

Overview

Lung cancer is the cancer most commonly suffered by men and women worldwide, and as such represents a leading cause of death. It was estimated to be responsible for 1.7 million deaths; more than cancers of the colon, prostate, and breast combined.¹ With cancers of the trachea and bronchus, it ranks as the fifth most common cause of death globally, behind heart disease, stroke, lower respiratory infections, and lung disease.² Lung cancer is the number one form of cancer in men, representing approximately 16.7% of all cancers in men in 2012.³ For women, it ranks behind breast and colorectal cancers, but still accounts for roughly 8.8% of all cancers suffered by women worldwide.

In 2014, lung cancer was the cause of death of 272,000 people in the European Union, making it responsible for 20.1% of total deaths from cancer in that region.⁴ The gender gap that is present in the global data is also observed in the region. Lung cancer accounted for 7.5% of all deaths among men in the EU that year, while for women that share was much lower at 3.5%. *Figure 1* below presents the number of deaths from lung cancer within EU Member States in 2015.⁵ There is substantial variation across member states. In all countries except Sweden, more men than women died of lung cancer that year. More remarkable is the substantial variation in the size of the gender gap across countries; it is very narrow in countries like Luxembourg, Malta, Denmark, and Ireland, but in other Member States (Germany, France, and Italy) over 15,000 more men than women died from lung cancer that year.

Across the EU, lung cancer represents a substantial economic burden. In 2011, the disease was estimated to be responsible for €3.35 billion in direct costs (this covers primary care, hospital outpatient and inpatient care, drugs, and oxygen).⁶ In addition to these sums disbursed on healthcare costs, there are also costs incurred by people who provide unpaid care to those who suffer from the disease, lost earnings resulting from premature death, and costs associated with sufferers' temporary or permanent absence from employment due to illness.⁷ Lung cancer then represents a significant economic burden to patients, their friends and family, and European healthcare systems.

Since 80-90% of instances of lung cancer globally are due to smoking,^{8,9,10} it is a highly preventable disease. As such if policymakers, medical professionals, and other relevant stakeholders work together to target the disease, it is possible to achieve a substantial reduction in new diagnoses of lung cancer and to achieve substantial relief from its associated burdens for healthcare systems across the EU.

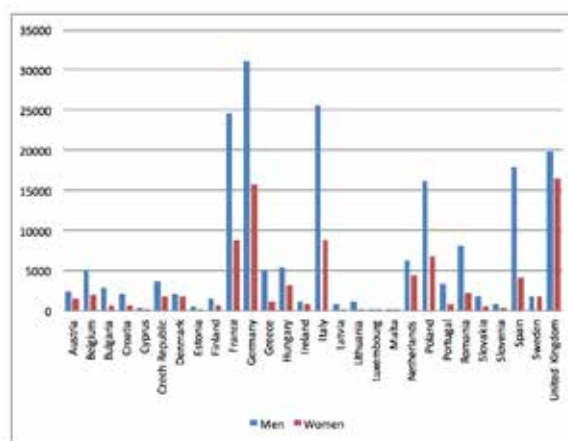


Fig. 1. Number of deaths from lung cancer EU member states (by gender), 2015

Source: WHO, 2016. *Global Health Estimates 2015: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015.*

Lung cancer: the basics

Lung cancer, also called lung carcinoma, occurs when the cells in the lung mutate, growing uncontrollably, and clustering together to form a malignant tumour.¹¹ There are three main types of lung cancer:¹²

- **Non-small cell lung cancer:** this is the most common type of lung cancer, making up roughly 85% of all cases.
- **Small cell lung cancer:** between 10 and 15% of lung cancers take this form. It is a type of cancer that spreads quickly.
- **Lung carcinoid tumour:** this is a small tumour which grows slowly and rarely spreads. It constitutes less than 5% of lung cancers.

Treatment for lung cancer varies according to the type, but radiotherapy, chemotherapy, surgery, or some combination of these treatments are most commonly employed.^{13,14,15} As well as the type of cancer, the stage of the cancer is will also impact on treatment.

Lung cancer can be divided into various stages using the tumour, node, and metastasis (TNM) categorisation, a coding system for cancer staging. Stages describe the size of the cancer and whether or not it has spread to other parts of the body. The staging is used for treatment decisions:^{16,17}

- **Tumour (T):** T describes the size of the tumour
- **Node (N):** N indicates whether (or not) and to what extent the tumour has spread to the lymph nodes (small, ball-shaped organs of the immune systems, distributed throughout the body)
- **Metastasis (M):** M specifies whether or not the tumour has spread to other areas of the body.

