DRAFT FOR CONSULTATION

National Clinical Guideline:
GP Guideline for the Referral of Patients with Suspected Lung Cancer

Cover page

HSE National Clinical Guideline: GP Guideline for the Referral of Patients with Suspected Lung Cancer

National Policy ☐ National Procedure ☐ National Protocol ☐ National Guideline ☐
National Clinical Guideline ☒

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Document Owner:	Head of Evidence and Quality Hub, National Cancer Control Programme (NCCP)
Document Owner name:	Dr Eve O'Toole
Document Owner email contact:	guidelines@cancercontrol.ie
Document Commissioner(s):	NCCP
Document Approver(s):	NCCP National Executive
Development Group Name:	Lung Cancer GP Referral Guideline Development Group
Development Group Chairperson(s):	Dr David Breen, Consultant Respiratory Physician, Galway University Hospitals; Dr Eve O'Toole, Head of Evidence and Quality Hub, NCCP

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Short summary:
An evidence-based guideline on the referral of patients with suspected lung cancer from Primary Care
Description:
The purpose of this National Clinical Guideline is to provide evidence based recommendations to General Practitioners on which patients with symptoms suspicious for lung cancer to refer to a Rapid Access Lung Cancer Clinic or for a chest x-ray. The guideline integrates the best research evidence with clinical expertise, patient values and experiences.

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Disclaimer

This guideline ("the Guideline") was developed by a multidisciplinary Guideline Development Group ("the Group") and is based upon the best clinical evidence available together with the clinical expertise of the Group members. The Guideline supersedes all previous Health Service Executive (HSE), National Cancer Control Programme (NCCP) GP referral guidelines for suspected lung cancer. The NCCP is part of the HSE and any reference in this disclaimer to the NCCP is intended to include the HSE. Please note, the Guideline is for guidance purposes only. The appropriate application and correct use of the Guideline is the responsibility of each health professional, as an autonomous practitioner, at all times. Each health professional should exercise his or her clinical judgment in deciding when and how to make a referral to a Rapid Access Lung Clinic, or for a chest x-ray. In the event of any uncertainty as to the application and/or use of the Guideline or whether a referral should be made to a Rapid Access Lung Clinic it is the responsibility of each health professional to seek further clarity from the appropriate clinician or specialist. The NCCP accepts no liability nor shall it be liable, whether arising directly or indirectly, to the user or any other third party for any claims, loss or damage resulting from any use of the Guideline.

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1 Background

1.1 Purpose

This guideline was developed to aid General Practitioners (GPs) to identify patients in Primary Care with signs or symptoms which may be suspicious for lung cancer, and who require referral for further investigations. It was developed by a multi-disciplinary Guideline Development Group and provides evidence-based recommendations through the integration of the best current research evidence with clinical expertise, patient values and experiences. It is an update of and supersedes the Lung Cancer Rapid Access Service GP Referral Guidelines (National Cancer Control Programme, 2012).

1.2 Mandate

In line with the Standards for Clinical Practice Guidance (Department of Health, 2015), the Lung Cancer Rapid Access Service GP Referral Guidelines (National Cancer Control Programme, 2012)) was due to be updated.

1.3 Scope

The guideline covers patients in a Primary Care setting who have signs and/or symptoms that may be suspicious for lung cancer. It describes which patients a GP may refer to a Rapid Access Lung Clinic or for a chest x-ray. Out of the scope of this guideline are patients who have signs or symptoms that require an immediate referral to an Emergency Department, and patients in secondary care who may have signs and symptoms of lung cancer.

1.4 Target audience

The guideline was developed by a multidisciplinary Guideline Development Group (GDG) – a full list of members can be found in Appendix I.

The guideline is intended for use by GPs as an aid to determine which patients to refer for further diagnostic investigations because they have signs or symptoms that may be suspicious for lung cancer. This guideline also tells them where to refer their patient.

The guideline may be used by a GP with their patient during a consultation. The guideline may also be of interest to people in the community who think they have signs or symptoms suspicious for lung cancer, and to those working in secondary care who may encounter patients with signs or symptoms suspicious for lung cancer. A Plain Language Summary of this guideline is available in Appendix VI This outlines the scope of the guideline and contains a suggested list of questions a patient may want to ask their GP.

1.5 Target population

The population covered by this guideline are adults in Ireland who present to their General Practitioner with signs and/or symptoms that may be suspicious for lung cancer.

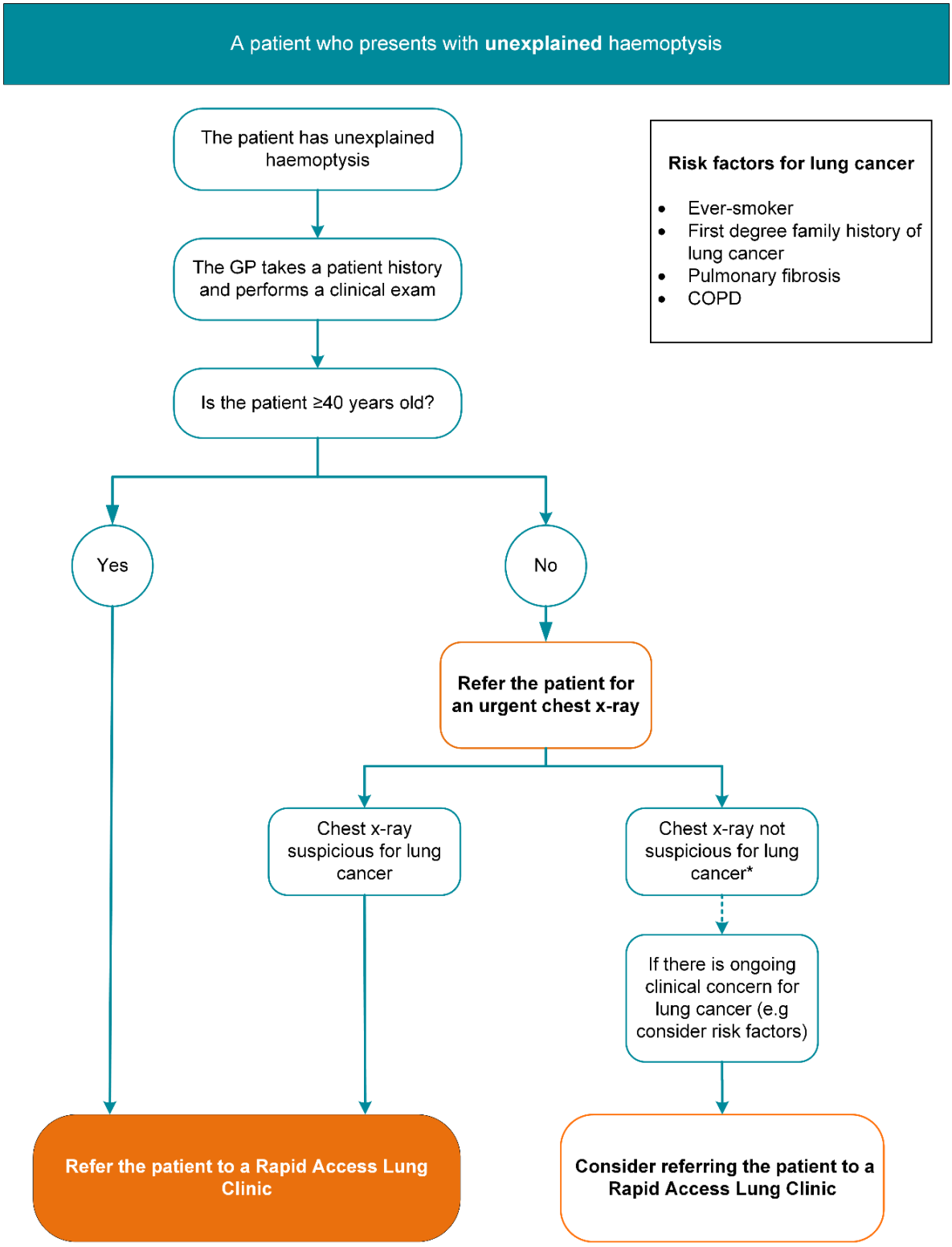
1.6 Summary of changes from the Lung Cancer Rapid Access Service GP Referral Guidelines (2012)

This updated guideline was developed as a full national clinical guideline in line with the Standards for Clinical Practice Guidance (Department of Health, 2015). The guideline and its recommendations follow an amended GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. Further details on the grading of recommendations in this guideline is available in Appendix III.

