy for people with stage II or III NSCLC that are
 19 not suitable for or decline surgery. Balance potential benefit in survival
 20 with the risk of additional toxicities. [2011]
- 1.4.33 Ensure that all people for whom multimodality treatment is potentially
 suitable (surgery, radiotherapy and chemotherapy in any combination) are
 assessed by a thoracic oncologist and by a thoracic surgeon. [2011]

1	1.4.34	Offer postoperative chemotherapy to people with good performance
2		status (WHO 0 or 1) and T1a–4, N1–2, M0 NSCLC. [2011]
-		
3	1.4.35	Consider postoperative chemotherapy for people with good performance
4		status (WHO 0 or 1) and T2b–4, N0, M0 NSCLC with tumours greater
5		than 4 cm in diameter. [2011]
6	1.4.36	Offer a cisplatin-based combination chemotherapy regimen for adjuvant
7		chemotherapy. [2011]
8	1.4.37	For people with stage I–II NSCLC that is suitable for surgery, do not offer
9		neo-adjuvant treatment outside a clinical trial. [2011, amended 2019]
-		
10	1.4.38	Ensure eligible people have the benefit of detailed discussion of the risks
11		and benefits of adjuvant chemotherapy. [2011]
40	4 4 9 9	Treat Developed to the server of the stress of NOOL O. Offer
12	1.4.39	Treat Pancoast tumours in the same way as other types of NSCLC. Offer
13		multimodality therapy according to resectability, stage of the tumour and
14		performance status of the person. [2011]
15	1.4.40	For people with stage IIIA–N2 NSCLC who are well enough for
16		multimodality therapy and who can have surgery, consider
17		chemoradiotherapy with surgery. [2019]
18	1.4.41	For people with stage IIIA–N2 NSCLC who are having chemoradiotherapy
19		and surgery, ensure that their surgery is scheduled for 3–5 weeks after
20		the chemoradiotherapy. [2019]
01	1 4 4 2	Control porforming lung reportions for lung concer should validate their
21	1.4.42	Centres performing lung resections for lung cancer should validate their
22		data for the Lung Cancer Clinical Outcomes publication. [2019]
	To find c	out why the committee made the 2019 recommendations on

To find out why the committee made the 2019 recommendations on chemoradiotherapy and surgery and how they might affect practice, see <u>rationale</u> <u>and impact</u>.

1	Systemic anti-cancer therapy (SACT) for non-small-cell lung cancer				
2	Non-squamous non-small-cell lung cancer				
3	EGFR-TK mutation				
4	1.4.43	For guidance on treatment for non-squamous non-small-cell lung cancer			
5 6		in people with the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation:			
7 8		 for initial treatment, see the NICE technology appraisal guidance on <u>afatinib</u>, <u>erlotinib</u> and <u>gefitinib</u>. 			
9 10		 on progression for people with the EGFR T790M mutation, see the NICE technology appraisal guidance on <u>osimertinib</u>. 			
11 12		 on progression, offer platinum doublet chemotherapy or see the NICE technology appraisal guidance on <u>pemetrexed</u> 			
13 14		 if patients do not immediately progress after chemotherapy, see the NICE technology appraisal guidance on <u>pemetrexed maintenance</u> after 			
15 16		pemetrexed and <u>pemetrexed maintenance after other platinum doublet</u> <u>chemotherapy</u>			
17		 on progression after first-line chemotherapy, offer docetaxel 			
18		monotherapy or see the NICE technology appraisal guidance on			
19		atezolizumab, nivolumab, pembrolizumab and docetaxel with			
20 21		nintedanib. [2019]			
22	ALK gene	e rearrangement			
23	1.4.44	For guidance on treatment for non-squamous non-small-cell lung cancer			
24		in people with the anaplastic lymphoma kinase-positive gene			
25		rearrangement:			
26		for first-line systemic treatment, see the NICE technology appraisal			
27		guidance on <u>crizotinib</u> , <u>ceritinib</u> and <u>alectinib</u>			
28		• on progression after first-line crizotinib, ceritinib or alectinib, see the			
29		NICE technology appraisal guidance on crizotinib and ceritinib for			
30		second line treatment			

1 2 3 4 5 6 7 8 9 10		 on progression, offer platinum doublet chemotherapy or see the NICE technology appraisal guidance on <u>pemetrexed</u> if patients do not immediately progress after chemotherapy, see the NICE technology appraisal guidance on <u>pemetrexed maintenance</u> after pemetrexed and <u>pemetrexed maintenance</u> after other platinum doublet <u>chemotherapy</u> on progression after first-line chemotherapy, offer docetaxel monotherapy or see the NICE technology appraisal guidance on <u>atezolizumab</u>, <u>nivolumab</u>, <u>pembrolizumab</u> and <u>docetaxel with nintedanib</u>. [2019]
11 12	PDL1≥50	%
 13 14 15 16 17 18 19 20 21 22 23 24 25 26 	1.4.45	 For guidance on treatment for non-squamous non-small-cell lung cancer in people whose tumours express PD-L1 at or above 50%: for initial treatment, see the NICE technology appraisal guidance on <u>pembrolizumab</u>. on progression after pembrolizumab, offer platinum doublet chemotherapy or see the NICE technology appraisal guidance on <u>pemetrexed</u>. if patients do not immediately progress after chemotherapy, see the NICE technology appraisal guidance after pemetrexed and <u>pemetrexed maintenance after other platinum doublet chemotherapy</u>. on progression after first-line chemotherapy, offer docetaxel monotherapy or see the NICE technology appraisal guidance on <u>docetaxel with nintedanib</u>. [2019]
27	ROS-1	
28 29	1.4.46	For guidance on treatment for ROS1-positive non-squamous non-small- cell lung cancer:

