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Review article

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The global burden of lung cancer: current status and future trends

Amanda Leiter [1] ✉, Rajwanth R. Veluswamy[2,4] & Juan P. Wisnivesky[3]

Abstract

Lung cancer is the leading cause of cancer-related death worldwide. However, lung cancer incidence and mortality rates differ substantially across the world, reflecting varying patterns of tobacco smoking, exposure to environmental risk factors and genetics. Tobacco smoking is the leading risk factor for lung cancer. Lung cancer incidence largely reflects trends in smoking patterns, which generally vary by sex and economic development. For this reason, tobacco control campaigns are a central part of global strategies designed to reduce lung cancer mortality. Environmental and occupational lung cancer risk factors, such as unprocessed biomass fuels, asbestos, arsenic and radon, can also contribute to lung cancer incidence in certain parts of the world. Over the past decade, large-cohort clinical studies have established that low-dose CT screening reduces lung cancer mortality, largely owing to increased diagnosis and treatment at earlier disease stages. These data have led to recommendations that individuals with a high risk of lung cancer undergo screening in several economically developed countries and increased implementation of screening worldwide. In this Review, we provide an overview of the global epidemiology of lung cancer. Lung cancer risk factors and global risk reduction efforts are also discussed. Finally, we summarize lung cancer screening policies and their implementation worldwide.

Sections

[1]Division of Endocrinology, Diabetes, and Bone Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [2]Division of Hematology and Oncology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [3]Division of General Internal Medicine, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [4]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ✉e-mail: amanda.leiter@mssm.edu

Key points

- Lung cancer is the leading cause of cancer death globally, with incidence and mortality trends varying greatly by country and largely reflecting differences in tobacco smoking trends.
- Cigarette smoking is the most prevalent lung cancer risk factor, although environmental exposures, such as biomass fuels, asbestos, arsenic and radon, are all important lung factor risk factors with levels of exposure that vary widely across the globe.
- Lung cancer incidence and mortality rates are highest in economically developed countries in which tobacco smoking peaked several decades ago, although these rates have mostly now peaked and are declining.
- Reductions in lung cancer mortality in economically developed countries reflect decreased incidence (mirroring declines in tobacco smoking) and improvements in treatment of patients with advanced-stage disease, including immunotherapies and targeted therapies.
- In low-income and middle-income countries at the later stages of the tobacco epidemic, both lung cancer incidence and mortality are increasing, thus highlighting the importance of tobacco mitigation policies for reducing the global burden of lung cancer.
- Low-dose CT-based lung cancer screening reduces lung cancer mortality, although adoption of lung cancer screening programmes has been slow, with limited uptake compared with other cancer screening programmes.

Introduction

Lung cancer is a very aggressive and highly prevalent disease worldwide, with an estimated 2.2 million new cases and 1.8 million deaths in 2020. Globally, lung cancer is the leading cause of cancer mortality in men and is the second highest cause of cancer death in women, behind only breast cancer[1]. Lung cancer incidence and mortality are, overall, approximately twice as high in men as in women, although the male-to-female incidence and mortality ratios vary greatly across different regions of the world[1]. Tobacco exposure is by far the main risk factor for lung cancer worldwide; however, environmental exposures (such as biomass fuels, arsenic, radon, industrial carcinogens and air pollution), which can vary substantially by country, also contribute to lung cancer incidence and mortality trends. Furthermore, the extent of certain histopathological features of lung cancer, such as subtype (adenocarcinoma or squamous cell carcinoma) and the frequency of somatic mutations (such as (*EGFR*) alterations) vary in different parts of the world, which might reflect region-specific variations in smoking patterns, environmental exposures and genetics. Lung cancer also has certain characteristics that can be seen in certain patient populations such as women, people living with HIV and never-smokers.

Epidemiology of lung cancer

Lung cancer is broadly categorized into small-cell and non-small-cell histologies; non-small-cell lung cancer (NSCLC) comprises >85% of all cases and can be further classified by histological subtype. Globally, the most common histological subtype of NSCLC is adenocarcinoma (40%), followed by squamous cell carcinoma (25%)[2,3]. Adenocarcinoma overtook squamous cell carcinoma as the most common subtype in more economically developed countries in the 1990s and is also the most prevalent subtype in women (27–54%) and never-smokers (53–70%)[2,4,5]. This increase in the incidence of lung adenocarcinoma has also occurred more recently in low- and middle-income countries (LMICs)[4].

Lung cancer incidence and mortality vary greatly internationally. Global differences in lung cancer incidence across the world largely reflect differences in tobacco smoking patterns, which vary by sex and economic development trends (Fig. 1). Both the incidence and mortality rates of lung cancer are three to four times higher in countries with higher levels of economic development as defined by the human development index (HDI), a score that combines gross domestic income per capita, life expectancy and levels of education[1,6] (Fig. 1c).

Economically developed countries

In economically developed countries, defined as those with the highest HDI scores, lung cancer incidence started to decline in men in the 1980s, reflecting trends in tobacco smoking, which peaked decades ago and have consistently decreased since in most of these countries (Figs. 2–4). In women, peak lung cancer incidence occurred more recently (in the 1990s), with a slight decrease in annual incidence rates since then. However, the degree of decline in lung cancer incidence varies substantially by country[1]. In the USA, lung cancer incidence is declining in both men and women, albeit with substantially greater decreases in men[1,7,8]. In fact, the lung cancer incidence rates among women in the USA are now higher than those in men, particularly in women born after 1960. Interestingly, this trend is not entirely explained by historical changes in tobacco use patterns[8]. Women in the USA and several other geographical regions are more likely than men to have non-smoking-related lung cancer[9]. Between 2011 and 2016, 90% of lung cancers in men and 84% in women were smoking-related (occurring in either current or former smokers). However, rates among never-smokers are higher in younger (20–49 years of age) people, with only 81% of men and 74% of women with lung cancer having a history of smoking exposure (either current or former smokers)[10]. Other epidemiological studies investigating lung cancer incidence rate trends in never-smokers (of all ages) in the USA have been conflicting, with some studies suggesting an increase and some suggesting no change[11,12]. Regarding race and ethnicity, data from the USA indicate that non-Hispanic white and Black individuals have the highest incidence of lung cancer; these patterns largely reflect differences in smoking patterns, although ethnicity-related differences in susceptibility to the carcinogenic effects of tobacco smoking and differences in nicotine metabolism have also been reported[1,13–15].

Lung cancer mortality in the USA still accounts for almost a quarter of all cancer deaths[16]. However, mortality rates have declined in recent years, which can probably be attributed to improvements in treatment and an increase in the number of patients diagnosed at an earlier disease stage, as a consequence of screening[17]. Early diagnosis can translate into improved outcomes, although mortality rates were already declining between 2013 and 2016, prior to the broader implementation of lung cancer screening in the USA that started around 2016 (ref. 18). In 2019, death rates had declined by 56% in men compared to the peak in 1990 and by 32% among women since peaking in 2002 (ref. 17). Lung cancer mortality also varies substantially by ethnicity with Black and non-Hispanic white people having the highest mortality rates (39 per 100,000 and 40 per 100,000, respectively), and those of Hispanic (16 per 100,000) and Asian American (21 per 100,000)

ethnicity having the lowest lung cancer mortality rates[17]. Lung cancer death rates have declined more quickly in Black men than in white men, which has reduced the historical disparity in lung cancer mortality between these two groups[19]. Unfortunately, however, persistent racial inequalities in outcomes continue to exist and have been attributed to delays in diagnosis and lower rates of treatment among Black men[20,21].

In Europe, lung cancer incidence is generally highest in western countries. The UK has similar trends to those seen in the USA, with lung cancer incidence rates declining more quickly in men than in women. Other economically developed European countries with very high HDI scores also have declining lung cancer incidence rates in men, with the exceptions of France and Spain where these rates have remained largely stable, reflecting a higher prevalence of smoking in these countries[1,22]. Among European women, lung cancer incidence rates are still increasing, with the exceptions of the UK, Denmark and Netherlands, where rates in women have plateaued or are declining, probably reflecting an early peak of tobacco smoking among women in these countries[1].