Some of the most common symptoms of lung cancer are the following:^{18,19,20,21,22}

- Unexplained weight loss
- Loss of appetite
- A new or changed cough
- A chest infection that is long-lasting
- Repeated incidents of pneumonia or bronchitis
- A dull or sharp pain when coughing
- Shortness of breath and wheezing
- Chest pain and/or shoulder discomfort
- Difficulty swallowing
- Swelling around the face or neck
- Fatigue and lethargy
- Coughing up blood in sputum (phlegm)
- Hoarseness or changed voice

Risk factors for lung cancer

There are various risk factors that studies have found to be associated with developing lung cancer, the most common are listed below:^{23,24,25,26,27}

- Smoking
- Exposure to second-hand smoke (i.e. passive smoking)
- Age (most lung cancers occur in people over 60)
- Exposure to radon (a radioactive gas, existing naturally in soil)
- Exposure to hazardous chemicals (e.g. asbestos, uranium, arsenic, chromium, nickel etc.)
- Particle pollution (coming from sources like exhaust smoke)
- Family history of lung cancer
- Previous experience of lung disease (e.g. chronic bronchitis, emphysema, pulmonary tuberculosis)
- Suffering from HIV
- Lower socioeconomic status

Lung cancer, sex and gender

Biological and gender differences

Lung cancer results from the interactions between genetic, hormonal, behavioural, and environmental factors. It appears that lung cancer differs between men and women. Researchers are just beginning to understand these differences. For example, one study finds that the risk of developing lung cancer is 19 times higher for women who have ever smoked heavily, compared with women who have never smoked.²⁸ However, for men the associated increase in the odds of developing lung cancer is less than 13 times higher. This suggests that for women the adverse effect of smoking tobacco products is greater than for men, something which needs to be taken account of by healthcare professionals and effectively communicated to at-risk women.

Existing research on this issue suggests that the following biological differences between men and women exist for lung cancer:

- Women's are more vulnerable to the harmful effects of smoking (it is thought that this is due to genetic factors)^{29,30,31,32}
- Various genetic associations with lung cancer are specific to either males or females, which either increase their risk of developing the disease or being protected from it.³³
- Women have better lung cancer survival rates than do men (this advantage decreases with age, so it is thought that sex hormones play a role)³⁴
- Low DNA repair capacity (DRC) appears to be associated with an increased risk of lung cancer (women's DRC is on average lower than men's)³⁵

- Women's sex hormones, such as oestrogen, may directly or indirectly influence cancer progression³⁶
- Some treatments appear to work better for women than men^{37,38,39}
- Women with lung cancer tend to be diagnosed earlier than men⁴⁰

Additional research into the gender and biological differences in cancer susceptibility should be encouraged.

Screening and treatment

The goal of cancer screening is to enable detection of the disease before symptoms are evident. Though other cancers have agreed upon screening methods (for example, mammography for breast cancer), there is no such accepted screening protocol for lung cancer.⁴¹ Often lung cancer is detected unintentionally when a patient undergoes an X-ray or CT scan for another reason. As a result, rates of early detection for lung cancer can be as low as 16%, something which is likely to contribute to the disease's very low 5-year survival rate.⁴² In contrast with breast and cervical cancers, the Member States of the European Union do not currently offer nationwide screening programmes for lung cancer, though several are in the process of undertaking pilot programmes.⁴³

Few studies have explored the differences between women and men in the procedures and outcomes of lung cancer screening. However, since women and men develop different histological subtypes of lung cancer, various experts believe that radiological screening varies in effectiveness by sex/gender. In addition, it is thought that women are better-placed to be screened for cancers in general.⁴⁴ They tend to have more frequent contact with healthcare professionals in general (during pregnancy, due to contraception, during childbirth and childrearing), providing them with more opportunities to discuss potential symptoms and to be given information.

Treatment also varies between men and women for lung cancer. Women are more commonly treated using surgery alone than are men; those who are treated with radiotherapy alone are more often men.^{45,46} Women also have better survival rates than men following surgery even when adjusting for confounders for both non-small cell and small cell lung cancers as well as various types of treatments (surgery, chemotherapy, radiation therapy, no treatment). The reasons for these differences in outcomes are currently unknown.