1		 for initial treatment, see the NICE technology appraisal guidance on
2		<u>crizotinib</u>
3		 on progression, offer platinum doublet chemotherapy or see the NICE
4		technology appraisal guidance on pemetrexed
5		 if patients do not immediately progress after chemotherapy, see the
6		NICE technology appraisal guidance on pemetrexed maintenance after
7		pemetrexed and pemetrexed maintenance after other platinum doublet
8		<u>chemotherapy</u>
9		 on progression after first line chemotherapy, offer docetaxel
10		monotherapy or see the NICE technology appraisal guidance on
11		atezolizumab, nivolumab, pembrolizumab and docetaxel with
12		nintedanib. [2019]
13	No gene	mutation or fusion protein and PD-L1<50%
14	1.4.47	For guidance on treatment for non-squamous non-small-cell lung cancer
15		in people who do not have a gene mutation, fusion protein or biomarker or
16		in whom chemotherapy is otherwise indicated:
17		 offer platinum doublet chemotherapy or see the NICE technology
18		appraisal guidance on pemetrexed
19		 if patients do not immediately progress after chemotherapy, see the
20		NICE technology appraisal guidance on pemetrexed maintenance after
21		pemetrexed and pemetrexed maintenance after other platinum doublet
22		<u>chemotherapy</u>
23		 on progression after first line chemotherapy, offer docetaxel
24		monotherapy or see the NICE technology appraisal guidance on
25		atezolizumab, nivolumab, pembrolizumab and docetaxel with
26		nintedanib. [2019]
27	Squamo	us NSCLC
28	PDL1≥50	0%

1.4.48 For guidance on treatment for squamous non-small-cell lung cancer in
people whose tumours express PD-L1 at or above 50%:

1		 for initial treatment, see the NICE technology appraisal guidance on
2		pembrolizumab
3		 on progression, offer gemcitabine or vinorelbine and cisplatin or
4		carboplatin
5		 on progression after first line chemotherapy, offer docetaxel
6		monotherapy. [2019]
7	PDL1<5	0%
8	1.4.49	For guidance on treatment for squamous non-small-cell lung cancer in
9		people whose tumours express PD-L1 below 50%:
10		 for initial treatment, offer gemcitabine or vinorelbine and cisplatin or
11		carboplatin
12		• on progression after first line chemotherapy, see the NICE technology
13		appraisal guidance on <u>atezolizumab, nivolumab</u> and <u>pembrolizumab</u> or
14		offer docetaxel monotherapy. [2019]
15	Assessi	ng people with small-cell lung cancer
16	1.4.50	Arrange for people with small-cell lung cancer (SCLC) to have an
17		assessment by a thoracic oncologist within 1 week of deciding to
18		recommend treatment. [2011]
19	First-line	e treatment for limited-stage disease small-cell lung cancer
20	1.4.51	Offer people with limited-stage disease SCLC (broadly corresponding to
21		T1–4, N0–3, M0) 4 to 6 cycles of cisplatin-based combination
22		chemotherapy. Consider substituting carboplatin in people with impaired
23		renal function, poor performance status (WHO 2 or more) or significant
24		comorbidity. [2011]
25	1.4.52	Offer concurrent chemoradiotherapy to people with limited-stage disease
26		SCLC (broadly corresponding to T1–4, N0–3, M0) and a WHO
27		performance status of 0 or 1 if they present with disease that can be
28		encompassed in a radical thoracic radiotherapy volume. Start the
29		radiotherapy during the first or second cycle of chemotherapy. [2019]

11.4.53Offer sequential radical thoracic radiotherapy to people with limited-stage2disease SCLC (broadly corresponding to T1-4, N0-3, M0) who are not3well enough for concurrent chemoradiotherapy but who respond to4chemotherapy. [2019]

In 2019, the committee reviewed the evidence on radiotherapy for first-line treatment of limited-stage disease SCLC. To find out why they did not make new recommendations on this, see <u>rationale and impact</u>.

5 Surgery for small-cell lung cancer

6 1.4.54 Consider surgery in people with early-stage SCLC (T1–2a, N0, M0).
7 [2011]

8 First-line treatment for extensive-stage disease small-cell lung cancer

- 9 1.4.55 Offer platinum-based combination chemotherapy to people with
 10 extensive-stage disease SCLC (broadly corresponding to T1–4, N0–3,
 11 M1a/b including cerebral metastases) if they are fit enough. [2011]
- 1.4.56 Assess the person's condition before each cycle of chemotherapy for
 extensive-stage disease SCLC (broadly corresponding to T1–4, N0–3,
 M1a/b) and offer up to a maximum of 6 cycles, depending on response
 and toxicity. [2011]
- 16 1.4.57 Consider thoracic radiotherapy with prophylactic cranial irradiation for
 17 people with extensive-stage disease SCLC who have had a partial or
- 18 complete response to chemotherapy within the thorax and at distant sites.
- 19 **[2019]**

To find out why the committee made the 2019 recommendation on thoracic radiotherapy with prophylactic cranial irradiation and how it might affect practice, see <u>rationale and impact</u>.

- 20 Maintenance treatment for small-cell lung cancer
- 21 1.4.58 Only offer maintenance treatment to people with SCLC in the context of a
 22 clinical trial. [2011]

1 Prophylactic cranial irradiation in small-cell lung cancer

- 1.4.59 Offer prophylactic cranial irradiation at a dose of 25 Gy in 10 fractions to
 people with limited-stage disease SCLC and WHO performance status
 2 or less, if their disease has not progressed on first-line treatment. [2011]
- 5 1.4.60 Consider prophylactic cranial irradiation for people with extensive-stage
 6 disease SCLC and WHO performance status 2 or less, if their disease has
 7 responded to first-line treatment. [2019]

To find out why the committee made the 2019 recommendation on prophylactic cranial irradiation and how it might affect practice, see <u>rationale and impact</u>.

