

# A disease of women

Once found mainly in men, lung cancer now afflicts an increasing number of women. Researchers and clinicians need to adjust to this change, says Narjust Duma.

In the United States, lung cancer kills more women than does any other cancer, having surpassed breast cancer in 1987. The age-adjusted death rate for lung cancer in women has risen in parallel with the smoking rate but with a lag of about 20 years.

The smoking rate for women rose significantly between 1930 and 1960 as tobacco companies increasingly directed advertisements towards women. The ads, which almost all featured young, svelte women, were designed to prey on women's insecurities about weight and diet. They also portrayed smoking as a sign of strength and independence, two traits cherished by women as they were surging into the workforce. These strategies increased cigarette sales during those three decades by more than 300% among women.

As a result, in the 30–49-year age group, the incidence of lung cancer is now higher in white and Hispanic women than it is in men – a remarkable reversal of the historical pattern.

Smoking behaviour is not the only factor that has affected the incidence of lung cancer in women. Other potential risk factors include air pollution, radiation therapy from previous cancers, and hormonal supplements. Indeed, when we take smoking out of the equation, we find some surprising patterns in the incidence of lung cancer in men and women. In the United States, 19% of lung cancer in women arises in those who have never smoked, compared with only 9% in men. So we need to ask: is lung cancer a disease of women?

As a thoracic oncologist who specializes in treating women with lung cancer, I would dare to say that the answer is yes – as long as we restrict ourselves to the population of never-smokers or light smokers. Unfortunately, the research community continues to see lung cancer as a disease of old men, and the consequences of this stereotype can be detrimental for women, causing significant delays in diagnosis.

Clinical outcomes for non-small-cell lung cancer – the most common form of the disease – are directly related to the stage of cancer at the time of diagnosis. The US National Lung Screening Trial showed that annual low-dose computed tomography (CT) scans in people who smoked one pack of cigarettes a day for 30 years or more, including



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those who quit smoking within 15 years, demonstrated a decrease in lung cancer mortality, which in turn reduced all-cause mortality<sup>1</sup>. These results led to lung cancer screening being added to health guidelines.

The effectiveness of lung cancer screening was later supported by the results of the NELSON trial, a randomized CT-based lung cancer trial involving about 15,000 current or former smokers in the Netherlands and Belgium. Unfortunately, women represented only 16% of the study participants<sup>2</sup>. The authors argued that the reason for such low representation was lower smoking prevalence and intensity in women. Despite women's meagre presence in the study, its results were encouraging. After ten years, lung cancer mortality for women was reduced by 48%, compared with a reduction of only 24% among men<sup>3</sup>.

The neglect of women with lung cancer is not limited to exclusionary studies – it also applies to their treatment by caregivers. A 2017 survey showed that women were 32% less likely than men to have talked to their doctor about screening for lung cancer<sup>4</sup> – even if the women were at high risk for the disease.

Women's second-class status among people with lung cancer has implications far beyond a lack of screening. There is also an unsettling lack of awareness about the problem of sexual dysfunction among women with lung cancer.

It has long been known that chemotherapy, radiation and surgery interfere with sexual desire. Unfortunately, most of the data regarding sexual dysfunction in both women and men with lung cancer is out of date because it preceded the approval of immunotherapy and targeted therapies. Moreover, much of the information gathered regarding sexual dysfunction in cancer relates to breast and gynaecological cancers. It is inappropriate to extrapolate these data to a disease such as lung cancer that is not clearly related to hormonal changes or surgical interventions to the genital organs.

Sexual dysfunction is only rarely discussed during routine oncology visits. Sexual health in women with lung cancer is a complex subject that involves social, psychological, physiological and environmental factors, all affecting women's sexual health at different levels. However, many clinicians do not feel comfortable asking about this issue. As a result, women often suffer in silence, and consider this to be the price they have to pay for their cancers to be treated effectively.

Low screening rates and inadequate attention to sexual dysfunction are stark reminders that lung cancer researchers and clinicians need to sharpen their focus on women. However, those are not the only examples of inequity. Women with lung cancer also suffer from delays in diagnosis, less counselling regarding smoking cessation, and fewer referrals to palliative-care services. We need to see lung cancer as a disease that affects women as well as men and realign both research funding and caregiving practices accordingly.

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4. Warner, E. T. & Lathan C. S. *Prevent. Med.* **124**, 84–90 (2019).