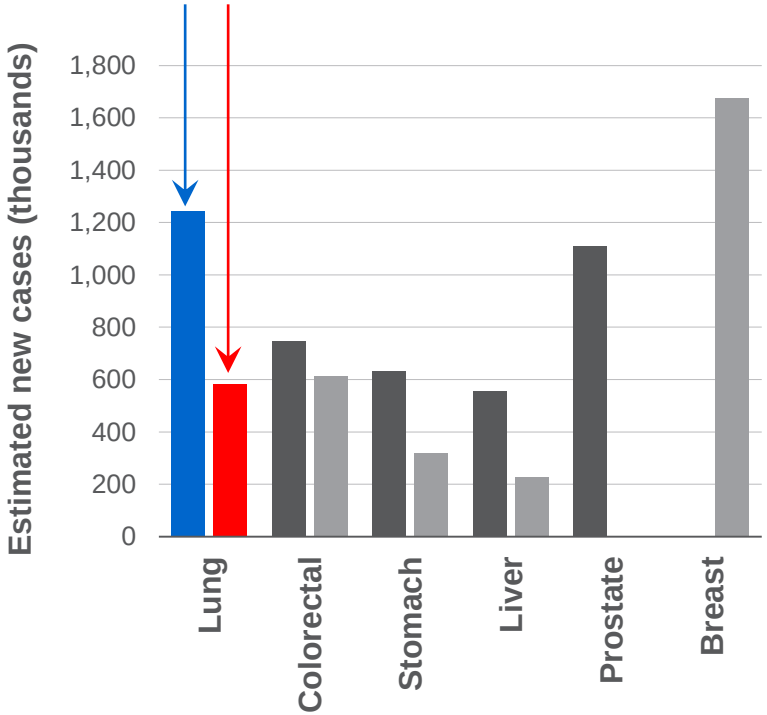
NSCLC

NSCLC

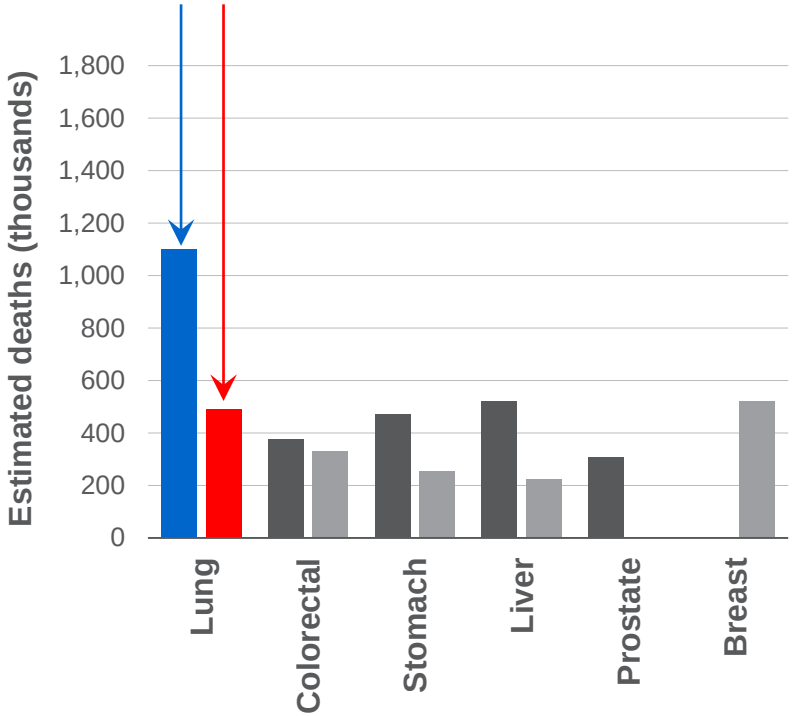
Epidemiology

Lung cancer incidence and mortality[1,2]

One of the most common cancers, with **1.8 million new cases** worldwide in 2012



The most common cause of cancer death, causing nearly **1 in 5** of all **cancer deaths** worldwide in 2012