8 Second-line treatment for small-cell lung cancer that has relapsed after first-

9 line treatment

- 10 1.4.61 Offer people with SCLC that has relapsed after first-line treatment
 assessment by a thoracic oncologist. [2011]
- 12 1.4.62 Inform people whose disease has not responded to first-line treatment
 13 that there is very limited evidence that second-line chemotherapy will be
 14 of benefit. [2011]
- 15 1.4.63 Offer people with relapsed SCLC in whom chemotherapy is suitable
 16 treatment with an anthracycline-containing regimen or further treatment
- 17 with a platinum-based regimen to a maximum of 6 cycles. [2011]
- 18 1.4.64 Offer radiotherapy for palliation of local symptoms to people with SCLC
 19 that has relapsed after first-line treatment. [2011]
- 20 *Topotecan*21 1.4.65 Refer to <u>Topotecan for the treatment of small-cell lung cancer</u> (NICE
 22 technology appraisal guidance 184 [2009]).

1.5 Palliative interventions and supportive and palliative care 1 2 **Providing palliative care** 3 1.5.1 Supportive and palliative care of the person should be provided by 4 general and specialist palliative care providers in line with the NICE 5 guidance on improving supportive and palliative care for adults with cancer. [2005] 6 7 1.5.2 Identify and refer people who may benefit from specialist palliative care 8 services without delay. [2005] 9 Palliative radiotherapy 10 1.5.3 Provide palliative radiotherapy, either as symptoms arise or immediately, 11 for eligible people who cannot be offered curative treatment. [2005] 12 Managing endobronchial obstruction 13 1.5.4 When people have large airway involvement, monitor (clinically and 14 radiologically) for endobronchial obstruction to ensure treatment is offered 15 early. [2011] 16 1.5.5 Offer external beam radiotherapy and/or endobronchial debulking or 17 stenting to people with impending endobronchial obstruction. [2011] 1.5.6 18 Every cancer alliance should ensure that people have rapid access to a 19 team capable of providing interventional endobronchial treatments. [2011] 20 Other palliative treatments 21 Perform pleural aspiration or drainage in an attempt to relieve the 1.5.7 22 symptoms of a pleural effusion. [2005] 23 1.5.8 Offer talc pleurodesis for longer-term benefit to people who benefit 24 symptomatically from aspiration or drainage of pleural fluid. [2005, 25 amended 2019] 26 1.5.9 Consider non-drug interventions based on psychosocial support, 27 breathing control and coping strategies for people with breathlessness. 28 [2005]

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1	1.5.10	Non-drug interventions for breathlessness should be delivered by a
2		multidisciplinary group, coordinated by a professional with an interest in
3		breathlessness and expertise in the techniques (for example, a nurse,
4		physiotherapist or occupational therapist). Although this support may be
5		provided in a breathlessness clinic, people should have access to it in all
6		care settings. [2005]
7	1.5.11	Consider opioids, such as codeine or morphine, to reduce cough. [2005]
8	1.5.12	Refer people with troublesome hoarseness due to recurrent laryngeal
9		nerve palsy to an ear, nose and throat specialist for advice. [2005]
10	1.5.13	Offer people who present with superior vena cava obstruction
11		chemotherapy and radiotherapy according to the stage of disease and
12		performance status. [2005]
13	1.5.14	Consider stent insertion for the immediate relief of severe symptoms of
14		superior vena caval obstruction or following failure of earlier treatment.
15		[2005]
15		
16	Managin	g brain metastases
	Managin 1.5.15	
16	•	g brain metastases
16 17	•	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and
16 17 18	•	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic
16 17 18 19	1.5.15	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011]
16 17 18 19 20	1.5.15 1.5.16	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see
16 17 18 19 20 21	1.5.15 1.5.16	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on <u>brain tumours</u> . [2019]
16 17 18 19 20 21 22	1.5.15 1.5.16 Bone me	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on brain tumours. [2019]
16 17 18 19 20 21 22 23	1.5.15 1.5.16 Bone me	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on brain tumours. [2019] etastases Administer single-fraction radiotherapy to people with bone metastasis
16 17 18 19 20 21 22 23 24	1.5.15 1.5.16 Bone me	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on brain tumours. [2019] stastases Administer single-fraction radiotherapy to people with bone metastasis who need palliation and for whom standard analgesic treatments are
 16 17 18 19 20 21 21 22 23 24 25 	1.5.15 1.5.16 Bone me 1.5.17	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on brain tumours. [2019] stastases Administer single-fraction radiotherapy to people with bone metastasis who need palliation and for whom standard analgesic treatments are inadequate. [2005]
 16 17 18 19 20 21 21 22 23 24 25 26 	1.5.15 1.5.16 Bone me 1.5.17	g brain metastases Offer dexamethasone to people with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [2011] For guidance on whole-brain radiotherapy for brain metastases, see recommendation 1.7.8 in the NICE guideline on brain tumours. [2019] tastases Administer single-fraction radiotherapy to people with bone metastasis who need palliation and for whom standard analgesic treatments are inadequate. [2005] For more guidance on preventing complications from bone metastases,

1	Managing other symptoms: weight loss, loss of appetite, difficulty swallowing,				
2	fatigue and depression				
3	1.5.19	Other symptoms, including weight loss, loss of appetite, depression and			
4		difficulty swallowing, should be managed by multidisciplinary groups that			
5		include supportive and palliative care professionals. [2005]			
6	1.6	Follow-up and patient perspectives			
7	1.6.1	Offer all people with lung cancer an initial specialist follow-up appointment			
8		within 6 weeks of completing treatment to discuss ongoing care. Offer			
9		regular appointments after this, rather than relying on the person			
10		requesting appointments when they experience symptoms. [2011]			
11	1.6.2	Offer protocol-driven follow-up led by a lung cancer clinical nurse			
12		specialist as an option for people with a life expectancy of more than			
13		3 months. [2011]			
14	1.6.3	Ensure that people know how to contact the lung cancer clinical nurse			
15		specialist involved in their care between their scheduled hospital visits.			
16		[2011]			
17	1.6.4	The opinions and experiences of people with lung cancer and their family			
18		members or carers (as appropriate) should be collected and used to			
19		improve the delivery of lung cancer services. People should receive			
20		feedback on any action taken as a result of such surveys. [2005]			
21	Recommendations for research				
22	The guideline committee has made the following recommendations for research.				