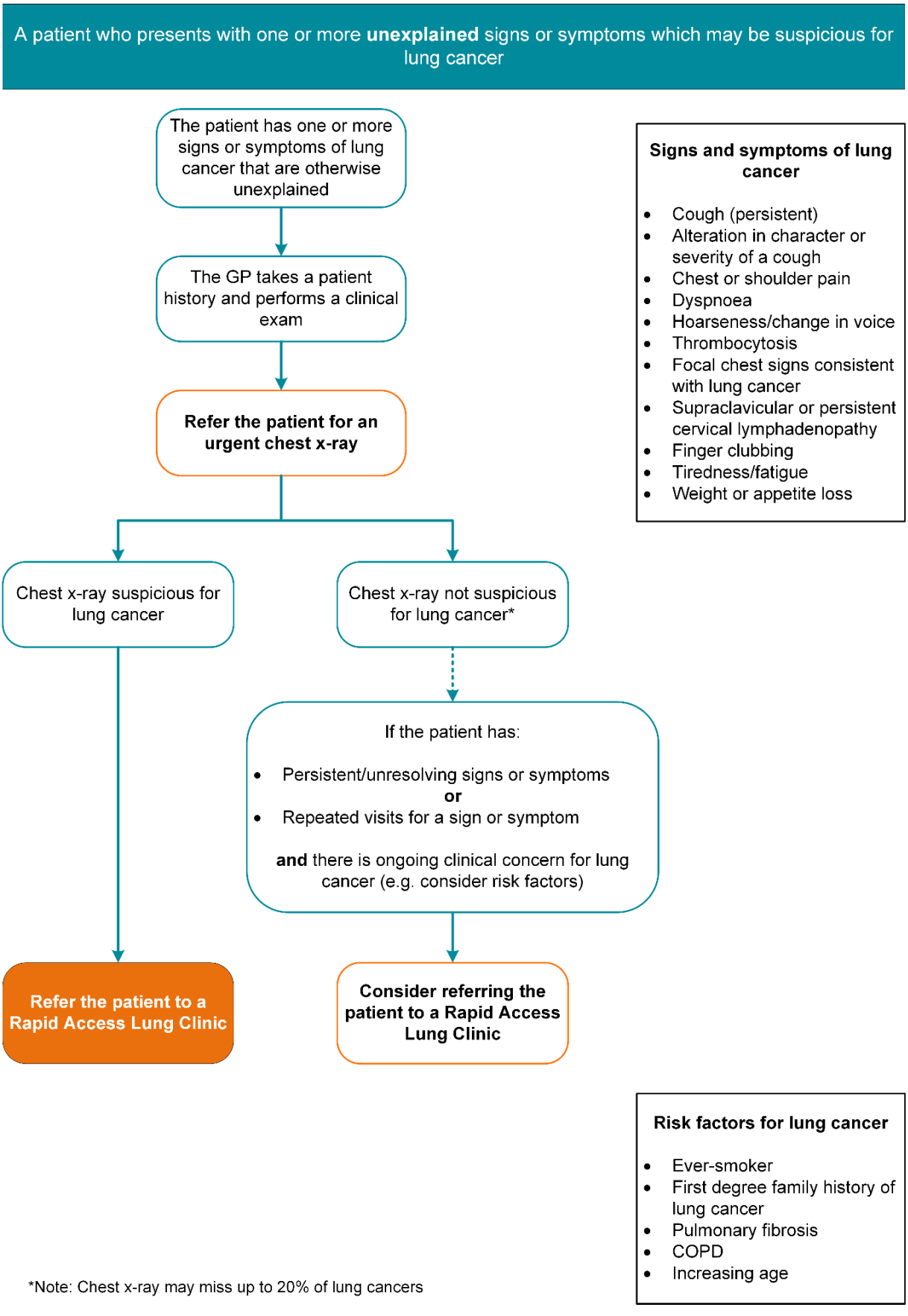
A literature search of the clinical questions outlined in Section 3.2 was carried out to collect the evidence which underpins this guideline. This evidence is summarised and was considered together with potential benefits and harms, patient preferences and values, and resources, capacity, equity and other considerations to generate the recommendations. These are presented in the text. The recommendations are summarised in two algorithms presented in section 2.1.

2 Clinical Guideline & Recommendations

2.1 Summary of Recommendations (Algorithms)



*Note: Chest x-ray may miss up to 20% of lung cancers


A patient who presents with one or more **unexplained** signs or symptoms which may be suspicious for lung cancer
The patient has one or more signs or symptoms of lung cancer that are otherwise unexplained
The GP takes a patient history and performs a clinical exam
Refer the patient for an urgent chest x-ray
Chest x-ray suspicious for lung cancer
Chest x-ray not suspicious for lung cancer*
If the patient has:
• Persistent/unresolving signs or symptoms
or
• Repeated visits for a sign or symptom
and there is ongoing clinical concern for lung cancer (e.g. consider risk factors)
Refer the patient to a Rapid Access Lung Clinic
Consider referring the patient to a Rapid Access Lung Clinic
Signs and symptoms of lung cancer
• Cough (persistent)
• Alteration in character or severity of a cough
• Chest or shoulder pain
• Dyspnoea
• Hoarseness/change in voice
• Thrombocytosis
• Focal chest signs consistent with lung cancer
• Supraclavicular or persistent cervical lymphadenopathy
• Finger clubbing
• Tiredness/fatigue
• Weight or appetite loss
Risk factors for lung cancer
• Ever-smoker
• First degree family history of lung cancer
• Pulmonary fibrosis
• COPD
• Increasing age
*Note: Chest x-ray may miss up to 20% of lung cancers

Key points for communicating with the patient

- The GP should communicate sufficient information to meet the patient's needs
- Safety-netting should be in place for those patients with signs or symptoms who have not been referred for further tests
- Provide smoking cessation advice if the patient is a current smoker.

Key points for communicating with the Rapid Access Lung Clinic

- Referrals to a Rapid Access Lung Clinic should be made electronically where possible, via Healthlink or by using an ICGP-accredited software system
- Any relevant information regarding additional supports that the patient might require to attend their appointment should be included with the referral

2.2 Clinical questions, evidence statement, and recommendations

For symptomatic people in Primary Care, which signs and symptoms (or combinations of signs and symptoms) are predictive of lung cancer?

- **Does age effect the positive predictive value?**
- **What additional risk factors increase the predictive value?**

In patients with signs and symptoms suspicious for lung cancer, how does chest x-ray compare with CT for diagnostic utility?

Evidence Summary

Which signs and symptoms are predictive of lung cancer?

Three prospective cohort studies (Haastrup et al., 2020, Bradley et al., 2021, Hippisley-Cox and Coupland, 2011) and three case control studies (Hamilton et al., 2005, Iyen-Omofoman et al., 2013, Prado et al., 2023) answer this question. The studies are heterogeneous in terms of study design, population characteristics and length of the study/follow-up period.

Five of these studies report the positive predictive values (PPV) for any signs or symptoms of lung cancer, or give values from which the PPV can be calculated: Hamilton et al. (2005), Iyen-Omofoman et al. (2013), Bradley et al. (2021), Haastrup et al. (2020) and Hippisley-Cox and Coupland (2011).

The signs and symptoms reported in these studies variously include haemoptysis, weight loss, appetite loss, dyspnoea, chest pain, tiredness/fatigue, cough, thrombocytosis, abnormal spirometry, and hoarseness. Table 1 shows the PPVs for the individual signs or symptoms within each of these studies. The evidence shows that there is no single clear and unambiguous sign or symptom of lung cancer. Haemoptysis is the most predictive single sign of lung cancer, with a reported PPV of between 1.3% (Iyen-Omofoman et al., 2013) to 6.4% (95% CI 5.9–7.0) (Hippisley-Cox and Coupland, 2011). These studies are of patients in primary care aged ≥39 followed-up for at least 12 months (Iyen-Omofoman et al., 2013) or aged ≥40 followed-up for up to 2 years (Hippisley-Cox and Coupland, 2011).

There was variability across all other signs and symptoms in the predictive values reported, with only weight loss and dyspnoea showing a PPV of >2% in any study (Bradley et al., 2021).

Signs and symptoms in combination are more predictive of cancer than signs and symptoms in isolation. The positive predictive values for combinations of

signs/symptoms are calculated by Hamilton et al. (2005) for patients ≥40 years in Primary Care. Bradley et al. (2021) reported PPVs for combinations of signs and symptoms in patients >50 years who had self-referred for a chest x-ray. These are detailed in Table 2.