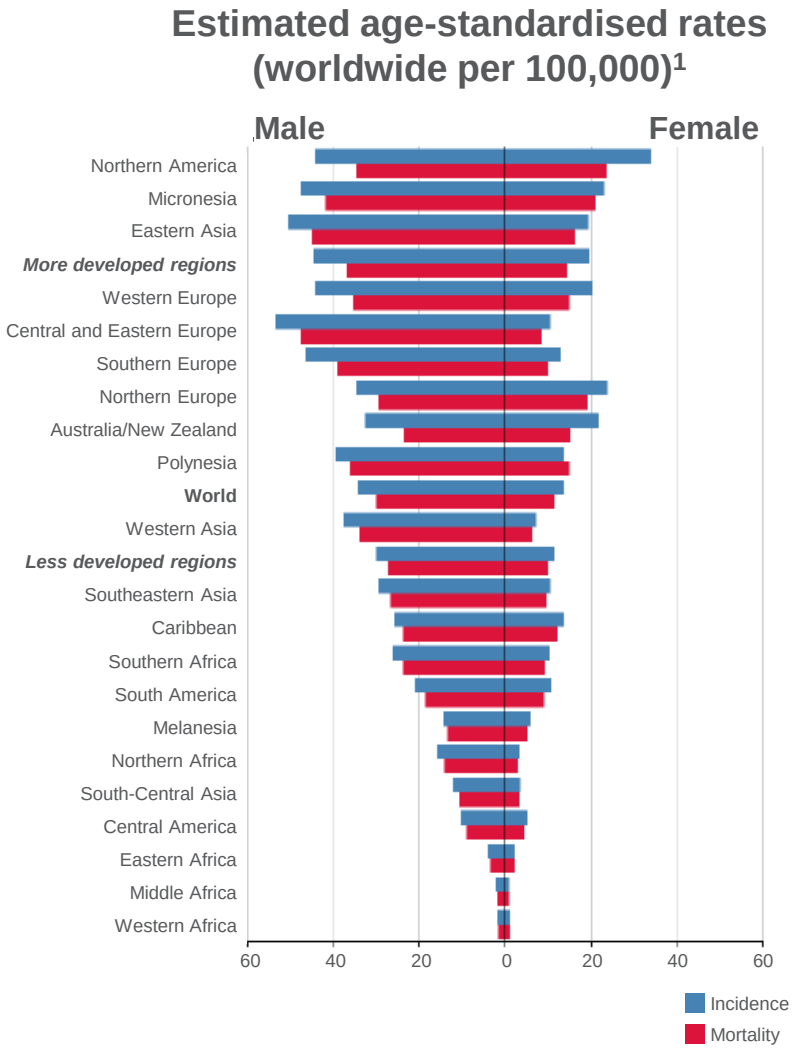


Male Female

This information is from an international website which is intended for healthcare professionals not located in the United States of America (US) and the United Kingdom (UK).

1. International Agency for Research on Cancer, World Health Organization. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (Accessed: 30 June 2017).
2. International Agency for Research on Cancer, World Health Organization. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx (Accessed: 30 June 2017).

Rates of lung cancer incidence and mortality differ worldwide



Highest incidence rates are in North America, East Asia, Europe: 48.5 to 56.5 per 100,000 men[2]

The most common cancer in men worldwide (1.2 million, 16.7% of total)[1]