Targeted therapies, adjusting for tumour characteristics, are improving lung cancer treatment. One of the most promising innovations in lung cancer treatment focuses on the epidermal growth factor receptor gene (EGFR)⁴⁷ This is one of the genetic mutations that are more common in women.⁴⁸

Smoking and lung cancer

Although lung cancer is deadly, it is highly preventable. The most important cause of lung cancer is smoking, accounting for between 80 and 90% of cases.^{49,50,51} In 2015 it was estimated that globally more than 1.1 billion people were tobacco smokers,⁵² this means that a substantial share of the global population is at risk of developing this disease.

There is a gender gap in smoking behaviour. Around the world, the prevalence of smoking is much lower among women than it is among men (the share of men who are smokers is more than five times that of women according to the most recent WHO estimates⁵³), however the size of the gender gap in tobacco use is at its smallest in high-income countries where the share of male smokers is less than twice that of female smokers. Of course, even within these high-income countries, there are substantial differences in tobacco consumption between men and women.

Across Europe, men are heavier smokers than women (it is only in Sweden where smoking is very slightly more prevalent among women than it is among men).⁵⁴ This gender gap has been narrowing due to a decrease in the number of male smokers, accompanied by an increase in the number of female smokers in some countries.⁵⁵ In addition, breaking down the available data according to gender and age, we find that young girls are more likely to smoke than boys, particularly in Northern and Western European countries.^{56,57} In the 2002-2005 period, more girls than boys smoked in Italy, Sweden, Finland, the Czech Republic, France, Spain, Denmark, Ireland, the UK, Norway, Belgium, the Netherlands, Hungary, Germany, Austria, Greece, Portugal, and Slovenia.⁵⁸

The gender and biological differences in lung cancer discussed above indicate that there is a need to target women directly in order to reduce their prevalence of the disease. Since smoking is the single most important predictor of lung cancer, it is important to target female smokers. One UK study finds that if women can be persuaded to stop smoking before the age of 40, this could lead to the avoidance of 90% of the excess mortality caused by continuing to smoke.⁵⁹ While the most effective approach to preventing lung cancer in women is to persuade them not to start in the first place, the earlier that women who smoke can be persuaded to stop, the better.

The tobacco industry has long targeted young people in the promotion of their products.⁶⁰ However, it is important to take account of the aggressive marketing strategies increasingly aimed at women who are considered to be a lucrative, unexplored market. Creating women-only brands, their packaging plays on the appeal of glamorous images such as cigarettes as party accessories, sponsored events, like women's tennis games and dances. Female-targeted branding includes light or

slim cigarettes, low prices, easy availability and free samples.^{61,62} Despite the industry aggressively targeting women with their promotional activities, few anti-smoking initiatives have taken a gender-based approach.⁶³

Smoking is more common among groups with lower socio-economic status.^{64,65,66,67} Not only is uptake higher among these groups, but attempts to quit smoking are less likely to be successful. It has been suggested that this may be due to factors such as increased likelihood of not completing interventions designed to lead to smoking cessation, a lower level of social support for smoking cessation, or lower motivation to quit.⁶⁸ It is important therefore that members of such groups be targeted in order to promote smoking cessation.

However, women are on average more likely than men to be part of a low socioeconomic status group. They tend to be poorer^{69,70}, have lower employment status^{71,72} and are often economically dependent.⁷³ Increasingly, they are heading single parent and low-income households. Their lower-paid work may expose them to a smoking environment through part-time house or hospitality work. Maternal smoking has a devastating effect on their offspring, causing miscarriages, birth defects, premature births, and still births among other complications.^{74,75,76,77,78}

It is crucial then to promote smoking cessation programmes among women, particularly those women who are made vulnerable by their socio-economic status, if the prevalence of lung cancer is to be successfully reduced. Smoking cessation programmes for vulnerable women must offer a way to break the cycle of deprivation and tobacco dependency.

Finally, it is important to note that the remaining 10-20% of people that develop lung cancer that is not linked to smoking behaviour (i.e. those who have never smoked) are two to three times more likely to be women, indicating that environmental factors such as passive smoking also need to be considered in developing measures targeting the disease.⁷⁹ Further research on these cases is urgently required.

European and national strategies for lung cancer prevention

The European Union and its Member States take the issue of smoking seriously.⁸⁰ The Tobacco Products Directive (2001/37/EC) is a key legal instrument of tobacco control in the EU.⁸¹ The Directive establishes maximum tar, nicotine and carbon monoxide yields for cigarettes. It specifies labelling provisions, bans the use of misleading descriptors and the marketing of oral tobacco in the EU, except in Sweden. The Tobacco Advertising Directive (2003/33/EC) places strict limits on advertising or sponsorship which promotes a tobacco product. The EU has also run several anti-tobacco campaigns targeting different age groups (the HELP campaign targeted young people aged 15 to 25, while Ex-Smokers are Unstoppable focused on 25 to 34 year olds)⁸².

