

Air pollution affects lung cancer survival

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Lung cancer is one of the most commonly occurring cancers in the USA. The American Cancer Society estimates that a total of 221 200 individuals were newly diagnosed with lung cancer in 2015, representing approximately 13% of all new cancer diagnoses.¹ Worldwide, lung cancer is the most commonly diagnosed malignancy. In their most recent report, WHO estimated that there were 1.8 million new lung cancer cases diagnosed in 2012.²

In addition to being one of the most commonly diagnosed cancers, survival from lung cancer is poor, making it the leading cause of cancer death in the USA.³ The 5-year lung cancer survival rate for cases diagnosed in 2011 was only 17.8%, with wide variations in survival rates by stage at diagnosis and specific histological subtype.⁴ The survival rate has only improved modestly in recent decades; the Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute estimated that overall 5-year survival rates were 12.2% for cases diagnosed in 1975–1977, 13.0% for cases diagnosed in 1987–1989 and 14.6% for cases diagnosed in 1996–1998.⁴ Therefore, interventions or other strategies to increase survival are a source of consistent research, with a focus on lifestyle and treatment interventions.^{5 6}

Given the large impact of lung cancer and the modest improvement in survival rates, population level prevention and intervention strategies are appealing as a public health tool. In addition to advances in early detection and strategies to reduce exposures from active and passive cigarette smoking, environmental exposures, especially radon and air pollution, have

emerged as potential public health targets. The International Agency for Research on Cancer recently declared air pollution generally, and particulate matter (PM) specifically, carcinogenic to humans.⁷ This determination was mainly based on the evidence for lung cancer incidence and mortality, where a rapidly growing number of studies have observed positive associations.^{7–9} However, to date, there has been no clear evidence of the impact of air pollution after a lung cancer diagnosis. In *Thorax*, Eckel *et al*¹⁰ publish the results of the first study to examine the impacts of air pollution exposures on the risk of subsequent all-cause or lung-cancer mortality among newly diagnosed individuals with lung cancer in California.

The authors used information collected on lung cancer cases diagnosed between 1988 and 2009 that were reported to the California Cancer Registry. Information on four different air pollution measures (PM <10 microns in aerodynamic diameter (PM₁₀), PM <2.5 microns in aerodynamic diameter (PM_{2.5}), nitrogen dioxide (NO₂) and ozone (O₃)) were interpolated from regulatory monitoring stations to the residential addresses of each individual at the time of diagnosis. Individuals were excluded if the necessary geographic information to locate their home address was not available, or if their address was further than 25 km from a monitoring location. Using daily exposure information, exposures were calculated from the date of diagnosis to the date of death, or end of study follow-up (21 December 2011). From the registry, information was available at an individual-level on age, race/ethnicity, sex, marital status, tumour characteristics at the time of diagnosis (stage, anatomical site, histology) and treatments occurring within 6 months of diagnosis. For each address, the authors calculated the distance to the nearest primary interstate highway and primary US and state highways to account for exposures to local traffic. For each address, they also obtained area-level information on measures of urbanicity and socioeconomic status from the Census. Information on vital status and cause of death were also available from the registry and were used to identify cases.

In multivariable adjusted models for all lung cancer stages considered together, there were elevations in both all-cause and lung cancer-specific mortality with increases in each of the pollutants examined, ranging from a 2% increased risk on all-cause mortality per IQR increase in O₃ to a 16% increased risk per IQR increase in PM_{2.5}. As the authors note, the most interesting findings were those from models stratified by stage at diagnosis and adjusted for histology and those stratified by both stage and histology. Across all pollutants, larger HRs were consistently observed for patients diagnosed at earlier stages and there were suggestions that the effects for PM₁₀, PM_{2.5}, and NO₂ were larger for adenocarcinoma cases compared with small-cell cases of the same stage.