- As part of the 2019 update, the guideline committee plans to remove two 2011guideline research recommendations on:
- the effectiveness of surgery with or without multimodality treatment in stage
 IIIA-N2 non-small-cell lung cancer and
- new regimens for radiotherapy with curative intent for people with non-small-cell
 lung cancer.

1 Key recommendations for research

2 1 Immunotherapy after multimodality treatment

- 3 What is the effectiveness and cost effectiveness of immunotherapy in people with
- 4 stage IIIA-N2 non-small-cell lung cancer following multimodality treatment including
- 5 surgery?
- 6 To find out why the committee made the research recommendation on
- 7 immunotherapy after multimodality treatment, see <u>rationale and impact</u>.

8 2 Stereotactic ablative radiotherapy compared with surgery

- 9 What is the effectiveness and cost effectiveness of stereotactic ablative radiotherapy
- 10 (SABR) compared with surgery (for example, sublobar, wedge resection, lobectomy)
- 11 for people with non-small-cell lung cancer (stage I and IIA) in whom surgery is
- 12 suitable?
- 13 To find out why the committee made the research recommendation on SABR
- 14 compared with surgery, see <u>rationale and impact</u>.

15 3 Routine contrast-enhanced brain CT

- 16 What is the effectiveness and cost effectiveness of routinely performing contrast-
- 17 enhanced brain CT at the time of initial diagnosis and/or staging CT?
- 18 To find out why the committee made the research recommendation on routinely
- 19 performing contrast-enhanced brain CT, see <u>rationale and impact</u>.

20 4 Prophylactic cranial irradiation compared with routine MRI follow-up in

21 extensive-stage SCLC

- 22 What is the effectiveness and cost effectiveness of prophylactic cranial irradiation
- 23 compared with routine MRI follow-up in people with extensive-stage small-cell lung
- 24 cancer without brain metastases?
- 25 To find out why the committee made the research recommendation on prophylactic
- 26 cranial irradiation compared with routine MRI follow-up in extensive-stage SCLC, see
- 27 <u>rationale and impact</u>.

1

1 Rationale and impact

- 2 These sections briefly explain why the committee made the recommendations and
- 3 how they might affect services. They link to details of the evidence and a full
- 4 description of the committee's discussion.

5 Diagnosis and staging

6 Why the committee made the recommendations

7 Effectiveness of diagnostic and staging investigations

- 8 Recommendation <u>1.3.10</u>
- 9 Clinical audit is an important tool for maintaining high standards in the use of
- 10 endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)
- 11 and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). This is
- 12 consistent with the British Thoracic Society guideline and guality standards (which
- 13 are endorsed by NICE).

14 EBUS-TBNA and EUS-FNA

- 15 Recommendations <u>1.3.19–1.3.21</u>
- 16 The recommendations cover:
- initial invasive investigations for people with an intermediate probability of
 mediastinal malignancy
- subsequent investigations for people with a high probability of mediastinal
 malignancy, when neck ultrasound and biopsy are negative.
- In these circumstances, when compared with alternative investigations EBUS-TBNAand EUS-FNA:
- produce a diagnosis and stage faster than bronchoscopy or CT-guided biopsy
- are more acceptable to patients than surgery
- reduce the need for further investigations and hospital visits compared with
- 26 bronchoscopy.

1 The decision on which procedure to use depends on where suspicious lesions are

- 2 located. For example, EUS-FNA enters the area between the lungs through the
- 3 oesophagus, so can more easily access lung stations 8, 9 and 4L. By contrast,
- 4 EBUS-TBNA enters the area between the lungs through the trachea, so can more
- 5 easily access lung stations closer to the large airways. The recommendations do not
- 6 specify when one procedure is better than the other because there is variation in the
- 7 way that abnormal lesions appear on imaging, so evidence is not available for every
- 8 possible situation. Because of this, clinicians will need to use their judgement on
- 9 whether to use EBUS-TBNA, EUS-FNA, or both.
- 10 The availability of PET-CT is more limited than EBUS-TBNA and EUS-FNA, so
- 11 specifying that PET-CT is done first may cause delays in diagnosis. As a result, the
- 12 committee did not mandate a specific order for the investigations.

13 Surgical mediastinal staging

- 14 Recommendation <u>1.3.22</u>
- 15 When EBUS-TBNA and/or EUS-FNA are negative but clinical suspicion of
- 16 mediastinal malignancy is high, surgical mediastinal staging is the final staging
- 17 option. Nodal status may affect the treatment plan. While there are potential harms
- 18 from the invasive nature of surgical staging, there is no evidence that these outweigh
- 19 the benefits in this population. With these points in mind, the committee
- 20 recommended consideration of surgical mediastinal staging based on their
- 21 knowledge and experience.

22 **Procedures that were not recommended**

- 23 Transthoracic needle biopsy, bronchoscopy and non-ultrasound-guided TBNA are no
- 24 longer recommended for diagnosing and staging lung cancer in mediastinal lymph
- 25 nodes because:
- bronchoscopy and non-ultrasound-guided TBNA are unlikely to reach the
- 27 minimum sensitivity required by the British Thoracic Quality Standards and
- they may discourage people from having more effective procedures (such as
 EBUS-TBNA) and subsequent investigations.

- 1 The word 'fibreoptic' has been removed because bronchoscopy can be fibreoptic,
- 2 video or hybrid.
- 3 How the recommendations might affect practice
- 4 The recommendations on PET-CT reflect current practice, so will not incur an extra5 cost.
- 6 EBUS-TBNA and EUS-FNA are widely used. The recommendations will reinforce
- 7 best practice and result in a more streamlined diagnostic service with more timely
- 8 diagnosis and staging.
- 9 The surgical mediastinal staging recommendation will also reinforce best practice
- 10 and restrict this procedure to people most likely to benefit.
- 11 Full details of the evidence and the committee's discussion are in evidence review A:
- 12 Investigations for staging the mediastinum.
- 13 <u>Return to recommendations</u>

14 Brain imaging for people having treatment with curative intent

15 Recommendations <u>1.3.24–1.3.26</u>

16 Why the committee made the recommendations

- 17 Brain imaging is helpful before starting treatment with curative intent, because if
- 18 brain metastases are detected then the treatment plan is likely to change. However,
- 19 routine brain imaging is expensive, and the evidence showed that it does not offer a
- 20 good balance of benefits and costs for everyone with NSCLC.
- 21 In people with stage II and IIIA disease, the benefits of brain imaging outweigh the
- 22 costs because:
- brain metastases are more common than in stage I disease
- people can start early treatment for metastases if they are identified, which
 improves prognosis
- some people with brain metastases will not have radical treatment (depending on
- factors such as the number of metastases, prognosis and patient preference), andthis reduces costs.