Some Member States have gone further in implementing legislation aimed at curbing tobacco consumption and protecting their citizens from passive smoke. Ireland, for example has passed laws prohibiting smoking in the workplace, with other countries (Greece, Hungary, Spain, Bulgaria, the UK) following suit with smoke-free provisions of their own.⁸³ Ireland has also passed legislation standardising the packaging of tobacco products.⁸⁴

With respect to policies that specifically target lung cancer, several member states have either completed or are currently running randomized trials for CT screening.⁸⁵ This method of screening has been recommended by a variety of organisations including the European Society of Medical Oncology⁸⁶ and the European Society of Radiology.⁸⁷ The countries engaged in such research include Italy, the Netherlands (part of the NELSON trial) and Denmark. There has been substantial debate over whether the benefits of lung cancer screening outweigh the costs (which include exposure to radiation, over-diagnosis, and false-positive results). Critics argue that rather than reducing rates of death from lung cancer, screening simply increases survival time since the disease is detected earlier.⁸⁸ However, increasingly a consensus is developing that screening for lung cancer will lead to a reduction in mortality rates from that disease.

The European Commission's *Communication on Action Against Cancer: European Partnership* sets a goal to reduce incidence of cancers in the European Union by 20% by 2020. Running between 2009 and 2013 its aim was to provide necessary support to Member States, such as engaging relevant stakeholders across the union, in their efforts to tackle cancer in general. Another important initiative, CANCON Joint Action 2014-17, is funded by the EU as well as universities, health institutes, and other organisations. It aims to develop the content of cancer control, producing a *Cancon Guide* containing good practice recommendations to be applied in national settings.

Steps for Policy Action

1. Improve existing EU data collection to track smoking prevalence and lung cancer.

Annually collect data on the prevalence and incidence of lung cancer, disaggregating by gender and age in order to fully understand trends. At the EU-level, set up a robust comparable monitoring system to track smoking prevalence across the EU Member States.

2. Make women and the public health community aware that women are at risk of developing lung cancer.

Target effective smoking cessation programmes at girls and young women as a priority in all EU countries. Promote an understanding in young women of the impact smoking has on their own health and that of their children. Develop anti-smoking campaigns to reach out with convincing messages to women during pre-natal care when they may be most receptive to advice.

3. Make tobacco control policies and interventions more gender-sensitive according to the Framework Convention on Tobacco Control (FCTC) recommendations, taking account of socio-economic factors and vulnerable groups.

4. Ensure that the revision of the EU Tobacco Products Directive provides for plain packaging.

The European Commission has revised the 2001 Tobacco Products Directive. This provides an opportunity for Europe to follow the leadership of countries like Australia and Ireland to make plain packaging mandatory.

5. Remove the stigma of lung cancer and increase research funding for both women and men to ensure optimal care for patients, improve their chances of survival and reduce the high financial and social burden of this disease.

Increase funding for basic and clinical research into early detection, diagnosis, appropriate biomarkers to enable earlier diagnosis and hence more effective treatment. Develop effective screening tests and screening criteria to detect lung cancer early. Develop affordable biotherapies for all stages of lung cancer.

6. Increase understanding of the disease differences between men and women, such as different patterns, causes and mechanisms to develop a comprehensive strategy for the prevention, diagnosis and treatment of lung cancer in both genders.

Fund research into the differences of lung cancer prevention, diagnosis and treatment between women and men and develop effective gender-sensitive guidelines for health professionals.

7. Expand and support lung cancer advocacy through interdisciplinary collaboration and coordination including epidemiologists, public health policy leaders, oncologists, behavioural scientists, researchers, politicians, women's and patient groups and lung cancer advocates.

Interdisciplinary collaborations can best address the complex interaction between the social and biological determinants of health that lead to differences in the development, diagnosis, and treatment of lung cancer between men and women.

A warm thank you to our expert reviewers:**Norma Cronin:** Board Member, International Network of Women Against Tobacco (INWAT)**Pilar Garrido:** MD PhD, Head of Thoracic Tumor Unit, Medical Oncology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain**Contributors:** Peggy Maguire, Kristin Semancik, Hildrun Sundseth and Lisa Keenan
December 2017**European Institute of Women's Health, CLG**

33 Pearse Street, Dublin 2, Ireland

Telephone: +353-1-671 5691

Email: info@eurohealth.ie

Website: www.eurohealth.ie

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