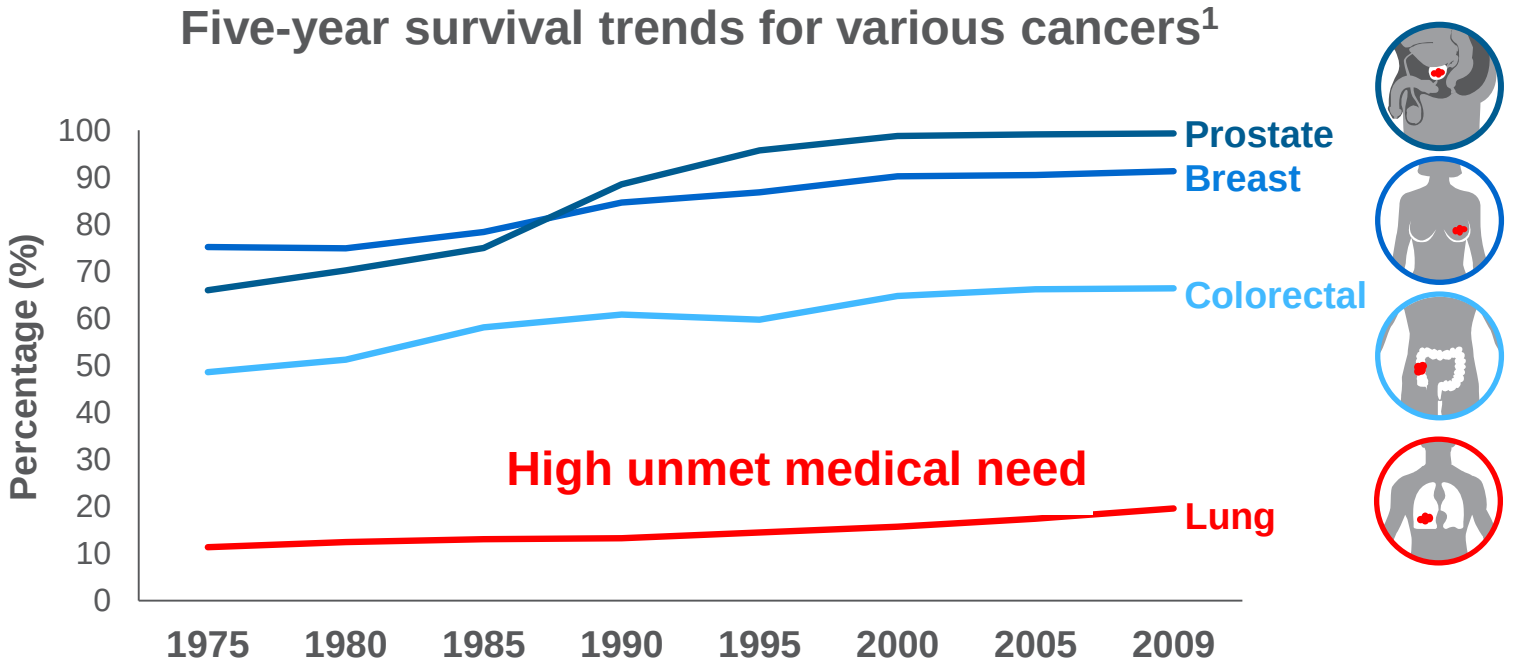
The fourth most common cancer in women (13.5 per 100,000)[2]

Global lung cancer **mortality** is slightly higher in less developed countries:[1]
39% of deaths occurred in **developed** countries
61% of deaths occurred in **less developed** countries

Global lung cancer **cases** are slightly higher in less developed countries:[1]
42% of cases occur in **developed** countries
58% of cases occur in **less developed** countries

1. International Agency for Research on Cancer, World Health Organization. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (Accessed: 30 June 2017).
2. Ridge CA, et al. Semin Intervent Radiol 2013;30(2):93–8.

Survival rates for lung cancer are generally low



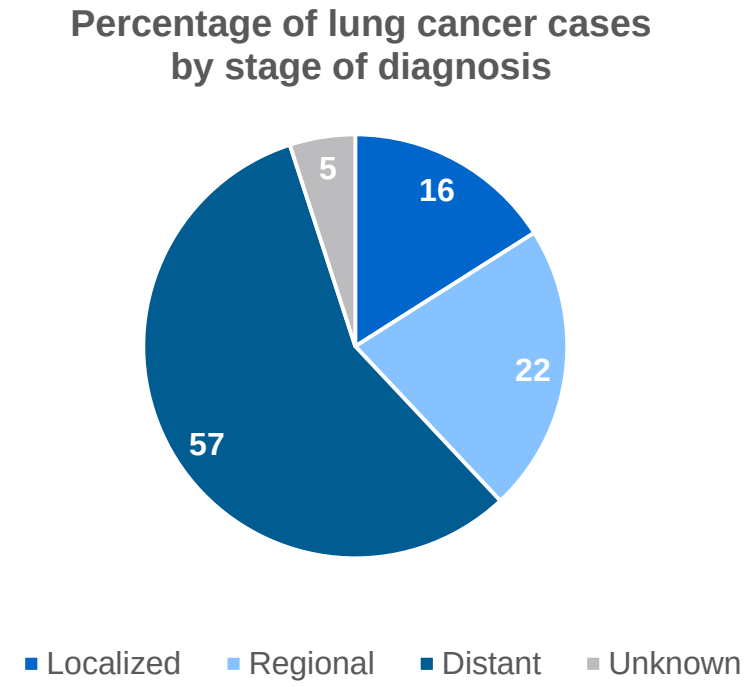
Survival rates vary depending on stage at diagnosis.