Lung cancer is the leading and second leading cause of cancer death in European men and women, respectively, with lung cancer mortality rates varying substantially by country. In Europe, the mean 5-year survival of patients with NSCLC is 15%, but this percentage ranges widely (from 10% in Lithuania to 20% in Switzerland)[23]. Reflecting incidence patterns, lung cancer mortality is decreasing in both men and women in European countries with the highest HDI scores, such as the UK. Lung cancer mortality is decreasing in men throughout Europe, although it is not decreasing among women in most European countries[24]. However, as of 2023, lung cancer mortality has stopped increasing for women in Europe overall, with declines in mortality rates projected for the future[25]. Lung cancer mortality trends are generally less favourable in countries located in central or eastern Europe compared with those in western Europe, with less precipitous declines in lung cancer mortality particularly apparent in southern and central or eastern European countries than in western European countries[26]. For example, lung cancer mortality increased in Bulgaria, Portugal and Romania between 2000 and 2017. These mortality trends can largely be attributed to these countries being in a later stage of the smoking epidemic, with higher rates of smoking and fewer restrictions on smoking[27,28]. When comparing mortality rates between European countries and the USA, differences in the quality of cancer registry data must be taken into account. For example, countries located in central or eastern Europe (such as Hungary and Romania) developed their cancer registries later than most countries in western Europe, and such registries often have lower levels of population coverage and more missing data regarding lung cancer diagnosis and mortality[24,29].

In Asia, countries with very high HDI scores, such as Japan and Korea, have high lung cancer incidence and mortality rates, similar to those seen in the USA and Europe. However, the gap in incidence between men and women is wider because lung cancer rates in men are not declining as precipitously, and the incidence in women, although increasing, remains very low[1]. These patterns reflect a wide gender gap in the prevalence of smoking in these countries[22]. Lung cancer mortality has been decreasing in both men and women in Japan and Korea[1], possibly owing to the availability of effective targeted therapies for lung cancers harbouring oncogenic driver mutations, which are more prevalent in these populations than in the USA or Europe[30] (Fig. 5).

Emerging economies

Emerging economies are characterized by rapid economic growth over the past 20 years. Lung cancer incidence and mortality patterns largely correlate with the degree of economic development in these countries. In Brazil, a country with a high HDI score that is also the largest emerging economy in South America, lung cancer incidence peaked in 2008, reflecting the high rates of smoking in the 1970s (as compared to the USA and Europe, where smoking rates in men peaked in the 1950s)[31,32]. Lung cancer mortality in Brazil has been declining since the late 2000s; however, this statistic reflects opposite trends by sex. Lung cancer mortality peaked in the early 1990s in men and has decreased since then, whereas lung cancer mortality rates among women are still increasing[1,31].

China, the largest emerging economy in the world, has reported high rates of lung cancer incidence (815,000 new lung cancers in 2020) and mortality[1]. The burden of lung cancer in China is directly related to the high prevalence of tobacco smoking, particularly in men. Smoking rates in Chinese men, while declining, remain very high (50% in 2019). Smoking is much less common in Chinese women, with rates below 4% in the same analysis[22]. Despite this limited smoking prevalence, lung cancer incidence rates are increasing in Chinese women, which is likely to be linked to exposure to other carcinogens such as household and/or outdoor air pollution or second-hand smoke[33–37].

Tobacco use, as well as lung cancer incidence and mortality, varies greatly across different regions of China. In urban areas, lung cancer incidence and mortality are higher owing to earlier adoption of smoking. Fortunately, public health measures in urban areas (such as Beijing and Shanghai) have already led to a decline in population smoking rates since 2007 (ref. 38). Conversely, lung cancer incidence and mortality are still increasing in rural regions of China, where tobacco smoking is still high and access to medical care is more limited[33,38]. In China, the National Cancer Registration and Follow-up Programme covers approximately 40% of the Chinese population with worse coverage in rural regions, and this might lead to under-reporting of both cancer incidence and mortality data[39,40].

In India, lung cancer incidence and mortality rates are low compared with those of other emerging economies and comparable with those in certain LMICs[1]. Nonetheless, lung cancer incidence rates in India increased between 2012 and 2016 in both men and women, mirroring smoking patterns, albeit with high levels of heterogeneity between different regions. In particular, lung cancer incidence has been increasing in northeastern and urban regions, which has been attributed to higher tobacco smoking rates and air pollution in these areas[41,42]. The proportion of squamous cell carcinomas (16–48%) remains higher than that in more economically developed countries, although the proportion of adenocarcinomas (24–51%) has started to increase over the past decade. These patterns have been attributed to the consumption of handmade cigarettes called 'bidi' (rather than manufactured cigarettes, which are filtered and contain less nicotine)[43–45]. In India, the predominant form of tobacco use is smokeless tobacco, which is instead consumed orally and thus increases the risks of oropharyngeal and oesophageal cancers but not necessarily that of lung cancer. Regional differences in tobacco consumption time might also contribute to heterogeneity in lung cancer incidence among different regions of India[46,47].

LMICs

In general, lung cancer registry data from LMICs are limited. Lung cancer age-standardized incidence and mortality rates are generally lower in LMICs owing to historically lower smoking rates and the competing risks of death from other causes (such as infectious diseases). However, these rates are largely variable by country and even within countries,

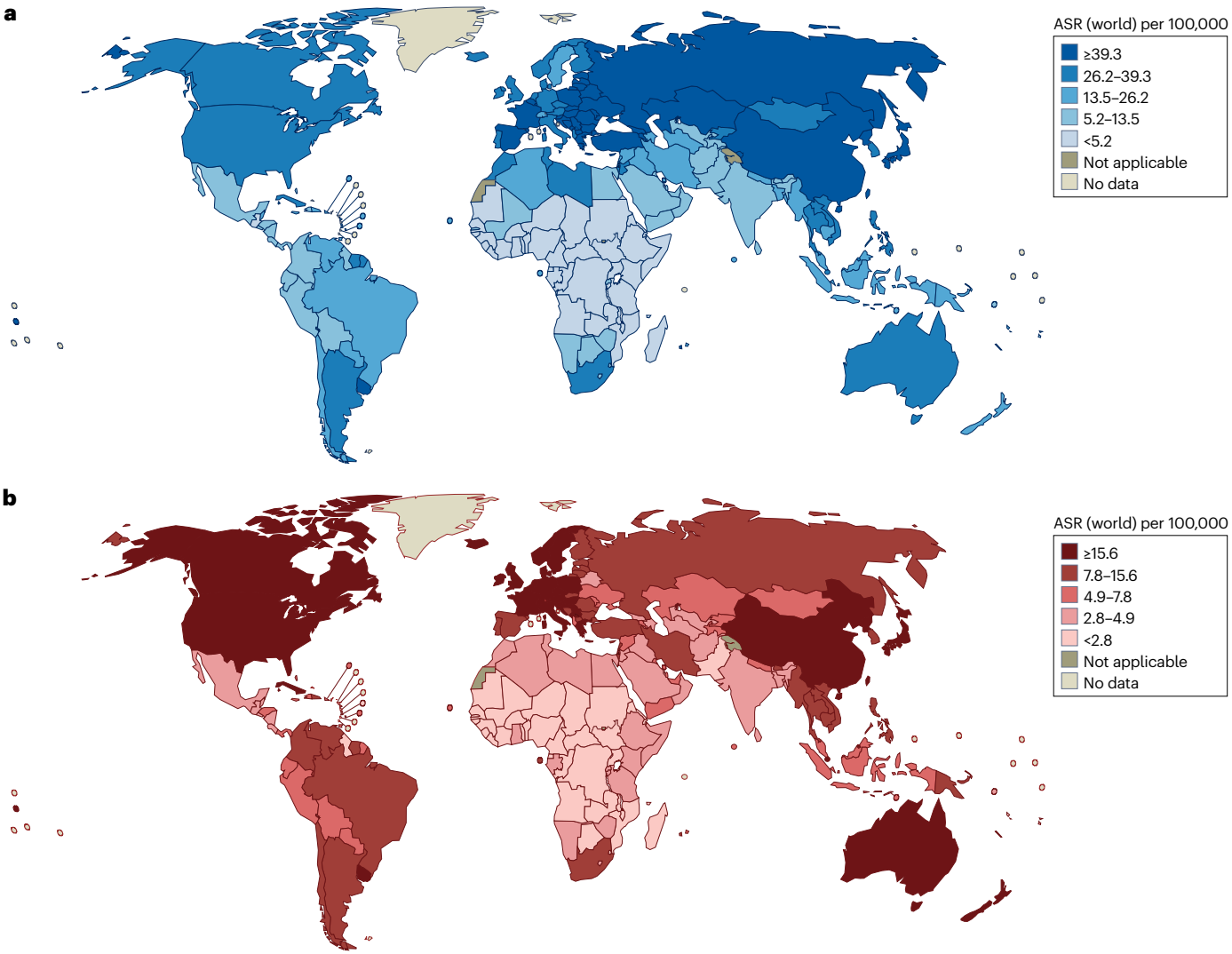
a
ASR (world) per 100,000
≥39.3
26.2–39.3
13.5–26.2
5.2–13.5
<5.2
Not applicable
No data
b
ASR (world) per 100,000
≥15.6
7.8–15.6
4.9–7.8
2.8–4.9
<2.8
Not applicable
No data
c
World 32 42.4
Very high HDI 30 20.6
Hungary 50 42.4
Denmark 37 27.0
USA 33 18.9
UK 32 20.8
Republic of Korea 26 16.5
New Zealand 25 18.4
High HDI 26 22.8
Turkey 40 35.9
China 35 30.2
Uruguay 31 25.5
Bulgaria 29 24.4
Brazil 14 12.3
Medium HDI 8 7.2
Vietnam 23 20.6
Philippines 21 18.8
South Africa 18 15.8
India 5 4.9
Guatemala 3 3.3
Low HDI 4 3.2
Syria 15 14.1
Papua New Guinea 13 11.2
Haiti 7 6.7
Uganda 3 2.6
Incidence
Mortality
Number of cases diagnosed or deaths in 2020 (per 100,000 persons)