Similarly, patients presenting to their General Practitioner (GP) for a single sign or symptom on more than one occasion is more predictive of lung cancer than presenting with that sign or symptom once. For example, Hamilton et al. (2005) calculated that upon the second presentation to the GP, the PPV for loss of appetite more than doubled (0.87 vs 1.7%), while the PPV for haemoptysis was more than seven fold (2.4 vs 17%). Therefore, repeated visits for the same sign or symptom should increase the suspicion for lung cancer.

A case control study of 698 patients with lung cancer and 6,841 matched controls support these findings (Prado et al., 2023). On multivariate analysis and after adjusting for comorbidity scores, the following signs and symptoms were associated with a significantly higher odds of having a diagnosis of lung cancer: finger clubbing (Odds Ratio 50.1 (95% CI 8.9–283.3); lymphadenopathy (5.8 (3.8–8.8)); cough (4.7 (3.5–6.3)) haemoptysis (3.5 (2.2–5.5)); chest crackles or wheezes (3.2 (2.4–4.3)); weight loss (2.9 (2.2–3.9)); back pain (2.4 (1.8–3.1)); bone pain (2.3 (1.7–3.1)); shortness of breath (1.9 (1.4–2.5)); fatigue (1.8 (1.4–2.4)); and chest pain (1.4 (1.1–1.8)) (Prado et al., 2023).

Does age affect the Positive Predictive Value?

In a retrospective cohort study of 762,325 people Jones et al. (2007) looked at the PPV of haemoptysis in different age groups in both women and men. In women, the PPV steadily increased from 0.36 (95% CI 0.04–1.30) in women under 45 years to 10.47 (7.01–14.9) in women aged between 75–84. In men the PPV also increased with age from 0.21 (0.03–7.55) in men under 45 years to 20.42 in men aged 85 and older.

In a case control study of 247 cases and 1,235 controls, Hamilton et al. (2005) calculated a PPV for haemoptysis of 7.1% in people aged 70 and older. Abnormal spirometry had a PPV of 4.3% in the same age group. Both of these had PPVs of <1% in patients aged 40–69.

National Cancer Registry of Ireland (NCRI) data show that between 2012 and 2021 on average, more than 98% of lung cancers occurred in people aged 50 years or older, and more than 99.6% of lung cancers occurred in people aged 40 or older (National Cancer Registry of Ireland, 2024).

What additional risk factors increase the Positive Predictive Value?

Smoking

Hamilton et al. (2005) found that the positive predictive values of lung cancer signs and symptoms for ever-smokers (current and ex-smokers combined) were approximately twice those for the whole study population (i.e. non-smokers and ever-smokers). The PPVs for the same signs and symptoms in non-smokers were about one-third to one-half of those in the study as a whole.

A meta-analysis by O'Keeffe et al. (2018) compared the sex-specific relative risks of lung cancer in current, former, and never-smokers. When adjusted for age, the relative risk for lung cancer in current smokers versus non-smokers (including former smokers) was 7.48 (95% CI 5.29–10.60) in women and 8.78 (95% CI 6.13–12.57) in men. The relative risk in former smokers versus never-smokers was 2.82 (95% CI 2.25–3.54) in women and 3.01 (95% CI 2.23–4.08) in men.

Chronic Obstructive Pulmonary Disease

No studies were identified that examined the effect of Chronic Obstructive Pulmonary Disease (COPD) on the PPV of lung cancer signs and symptoms. However, two studies calculated the risk of developing lung cancer in patients with COPD compared to those without COPD. In a retrospective cohort study of 139,414 patients aged ≥40 years, Cave et al. (2021) reported that, after adjusting for age, sex, smoking status and urban/rural living, patients with COPD had a greater than seven-fold risk of developing lung cancer compared to patients without COPD (adjusted Relative Risk 7.57 (95% CI 4.74–12.09)). Similarly, Kiri et al. (2010) investigated the trends in annual incidence of lung cancer in individuals aged ≥45 years already diagnosed with COPD compared to the general population over a 15-year period in a UK primary care setting. Among those with a prior COPD diagnosis annual lung cancer incidence rates were four and five times higher than in the general population for men and women, respectively.

Pulmonary fibrosis

No studies were identified that examined the effect of pulmonary fibrosis on the PPV of lung cancer signs and symptoms. However, a systematic review and meta-analysis conducted by Whittaker Brown et al. (2019) to determine the association between idiopathic pulmonary fibrosis (IPF) and the incidence of lung cancer found that the estimated incidence rate ratio for lung cancer in patients with IPF was 6.42 (95% CI 3.21–9.62) [two studies, I^2= 56.2%]. As this was adjusted for known confounders — age, sex and smoking status — the analysis thus showed an independent association between IPF and lung cancer.

Family history of lung cancer in a first-degree relative

No studies were identified that examined the effect of a family history of lung cancer on the PPV of lung cancer signs and symptoms. However there are a number of studies that examine whether there is an association between development of lung cancer and a family history of the disease: Cannon-Albright et al. (2019), Coté et al. (2012), Kim et al. (2024), Lissowska et al. (2010), Cassidy et al. (2009), Gorlova et al. (2007), Cassidy et al. (2006) (see Table 3 and Table 4). This body of evidence has some limitations, notably almost all studies were subject to recall bias as presence of lung cancer in a family history was not validated. Studies were also subject to confounding due to either a lack of information on tobacco exposure in individuals or their relatives, or both. In all case control studies there was a significant difference in the proportion of smokers between cases and controls, although this is adjusted for in statistical analyses. Despite these limitations, the body of evidence is consistent in showing that, in the population overall, individuals with a first-degree family history of lung cancer have a higher odds of having a personal diagnosis of lung cancer than those who do not have a family history. Where never-smokers are analysed separately this association is also present (Table 3).

Studies are also consistent in showing that the strength of the association between lung cancer and a first-degree family history of the disease is related to the age at diagnosis of the affected relative: the odds of developing lung cancer are higher for individuals whose affected relative was diagnosed at a young age (Table 4).

Personal history of cancer

No studies were identified that examined the effect of a personal history of any cancer on the PPV of lung cancer signs and symptoms. However, one retrospective review examined the relative risk of developing lung cancer amongst 5-year survivors of a first primary cancer. Sung et al. (2020) calculated the Standardised Incident Ratio (SIR), that is, the ratio of observed incidence of second primary cancers in 5-year cancer survivors to the expected incidence in the general population.

Table 5 5 details the statistically significant SIRs for lung cancer as a second primary cancer. However, many of these first primary cancers are also smoking-related. Where breast cancer or Hodgkin lymphoma was the first primary cancer, the subsequent development of lung cancer may have been related to previous radiotherapy treatment to the chest.

How does chest x-ray compare with CT for diagnostic utility?

No studies were identified that directly compared CT with chest x-ray in people with signs and symptoms suspicious for lung cancer. As chest x-ray is readily available, the diagnostic performance of chest x-ray alone for the diagnosis of lung cancer was considered. A meta-analysis by Dywer-Hemmings and Fairhead (2021) reported that chest x-ray performed in symptomatic primary care populations has a sensitivity of 81% (95% CI 74–87%) and a specificity of 68% (49–87%). Because chest x-ray may therefore miss approximately 20% of lung cancers, additional follow-up tests may be required if there is ongoing clinical suspicion following a normal chest x-ray result.

Benefits and Harms

The purpose of this guideline is to identify people who have signs or symptoms that may indicate lung cancer and to support GP decision-making regarding which patients require further investigation or referral to a Rapid Access Lung Clinic. Timely diagnosis of lung cancer through a structured referral pathway can facilitate improved patient outcomes and experience.

Signs and symptoms

The predictive value of different signs and symptoms, alone or in combination, provides useful information regarding what proportion of patients with those signs or symptoms have lung cancer. Lung cancer frequently presents with the same signs and symptoms as common benign respiratory illnesses. When establishing a threshold for referral of patients with suspected lung cancer, setting the predictive value too low may result in unnecessary referral and investigations. This can result in anxiety for the patient and exposure to ionising radiation. Potential harms associated with setting the predictive value for signs and symptoms too high include delayed referrals and diagnoses resulting in poorer outcomes.

It is important to note that early stage lung cancer is often asymptomatic. Symptomatic patients subsequently diagnosed with lung cancer may already have late stage disease at the time of presentation. However, timely diagnosis of lung cancer through a structured referral pathway can facilitate improved patient outcomes and experience, regardless of stage at diagnosis.