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- 1 In people with stage I NSCLC and no neurological symptoms, brain metastases are
- 2 relatively rare. Because of this, the benefits of imaging are too low to justify the
- 3 costs.
- 4 There was some uncertainty around the sensitivity and specificity of CT for detecting
- 5 brain metastases. In addition, it was unclear if the benefits outweighed the costs,
- 6 because:
- 7 positive findings often need to be confirmed with MRI
- the prevalence of detectable brain metastases is fairly low (around 4%)
- 9 a diagnosis of brain metastases will not always mean a change to the treatment10 plan.
- 11 This review only examined the clinical and cost-effectiveness of imaging after the
- 12 treatment plan has been decided but the committee noted that it could be more
- 13 efficient to conduct CT brain imaging alongside initial staging CT. With this in mind,
- 14 the committee made a <u>recommendation for further research into routine brain</u>
- 15 imaging with CT at initial diagnosis and/or staging.

16 How the recommendations might affect practice

- 17 Practice in this area is variable. The committee estimated that the recommendations
- 18 will increase the number of people who have brain imaging. In turn, they thought this
- 19 should prevent the use of treatment options (such as lobectomy and sublobar
- 20 resection) in some patients for whom it is not expected to be beneficial. The
- 21 recommendations may also lead to an increase in radical radiotherapy, stereotactic
- 22 radiosurgery and brain surgery, which would be expected to improve their prognosis
- although each treatment would carry its own risks and side effects.
- 24 Full details of the evidence and the committee's discussion are in evidence review B:
- 25 Brain imaging for people with NSCLC selected for treatment with curative intent
- 26 Return to recommendations

27 Surgery and radiotherapy with curative intent for non-small-cell

- 28 lung cancer
- 29 Recommendations <u>1.4.20, 1.4.24–1.4.28</u>

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1 Why the committee made the recommendations

- 2 For people with non-small-cell lung cancer (NSCLC) who are well enough and for
- 3 whom treatment with curative intent is suitable, the evidence showed that lobectomy
- 4 provides better survival outcomes than stereotactic ablative radiotherapy (SABR).
- 5 Lobectomy is a good compromise between preserving pulmonary function and being
- 6 more likely to remove cancerous cells compared with sublobar resection.

7 For people with stage I-IIA (T1a–T2b, N0, M0) NSCLC, the evidence showed that:

- if they decline lobectomy or it is contraindicated, sublobar resection and SABR
- 9 both provide better survival outcomes than conventionally fractionated
- 10 radiotherapy, and it is not clear which of these 2 is better
- if they decline any surgery or it is contraindicated, SABR provides better survival
- outcomes than conventionally fractionated radiotherapy, and people often prefer it
 because it involves fewer hospital visits
- if surgery and SABR are contraindicated, conventionally fractionated radiotherapy
 provides better survival outcomes than no radiotherapy.
- 16 For people with stage IIIA or IIIB NSCLC who cannot tolerate chemoradiotherapy or
- 17 who decline it, the evidence was not strong enough to recommend conventional
- 18 radiotherapy over hyper-fractionated regimens or vice versa. However, people who
- 19 cannot tolerate chemoradiotherapy may also be unable to tolerate radical
- 20 radiotherapy, so this will not be an option for everyone with stage IIIA or IIIB NSCLC.
- 21 For an explanation of the recommendations covering surgery in this group, see the
- 22 rationale on management of stage IIIA-N2 NSCLC.
- 23 55 Gy in 20 fractions is the most common conventional radical radiotherapy regimen
- 24 in the UK. If conventionally fractionated radiotherapy is used, a total radiation dose of
- 25 60 Gy provides better survival outcomes and fewer adverse events than 74 Gy. A
- total dose of 60–66 Gy is also normal NHS practice.
- 27 There are not many randomised controlled trials comparing SABR with surgery
- 28 (lobectomy or sublobar resection). SABR is non-invasive, so if it is as effective as
- surgery then it may be a preferable option for many people with lung cancer. It is
- 30 also possible that SABR, which is usually delivered as outpatient treatment, is more

- 1 cost effective than surgery. There might also be subgroups for whom different forms
- 2 of surgery or SABR might be the most cost-effective options. The committee made a
- 3 <u>research recommendation</u> to investigate these uncertainties.

4 How the recommendations might affect practice

- 5 The new recommendations on SABR are a change from the 2011 guideline and
- 6 improve choice for people with NSCLC. However, practice has also changed since
- 7 2011, and SABR is now widely used, so implementing the recommendations may
- 8 not involve a significant change in practice. The remaining changes to the
- 9 recommendations reflect current practice.
- 10 Full details of the evidence and the committee's discussion are in evidence review D:
- 11 Radiotherapy with curative intent for NSCLC
- 12 Return to recommendations

13 Management of stage IIIA–N2 non-small-cell lung cancer

14 Recommendations <u>1.4.40–1.4.42</u>

15 Why the committee made the recommendations

- 16 The available evidence showed that chemoradiotherapy and surgery are more
- 17 effective than chemoradiotherapy alone in people who are well enough for surgery.
- 18 For chemotherapy and surgery, there was no evidence that outcomes were better
- 19 than for chemoradiotherapy, so the additional costs outweighed the benefits. The
- 20 key benefit associated with chemoradiotherapy and surgery is the longer progression
- 21 free survival time. However, there are some uncertainties in the evidence:
- it was not possible to tell whether chemoradiotherapy alone or chemotherapy and
 surgery provide better survival outcomes
- the evidence in favour of chemoradiotherapy and surgery involved indirect
- comparisons, and no head-to-head trials showed meaningful differences in
- 26 outcomes for any of the interventions.