Fig. 1 | The global epidemiology of lung cancer. a,**b**, Age-standardized estimated lung cancer incidence rates (per 100,000 persons per year) for men (part **a**) and women (part **b**) across the globe in 2020, demonstrating substantial variability in lung cancer incidence by country. **c**, Lung cancer age-standardized incidence and mortality rates in 2020 categorized by human development index (HDI), an economic development score that combines income, life expectancy and education. ASR, age-standardized rate. Adapted from ref. 1 https://gco.iarc.fr/today/home (accessed July 2023).

owing to differences in smoking patterns, environmental exposures and access to health-care services[1]. For example, in Latin America, higher lung cancer incidence and greater mortality are usually seen in countries with greater levels of economic development as defined by HDI score (such as Argentina and Uruguay) both of which have an increased prevalence of tobacco smoking. Overall, while lung cancer is the leading cause of cancer mortality in Latin America, lung cancer incidence is declining and remains higher in men than in women[48,49].

Among Asian LMICs, lung cancer incidence and mortality are also highly variable and correlate closely with tobacco smoking patterns. Countries geographically closer to eastern Europe, such as Kazakhstan and Turkey, have higher lung cancer incidence rates. In the Middle East, LMICS with a low prevalence of tobacco smoking, such as Yemen and Pakistan, have the lowest lung cancer incidence and mortality rates[1,50].

Africa is the continent with the lowest lung cancer incidence and mortality rates, which reflects lower smoking rates. Additionally, lower life expectancy owing to the presence of several other major competing causes of death might have a role in lower lung cancer incidence and mortality rates. However, increases in both life expectancy and smoking led to higher lung cancer mortality rates between 2002 and 2018, particularly in men in northern and southern Africa. Tunisia, Morocco and South Africa have the highest incidences of lung cancer; countries with the lowest rates include Niger and Mozambique[1,51].

Lung cancer risk factors across the globe

Cigarette smoking is the most established and widely recognized risk factor for lung cancer, with incidence trends that largely mirror those of regional smoking patterns. Other lifestyle and environmental exposures that increase lung cancer risk include exposure to biomass fuels, occupational exposures and pollution. Other lung cancer risk factors include genetics and sex (Table 1).

Smoking

Cigarette smoking increases lung cancer risk by 10-fold to 30-fold, with a proportional relationship between the number of cigarettes and the number of years smoked and risk of malignancy[52,53]. Cigar, pipe and bidi smoking are also associated with an increased risk[54,55]. The link between tobacco consumption and lung cancer began to be recognized in the 1930s through epidemiological case–control studies. Around this time, polycyclic aromatic hydrocarbons present in coal tar and cigarette smoke were identified as carcinogens[56]. In the 1950s, dozens of other tobacco-related carcinogens had been characterized and further epidemiological data confirmed the link between tobacco smoking and lung cancer, with a 1954 study showing that heavy smoking (>35 cigarettes per day) increases the risk of lung cancer by a factor of 40 (refs. 56,57). Despite a global consensus as early as the 1950s, the first national public health effort to reduce cigarette smoking did not occur until the US Surgeon General's report on smoking and health was published in 1964 (ref. 58). At this time, 52% of men and 35% of women in the USA smoked cigarettes. Following this report, cigarette smoking in the USA and other higher-HDI nations began to decline markedly, a trend that translated a few decades later to declines in lung cancer incidence rates[59]. By contrast, smoking rates in LMICs have seen little decline over the past three decades[22]. Given the high worldwide health burden of smoking, the WHO developed the Framework Convention for Tobacco Control (FCTC), an international treaty designed to support participating nations in the implementation of tobacco control laws up to an agreed minimum standard, which was implemented in 2005 and has expanded to include 182 countries as of 2021. FCTC interventions include pictorial health warning labels on cigarette packaging and tobacco advertising bans[60]. Despite these efforts, more than a billion people worldwide were estimated to have regularly smoked cigarettes in 2019. Global smoking rates have decreased by 27% since 1990, although these declines have mostly occurred in economically developed, and certain Latin American countries[22].

Second-hand smoke is also a recognized risk factor for lung cancer (conferring an estimated 20–30% increase in risk), with this increase being proportional to the degree of exposure[61,62]. Since the harmful effects of second-hand smoke exposure were recognized in the 1980s, many countries have implemented policies to either ban or strictly limit smoking in public places. Second-hand smoke exposure, as measured using the second-hand smoke index (individuals who smoked associated with one death of an individual who did not smoke), has declined worldwide in the past 20 years except in Africa and eastern Mediterranean countries[63]. Unfortunately, however, mortality from second-hand smoke exposure continues to increase in some parts of the world, including southern parts of Asia and Latin America[63].

The use of electronic cigarettes (e-cigarettes) and vaping devices has emerged over the past decade, particularly amongst younger individuals (13–25 years of age) and non-smokers[64,65]. While establishing an epidemiological link between these forms of smoking and lung cancer will require longer follow-up, e-cigarette smoke is likely to contain several human carcinogens including polycyclic aromatic hydrocarbons and aldehydes. The availability of e-cigarettes might promote the cessation of traditional cigarette smoking, but conversely might also be linked to smoking initiation in previous never-smokers[64]. Despite legal age restrictions for purchasing e-cigarettes and other tobacco products in the USA (a minimum of 18–21 years of age), adolescents and young adults are the main e-cigarette users. In the USA, e-cigarette use declined for the first time in 2020 after consistent increases in use among middle-school and high-school students in the previous years[65]. US policies designed to further control e-cigarette use have included flavour bans and taxes[66]. In other parts of the world, regulatory strategies for limiting the use of e-cigarettes have varied and include complete prohibition, only allowing use for smoking cessation therapy, taxation and flavour bans[67].