Age

The majority of lung cancers occur in people aged 40 and older (>99% according to NCRI statistics (National Cancer Registry of Ireland, 2024)). This guideline does not include an age threshold for referral to a RALC, as an age threshold could result in patients who are under that age having a slower route to diagnosis. GPs should therefore have the facility to refer patients, regardless of age, if they have a strong

clinical suspicion of lung cancer while noting increasing age is an independent risk factor.

Other risk factors

The evidence supports the inclusion of the risk factors listed above as important considerations in assessing lung cancer risk. They are included in this guideline as a prompt for the GP in their clinical reasoning and to aid the GP to come to a decision about whether a referral to a RALC is warranted. However, while they are a factor in referral they should not the only reason for referral. They should be considered in combination with signs and symptoms. Patients may still be referred in the absence of these risk factors.

Chest x-ray versus CT

The benefit of a chest x-ray as a first line test when compared to CT is its ease of access and lower exposure to ionising radiation for the patient. However, some lung cancers may be missed on chest x-ray alone. Therefore, a chest x-ray not suspicious for lung cancer in a patient with an ongoing clinical suspicion of lung cancer may require further diagnostic investigations.

Preferences and values

Patients value knowledge and understanding, disclosure, and good communication regarding what is happening and how their care is being managed. They value feeling listened to and having their concerns understood and addressed. Patients report feeling that there is a stigma associated with lung cancer when compared with other cancer diagnoses. They therefore value openness in their discussions with their healthcare provider.

For patients who are referred for either a chest x-ray or to a Rapid Access Lung Clinic, the GP should communicate sufficient information to meet the individual patient's needs. To assist patients (or their carers) to be informed advocates for their own health this information could include, for example, why they are being referred for tests, where those tests will happen, and who will communicate the results of those tests to them.

As advocates for their own care, patients are often aware that something is wrong or different for them and they should be encouraged to contact their GP if they have ongoing signs or symptoms, which, if persistent, may indicate lung cancer.

Resources, capacity, equity and other considerations

The Guideline Development Group noted anecdotal reports of variation in timely access to imaging modalities (e.g. chest x-ray and CT) in the community.

In Ireland, both males and females residing in the most deprived quintile have significantly higher age-standardised incidence of lung cancer compared with those in the least deprived quintile (59% higher and 71% higher for males and females, respectively, between 2014–2018) (Bambury et al., 2023). Additionally, patients with lung cancer tend to have co-morbidities, thus travel distance to and from a RALC is a consideration. This is particularly true in areas outside of Dublin where access to a RALC can involve long travel distances for many patients.

There may be an increase in referral numbers to the RALCs as a result of this updated guideline.

The impact of vaping on lung cancer incidence is uncertain.

Recommendation 1

All people aged 40 and over who present to primary care with unexplained haemoptysis should be referred to a Rapid Access Lung Clinic.

Quality of Evidence: Moderate **Grade of recommendation: Strong**

Recommendation 2

All patients who present to primary care with any of the following signs or symptoms suspicious for lung cancer (which are otherwise unexplained) should be referred for an urgent chest x-ray.

Signs and symptoms:

- Cough (persistent)
- Alteration in character of severity of a cough
- Dyspnoea
- Chest or shoulder pain
- Hoarseness/change in voice
- Thrombocytosis
- Haemoptysis (aged ≤39)
- Focal chest signs consistent with lung cancer
- Supraclavicular or persistent cervical lymphadenopathy
- Finger clubbing
- Tiredness/Fatigue
- Weight or appetite loss

Quality of Evidence: High **Grade of recommendation: Strong**

Recommendation 3

All patients in primary care who have a chest x-ray suspicious for lung cancer should be referred to a Rapid Access Lung Clinic.

Quality of Evidence: High **Grade of recommendation: Strong**

Recommendation 4

For patients who have had a chest x-ray, that is not suspicious for lung cancer, but who have unresolving or persistent signs or symptoms (that are otherwise unexplained), consider referral to a Rapid Access Lung Clinic if there is an ongoing clinical concern* for lung cancer.

*The following risk factors should be considered: increasing age, ever-smoker, first-degree family history of lung cancer, presence of COPD or pulmonary fibrosis.

Quality of Evidence: Low **Grade of recommendation: Conditional**

Good practice points

- Referrals to a Rapid Access Lung Clinic should be made electronically where possible, via Healthlink or by using an ICGP-accredited software system
- The GP should communicate sufficient information to meet the individual patient's needs
- Safety-netting processes should be in place for those patients with signs or symptoms who have not been referred for further tests.
- Provide smoking cessation advice if the patient is a current smoker.

Practical considerations for patient care

- Patients should be aware that the RALC may contact them for further information in advance of their appointment
- Any relevant information regarding additional supports that the patient might require to attend their appointment should be included with the referral.

Table 1: Positive predictive values of each sign or symptom as reported in each study, with the study characteristics.

Study	Study design	Population characteristics	Study period (follow-up)	PPV [%] (95% CI)[1]
Haemoptysis				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	2.4 (1.4–4.1)
Hippisley-Cox & Coupland (2011)	Prospective cohort	Patients in primary care aged ≥40 years	2 years	6.4
Bradley et al. (2021)	Prospective cohort	Patients aged >50 years self-referred for chest x-ray (all patients)	12 months	4.67 (2.09–7.25)
			24 months	5.54 (2.67–8.22)
		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	2.94 (0.62–5.26)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort — patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,8226,293)	12 months	1.3
Weight loss				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls.	2 years	1.1 (0.8–1.6)
Bradley et al. (2021)	Prospective cohort	Patients aged >50 years self-referred for chest x-ray (all patients)	12 months	2.31 (1.11–3.50)
			24 months	3.14 (1.75–4.52)
		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	0.80 (0.02–1.58)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort– patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,8226,293)	12 months	0.33
Appetite loss				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and	2 years	0.87 (0.6–1.3)

[1] Unlike the other studies which use the equation PPV= $\frac{True\ Positive}{True\ Positive+False\ Positive}$, Hamilton et al. (2005) calculated the PPV from the likelihood ratio and the observed incidence of cancer during the study.

Study	Study design	Population characteristics	Study period (follow-up)	PPV [%] (95% CI)[1]
		general practice-matched controls		
Haastrup et al. (2020)	Prospective cohort	37,455 respondents to a health survey, aged ≥40 years from the general population. Symptoms and certain participant characteristics self-reported, with information on age, sex taken from the Danish Civil Registration System, and information on lung cancer diagnoses (C34) from the Danish Cancer Registry	1 year	0.3 (0.1–0.6)
			6 months	0.3 (0.1–0.6)
Dyspnoea				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	0.66 (0.5–0.8)
Haastrup et al. (2020)	Prospective cohort	37,455 respondents to a health survey, aged ≥40 years from the general population. Symptoms and certain participant characteristics self-reported, with information on age, sex taken from the Danish Civil Registration System, and information on lung cancer diagnoses (C34) from the Danish Cancer Registry	1 year	0.2 (0.1–0.5)
			6 months	0.2 (0.1–0.4)
Bradley et al. (2021)[2]	Prospective cohort	Patients aged >50 years self-referred for chest x-ray (all patients)	12 months	1.49 (0.93–2.05)
			24 months	2.11 (1.69–2.53)
		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	0.40 (0.21–0.60)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort — patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,8226,293)	12 months	0.51
Chest, shoulder or rib pain				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	0.82 (0.6–1.1)
			12 months	1.49 (0.93–2.05)

[2] Recorded as breathlessness in study

Study	Study design	Population characteristics	Study period (follow-up)	PPV [%] (95% CI)[1]
Bradley et al. (2021)	Prospective cohort	Patients aged >50 years self-referred for chest x-ray (all patients)	24 months	1.99 (1.35–2.46)
		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	0.55 (0.19–0.91)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort — patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,8226,293)	12 months	0.18
Tiredness/Fatigue				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	0.43 (0.3–0.6)
Haastrup et al. (2020)[3]	Prospective cohort	37,455 respondents to a health survey, aged ≥40 years from the general population. Symptoms and certain participant characteristics self-reported, with information on age, sex taken from the Danish Civil Registration System, and information on lung cancer diagnoses (C34) from the Danish Cancer Registry	1 year	0.1 (0.1–0.2)
			6 months	0.1 (0.0–0.1)
Cough				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years (1st attendance)	0.40 (0.3–0.5)
			2 years (2nd attendance)	0.58 (0.4–0.8)
Haastrup et al. (2020)	Prospective cohort	37,455 respondents to a health survey, aged ≥40 years from the general population. Symptoms and certain participant characteristics self-reported, with information on age, sex taken from the Danish Civil Registration System, and information on lung cancer diagnoses (C34) from the Danish Cancer Registry	1 year	0.2 (0.1–0.4)
			6 months	0.1 (0.0–0.3)
Bradley et al. (2021)	Prospective cohort	Patients aged >50 years self-referred for chest x-ray (all patients)	12 months	1.24 (1.01–1.48)
			24 months	1.66 (1.39–1.93)