The later the stage of diagnosis, the lower the 5-year survival[2]

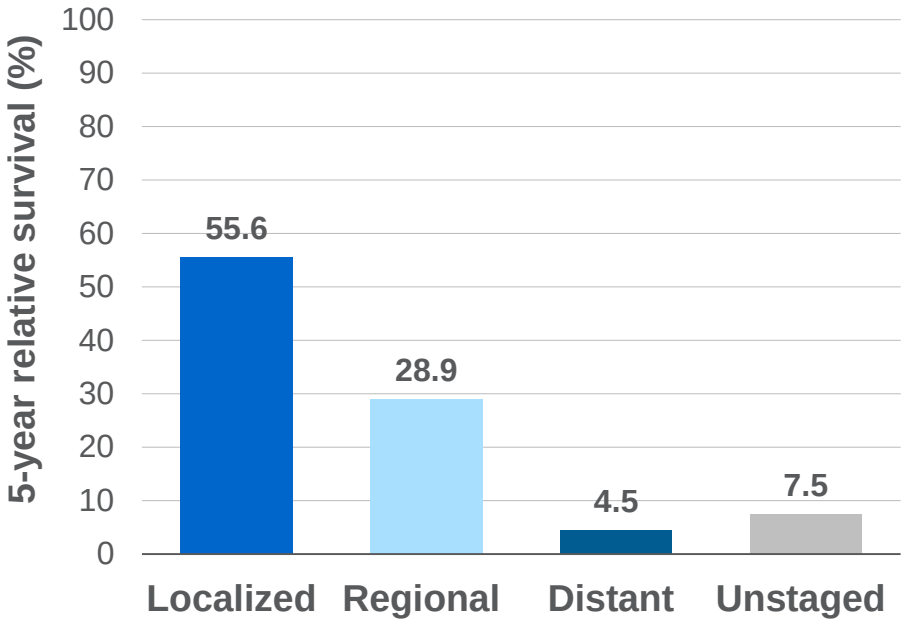
1. National Cancer Institute Surveillance, Epidemiology, and End Results (SEER). https://seer.cancer.gov/faststats/selections.php (Accessed: 30 June 2017).
2. Ridge CA, et al. Semin Intervent Radiol 2013;30(2):93–8.

The later the stage of diagnosis, the lower the 5-year survival[1]

Almost 60% of patients with lung cancer have late-stage disease at diagnosis



The 5-year survival rate is low in patients with late-stage disease



1. National Cancer Institute Surveillance, Epidemiology, and End Results (SEER). https://seer.cancer.gov/statfacts/html/lungb.html (Accessed: 30 June 2017).

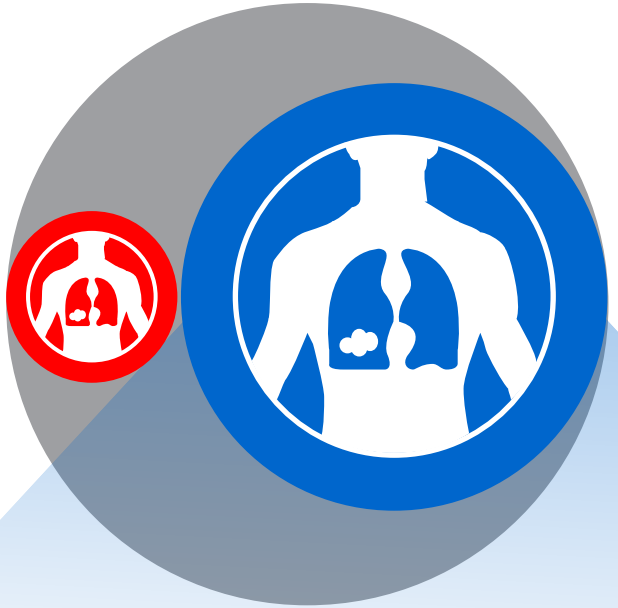
NSCLC

Histological subtypes

There are two main types of lung cancer[1,2]