Environmental exposures

Emissions from unprocessed biomass fuels are known to contain carcinogens, such as benzene and cyclic aromatic hydrocarbons, both of which are linked to an increased risk of lung cancer[68]. Approximately half of the global population is exposed to domestic biomass fuels, such as combustible products for cooking and heating, including wood and coal. Exposure to biomass fuel emissions is associated with an increased lung cancer risk (odds ratio (OR) 1.56, 95% confidence interval (CI) 1.44–1.69), with a particularly high risk in coal users in

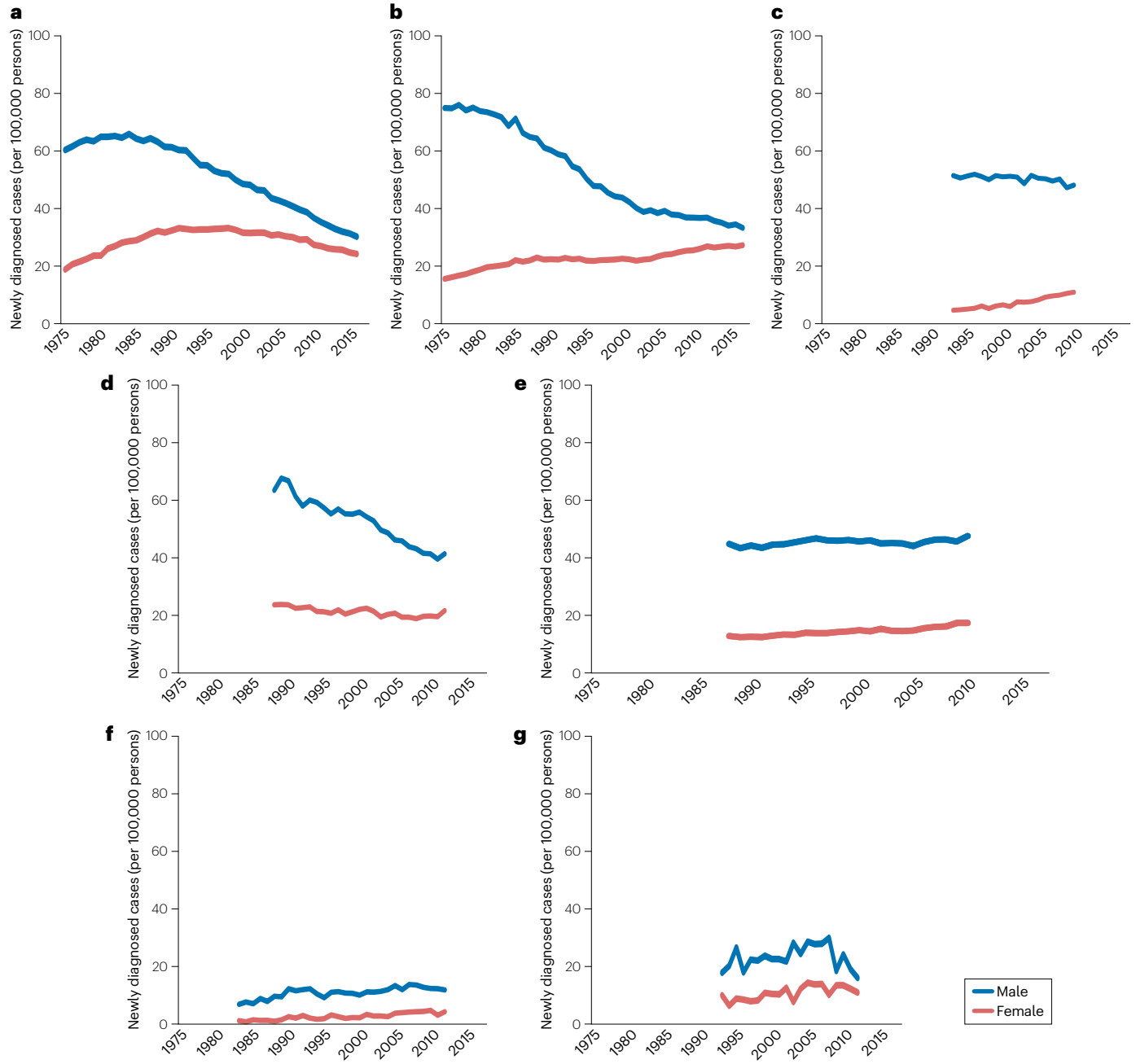

Fig. 2 | Changes in lung cancer epidemiology for men and women over time. Age-standardized lung cancer incidence rates (per 100,000 persons per year) over time by sex in selected countries: USA (part **a**), England and Wales (part **b**), Spain (part **c**), China (part **d**), Japan (part **e**), India (part **f**) and Brazil (part **g**). Data source: Global Cancer Observatory: Cancer Over Time[198].

Asia (OR 4.93, 95% CI 3.73–6.52), but also with a more limited increase in risk in wood users in North America and Europe (OR 1.21, 95% CI 1.06–1.38) when compared with non-solid-fuel users[35]. Data from meta-analyses also indicate that both cooking and heating with biomass fuels are associated with an increased risk of lung cancer, with a higher risk in women than in men, which is suggested to reflect greater levels of exposure in women[36,68]. Interventions designed to reduce the extent of indoor air pollution from biomass fuels include woodstove change-out programmes, adding chimneys and switching fuel type to petroleum; however, these efforts have not yet been shown to ameliorate the health hazards associated with domestic use of biofuels[37,69]. The increasing frequency and scale of wildfires globally has augmented the potential for exposure to biomass fuel emissions[70]. Long-term exposure to wildfires (within 50 km) might increase the risk of lung

cancer compared with that of unexposed populations (HR 1.05, 95% CI 1.03–1.07)[71].

Environmental exposure to arsenic, a group 1 carcinogen according to the International Agency for Research on Cancer (IARC), is known to increase the risk of lung cancer[72–78]. Millions of people globally are exposed to high arsenic levels through contaminated drinking water and/or food[79]. As a consequence, the WHO recommends a maximum arsenic concentration of 10 µg per litre in water. Strategies for lowering arsenic exposure include substituting water from high-arsenic sources (such as groundwater) with water from other sources for drinking and the use of arsenic removal systems[80].

Radon is another carcinogen associated with an increased risk of lung cancer. Exposure can occur in residential settings owing to the presence of this element in soil and building materials, and in some occupational settings. In the Cancer Prevention Study-II, residential radon exposure was associated with an increased risk of lung cancer mortality (HR 1.15, 95% CI 1.00–1.31, per 100 Bq/m^3 increase in radon)[81]. A meta-analysis incorporating data from 39 lung cancer case–control studies demonstrated that elevated radon exposure is associated with a higher risk of lung cancer (relative risk 1.38, 95% CI 1.19–1.60)[82]. Over time, the incidence of lung cancer attributable to radon exposure has declined across the globe. However, changes in rates of lung cancer attributable to radon exposure vary considerably between countries, with increased levels of radon-attributable lung cancer emerging between 1990 and 2019 in countries with moderate HDI scores[83]. The WHO has provided detailed recommendations regarding indoor radon levels and suggested policies for radon exposure prevention[84]. These plans incorporate strategies such as radon testing, radon mitigation and radon-resistant construction. For example, the US Environmental Protection Agency implemented a National Radon Action Plan in 2010 to launch several projects designed to reduce the risk of radon exposure, which have been successful in that rules and standards regarding radon exposure have been established and awareness of the risks associated with such exposures has increased[85].

Occupational exposures commonly associated with lung cancer include asbestos, arsenic, beryllium, silica and diesel exhaust. Other exposures also include nickel, cadmium and chromium[86]. Asbestos fibre exposure can occur in occupations such as mining, ship and building construction, and insulation, and is notorious for increasing the risk of cancer (particularly mesothelioma, but also NSCLC)[87–89]. Asbestos exposure also has a synergistic effect with tobacco smoking regarding increasing the risk of lung cancer[90,91]. Possible mechanisms for the carcinogenic effects of asbestos include altered DNA methylation in lung epithelial cells, changes in lung epithelial cell signalling pathways that promote inflammation and cellular proliferation, and increased levels of oxidative stress[92]. In the USA, levels of asbestos use and mining peaked in the 1940s (during and after the Second World War). Asbestos use in the USA was partially banned in 1973 and this material has not been mined since 2002. Russia, China, Brazil and Kazakhstan are now the leading producers of asbestos. Asbestos use is currently banned in 71 countries and was eliminated in the European Union in 2005. However, many countries around the world, including the USA, Canada, China, Russia, India and Mexico, continue to consume asbestos products, most commonly for insulation materials and automobile brakes[93].

Diesel exhaust is another common occupational exposure associated with lung cancer development and is classified as a group 1 human carcinogen by the IARC[94]. Epidemiological studies have consistently demonstrated a link between occupational diesel exhaust exposure and increased lung cancer risk. A pooled case–control analysis demonstrated ORs of 1.1 (95% CI 1.0–1.2) and 1.4 (95% CI 1.3–1.5) for low versus high cumulative elemental carbon exposure, respectively[95], and these results have been confirmed in multiple other epidemiological studies[96–98]. These findings highlight the importance of reducing potential diesel exhaust exposures in occupational and domestic settings. In the USA, multiple programmes have been implemented to promote the development and implementation of technologies intended to reduce diesel emissions including the Diesel Emissions Reduction Act Program of 2005 and 2010, which was re-authorized in 2020.