[3] Lack of energy listed as a separate symptom in this study

Study	Study design	Population characteristics	Study period (follow-up)	PPV [%] (95% CI)[1]
		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	0.33 (0.20–0.46)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort — patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,826,293)	12 months	0.24
Thrombocytosis				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	1.6 (0.8–3.1)
Abnormal spirometry				
Hamilton et al. (2005)	Case control	Aged ≥40 years from primary care, 247 cases with lung cancer, 1,235 sex, age and general practice-matched controls	2 years	1.6 (0.9–2.9)
Hoarseness/Change in voice				
Haastrup et al. (2020)[4]	Prospective cohort	37,455 respondents to a health survey, aged ≥40 years from the general population. Symptoms and certain participant characteristics self-reported, with information on age, sex taken from the Danish Civil Registration System, and information on lung cancer diagnoses (C34) from the Danish Cancer Registry	1 year	0.3 (0.1–0.7)
			6 months	Not recorded
Bradley et al. (2021)	Prospective cohort	8996 patients aged >50 years self-referred for chest x-ray (all patients)	12 months	0.75 (0.34–1.15)
Bradley et al. (2021)			24 months	1.27 (0.74–1.79)
Bradley et al. (2021)		Patients aged >50 years self-referred for CXR who have a **negative x-ray result**	12 months	0.26 (0.01–0.51)
Iyen-Omofoman et al. (2013)	Case control	Validation cohort– patients in general practice, aged ≥39 years with ≥1 year of follow up and were free from lung cancer at start date (n=1,8226,293)	12 months	0.17

[4] Symptom persisting greater than four weeks

Table 2: Positive predictive values for lung cancer of sign/symptom combinations reported by two studies (Hamilton et al. (2005) and Bradley et al. (2021)).

Symptom 1	Symptom 2	PPV (95% CI) Hamilton et al. (2005)	PPV (95% CI) Bradley et al. (2021)
Cough	Fatigue	0.63 (0.5–0.9)	NR
Cough	Dyspnoea/breathlessness	0.79 (0.6–1.0)	2.07 (1.63–2.50)
Cough	Chest pain	0.76 (0.6–1.0)	1.95 (1.26–2.60)
Cough	Loss of weight	1.8 (1.1–2.9)	3.20 (1.75–4.67)
Cough	Loss of appetite	1.6 (0.9–2.7)	NR
Cough	Thrombocytosis	2.0 (1.1–3.5)	NR
Cough	Abnormal spirometry	1.2 (0.6–2.6)	NR
Cough	Haemoptysis	2.0 (1.1–3.5)	5.08 (2.29–7.89)
Cough	Change in voice	NR	1.08 (0.59–1.58)
Fatigue	Dyspnoea/breathlessness	0.89 (0.6–0.3)	NR
Fatigue	Chest pain	0.84 (0.5–1.3)	NR
Fatigue	Loss of weight	1.0 (0.6–1.7)	NR
Fatigue	Loss of appetite	1.2 (0.7–2.1)	NR
Fatigue	Thrombocytosis	1.8	NR
Fatigue	Abnormal spirometry	4.0	NR
Fatigue	Haemoptysis	3.3	NR
Dyspnoea/breathlessness	Chest pain	1.2 (0.9–1.8)	1.83 (1.07–2.59)
Dyspnoea/breathlessness	Loss of weight	2.0 (1.2–3.8)	3.27 (1.59–4.98)
Dyspnoea/breathlessness	Loss of appetite	2.0 (1.2–3.8)	NR
Dyspnoea/breathlessness	Thrombocytosis	2.0	NR
Dyspnoea/breathlessness	Abnormal spirometry	2.3	NR
Dyspnoea/breathlessness	Haemoptysis	4.9	6.37 (2.55–10.19)
Dyspnoea/breathlessness	Change in voice	NR	1.62 (0.88–2.36)
Chest pain	Loss of weight	1.8 (1.0–3.4)	3.61 (0.78–6.45)
Chest pain	Loss of appetite	1.8 (0.9–3.9)	NR
Chest pain	Thrombocytosis	2.0	NR
Chest pain	Abnormal spirometry	1.4	NR
Chest pain	Haemoptysis	5.0	4.94 (0.22–9.66)*
Chest pain	Change in voice	NR	1.30 (0.27–2.33)
Loss of weight	Loss of appetite	2.3 (1.2–4.4)	NR
Loss of weight	Thrombocytosis	6.1	NR
Loss of weight	Abnormal spirometry	1.5	NR
Loss of weight	Haemoptysis	9.2	12.50 (1.04–23.96)*
Loss of weight	Change in voice	NR	1.76 (0.00–3.74)*
Loss of appetite	Thrombocytosis	0.9	NR
Loss of appetite	Abnormal spirometry	2.7	NR
Loss of appetite	Haemoptysis	>10	NR
Thrombocytosis	Abnormal spirometry	3.6	NR
Thrombocytosis	Haemoptysis	>10	NR
Abnormal spirometry	Haemoptysis	>10	NR
Haemoptysis	Change in voice	NR	1.45 (0.00–4.27)*

NR = not reported; * indicates data is from fewer than five cases.

Note the follow-up period for both studies was two years; however, the study population differed. Hamilton et al. (2005) is a case control study of 247 cases aged ≥40 years from Primary Care, with 1,235 sex-, age- and GP practice-matched controls. Bradley et al. (2021) is a prospective cohort study of 8996 patients aged >50 years who self-referred for a chest x-ray (data extracted from the supplementary material). Additionally, Hamilton et al. (2005) calculated the PPV from the likelihood ratio and the observed incidence of cancer during the study.

Table 3: Association between lung cancer development and family history of lung cancer in a first-degree relative.

Study	Study type	Population	Results*	Adjusted for
Cannon-Albright (2019)	Retrospective cohort	Utah Population Database linked to Cancer Registry: 1.3m probands, 5,408 lung cancer cases.	RR 2.57 (2.39–2.76)	
Coté (2012)	Pooled analysis of case control studies	24,380 lung cancer cases and 23,399 controls	aOR 1.51 (1.39–1.63)	Age, gender, ethnicity, smoker-type, pack years and study site where appropriate
Kim (2024)	Cross sectional	198,980 participants from Korea, of which 140 had lung cancer	OR 1.86 (0.91–3.79) aOR 2.28 (1.11–4.66)	Age, sex, smoking status
Lissowska (2021)	Case control	2,861 lung cancer cases and 3188 controls	aOR 1.63 (1.31–2.01)	Age, sex, study centre, education, smoking status (pack years), number of relatives
Cassidy (2009)	Case control	733 cases with NSCLC and 1312 controls	aOR[1] 1.55 (1.19–2.03) aOR[2] 1.33 (0.97–1.81)	[1]Family size [2]Family size, tobacco consumption (pack years) occupational asbestos exposure, education level
Gorlova (2009)	Case control	316 cases and 318 controls with 2,465 and 2,441 first degree relatives respectively	aOR 1.39 (0.91–2.13)	Ethnicity, gender and age of proband, gender, age smoking status, birth cohort of relative, and type of relationship to proband
Kim (2024)	Cross sectional	144,291 never smoking participants from Korea, of which 59 had lung cancer	OR 2.85 (1.14–7.13) aOR 3.25 (1.30–8.16)	Age, sex
Coté (2012)	Pooled analysis of case controls	3,301 cases and 8,497 controls	aOR 1.25 (1.03–1.52)	Age, gender, ethnicity, education, study site

*RR=Relative risk; OR=Odds ratio; aOR=adjusted odds ratio.

Table 4: Association between age of diagnosis of affected first degree relative and lung cancer development.