There are two main types of lung cancer

13%
Small cell lung cancer (SCLC)

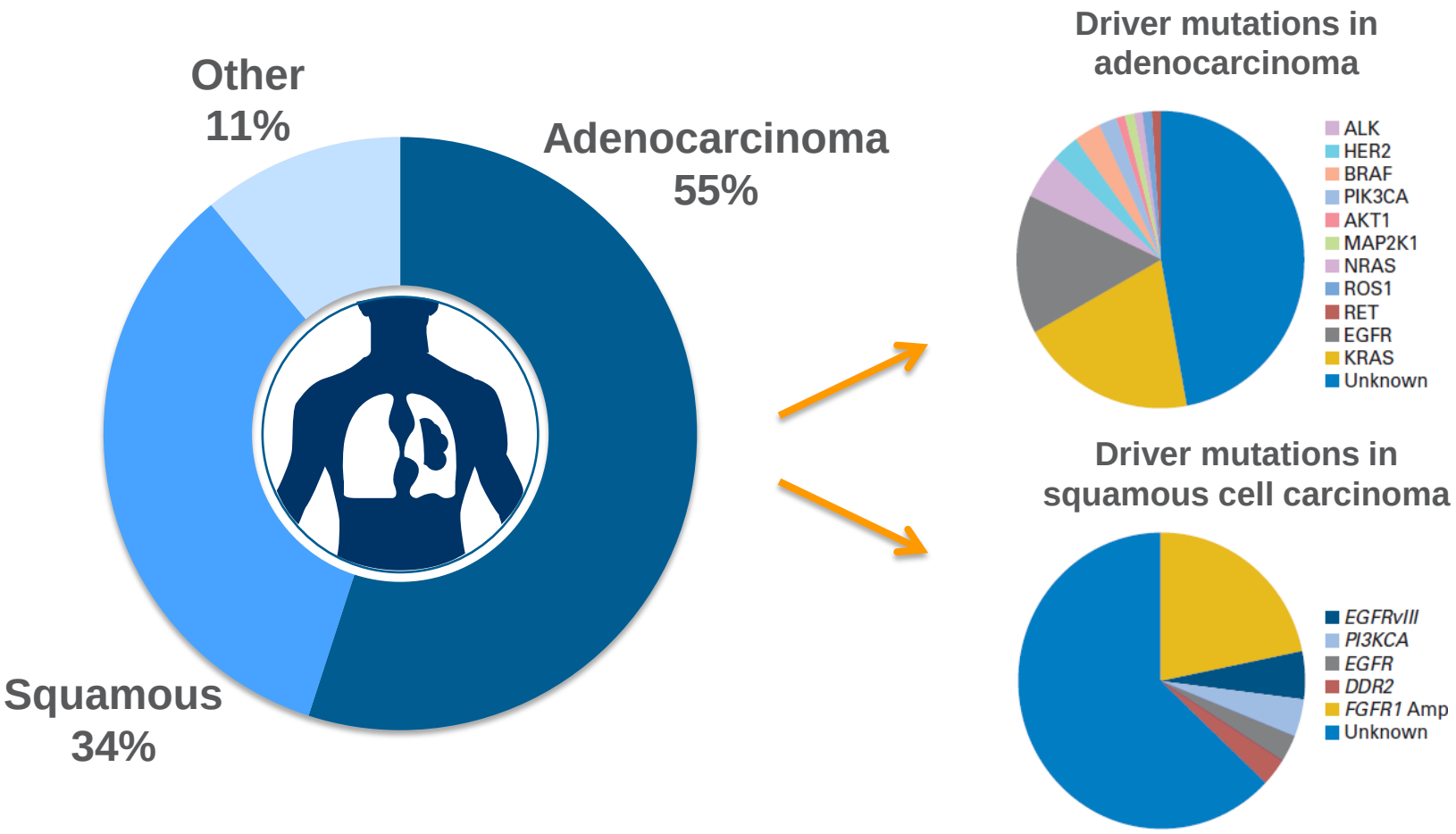


84%
Non-small cell lung cancer (NSCLC)

NSCLC usually **grows** and **spreads more slowly** than small cell lung cancer (SCLC)

1. Howlader N, et al. National Cancer Institute Surveillance, Epidemiology, and End Results (SEER). https://seer.cancer.gov/csr/1975_2013 (Accessed: 30 June 2017).
2. Lozić AA, et al. Coll Antropol 2010;34(2):609–12.