Chronic obstructive pulmonary disease

Smoking is a common risk factor for both chronic obstructive pulmonary disease (COPD) and lung cancer. However, several studies have demonstrated that regardless of smoking duration and total

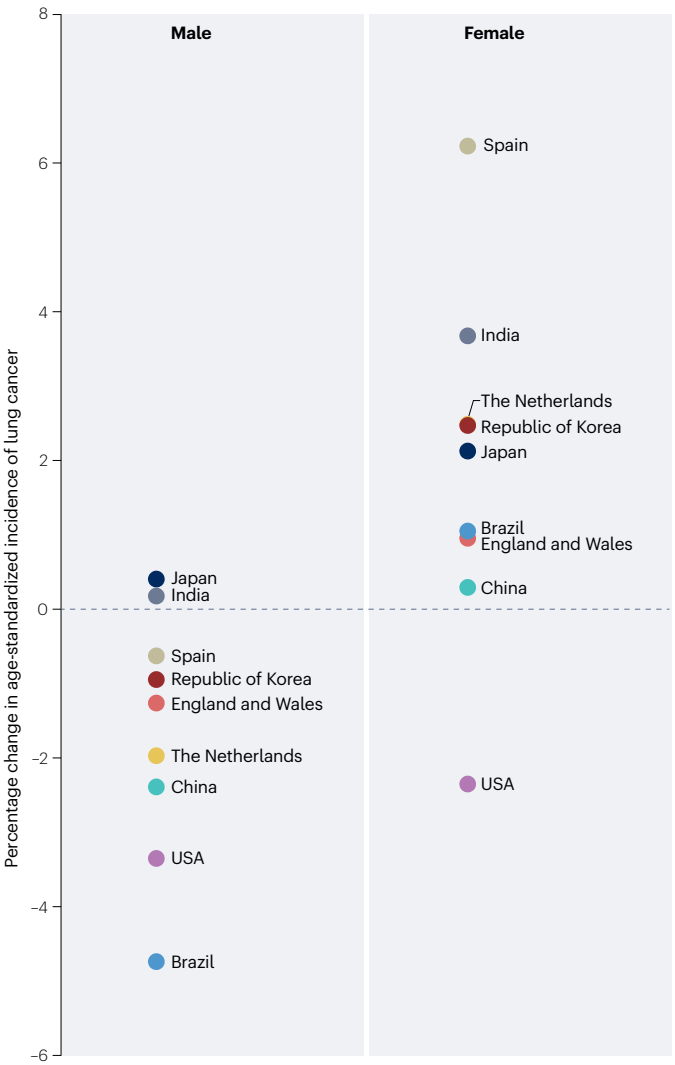

Fig. 3 | Changes in overall lung cancer epidemiology over time. Percentage changes in lung cancer incidence rates (per 100,000 persons per year) in the USA (2007–2016), England and Wales (2008–2017), Spain (2001–2010), Netherlands (2004–2013), Brazil (2003–2012), Japan (2001–2010), Republic of Korea (2003–2012), China (2003–2012) and India (2003–2012). Data source: Global Cancer Observatory: Cancer Over Time[198].

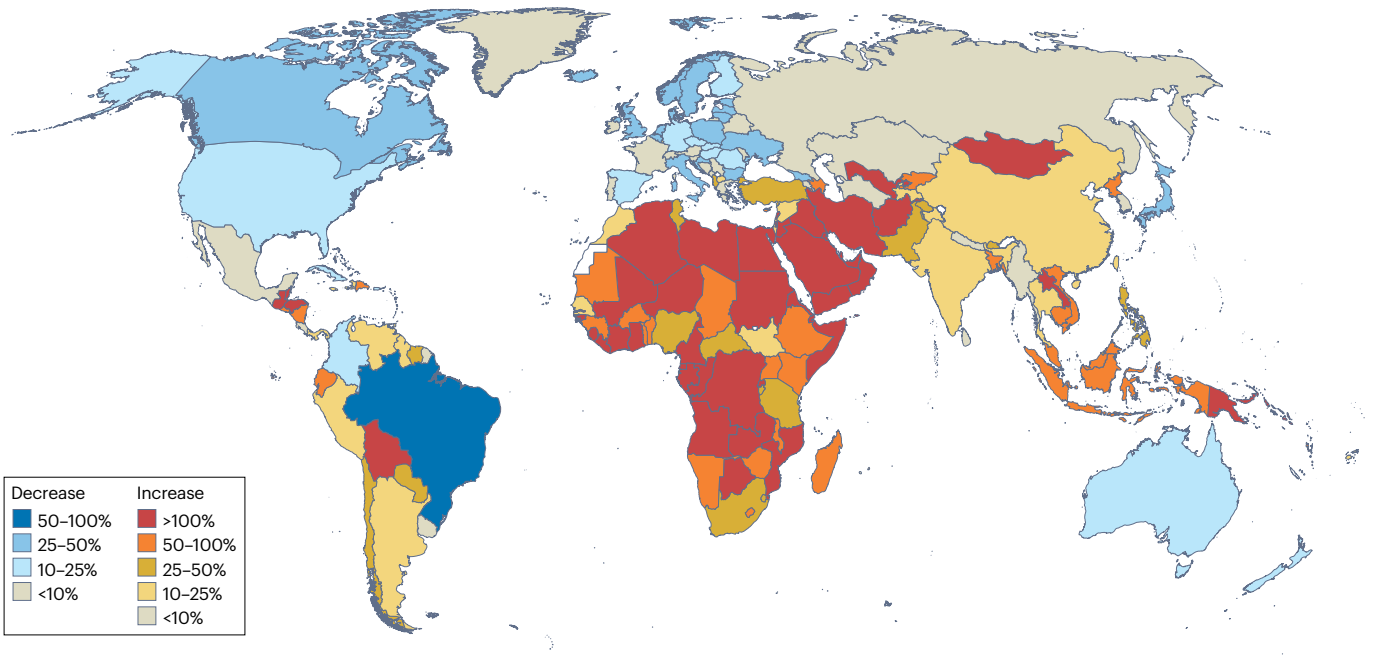

Fig. 4 | Changes in number of individuals who smoke, by country (1990–2019). These data indicate a reduction or plateauing in the percentage of the population who smoke in most economically developed countries, alongside an increase in the percentage of smokers in many economically developing countries. Globally, despite an approximately 10% decrease in the percentage of smokers, the number of smokers continues to increase owing to population growth. Modified from ref. 22, CC BY 4.0 (https://creativecommons.org/licenses/by/4.0/).

pack-years, COPD is an independent risk factor for developing lung cancer. In a case–control study, the number of newly diagnosed cases of lung cancer was sixfold higher in patients with COPD than in matched smokers without the disease[99]. Data from further studies indicate that increased severity of COPD, including worse airway obstruction, worse diffusing lung capacity and greater extent of emphysema on CT, are all associated with both increased lung cancer incidence and mortality[100]. Postulated mechanisms underlying the link between COPD and lung cancer include enhanced expression of inflammatory cytokines and oxidative stress, leading to the development of a carcinogenic tissue microenvironment[101]. Data from large-scale genetic studies have demonstrated a genetic link between COPD, emphysema and lung cancer, and have identified genetic loci that contribute independently to both lung cancer and COPD[102]. These genetic variants influence epithelial remodelling and the presence of inflammatory mediators in the lung[103].

HIV infection

Lung cancer is the leading cause of non-AIDS-defining cancer death in people living with HIV[104]. Numerous studies have demonstrated that HIV infection increases the risk of lung cancer by twofold to fivefold[105–111]. This increased risk is partially attributable to higher smoking rates in people living with HIV, although data from numerous studies indicate a persistent increased risk of lung cancer even when controlling for smoking exposure[105–107,109]. People living with HIV who also smoke have greater than double the lung cancer risk of people living with HIV who do not smoke[105,106]. Furthermore, lung cancer typically develops at a younger age and with fewer pack-years of smoking in this population[105,112,113]. People living with HIV are also more likely to be diagnosed with lung cancer at more advanced stages and are more likely to have disease of an adenocarcinoma histology[106,108,113,114]. Lung cancer risk and characteristics might differ in people living with HIV owing to the virus itself directly promoting oncogenesis, virus-related immunosuppression (resulting in the need to maintain low CD4 counts over prolonged periods of time) and infection-related and non-infection-related lung inflammation[104].