Study	Study type	Age at diagnosis of FDR	Result*	Population
Cannon-Albright (2019)	Retrospective cohort	<50 years	RR 3.04 (2.13–4.21)	General
		50–59 years	RR 3.66 (3.11–4.28)	
		60–69 years	RR 2.82 (2.49–3.18)	
		70–79 years	RR 2.19 (1.91–2.50)	
		≥80 years	RR 1.74 (1.38–2.17)	
Kim (2024)	Cross sectional	<60 years	OR 3.05 (0.97– 9.60) aOR 3.77 (1.19–11.88)	General
		≥60 years	OR 1.50 (0.61–3.67) aOR 1.84 (0.75–4.50)	
Kim (2024)	Cross sectional	<60 years	OR 7.31 (2.28–23.41) aOR 8.52 (2.65–27.39)	Never smokers
		≥60 years	OR 1.49 (0.36–6.11) aOR 1.69 (0.41–6.94)	
Gorlova (2007)	Case control	<50 years	aOR 5.52 (1.19–25.51)	Never smokers
Cassidy (2006)	Case control	<60 years	aOR 2.08 (1.20–3.59)	General
		≥60 years	aOR 1.27 (0.83–1.95)	

*RR=Relative risk; OR=Odds ratio; aOR=adjusted odds ratio.

Table 5: Standardized Incident Ratios for lung cancer as a second primary cancer, where statistically significant, by sex and first primary cancer type.

	Standardised Incident Ratio for subsequent lung cancer (95% Confidence Intervals)	
First primary Cancer	**Males**	**Females**
Larynx	3.97 (3.7–4.27)	8.09 (7.08–9.2)
Oesophagus	1.93 (1.54–2.38)	3.78 (2.7–5.14)
Acute lymphocytic leukaemia	Not significant	2.85 (1.05–6.21)
Oral cavity and pharynx	2.47 (2.31–2.46)	2.81 (2.52–3.12)
Hodgkin lymphoma	2.22 (1.82–2.69)	2.45 (1.96–3.1)
Urinary bladder	1.78 (1.71–1.86)	2.35 (2.17–2.55)
Anus, anal canal and anorectum	2.29 (1.77–2.92)	2.11 (1.67–2.63)
Pancreas	Not significant	2.23 (1.54–3.12)
Vulva and other genital organs	Not applicable	1.92 (1.62–2.26)
Cervix uteri	Not applicable	1.9 (1.7–2.12)
Liver and intrahepatic bile duct	Not significant	1.85 (1.13–2.85)
Gallbladder	Not significant	1.76 (1.19–2.5)
Penis	1.71 (1.28–2.23)	Not applicable
Non-Hodgkin lymphoma	1.21 (1.13–1.29)	1.48 (1.37–1.59)
Kidney and renal pelvis	1.13 (1.03–1.24)	1.39 (1.23–1.56)
Stomach	1.36 (1.15 -1.59)	Not significant
Colon and rectum	1.06 (1.01–1.11)	1.13 (1.07–1.2)
Breast	Not significant	1.12 (1.09–1.15)

3 Methodology

3.1 Establishment of a Guideline Development Group

A Guideline Development Group (GDG) was responsible for the development and delivery of this National GP Referral Guideline and included representatives from relevant medical professionals and stakeholders (see Appendix I for a list of the members of the GDG).

3.2 List of clinical questions

Four clinical questions were developed to guide the literature searches that underpin the evidence in this guideline. Following literature retrieval for one of the questions (Clinical Question LGP3) and after discussion with the Guideline Development Group, two additional and more specific literature searches were conducted to retrieve more focussed results for this question. These are indicated in the footnotes below. A fifth clinical question (LGP5) regarding the incidence of lung cancer by age in Ireland was also developed. Data from the National Cancer Registry Ireland was retrieved to answer this question and a literature search was not performed.

The clinical questions are as follows:

Clinical question code: LGP1

For symptomatic people in Primary Care, which signs and symptoms (of combination of signs and symptoms) are predictive of lung cancer?

Population	Symptomatic people in Primary Care
Prognostic factor	Signs and symptoms of lung cancer – alone or in combination: • Haemoptysis • Dyspnoea • Cough (persistent or change to existing) • Hoarseness • Stridor • Chest pain or shoulder pain • Finger clubbing • Lymphadenopathy • Dysphagia • Paraneoplastic syndromes • Loss of appetite • Weight loss • Change in symptom burden • Tiredness/fatigue
Outcome	Positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio

Clinical question code: LGP2
For people in primary care with signs and symptoms suspicious of lung cancer, does age affect the predictive value?

Population	People in primary care with symptoms suspicious of lung cancer
Prognostic factor	Age
Outcome	Positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio

Clinical question code: LGP3
For people in primary care with symptoms suspicious of lung cancer, what additional risk factors increase the predictive value?

Population	People in primary care with symptoms suspicious of lung cancer
Prognostic factor	Additional risk factors: • Family history of lung cancer in a first degree relative[5] • Personal history of head and neck cancer • Previous radiation to chest • Smoking history • Chronic lung disease • Pulmonary fibrosis[6] • Occupational exposure/environmental factors • Radon • Social deprivation
Outcome	Increased positive predictive value, positive likelihood ratio

Clinical question code: LGP4
In patients with signs and symptoms suspicious for lung cancer how does chest x-ray compare with CT for diagnostic utility (sensitivity, specificity, false positive rate, false negative rate, recall rate)?

Population	Patients with signs and symptoms suspicious of lung cancer
Intervention	Chest x-ray
Comparison	CT
Outcome	Sensitivity, specificity, false positive rate, false negative rate, recall rate, incidental findings

[5] Additional literature search carried out on family history of lung cancer to provide more focussed results
[6] Additional literature search carried out on Pulmonary fibrosis to provide more focussed results

Clinical question code: LGP5[7]
What is the incidence of lung cancer by age range in people living in Ireland?

Condition	Lung cancer
Context	Incidence by age ranges
Population	People living in Ireland

3.3 Describe and document the evidence search

A systematic literature review protocol was developed for the guideline development process by the HSE librarians in conjunction with the NCCP and is available upon request. The literature search strategies for each clinical question (including the additional searches conducted for Clinical Question LGP3) are available upon request.

3.4 Describe the method of screening and evidence appraisal

Two NCCP senior research officers screened the literature searches independently to identify any relevant primary papers. Any disagreements on primary paper inclusion were agreed through discussion.

All primary papers deemed suitable for inclusion were appraised using validated checklists developed by the Scottish Intercollegiate Guideline Network (SIGN).

There were three main points considered when appraising the research evidence:
- Are the results valid? (internal validity)
- What are the results? (statistical and clinical significance)
- Are the results applicable/generalisable to the patient/population of the guideline? (external validity)

3.5 Formulation and grading of recommendations

The evidence to address the clinical questions, both from primary literature and international guidelines, was extracted into evidence tables.

Recommendations were formulated through a formal structured process. An 'Evidence to Decision Framework' was completed for the clinical questions.

The following domains were discussed by the GDG for each updated question.

Evidence summary
The body of evidence was reviewed and discussed taking into account the types of studies available, the quality of those studies and their degree of bias, the precision

[7] Literature search not conducted for this question. Data were retrieved from the National Cancer Registry, Ireland.

of the results, and whether all studies were consistent in their findings. The directness of the evidence and generalisability to the target population were also considered.

Benefit and harm
The balance of potential benefits versus potential harms of the proposed recommendations were considered.

Preferences and values
The preferences and values of the patient were discussed and considered by the Guideline Development Group, noting particularly the acceptability of the proposed recommendations to patients and their carers' in the context of the balance of benefits and harms.

In endeavouring to achieve as broad a perspective as possible on patients' preferences and values, a patient focus group was also convened. This focus group was asked to advise on and discuss their preferences and values, and the preferences and values of patients like them. The key points from this discussion were then summarised and are presented in this guideline. Members of the patient focus group can be found in Appendix I.

Resources, capacity, equity and practical considerations
Any factors which may affect the implementation of the proposed recommendations were discussed and documented. Potential issues around equity was explicitly considered.

Following discussion on the four domains above the recommendations were agreed by the GDG. The following terms were considered for use in recommendations:

- is recommended
- should be considered
- may be considered
- is not recommended.

The use of these terms are dependent on all four domains outlined above. Each recommendation was assigned a quality of evidence and a grade of recommendation by the GDG. Good practice points and practical considerations for patient care were also agreed by the Guideline Development Group. Further information on the grading systems used are documented in Appendix III.

3.6 Consultation

National review

The draft guideline was signed-off by the GDG before going to national stakeholder review.

It was placed on the NCCP website and circulated to relevant organisations and individuals for comment between [date month] and [date month year].

Stakeholders were asked to comment on the comprehensiveness of evidence used to form the recommendations. Stakeholders were required to submit feedback with supporting evidence on a form provided along with a completed conflict of interest form.