The 3–5 week wait for surgery is recommended to give people time to recover fromthe chemoradiotherapy.

- 1 Immunotherapy has been shown to be effective in a variety of NSCLC indications but
- 2 there is currently no evidence on whether it is clinically or cost effective for people
- 3 with stage IIIA-N2 non-small-cell lung cancer following surgery. The committee made
- 4 a <u>research recommendation</u> to address this.

5 How the recommendations might affect practice

- 6 The committee felt that chemoradiotherapy and surgery is offered far less often than
- 7 chemoradiotherapy alone or chemotherapy and surgery for people with NSCLC
- 8 stage IIIA-N2. Therefore, these recommendations could lead to a change in current
- 9 practice.
- 10 Full details of the evidence and the committee's discussion are in evidence review C:
- 11 Management of NSCLC stage IIIA-N2
- 12 Return to recommendations

13 First-line treatment for limited-stage disease small-cell lung cancer

14 Recommendations <u>1.4.52 and 1.4.53</u>

15 Why the committee did not change the recommendations

The evidence showed a survival benefit from twice-daily radiotherapy compared with once-daily. However, the committee were concerned that the clinical trials are not representative of clinical practice. Very few people with small-cell lung cancer are well enough to tolerate twice-daily chemotherapy. It is more likely to cause oesophagitis, which has serious and long-term effects on quality of life and physical health. Oesophagitis may also stop people from having prophylactic cranial

- 22 irradiation, and this will reduce the effectiveness of treatment. With these concerns in
- 23 mind, the committee did not make recommendations on whether to use twice-daily or
- 24 once-daily radiotherapy.
- 25 The committee noted that in practice, radiotherapy is not started in chemotherapy
- 26 cycle 1, because this is when planning often takes place (see recommendation
- 27 1.4.53). However, there was no new evidence on when to start radiotherapy, so the
- 28 committee did not change the 2011 recommendation.

- 1 There were limited data available on whether continuous radiotherapy with
- 2 concurrent chemotherapy was more effective than alternating radiotherapy with
- 3 weekly breaks. Based on the available data, and their experience that people prefer
- 4 to complete treatment as quickly as possible, the committee did not change the 2011
- 5 recommendation on concurrent chemoradiotherapy (see recommendation 1.4.53).
- 6 Full details of the evidence and the committee's discussion are in evidence review F:
- 7 <u>Chemoradiotherapy for limited stage SCLC</u>
- 8 Return to recommendations

9 First-line treatment for extensive-stage disease small-cell lung

- 10 *cancer*
- 11 Recommendation <u>1.4.57</u>

12 Why the committee made the recommendation

- 13 There was some uncertainty in the evidence. However, the study most relevant to
- 14 UK practice showed that thoracic radiotherapy improves long-term survival for
- 15 people who have had a partial or complete response to chemotherapy, if they live
- 16 longer than 1 year after the radiotherapy. The committee specified that thoracic
- 17 radiotherapy should be given alongside prophylactic cranial irradiation. This is to
- 18 match recommendation 1.4.61. In addition, the reviewed clinical trials gave thoracic
- 19 radiotherapy alongside prophylactic cranial irradiation.
- 20 How the recommendations might affect practice
- 21 The 2011 recommendation only recommended thoracic radiotherapy for people with
- 22 a complete response to chemotherapy at distant sites. Therefore, this
- recommendation could increase the number of people who could be given thoracic
- 24 radiotherapy.
- 25 Full details of the evidence and the committee's discussion are in evidence review G:
- 26 <u>Thoracic radiotherapy for extensive stage SCLC</u>
- 27 Return to recommendations

1 Prophylactic cranial irradiation in small-cell lung cancer

2 Recommendation <u>1.4.60</u>

3

4 Why the committee made the recommendation

- 5 The evidence showed that prophylactic cranial irradiation improves survival versus
- 6 best supportive care.
- 7 Prophylactic cranial irradiation can adversely affect quality of life, and the survival
- 8 benefits are limited. There is also some evidence from a study outside the UK that
- 9 routine MRI follow-up may be more cost effective. The committee made a
- 10 <u>recommendation for further research</u>, to provide evidence more relevant to the UK
- 11 and to see if MRI could identify people who need whole-brain radiotherapy and so
- 12 reduce the number of people having unnecessary treatment.

13 Impact of the recommendation on practice

- 14 It is likely that the recommendation reflects current clinical practice.
- 15 Full details of the evidence and the committee's discussion are in evidence review H:
- 16 Prophylactic cranial irradiation for extensive stage SCLC
- 17 Return to recommendations

18 **Context**

- 19 Over 46,000 people were diagnosed with lung cancer in the UK in 2015⁵. An
- 20 estimated 89% of lung cancers are preventable, with 86% of these linked to
- smoking, 13% to occupational exposure, 9% to dietary factors and 7.8% to air
- 22 pollution. Lung cancer can be linked to more than one cause.
- 23 In 2015 in the UK, over 35,000 people died from lung cancer. The overall mortality
- rate from lung cancer has decreased by 9% over the last decade. However, while
- 25 there has been a decrease of 19% in mortality rates in men, there has been an
- 26 increase of 2% in women; this is linked to lifestyle factors such as smoking and is
- 27 driven by an increased incidence of lung cancer in older women.

⁵ All statistics in this section are from <u>Cancer Research UK</u>.

- 1 In the UK, lung cancer is more common in people of European family origin than in
- 2 people of African or Asian family origin. It is strongly linked to socioeconomic
- 3 deprivation. There are many risk factors for lung cancer, including age, genetics,
- 4 lifestyle (especially smoking) and occupation. Lung cancer is estimated to cost the
- 5 UK economy £2.4 billion per year.

6 Current practice

- 7 Lung cancer is diagnosed and staged using a variety of tests, including chest X-rays,
- 8 CT or positron-emission tomography CT (PET-CT). When biopsies are needed, they
- 9 are commonly taken using bronchoscopy, endobronchial ultrasound (EBUS) or a
- 10 percutaneous procedure (guided by CT or ultrasound).