Diet and metabolic factors

Numerous epidemiological studies have examined the effects of diet, including the use of vitamins and other dietary supplements, on lung cancer risk[115]. A meta-analysis of data from 33 published studies revealed pooled risk ratios of 1.44 (95% CI 1.29–1.61) for red meat consumption and of 1.23 (95% CI 1.10–1.37) for processed meat consumption. A dose–response analysis indicated that each 50 g per day increase in red meat intake increases the risk of lung cancer by 20%[116,117]. Conversely, data from several studies have demonstrated an inverse association between consumption of fruit and vegetables and lung cancer development[116,118]. Fruit and vegetables contain antioxidants that might negate the inflammatory, genotoxic and oncogenic effects of smoking on lung epithelial cells[119]. Cross-sectional and cohort studies have demonstrated associations between the consumption of specific vitamins, minerals and dietary supplements and lung cancer incidence[120]. For example, higher vitamin B_6 and methionine levels were associated with reduced lung cancer risk in the large European Prospective Investigation into Cancer and Nutrition (EPIC) study (OR 0.44 for the fourth versus first quartile for vitamin B_6 levels, 95% CI 0.33–0.60; OR 0.52 for the fourth versus first quartile of methionine levels, 95% CI 0.39–0.69) in both smokers and never-smokers[121]. In the Vitamins and Lifestyle study, a large prospective cohort study involving approximately 77,000 volunteers, vitamin E supplements were associated with an increased risk of lung cancer (HR 1.05, 95% CI 1.00–1.09, per 100 mg/day dose increase), with a

higher risk in current smokers (HR 1.11, 95% CI 1.03–1.19, per 100 mg/day dose increase)[122]. Many of these analyses adjust for both the dose and duration of any smoking, although residual confounding related to smoking (which might lead to different dietary and supplement ingestion habits) could be a source of bias in many of these studies[123].

In addition to epidemiological studies, several randomized controlled trials have assessed the effects of vitamin and/or other dietary supplement consumption on lung cancer risk. A Cochrane Review of data from randomized controlled trials found that vitamin D and calcium supplementation does not affect lung cancer risk among post-menopausal women and that selenium supplementation does not significantly reduce lung cancer risk in men[124]. The same review, analysing data from prospective studies, also showed that the use of β-carotene (a vitamin A precursor) and vitamin A supplements can increase lung cancer risk. The Alpha-Tocopherol, Beta Carotene Cancer Prevention trial (with randomization to α-tocopherol 50 mg per day alone, β-carotene 20 mg per day alone, both α-tocopherol and β-carotene, or placebo) showed that β-carotene supplementation increases the risk of lung cancer, whereas α-tocopherol has no association with lung cancer development[125]. The Beta-Carotene and Retinol Efficacy trial involving >18,000 smokers, former smokers and workers exposed to asbestos showed that daily dietary supplementation with β-carotene (30 mg) and vitamin A (25,000 IU) increased the relative risk of lung cancer (RR 1.28, 95% CI 1.04–1.57) relative to placebo[126]. Based on these data, the US Preventive Services Task Force (USPSTF) recommends against the use of β-carotene for cancer prevention and otherwise concludes that the current evidence is not sufficient to make a recommendation regarding the use of other dietary supplements for lung cancer prevention[115].

The prevalence of type 2 diabetes, insulin resistance and increased BMI (leading to overweight and obesity) are increasing steadily worldwide and have been associated with higher risk of many common types of cancer[127]. However, lung cancer has an inverse association with BMI, known as the 'obesity paradox'[128,129]. This finding has been attributed to residual confounding with smoking or reverse confounding in the setting of cachexia with more advanced-stage lung cancer. While BMI is inversely correlated with lung cancer incidence, emerging evidence indicates that obesity determined by measures other than BMI, such as increased waist circumference and increased waist to hip ratio, is associated with a higher risk of lung cancer[130,131]. Additionally, type 2 diabetes has not been associated with lung cancer incidence (including any histological subtype)[132,133]. However, Mendelian randomization studies have demonstrated a link between insulin resistance (a precursor to diabetes that is associated with higher waist circumference) and an increased risk of lung cancer[134]. Data from this study, along with data from preclinical studies showing the importance of insulin receptors in the pathogenesis of lung cancer, suggest that increased endogenous insulin levels (rather than high blood sugar) might have a role in lung cancer development[134,135].

Genetic risk factors

Major insights into the somatic mutations that drive lung cancer have been gained, with distinct subtype patterns (such as lung cancers harbouring *EGFR* alterations) found in different geographical regions (such as east Asia) and among specific patient groups (such as women and never-smokers) (Fig. 5). Regional differences in the percentages of tumours expressing specific molecular markers reflect the effects of varying risk factors (such as the prevalences of smoking and of unprocessed biomass fuel exposure) and have important implications for lung cancer detection and therapeutic management. Alterations in *EGFR* are more prevalent in east Asia (38–50%) than in the Americas (24%) and Europe (14%)[136–138], in adenocarcinomas (38% versus 12% in other histologies), in women (44% versus 24% in men) and in never-smokers (49% versus 22% in smokers)[138]. Other driver mutations associated with non-smokers include those in *ALK* (overall prevalence 4–5%), *ROS1* and *ERBB2*. The prevalence of cytosine–adenine nucleotide transversions (C:G to T:A) and tumour mutational burden are both higher in patients with a smoking history than in those who have never smoked[139]. Alterations in *KRAS* (27% of cases) are more prevalent in smokers with adenocarcinoma (34%) and also differ in prevalence across different parts of the world (25% in the USA versus 8% in China)[136,137,140,141]. Patients with lung cancers harbouring oncogenic driver mutations have increased treatment options owing to the availability of targeted therapies that are usually more effective than non-targeted approaches.

Having a family history of lung cancer is a known risk factor for lung cancer, although heritability (defined as the proportion of variance in cancer risk accounted for by inter-individual genetic differences) is complex and an area of active research[142–144]. In a large case–control study from the International Lung Cancer Consortium, having a first-degree relative with lung cancer was associated with a 1.51-fold increase in the risk of lung cancer after adjusting for smoking and other potential confounders[144]. A prospective study from several Scandinavian countries involving >120,000 monozygotic twins, an approach designed to take into account shared environmental risk factors, found that the heritability of lung cancer is 18%[145]. Certain pathogenic germline variants, such as pathogenic *TP53* variants (often referred to as Li–Fraumeni syndrome) and *EGFR* variants, can confer an increased risk of lung cancer, although these are exceedingly rare (linked to <1% of lung cancers)[146,147]. Genome-wide association studies

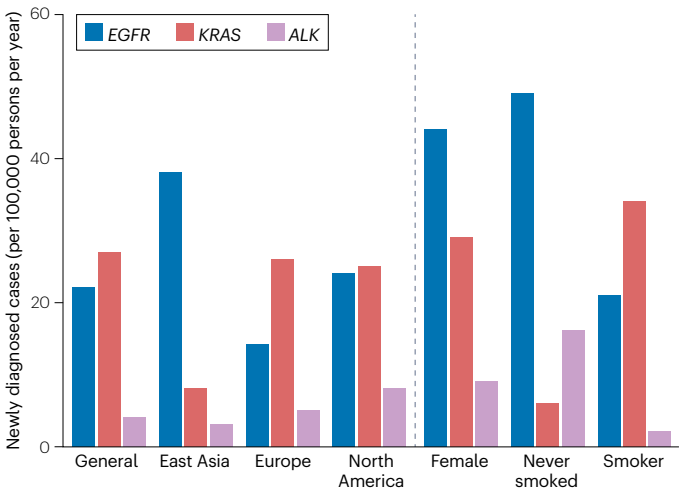

Fig. 5 | Prevalence of common NSCLC driver mutations by continent and patient characteristics. Mutations in *EGFR* or *KRAS*, and *ALK* fusions, are among the commonest driver alterations in patients with non-small-cell lung cancer (NSCLC). The incidence of these alterations can vary substantially by location and certain other patient characteristics and can have important implications owing to the availability of effective targeted therapies for patients with cancers harbouring these alterations. Data on the general prevalence of these alterations are derived from the Genomics Evidence Neoplasia Information Exchange (GENIE) consortium database and from large cohort studies for subpopulation prevalences[136–138,140,141,199–201].