NSCLC, the most common type of lung cancer, is genomically diverse



ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.
This information is from an international website which is intended for healthcare professionals not located in the United States of America (US) and the United Kingdom (UK).

1. Li T, et al. J Clin Oncol 2013;31(8):1039–49.

The distribution of NSCLC subtypes is changing

Squamous cell carcinoma (SqCC) rates have **declined** by around **30%** among males in North America and some European countries[1]

Adenocarcinoma incidence **(55%)** has greatly **increased**, replacing SqCC (34%) as the most prevalent type of NSCLC[2,3]

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1. Devesa SS, et al. Int J Cancer 2005;117(2):294–9. 2. Dela Cruz CS, et al. Clin Chest Med 2011;32(4):605–44. 3. Li T, et al. J Clin Oncol 2013;31(8):1039–49.

Lung adenocarcinoma classification: IASLC/ATS/ERS[1]

The **IASLC, ATS and ERS** have sought to account for aspects such as **genetic and clinical criteria** in a new classification for lung adenocarcinoma:

1

Re-characterises and expands certain histological designations (e.g. replacing ‘mixed’ subtype with histologic subtype characterisation)

2

Extrapolates the pathologic classification of resected specimens to a new additional classification system for small biopsy and cytology specimens

3

Addresses immunohistochemical/ molecular, radiologic and surgical considerations

ATS, American Thoracic Society; ERS, European Respiratory Society; IASLC, International Association for the Study of Lung Cancer.
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1. Tang ER, et al. J Thorac Dis 2014;6(Suppl. 5):S489–501.

NSCLC

Risk factors

Relative contribution of risk factors to lung cancer burden

Population
attributable risk

impact of exposure + likelihood of exposure

Nearly **90%** cigarette smoking[1]

9–15% Occupational exposure to carcinogens[1]

1–2% Outdoor air pollution[1]

10% Radon exposure[1]

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1. American Lung Association. http://www.lung.org/lung-disease/lung-cancer/resources/facts-figures/lung-cancer-fact-sheet.html#Other_Causes (Accessed: 30 June 2017).

Tobacco use is the most important risk factor[1]

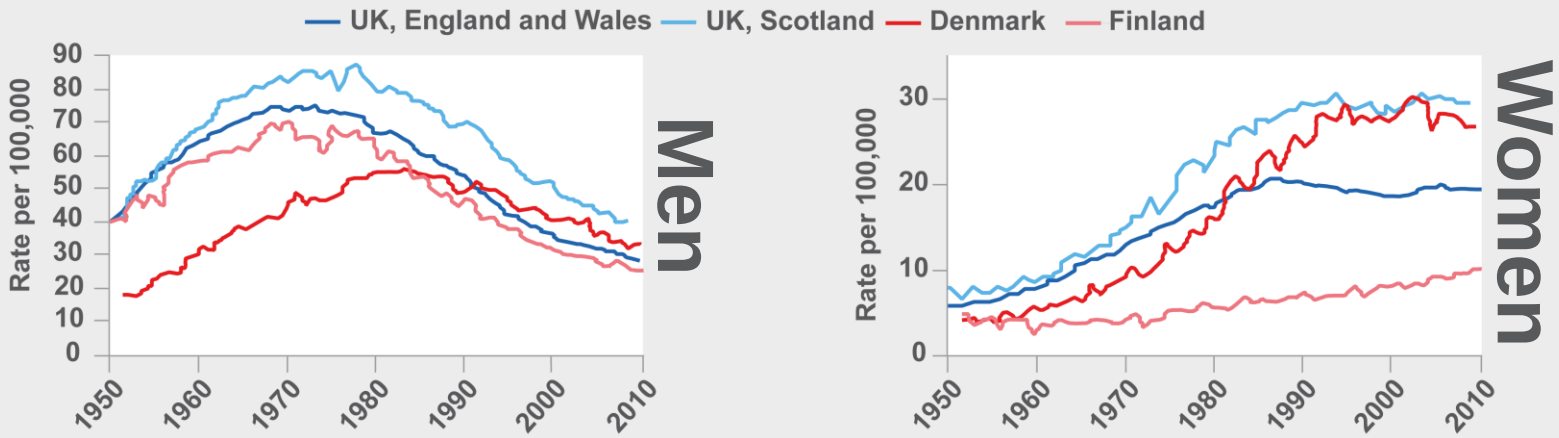
Tobacco smoking is the most important cause of lung cancer