11 Lung cancer has 2 main types:

- non-small-cell lung cancer (NSCLC), which is more common and spreads more
 slowly
- small-cell lung cancer (SCLC), which is rarer and spreads more quickly.
- 15 Treatment depends on the type, size, position and stage of the cancer, and the
- 16 person's health. Possible treatments include radiotherapy, systemic anti-cancer
- 17 therapies, surgery, supportive care cryotherapy, photodynamic therapy and ablation.
- 18 Since 2011, when the NICE lung cancer guideline was last updated, there have been
- 19 changes in the way that lung cancer is diagnosed and treated. The <u>2016 national</u>
- 20 <u>lung cancer audit</u> identified that only 72% of people have pathological confirmation of
- 21 their lung cancer. There is also inconsistency in the availability of molecular testing in
- 22 lung cancer diagnosis.
- 23 NHS England has taken steps to improve access to and uptake of radiotherapy, and
- 24 stereotactic ablative radiotherapy (SABR) is routinely used for certain subgroups of
- 25 people with early-stage NSCLC. There are now a variety of licensed
- 26 immunotherapies and biological targeted therapies for treating advanced NSCLC,
- and NICE has published technology appraisals covering many of these.

1 Finding more information and resources

- 2 To find out what NICE has said on topics related to this guideline, see our web page
- 3 on <u>lung cancer</u>.

4

1 Update information

- 2 We have reviewed the evidence on diagnosis and treatment for people with lung3 cancer.
- 4 Recommendations are marked **[2019]** if the evidence has been reviewed.

5 **Recommendations that have been deleted or changed**

- 6 We propose to delete some recommendations from the 2011 guideline. <u>Table 1</u> sets
- 7 out these recommendations and includes details of replacement recommendations.
- 8 If there is no replacement recommendation, an explanation for the proposed deletion
- 9 is given.
- 10 In recommendations shaded in grey and ending [2005, amended 2019] or [2011,
- amended 2019], we have made changes that could affect the intent without
- 12 reviewing the evidence. Yellow shading is used to highlight these changes, and
- 13 reasons for the changes are given in <u>table 2</u>.
- 14 In recommendations shaded in grey and ending [2005] or [2011], we have not
- 15 reviewed the evidence. In some cases minor changes have been made for
- 16 example, to update links, or bring the language and style up to date without
- 17 changing the intent of the recommendation. Minor changes are listed in <u>table 3</u>.
- 18 See also the previous NICE guideline and supporting documents.

1 Table 1 Recommendations that have been deleted

Recommendation in 2011 guideline	Comment
1.3.20 Offer neck ultrasound with biopsy of visible lymph nodes to patients that have neck nodes detected by initial CT. If negative, follow with non-ultrasound- guided TBNA or EBUS-guided TBNA or EUS-guided FNA. [new 2011]	This set of recommendations have been superseded by new recommendations on mediastinal staging (see 1.3.19 onwards)
1.3.21 Evaluate PET-CT-positive mediastinal nodes by mediastinal sampling (except when there is definite distant metastatic disease or a high probability that N2/N3 disease is metastatic [for example, if there is a chain of lymph nodes with high 18F-deoxyglucose uptake]). [new 2011]	
1.3.22 Consider combined EBUS and EUS for initial staging of the mediastinum as an alternative to surgical staging. [new 2011]	
1.3.23 Confirm negative results obtained by non- ultrasound-guided TBNA using EBUS-guided TBNA, EUS-guided FNA or surgical staging. [new 2011]	
1.4.27 Patients with stage I or II NSCLC who are medically inoperable but suitable for radical radiotherapy should be offered the CHART regimen. [2005]	These recommendations have been superseded by new recommendations on the use of radiotherapy with curative intent (see
1.4.29 Patients with stages IIIA or IIIB NSCLC who are eligible for radical radiotherapy and who cannot tolerate or do not wish to have chemoradiotherapy should be offered the CHART regimen. [2005]	1.4.25 onwards)
1.4.30 If CHART is not available, conventionally fractionated radiotherapy to a dose of 64–66 Gy in 32– 33 fractions over 61/2 weeks or 55 Gy in 20 fractions over 4 weeks should be offered. [2005]	
1.3.26 Consider MRI or CT of the head in patients selected for treatment with curative intent, especially in stage III disease. [new 2011]	This recommendation has been replaced by recommendations 1.3.24 – 1.3.26 on brain imaging.
1.4.31 Offer patients with stage I–III NSCLC who are not suitable for surgery an assessment by a clinical oncologist specialising in thoracic oncology for radiotherapy with curative intent. [new 2011]	This recommendation was deleted because it is the same as 1.4.19

 1.4.43 Offer SACT to people with stage III or IV NSCLC and good performance status (WHO 0, 1 or a Karnofsky score of 80–100), to improve survival, disease control and quality of life. [2005] 1.4.44 Chemotherapy for advanced NSCLC should be a combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine) plus a platinum drug. Either carboplatin or cisplatin may be used, taking account of their toxicities, efficacy and convenience. [2005] 1.4.45 For people who cannot tolerate a platinum 	These recommendations have been deleted and replaced with an anti- cancer therapy algorithm and related recommendations
 combination, offer single-agent chemotherapy with a third-generation drug. [2005] 1.4.46 Consider docetaxel monotherapy if second-line treatment is appropriate for people with locally 	
advanced or metastatic NSCLC in whom relapse has occurred after previous chemotherapy. [2005]	
1.4.51 For patients with extensive-stage disease SCLC, thoracic radiotherapy should be considered after chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax. [new 2011]	This recommendation has been replaced by recommendation 1.4.50
1.4.54 Offer prophylactic cranial irradiation to patients with extensive-stage disease SCLC and WHO performance status 2 or less, if their disease has not progressed on first-line treatment. [new 2011]	This recommendations has been replaced by recommendation 1.4.53