Table 1 | Common risk factors for lung cancer

Risk factor	Relative risk	Strategies to mitigate risk	Refs.
Smoking	10–40	National and global public awareness and education campaigns, tobacco taxes and policies supported by the WHO Framework Convention for Tobacco Control	52,53,57,60
Second-hand smoke	1.2–1.3	National policies to reduce smoking in public places	61,63
Biomass fuels	1.2–4.9	Woodstove change-out programmes	35–37,68,69
Arsenic	1.02–1.20 depending on degree of exposure	Arsenic removal systems, substituting high-arsenic water with water from other sources	72–78,80
Radon	1.15–1.38	National radon action plans to increase the extent of radon testing, increase radon mitigation and encourage radon-resistant construction	81,82,84,85
Asbestos	1.14–7 depending on degree of exposure	National and international asbestos bans	87–89,93
Diesel exhaust	1.1–1.4	International programmes designed to reduce diesel emissions internationally (such as the Diesel Emissions Reduction Act Program in the USA)	95–98,197
Chronic obstructive pulmonary disease	2–6	Smoking mitigation strategies (see above)	99,100
HIV	2–5	Large-scale education efforts on HIV infection prevention strategies and HIV infection treatment	105–111
Red meat	1.36 per 50 g/day	National nutritional education efforts	116,117
Fruit and vegetable consumption	0.86 (highest versus lowest intake)	National nutritional education efforts	119

(GWAS) have identified multiple low-penetrance variants that increase the risk of lung cancer. An aggregate of data from multiple GWAS identified 18 susceptibility loci that are potentially responsible for 12% of the added familial relative risk of lung cancer[148]. In diseases with complex heritability patterns with multiple low-penetrance genetic variants, such as lung cancer, polygenic risk scores have the potential to improve personalized disease risk predictions[149]. Several risk scores focusing on established susceptibility loci identified in previous GWAS have shown the potential to improve lung cancer risk stratification and provide guidance on the optimal timing of screening[150,151]. As the costs of genotyping continue to decrease and the technology becomes more widely available, polygenic risk scores, in combination with traditional lung cancer risk factors, will potentially become an important component of lung cancer risk prediction.

Screening and the global burden of lung cancer

Development of evidence-based guidelines

A large proportion of patients with lung cancer (48%) are diagnosed with distant metastases, and these patients have a 5-year relative survival rate of 8%. By contrast, patients diagnosed with localized lung cancer have a 5-year survival rate of ≥60%[152,153]. Thus, diagnosing lung cancer at the earlier stages is critical for improving outcomes. Data from multiple international lung cancer screening trials have demonstrated that screening with low-dose CT (LDCT) is an effective method of increasing the percentage of individuals diagnosed with stage I–II lung cancer and decreasing the percentage diagnosed with stage III–IV disease in high-risk populations (typically heavy smokers ≥50 years of age)[154–158]. Thus far, only the National Lung Screening Trial (NLST) and Nederlands–Leuvens Longkanker Screenings Onderzoek (NELSON) trial have sufficient statistical power and follow-up to assess reductions in lung cancer mortality, with both studies demonstrating that LDCT improves survival in high-risk populations[158,159].

The NLST was the definitive study that led to the incorporation of lung cancer screening into US national clinical guidelines in 2013. In the NLST, individuals 55–74 years of age with a smoking history of ≥30 pack-years and <15 years since smoking cessation were randomly assigned to either LDCT or chest radiography screening. The NLST found that LDCT reduced lung cancer mortality by 20% with a number needed to screen (NNS) to prevent one lung cancer death of 323 individuals (over 6.5 years of follow-up monitoring)[159]. The most recent USPSTF guidelines recommend annual LDCT screening for adults 50–80 years of age with a smoking history of ≥20 pack-years who either currently smoke or quit smoking within the past 15 years[160]. In 2016, the Canadian Preventive Task Force guidelines recommended annual LDCT screening for up to three consecutive years for adults 55–74 years of age with a smoking history of ≥30 pack-years who either currently smoke or quit within the past 15 years[161].

In Europe, the NELSON trial, conducted in Belgium and Netherlands, included patients 55–75 years of age, with a smoking history of >15 cigarettes per day for >25 years or >10 cigarettes per day for >30 years, and less than 10 years since quitting. Patients were randomly assigned to undergo LDCT screening versus no screening. This trial demonstrated a 24% reduction in lung cancer mortality (NNS to prevent one lung cancer death of 130 over 10 years of follow-up monitoring), with even greater effectiveness in women[158]. Based on data from the NELSON trial, the European Union issued a position statement in 2017 recommending that member countries delineate a timeline for implementing lung cancer screening and also outlined preparatory steps for implementation[162]. In September 2022, the UK National Screening Committee recommended a national targeted lung cancer screening programme[163] (Table 2).

Despite the major positive effect on lung cancer mortality observed in the NLST and the NELSON trial, LDCT screening comes with the risk of false-positive findings, which can lead to unnecessary invasive procedures. The number of screening procedures needed to cause unnecessary harm (false-positive results that led to unnecessary invasive procedures) was 59 in the NLST and 62 in the NELSON trial[158,159]. Other potential harms of screening include radiation-related cancers (considered extremely rare), patient distress and incidental (other than nodules) imaging findings that might not be clinically important but could nonetheless trigger additional investigations and the associated anxieties and/or costs[164]. Ongoing research attempting to improve the stratification of patients with LDCT-detected nodules (such as biomarkers and/or prediction models) might reduce the risk of unnecessary harms associated with screening in the future.

Following publication of the NLST results, clinicians in several Asian countries, including Japan, China and South Korea, developed lung cancer screening guidelines for use in individuals with a high risk of lung cancer (Table 2). In 2013, Japan issued guidelines recommending LDCT screening in adults >50 years of age with a smoking history of ≥30 pack-years[165]. The most recent screening guidelines published in China, from 2018, recommend LDCT screening in adults 50–74 years of age with a smoking history of at least 20 pack-years who are either current smokers or who quit smoking in the past 5 years[166]. Similarly, clinicians in South Korea issued guidelines in 2015 that recommended LDCT screening according to the NLST inclusion criteria[167]. Given the observed increase in the incidence of lung cancer in women with no history of smoking exposure in several Asian countries, the application of LDCT lung cancer screening in non-smoking populations is currently an active area of research. As of 2019, the China National Cancer Early Screening trial enrolled 78,500 smokers and non-smokers who were randomized to annual LDCT for three consecutive years versus biannual LDCT for 1 year versus no screening, with various screening tests for colorectal cancer included in each arm, to assess for differences in lung cancer mortality[168]. In Japan, an ongoing trial is evaluating the utility of 5-yearly LDCT versus chest roentgenography in never-smokers or lighter smokers (<30 pack-years)[169]. The results of these trials are expected to further inform lung cancer screening guidelines in Asia and other parts of the world.

In countries with lower HDI scores, the findings of lung cancer screening trials conducted in Europe and the USA might not be applicable owing to higher incidences of granulomatous disease (such as pulmonary tuberculosis), which might increase the risk of false-positive findings. The first Brazilian Lung Cancer Screening Trial (BRELT1) had the same inclusion criteria as the NLST. BRELT1 had a higher positive screen rate (40%) than the NLST (26%), albeit with a similar number of lung cancer diagnoses[170]. However, in BRELT1 (unlike in the NLST), indeterminate pulmonary nodules >4 mm in diameter were considered a positive finding. This trial did not examine lung cancer mortality, although the data demonstrate that LDCT screening needs to be further studied, and potentially refined, in countries with lower HDI scores and higher rates of tuberculosis. Brazilian national guidelines did not recommend lung cancer screening with LDCT as of 2014 (ref. 171).