Rates of lung cancer deaths attributable to smoking vary from **>80%** in the US and France to **61%** in Asia and **40%** in sub-Saharan Africa

Trends in lung cancer mortality rates in a country generally follow trends in **smoking prevalence**, with lung cancer trends lagging by 20–30 years

Lung cancer **mortality rates in men** have been **decreasing** in the last few decades; however, **in women this decline is more recent**, reflecting a later decline in smoking prevalence

Trends in lung cancer mortality rates in men and women in Northern Europe



1. Islami F, et al. Transl Lung Cancer Res 2015;4(4):327–38.

Radon exposure and asbestos exposure are also important risk factors

Radon

- Radon gas is the **second most common cause of lung cancer** after smoking[1]
- Worldwide, **3–20% of lung cancer deaths** are attributable to indoor radon exposure[1]
- The attributable risk is higher in never smokers vs ever smokers, but lung cancer death rates due to radon are higher in smokers as a result of a higher rate of lung cancer[1]

Asbestos

- Asbestos is associated with **various lung diseases**, including benign pleural disease, asbestosis, lung carcinoma and mesothelioma[2]
- Asbestos exposure **coupled with smoking increases the risk of developing lung cancer** compared with exposure to only one risk[2]

1. Kim SH, et al. Ann Occup Environ Med 2016;28:8. 2. Ngamwong Y, et al. PLoS One 2015;10(8):e0135798.

Other risk factors include indoor air pollution and alcohol

Indoor air pollution

Indoor air pollution is a **known** lung cancer risk **factor**[1,2]

- Wood burning
- Coal burning
- Cooking oil fumes

Dietary supplements

There are **conflicting reports** over the effects of dietary supplements such as beta-carotene, with some analyses indicating reduced risk of lung cancer[3] and others showing increased risk among smokers and asbestos workers[4]

Alcohol

There is evidence that those who consume alcohol in **high amounts** have increased lung cancer risk, although it is difficult to control for the confounding effect of smoking in studies[5]

1. Hosgood HD, et al. Environ Health Perspect 2010;118(12):1743–7. 2. Lam WK, et al. Int J Tuberc Lung Dis 2004;8(9):1045–57. 3. Yu N, et al. Nutrients 2015;7(11):9309–24. 4. Druesne-Pecollo N, et al. Int J Cancer 2010;127(1):172–84. 5. Bandera EV, et al. Cancer Epidemiol Biomarkers Prev 2001;10(8):813–21.

NSCLC

Clinical features

NSCLC is most often diagnosed at an advanced stage

Early lung cancer may not cause any symptoms[1]

25% Have **no symptoms** when lung cancer is diagnosed

75% Develop **some symptoms**[2]

Many of the symptoms that do appear with more advanced disease can be mistaken for other illnesses[3]

Early symptoms that may be difficult to notice include:

- Persistent cough
- Shortness of breath
- Dull and persistent pain in the chest
- Repeat infections such as bronchitis or pneumonia

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1. MedlinePlus Medical Encyclopedia. http://www.nlm.nih.gov/medlineplus/ency/article/007194.htm (Accessed: 30 June 2017). 2. WebMD. http://www.webmd.com/lung-cancer/lung-cancer-symptoms (Accessed: 30 June 2017). 3. American Cancer Society. http://www.cancer.org/cancer/lungcancer-non-smallcell/moreinformation/lungcancerpreventionandearlydetection/lung-cancer-prevention-and-early-detection-early-detection (Accessed: 30 June 2017).