All feedback received was reviewed by the GDG. Suggested amendments and supporting evidence were reviewed and consensus reached to accept or reject the amendments. These decisions, and their rationale, were documented in a Consultation Feedback Report and accepted amendments were applied to the guideline. A copy of the Feedback Report is available on request.

3.7 National implementation plan

An implementation plan was developed based on the NCEC Implementation guide (Department of Health, 2018). It outlines the actions required to implement this guideline, who has lead responsibility for delivering the action, the timeframe for completion and the expected outcomes of implementation (see Appendix IV). Implementation of the guideline was considered in tandem with the development and implementation of an update to the electronic referral form for GPs, which is the primary mechanism by which GPs refer patients into the Rapid Access Lung Clinics.

The National GP Referral Guideline has been circulated and disseminated through the professional networks who participated in developing and reviewing this document.

3.8 Governance and approval

The final draft of the guideline was Quality Assured internally by a member of the NCCP Evidence and Quality Team to confirm adherence to the National Standards for Clinical Practice Guidance (Department of Health, 2015).

The guideline, along with confirmation of the outcome of the Quality Assurance process, was then submitted to the NCCP National Executive on [date month year] for approval. A full list of the members can be found in Appendix II.

3.9 Communication and dissemination plan

This National Clinical Guideline is available on the HSE National Central Repository.

A Communication and Dissemination Plan was developed by the GDG to raise awareness of the development of this guideline, to ensure effective communication and collaboration with all key stakeholders throughout the various stages of guideline

development process and to maintain momentum for the widespread adoption of the guideline.

In conjunction with the HSE Communications Division, key stakeholders were identified and a list of strategies was developed to inform them of the new guideline. The implementation of the guideline will also be supported by communication and dissemination. Details of the Communication and Dissemination Plan are available in Appendix V.

3.10 Plan for national monitoring, evaluation and audit

Monitoring and evaluation

Referrals to the Rapid Access Lung Clinics (RALCs) are monitored on an ongoing basis using Healthlink data.

The impact of the referral guideline on clinics will be monitored through the NCCP Lung Leads forum, which has representation from each RALC. Additionally, a suite of Key Performance Indicators monitor the functioning of the clinics.

3.11 Review/update

This guideline was issued on [date month year] and will be considered for review by the NCCP in three years, or may be updated in the interim period if the NCCP are notified of evidence which may result in a change to the recommendations.

Surveillance of the literature base will be carried out periodically by the NCCP. Any updates to the guideline in the interim period where new evidence emerges or as a result of three year review will be noted in the guidelines section of the NCCP websites.

4 Abbreviations

CI	Confidence Interval
CT	Computed Tomography
CXR	Chest X-Ray
COPD	Chronic Obstructive Pulmonary Disorder
GDG	Guideline Development Group
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HSE	Health Service Executive
IPF	Idiopathic Pulmonary Fibrosis
NCCP	National Cancer Control Programme
NCEC	National Clinical Effectiveness Committee
NCRI	National Cancer Registry of Ireland
OR	Odds Ratio
PPV	Positive Predictive Value
RALC	Rapid Access Lung Clinic
RR	Relative Risk
SIR	Standardised Incident Ratio

5 Glossary of Terms

Case control study
The observational epidemiologic study of persons with the disease (or other outcome variable) of interest and a suitable control (comparison, reference) group of persons without the disease. The relationship of an attribute to the disease is examined by comparing the diseased and non-diseased with regard to how frequently the attribute is present or, if quantitative, the levels of the attribute, in each of the groups.

Cohort study
The analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of cohort study is observation of large numbers over a long period (commonly years) with comparison of incidence rates in groups that differ in exposure levels.

Comorbidity
The condition of having two or more diseases at the same time.

Confidence Intervals (CI)
Confidence intervals indicate the consistency, or variability of a result. If a study has 95% confidence interval calculated, this means that if the study was repeated multiple times with samples from the whole population and the confidence intervals were calculated for each of those repeated studies, then the true value would lie within the calculated confidence intervals 95% of the time.

Computed tomography (CT) Scan
A procedure that uses a series of x-rays to make detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional (3-D) views of tissues and organs. A dye may be injected into a vein or swallowed to help the tissues and organs show up more clearly. A CT scan may be used to help diagnose disease, plan treatment, or find out how well treatment is working. Also called CAT scan, computed tomography scan, computerized axial tomography scan, and computerized tomography.

Dyspnoea
Difficult, painful breathing or shortness of breath.

Ever smoker
A person who currently smokes cigarettes, or who has quit smoking but has smoked at least 100 cigarettes in their lifetime.

First degree relative
A way of describing how family members are related to each other when there are no other family members in the bloodline between them. Examples of a first-degree relative are a parent, sibling, or child. Also called FDR.

Haemoptysis
Coughing or spitting up blood from the respiratory tract.

Incidence
The number of new cases of illness commencing, or of persons falling ill, during a specified time period in a given population.

Lymphadenopathy
Disease or swelling of the lymph nodes.

Meta-analysis
A process that analyses data from different studies done about the same subject. The results of a meta-analysis are usually stronger than the results of any study by itself.

Never smoker
An adult who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime.

Odds ratio (OR)
An odds ratio (OR) is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure.

Positive Predictive Value (PPV)
The proportion of people with a positive test who have disease.

Relative Risk (RR)
A measure of the risk of a certain event happening in one group compared to the risk of the same event happening in another group. A relative risk of 1 means there is no difference between two groups in terms of their risk of cancer, based on whether or not they were exposed to a certain substance or factor, or how they responded to two treatments being compared. A relative risk >1 or <1 usually means that being exposed to a certain substance or factor either increases or decreases the risk of cancer, or that the treatments being compared do not have the same effects.

Sign
In medicine, a sign is something found during a physical exam or as a result of a laboratory or imaging test that shows that a person may have a condition or disease. Signs can be observed by a health care provider or other person. Some examples of signs are fever, swelling, skin rash, high blood pressure, and high blood glucose.

Spirometry
A test used to measure how well air moves in and out of the lungs.

Symptom
Something that a person feels or experiences that may indicate that they have a disease or condition. Symptoms can only be reported by the person experiencing them. They cannot be observed by a health care provider or other person and do not show up on medical tests. Some examples of symptoms are pain, nausea, fatigue, and anxiety.

Systematic review
The application of strategies that limit bias in the assembly, critical appraisal, and synthesis of all relevant studies on a specific topic. Systematic reviews focus on peer-reviewed publications about a specific health problem and use rigorous, standardized methods for selecting and assessing articles. A systematic review differs from a meta-analysis in not including a quantitative summary of the results.

Thrombocytosis
An elevated level of platelets in the blood.

6 Appendices

Appendix I Members of the Guideline Development Group and Patient Focus Group

A conflict of interest form was signed by all members of the Guideline Development Group. No conflicts of interest were declared.

Members of the Guideline Development Group		
Name	**Title/position**	**Role on GDG**
Chairs of the Guideline Development Group		
Dr David Breen	Consultant Respiratory Physician, GUH	Clinical chair and writing member
Dr Eve O'Toole	Head of Evidence and Quality, NCCP	Evidence Chair and writing member
Evidence Synthesis		
Dr Niamh Kilgallen	Senior Research Officer, NCCP	Researcher, project manager and writing member
General Practice		
Dr Una Kennedy	GP Adviser, NCCP	Writing member
Prof. Patrick Redmond	General Practitioner, RCSI	Writing member
Library		
Ms Dymphna McGettigan	HSE Librarian	Information services
NCCP		
Ms Nerissa Keating	General Manager, NCCP	Programme manager and writing member
Nursing		
Ms Noreen Lyons	Advanced Nurse Practitioner, CUH	Writing member
Ms Salomy Matthew	Clinical Nurse Specialist, Beaumont Hospital	Writing member
Ms Rosemarie Murphy	Advanced Nurse Practitioner, UHL	Writing member
Ms Gráinne Cogan	Lung Cancer Coordinator, OLOL Drogheda	Writing member
Patient/Service User Partners		
Ms Oonagh McArdle	Patient and public partner	Writing member
Ms Dolores Roberts	Patient and public partner	Writing member
Patient Support and Administration		

Ms Nainsi Corcoran	Rapid Access Lung Patient Navigator, GUH	Writing member
Public Health		
Dr Heather Burns	Consultant in Public Health Medicine, NCCP	Writing member
Radiology		
Dr Carmel Cronin	Consultant Radiologist, MMUH	Writing member
Dr Bryan Dalton	Specialist Registrar, SJH	Writing member
Dr John Kavanagh	Consultant Radiologist, SJH	Writing member
Respiratory Medicine		
Dr Ian Counihan	Consultant Respiratory Physician, OLOL Drogheda	Writing member
Dr Susan Foley	Consultant Respiratory Physician, UHW	Writing member
Dr Emmet O'Brien	Consultant Respiratory Physician, Beaumont Hospital	Writing member