Implications for early diagnosis

With the growing uptake of screening, lung cancer is increasingly being diagnosed at earlier stages. In the USA, the percentage of lung cancers diagnosed as localized disease (according to cancer registry summary stage) increased from 20% to 28% from 2013 to 2018 (refs. 17,152). Simulation modelling, a comparative effectiveness technique that enables the extrapolation of existing evidence to forecast long-term clinical outcomes, has been used to assess the potential benefits and harms of various different lung cancer screening strategies. A modelling study conducted to assess the cost effectiveness of the approach recommended in the 2021 USPSTF guidelines (that individuals ≥50 years of age with a minimum cumulative smoking exposure of ≤20 pack-years should undergo annual LDCT screening until 80 years of age and until 15 years following smoking cessation) found that screening is cost-effective in the USA, and also that expanding eligibility to patients who quit smoking <25 years previously would be even more cost-effective[172]. Data from another study demonstrated that the overall level of benefit from lung cancer screening in the USA was expected to peak in 2021 owing to lower smoking rates among younger birth cohorts[173]. Given the more recent implementation and the lack of coordinated national lung screening programmes, only limited data are available on the nationwide effects of lung cancer screening in other countries.

Challenges to widespread implementation

Despite robust evidence supporting the effectiveness of LDCT-based lung cancer screening, levels of adoption remain low. In the USA, where screening has been broadly recommended since 2013, only 18% of eligible patients in real-world settings had undergone lung cancer screening with LDCT as of 2018 (ref. 174). In China, uptake of LDCT screening in a study that actively recruited participants (including through the use of media advertisements, offers of rapid procedures and even certain financial incentives as well as traditional methods) was only 33%[175]. Similarly, only 52% of eligible individuals agreed to participate in a dedicated lung cancer screening study in the UK[176]. These rates are dramatically lower than those observed for other cancer screening tests, such as breast cancer (78% of eligible women) and colorectal cancer (67% of eligible adults)[177].

Multiple barriers to LDCT-based lung cancer screening might explain these low uptake rates, including patient-related, provider-related and health-care system-related factors. Patient-related barriers include a lack of knowledge of screening benefits and fatalistic views about lung cancer among screening candidates[178,179]. Provider-related and system-related barriers include a limited awareness of screening guidelines, eligibility and a lack of time for shared decision making[180]. The availability of multiple society guidelines with different screening

Table 2 | National lung cancer screening guidelines by country

Country or region	Year	Screening recommendation and interval	Age range (years)	Minimum pack-years	Maximum time since quitting smoking (years)
USA[160]	2021	LDCT	50–80	20	<15
Canada[161]	2016	LDCT (annually for three consecutive years)	55–74	30	<15
Brazil[171]	2014	Not recommended currently	NA	NA	NA
China[166]	2018	LDCT (annual)	50–74	20	<5
Japan[165]	2013	LDCT (screening interval not specified)	>50	30	Any
Republic of Korea[167]	2015	LDCT (annual)	50–74	30	<15
UK[163]	2022	LDCT (screening interval not specified)	55–74	Any	Any
European Union[162]	2017	Member countries should delineate timeline for implementation	NA	NA	NA

LDCT, low-dose CT; NA, not applicable.

eligibility criteria creates confusion among health-care providers[181,182]. Furthermore, approaches to automatically identify potential candidates for screening from electronic health records are limited given that detailed data on smoking history are often not available[183].

Internationally, a major system-related barrier to LDCT lung cancer screening is cost. In the USA, LDCT is covered by private insurance and Medicare (government-provided medical insurance for adults >65 years of age). Coverage for LDCT by Medicaid (a state and federal medical insurance programme for individuals with limited income) is variable by state and often uses different eligibility criteria to those recommended by the USPSTF, requires prior authorization and/or involves copayments[184]. In China, the costs of both screening and lung cancer treatment, which are only partially covered by the government in many regions, are major barriers to patient participation[185]. In Europe, where many countries have nationalized health-care systems, the cost effectiveness of LDCT screening is an important consideration when implementing national lung cancer screening guidelines. However, if nationally adopted, upfront costs will be largely covered by the national health systems, facilitating adoption[186]. Although LDCT screening might be cost-effective in the long term, upfront costs of implementation might impair screening uptake. However, even when payment-related barriers are removed, uptake among the target population has been between 25–50%[158,172,175,176,187].

Other system-related barriers to screening implementation include limited access to screening centres, as well as a lack of infrastructure for evaluation of screening-detected pulmonary nodules[180]. Given these multilevel barriers, interventions designed to improve implementation should include patient and provider education, system-level changes to enable the availability of staffing and resources to identify and counsel eligible patients, as well as improvements in infrastructure to enable screening tests and any follow-up investigations to be promptly conducted in order to rapidly diagnose and treat patients with screening-detected cancers.

Challenges regarding implementation on a global scale include the cost of CT scanners, as well as the limited availability of infrastructure for follow-up procedures including pathology-based diagnosis and treatment of any pulmonary nodules and/or cancers identified on LDCT[188,189]. False-positive results are of greater concern in countries with lower HDI scores owing to the often higher incidence of pulmonary tuberculosis and other granulomatous lung infections[170]. Given the challenges and costs associated with screening and the high smoking rates in several LMICs relative to economically developed countries, many policy experts advocate for implementing stricter tobacco control measures rather than LDCT screening programmes[188].

Future directions in lung cancer screening

In addition to LDCT screening, the development of blood tests involving the detection of circulating tumour material, also known as 'liquid biopsies', is an active area of research. Examples of non-invasive biomarker assays currently under evaluation include those based on the detection of microRNAs and cell-free DNA (cfDNA), circulating autoantibodies and nasal gene expression[190]. Multicancer early detection genomic blood tests use cfDNA sequencing, typically in combination with more traditional markers, to screen for multiple cancer types, with preliminary data demonstrating low false-positive rates (<1%)[191]. The successful development and implementation of these tests has the potential to reduce barriers to screening and thereby decrease lung cancer mortality[192,193]. The initial implementation of multicancer early detection genomic blood tests is likely to happen in conjunction with traditional screening methods in order to enhance sensitivity[193].

Effects of advances in treatment on lung cancer mortality

Lung cancer mortality is declining in the economically developed world largely owing to reductions in incidence (mirroring tobacco trends), although reduced lung cancer mortality owing to improved survival from the use of more advanced treatments might also have a role. In an assessment of lung cancer mortality trends in the USA, population-level reductions in lung cancer mortality between 2013 and 2016 were attributed to the increased uptake of targeted therapies for NSCLC driven by targetable alterations such as *ALK* rearrangements and *EGFR* mutations[18]. The use of immune checkpoint inhibitors (such as anti-PD-1 and anti-PD-L1 antibodies), which were approved for use in the USA as early as 2015, is another paradigm shift that has improved the survival outcomes in patients with advanced-stage NSCLC without a targetable driver alteration, and is expected to have population-level effects on lung cancer mortality in countries with widespread access to these treatments[194].

Given limited access to newer lung cancer therapies in most LMICs, the effects of targeted therapies and immune checkpoint inhibitors on lung cancer mortality are likely to be limited. Less than half of all patients globally have access to the molecular testing needed to select patient for targeted therapies, with practice patterns varying substantially depending on geographical location[195]. As well as a lack of infrastructure permitting the detection of specific targetable alterations, other barriers to accessing novel lung cancer therapies in LMICs include a lack of access to cancer centres and the unaffordability of therapies[196].

Conclusions

Lung cancer is a major source of morbidity and mortality across the globe. In this Review, we highlight the major international trends in the epidemiology of lung cancer, lung cancer risk factors and lung cancer screening. In economically developed countries, such as the USA and UK, where tobacco smoking peaked 40–50 years ago, both the incidence of and mortality from lung cancer are declining. The implementation of lung cancer screening in the USA and in other economically developed countries over the past decade has led to an increase in the diagnosis of early-stage lung cancer, which has led to further reductions in lung cancer mortality. Increasing the implementation of lung cancer screening will be critical for reducing global lung cancer burden. In most LMICs, the extent of tobacco smoking is declining but remains highly prevalent. Tobacco control will continue to be crucial in reducing lung cancer incidence and mortality in most parts of the world. To improve lung cancer outcomes, future studies designed to further refine lung cancer risk using genetics and other clinical risk factors and eligibility for screening, particularly in non-smokers, are likely to be important. The further characterization of lung cancer biology is expected to enable improvements in personalized therapies in patients with lung cancer.

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Author contributions

All authors made a substantial contribution to all aspects of the preparation of this manuscript.

Competing interests

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