Some common NSCLC symptoms

Irrespective of metastases[1–3]

Mortality rates are greatly improved when lung cancer is diagnosed early

Common symptoms

- Worsening long-term cough
- Chronic cough
- Wheezing or shortness of breath
- Hoarseness
- Loss of appetite
- Weight loss
- Recurrent pneumonia
- Haemoptysis
- Fatigue
- Constant chest pain
- Recurrent bronchitis

Metastatic NSCLC[3,4]

Symptoms may vary widely and often coincide with the site of tumour metastasis

Common symptoms

- Lumps near the surface of the body (lymph nodes), often in the neck or above the collarbone
- Jaundice
- Dizziness
- Seizures
- Headaches
- Bone pain
- Bleeding or blood clots
- Weakness or numbness of the arms or legs

1. MedlinePlus Medical Encyclopedia. http://www.nlm.nih.gov/medlineplus/ency/article/007194.htm (Accessed: 30 June 2017). 2. Thomas KW. UpToDate. http://www.uptodate.com/contents/lung-cancer-risks-symptoms-and-diagnosis-beyond-the-basics (Accessed: 30 June 2017). 3. WebMD. http://www.webmd.com/lung-cancer/lung-cancer-symptoms (Accessed: 30 June 2017). 4. American Cancer Society. http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-signs-symptoms (Accessed: 30 June 2017).

Diagnostic workup of NSCLC: laboratory evaluation and imaging[1]

Laboratory	Standard tests, including routine haematology, renal and hepatic function, and bone biochemistry
Radiology	CT scan of chest and upper abdomen; complete assessment of liver, kidneys and adrenal glands
	CNS imaging (MRI [more sensitive] or CT scan with iodine contrast) if available; required in patients with neurological symptoms
	If bone metastases suspected: PET, ideally coupled with CT, and bone scans. PET/CT is most sensitive for detecting bone metastases. MRI as needed
	Assessment of mediastinal lymph nodes and distant metastases: FDG–PET/CT scan offers highest sensitivity

CNS, central nervous system; CT, computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.
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1. Novello S, et al. Ann Oncol 2016;27(Suppl. 5):v1–27.

Lung cancer staging and TNM classification

- The system used most often to stage lung cancer is the American Joint Committee on Cancer TNM system, which is based on[1]
  - The size of the main tumour (T) and whether it has grown into nearby areas
  - Whether the cancer has spread to nearby (regional) lymph nodes (N)
  - Whether the cancer has metastasised (M) to other organs of the body
- Once the T, N and M categories have been defined, this information is combined to assign an overall Stage of 0, I, II, III or IV[1]
- This process is called stage grouping[1]
- It produces a range of anatomic stage or prognostic groups (right)[1]

ANATOMIC STAGE/PROGNOSTIC GROUPS			
Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b

M, metastasis; N, node; T, tumour.

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1. American Joint Committee on Cancer. Lung cancer staging. 7th ed. 2009. https://cancerstaging.org/references-tools/quickreferences/Documents/LungMedium.pdf (Accessed: 30 June 2017).

Lung cancer TNM classification in more detail[1]

T	Comments
TX	Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualised by imaging or bronchoscopy
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (for example, not in the main bronchus)*
T1a	Tumour 2 cm or less in greatest dimension
T1b	Tumour more than 2 cm but 3 cm or less in greatest dimension
T2	Tumour more than 3 cm but 7 cm or less or tumour with any of the following features (T2 tumours with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumour more than 3 cm but 5 cm or less in greatest dimension
T2b	Tumour more than 5 cm but 7 cm or less in greatest dimension
T3	Tumour more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumours), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumour in the main bronchus less than 2 cm distal to the carina* but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumour nodule(s) in the same lobe
T4	Tumour of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina, separate tumour

*The uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1a.
M, metastasis; N, node; T, tumour.
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1. American Joint Committee on Cancer. Lung cancer staging. 7th ed. 2009. https://cancerstaging.org/references-tools/quickreferences/Documents/LungMedium.pdf (Accessed: 30 June 2017).

Lung cancer TNM classification in more detail (cont'd)[1]

N	Comments
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M	Comments
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumour nodule(s) in a contralateral lobe, tumour with pleural nodules or malignant pleural (or pericardial) effusion*
M1b	Distant metastasis (in extrathoracic organs)

*Most pleural (and pericardial) effusions with lung cancer are due to tumour. In a few patients, however, multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumour, the effusion should be excluded as a staging element and the patient should be classified as M0.
M, metastasis; N, node; T, tumour.
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1. American Joint Committee on Cancer. Lung cancer staging. 7th ed. 2009. https://cancerstaging.org/references-tools/quickreferences/Documents/LungMedium.pdf (Accessed: 30 June 2017).