Members of the Patient Focus Group	
Name	**Role**
Mr Séamus Cotter	Patient and public partner
Ms Susan Leatham	Patient and public partner
Ms Oonagh McArdle	Patient and public partner
Ms Dolores Roberts	Patient and public partner
Ms Gillian Ryan	Patient and public partner
Ms Sally Stone	Patient and public partner
Dr Eve O'Toole	Moderator
Dr David Breen	Facilitator (RALC)
Dr Una Kennedy	Facilitator (GP)
Ms Nerissa Keating	Facilitator (NCCP)
Dr Niamh Kilgallen	Facilitator (NCCP)

Additional Contributors	
Name	**Role**
Dr Robert Conway	Public Health, Cancer Intelligence, NCCP
Mr Paul Flood	Research Officer, NCCP
Dr Ciara Grady	Specialist Registrar, NCCP
Ms Louise Murphy	Senior Research Officer, NCCP
Ms Mary O'Brien	Administration, CUH

Appendix II Membership of NCCP National Executive

Name	Role and position

Sign-off by Chair of Approval Governance Group

National Clinical Guideline: GP Guideline for the Referral of Patients with Suspected Lung Cancer was formally ratified and recorded in the minutes of the Approval Governance Group on [date month year].

Name:	
Title:	
Signature:	

Appendix III Grading the recommendations in this guideline

Grading system

The Guideline Development Group assigned each recommendation a quality of evidence and grade of recommendation. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach provides an explicit system for rating the quality of evidence and whether the recommendation is strong or conditional (Guyatt et al., 2008).

Quality of evidence

It is recognised in guideline development that just assessing the level of evidence does not take into account the methodological quality of each individual study or the quality of the body of evidence as a whole (Harbour and Miller, 2001). The Guideline Development Group used an amended GRADE system which considers the following factors when classifying the quality of evidence; high, moderate, low or very low (Guyatt et al., 2008):

- Study design
- Study design limitations
- Consistency of results
- Directness of the evidence
- Imprecision of results
- Reporting bias

Table i: Quality of evidence adapted from GRADE working group 2013

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Grade of recommendation

There are two grades of recommendation: strong or conditional. These reflects the balance of the following items:

- The quality of the body of evidence
- The balance between benefit and harm to patient
- Patient preferences and values
- Resources/cost

Table ii: Grade of recommendation adapted from GRADE working group 2013

Strong	A strong recommendation is one for which the Guideline Development Group is confident that the desirable effects of an intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention). Strong recommendations are not necessarily high priority recommendations. A strong recommendation implies that most or all individuals will be best served by the recommended course of action.
Conditional	A conditional recommendation is one for which the desirable effects probably outweighs the undesirable effects (conditional recommendation for an intervention) or undesirable effects probably outweigh the desirable effects (conditional recommendation against an intervention) but appreciable uncertainty exists. A conditional recommendation implies that not all individuals will be best served by the recommended course of action. There is a need to consider more carefully than usual the individual patient's circumstances, preferences, and values. When there are conditional recommendations caregivers need to allocate more time to shared decision-making, making sure that they clearly and comprehensively explain the potential benefits and harms to a patient.

Appendix IV National Implementation Plan

National Clinical Guideline	HSE National Clinical Guideline. GP Referral Guideline for Patients with Suspected Lung Cancer
Date National Clinical Guideline approved	[date month year]
Expected date of full implementation	[year]

Implementation action	Implementation barriers / enablers	List of tasks to implement the action	Lead responsibility for delivery of the action	Expected completion date	Expected outcomes
Removal of superseded guideline from HSE website.	Enabler: NCCP Website Editorial Board Barrier: None	Liaison with NCCP Website Editorial Board	Project manager (NCCP)	TBC	Outdated guideline removed from public access
Publication of this guideline update on National Central Repository	Enabler: National Central Repository Barrier: None	Liaison with NCR team	Project manager (NCCP)	TBC	Updated guideline published.
Creation of Healthlink e-referral form based on updated guideline and linking to summary of updated guideline	Enabler: Healthlink project/development team. Barrier: Healthlink scheduling constraints.	Liaison with Healthlink	Healthlink team	TBC	Updated e-referral form available to GPs, reflecting guideline

Implementation action	Implementation barriers / enablers	List of tasks to implement the action	Lead responsibility for delivery of the action	Expected completion date	Expected outcomes
Dissemination of guideline to GPs	Enabler: Healthlink GP contact list, ICGP Barrier: Gaps in the above	Email to GPs		TBC	
Dissemination of guideline to RALCs	Enabler: Lung Leads group, GDG Barrier: None	Email to RALCs, Cancer Centre managers, GDG.	Project manager (NCCP)	TBC	

Appendix V Communication & Dissemination Plan

Key stakeholders were identified by the GDG and in conjunction with the HSE Communications Division, a list of strategies was developed to inform these stakeholders of the new guideline. These include:

- Official publication and launch of the guideline.
- Direct communication from NCCP Director to ICGP.
- Circulation to GP Practices.
- Circulation to the networks who participated in developing and reviewing the guideline.
- Circulation to NCCP staff.
- Inform the relevant voluntary organisations and patient advocacy groups that the guideline has been updated and is available for representation in their patient and public information.
- Promotion through the HSE/NCCP website, internal HSE media, social and print media.
- NCCP to include details of the guideline in presentations by clinical leads, sub-group chairs, NCCP Director.
- NCCP to promote the guideline at Audit and Quality Reviews, conferences, workshops, and CPD sessions.

A plain language summary of the guideline is included as a key element of the Communication and Dissemination Plan — for patients, their families and other non-specialists who may be interested in the guideline and what it means for them.

Description of stakeholder communications	Communication method	Owner	Timeline
Patients			
Plain language summary	Guideline	Project team	Pre 'go live'
Guideline Development Group			
New guideline alert	Email	Project team	Pre 'go live'
National stakeholders			
New guideline to ICGP	Email	National Director, NCCP	Pre 'go live'
New guideline to relevant stakeholders (incl. GPs, patient advocacy groups)	Email	Project team	Within 1 week of 'Go live'
New guideline to NCCP staff	Email	Project team	Within 1 week of 'Go live'

Press Release (HSE website)	Article	Project team/HSE Comms	Official launch
Social media coverage (Irish & English)	“X” posts	Project team	‘Go live’ & official launch
News articles	Article	Project team/HSE Comms	Within 2 months of 'go live'

Appendix VI Plain Language Summary

Summary of National Clinical Guideline

The signs and symptoms of lung cancer can be the same as those for many common illnesses like chest infections or coughs. You should talk to your GP if you have any signs or symptoms that you are worried about. Your GP can use this guideline to help decide whether to refer you for further tests. The recommendations in the guideline are based on the signs or symptoms you have, how long you have had them, how old you are, and if there are any other reasons to think you might be at risk for having lung cancer.

Who is this for?

This guideline is for GPs. It was developed to help them decide if they need to refer you for further tests to check if you have lung cancer.

Questions you might want to ask your GP

- What happens next?

If your GP refers you for further tests:

- What tests will I have?
- How long should I expect to wait for an appointment?
- When will I get the results and who will give them to me?
- What happens then?
- Who do I contact if my symptoms get worse, or I have a new symptom?

If your GP does not refer you for further tests:

- What do I do if my symptoms do not improve or I have a new symptom?

Understanding the language

Medical term	Plain language explanation
Chronic Obstructive pulmonary disorder (COPD)	A group of lung conditions that can cause breathing difficulties
Computed tomography (CT)	An imaging scan that uses a combination of X-rays and computer technology to produce images of the inside of the body
Dyspnoea	Shortness of breath
First-degree relative	A parent, brother, sister, or child
Haemoptysis	Coughing up blood from your lungs or airways
Lymphadenopathy	Swelling of the lymph nodes

Pulmonary fibrosis	A serious, lifelong lung disease. It causes lung scarring (tissues scar and thicken over time), making it harder to breathe
Rapid Access Lung Clinic (RALC)	A hospital-based clinic that specialises in the diagnosis of lung cancer
Thrombocytosis	A condition where your body produces too many platelets. Platelets are a part of the blood that help you to form blood clots. Too many platelets can be produced when you have a disease or infection

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