1

- 1 Table 2 Amended recommendation wording (change to intent) without an
- 2 evidence review

Recommendation in 2011 guideline	Recommendation in current guideline	Reason for change
1.3.2 Patients with known or suspected lung cancer should be offered a contrast- enhanced chest CT scan to further the diagnosis and stage the disease. The scan should also include the liver and adrenals ² . [2005]	1.3.2 Offer people with known or suspected lung cancer a contrast-enhanced chest CT scan to further the diagnosis and stage the disease. Include the liver, and adrenals and lower neck in the scan. [2005]	The committee updated this to reflect current best practice and in light of recommendations made during this update about the use of EBUS.
1.3.5 Every cancer network should have a system of rapid access to PET-CT scanning for eligible patients. [2005]	1.3.5 Every cancer alliance should have a system of rapid access to PET-CT scanning for eligible people.[2005, amended 2019]	Updated to reflect current terminology.
1.3.10 The local test performance of non- ultrasound-guided TBNA, EBUS and EUS-guided FNA should be the subject of audit. [2011]	1.3.10 Audit the local test performance of EBUS-TBNA and endoscopic ultrasound- guided fine-needle aspiration (EUS-FNA). [2011, amended 2019]	Non-ultrasound- guided TBNA has been removed as a result of new update evidence and replaced with EBUS- TBNA.
1.3.11 Ensure adequate samples are taken without unacceptable risk to the patient to permit pathological diagnosis including tumour sub-typing and measurement of predictive markers. [new 2011]	1.3.11 When taking samples, ensure they are adequate (without unacceptable risk to the person) to permit pathological diagnosis, including tumour subtyping and assessment of predictive markers. [2011, amended 2019]	Updated to reflect current terminology.
 1.3.13 Chest CT should be performed before: an intended fibreoptic bronchoscopy any other biopsy procedure. [2005] 	 1.3.14 Perform CT of the chest, liver, adrenals and lower neck before: an intended bronchoscopy or EBUS any other biopsy procedure. [2005, amended 2019] 	The committee updated this to reflect current best practice and in light of recommendations made during this update about the use of EBUS.
1.3.14 Offer CT- or ultrasound-guided transthoracic needle biopsy to patients with peripheral lung lesions when treatment can be planned on the basis of this test. [new 2011]	1.3.15 Offer image-guided biopsy to people with peripheral lung lesions when treatment can be planned on the basis of this test. [2011, amended 2019]	Updated to reflect current practice.

1.3.16 Offer fibreoptic bronchoscopy to patients with central lesions on CT if nodal staging does not influence treatment.	1.3.17 Offer flexible bronchoscopy to people with central lesions on CT if nodal staging does not influence treatment.	The word 'fibreoptic' has been removed because bronchoscopy can be fibreoptic, video or hybrid.
1.3.29 Provide treatment without undue delay for people who have lung cancer that is suitable for radical treatment or chemotherapy, or who need radiotherapy or ablative treatment for relief of symptoms, according to the Welsh Government and Department of Health recommendations (within 31 days of the decision to treat and within 62 days of their urgent referral). [2005]	1.3.30 Provide treatment without undue delay for people who have lung cancer that is suitable for radical treatment or chemotherapy, or who need radiotherapy or ablative treatment for relief of symptoms. [2005, amended 2019]	The Welsh Government/ Department of Health recommendations on treatment times have been removed, as the <u>optimal lung</u> <u>cancer pathway</u> now covers this.
1.3.34 All cancer units/centres should have one or more trained lung cancer clinical nurse specialists to see patients before and after diagnosis, to provide continuing support, and to facilitate communication between the secondary care team (including the MDT), the patient's GP, the community team and the patient. Their role includes helping patients to access advice and support whenever they need it. [2005]	 1.3.34 All cancer units/centres should have one or more trained lung cancer clinical nurse specialists to: see people before, at the time of and after diagnosis provide continuing support facilitate communication between the secondary care team (including the multidisciplinary team), the person's GP, the community team and the person with lung cancer help people access advice and support whenever they need it. [2005, amended 2019] 1.3.35 For standards on lung cancer clinical nurse specialists, see quality statement 4 in the NICE quality standard on lung cancer. [2019] 	Updated to reflect current practice and to be in line with the NICE quality standard on lung cancer.

1.4.13 Perform spirometry in all patients being considered for treatment with curative intent. Measure TLCO if breathlessness is disproportionate or there is other lung pathology (for example, lung fibrosis). [2011]	1.4.13 Perform spirometry and transfer factor (TLCO) in all people being considered for treatment with curative intent. [2011, amended 2019]	Amended to reflect that SABR is now a treatment option, as TLCO measurements are relevant to this treatment.
1.4.15 Offer patients with predicted postoperative FEV1 or TLCO below the recommended limit of 30% the option of undergoing surgery if they accept the risks of dyspnoea and associated complications. [new 2011]	1.4.16 Offer people with predicted postoperative FEV1 or TLCO below the recommended limit of 30% the option of treatment with curative intent if they accept the risks of dyspnoea and associated complications. [2011, amended 2019]	Recommendation broadened because this applies to a range of treatment options with curative intent rather than only surgery.
1.4.37 For patients with NSCLC who are suitable for surgery, do not offer neo- adjuvant chemotherapy outside a clinical trial. [new 2011]	1.4.37 For people with stage I–II NSCLC that is not suitable for surgery, do not offer neo-adjuvant treatment outside a clinical trial. [2011, amended 2019]	Updated to reflect that there are surgical options in this space for stage IIIA NSCLC, so the recommendation now only applies to stage I–II.

1 Table 3 Minor changes to recommendation wording (no change to intent)

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [2019]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) where possible. Yellow highlighting has not been applied to these changes.
1.3.27 Offer people with clinical features suggestive of intracranial pathology CT of the head followed by MRI if normal, or MRI as an initial test. [2011]	The word 'clinical' has been added for clarification
1.5.8 Offer talc pleurodesis for longer-term benefit to people who benefit symptomatically from aspiration or drainage of pleural fluid. [2005]	Clarified 'pleural' fluid.

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3