This study, along with two other previously published analyses on the impact of air pollution on cancer survival, provide compelling initial evidence that air pollution may be a potential target for future prevention and intervention studies to increase cancer survival.^{11 12} With such a large number of cases with detailed stage and histological subtype information, this work has set the bar high for future analyses; however, it is important to note that this study does have limitations. First, with the exception of treatment within 6 months of diagnosis, this study was unable to account for potential confounding by changes in lifestyle habits, subsequent treatments or changes in time-activity patterns. Adjusting for these changes, which may differ by prognosis at diagnosis, would be important to address the potential for confounding.^{5 6} Second, although the density of regulatory monitors in California is higher than most other locations in the USA, future studies should improve on the exposure accuracy of the current analysis with the use of residence-level or individual-level predictions. The authors did not have information on changes in residence after diagnosis, which could introduce bias if there are differences in patterns of residential mobility by stage or subtype of cancer at diagnosis. The authors also focused on large-scale differences in pollution exposures in their analyses. Future work should also consider the impact of smaller-scale differences in exposures, as well as the impact of exposure to mixtures of pollutants. In conclusion, this emerging link between cancer survival and air pollution exposures should be seen as evidence of the importance of air pollution regulations, as well as a worthwhile target for interventions focused on increasing lung cancer survival rates.

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PRESS RELEASE

THORAX

Air pollution may shorten survival of patients with lung cancer

Trends most noticeable for early stage disease, particularly adenocarcinomas

Air pollution may shorten the survival of patients with lung cancer, suggests a population based study, published online in the journal *Thorax*.

The trends were most noticeable for early stage disease, particularly adenocarcinoma—the most common type of non-small cell lung cancer, which accounts for 80% of lung cancer cases—the findings show.

Air pollution has been linked to a higher incidence of lung cancer and death, but little is known about its potential impact on an individual's chances of survival after diagnosis.

In a bid to clarify this, the researchers tracked the health outcomes up until the end of 2011 of more than 352,000 people newly diagnosed with lung cancer between 1988 and 2009, and whose details had been entered into the US California Cancer Registry.

Their average age at diagnosis was 69. More than half (53%) of the cancers were diagnosed at an advanced stage (distant spread); and the average survival time for localised (early stage) disease was 3.6 years, falling to 1.3 years for regional spread, and just 4 months for distant spread.

For patients with early stage disease, average survival time was shortest for those with small and large cell cancers (around 1.5 years) and longest for those with adenocarcinoma (around 5 years).

Participants' average exposure to nitrogen dioxide (NO₂), ozone (O₃), particulate matter of less than 10 µm, and less than 2.5 µm, in diameter (PM₁₀ and PM_{2.5}) was calculated using data from US Environmental Protection Agency air quality monitoring stations, mapped to area of residence.

Almost half of the study participants (45.4%) lived more than 1500 metres away from a major interstate motorway. Less than 10% lived within a 300 metre radius of one.

Their risk of death from any cause was then estimated, according to disease stage and tumour cell type.

After taking account of these, and other potentially influential factors, the calculations showed that higher exposures to each of the four pollutants were associated with a correspondingly heightened risk of death and shorter average and 5-year survivals.

But the magnitude of heightened risk was greatest for patients with early stage disease, among whom average survival was 2.4 years for those with high PM_{2.5} exposure (at least 16 µg/m³) and 5.7 years for those with low exposure (less than 10 µg/m³), for example.

Overall, for patients with early stage disease, risk of death from any cause was 30% greater for NO₂; 26% greater for PM₁₀; and 38% greater for PM_{2.5}. The impact of exposure to O₃ was small (4%).

These trends were particularly evident among patients with early stage adenocarcinoma.

As might be expected, survival for patients with advanced disease was poor, irrespective of exposure to pollutants.

This is an observational study so no firm conclusions can be drawn about cause and effect. And the researchers point to several caveats, including a lack of data on potentially important risk factors, such as an individual's lifestyle, smoking status, and alcohol intake; and the inability to capture road traffic pollution.

Nevertheless, there are plausible biological mechanisms for the associations found, they say, as ambient air pollution has been classified as a cancer causing agent by the International Agency for Research on Cancer (IARC).

They conclude: "Our observed associations were clinically significant ([less than or equal to 38%] increased risk of death depending on stage and pollutant), suggesting that reductions in exposure have the potential to improve lung cancer survival."

In a linked editorial, Dr Jaime Hart, of the Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, points out that survival rates for lung cancer are poor, having improved only slightly in recent decades despite advances in treatment.

The most recent figures from the World Health Organization estimate that 1.8 million new cases of cancer were diagnosed in 2012 alone.

"This study, along with two other previously published analyses on the impact of air pollution on cancer survival, provide compelling initial evidence that air pollution may be a potential target for future prevention and intervention studies to increase cancer survival," she writes.

And the findings underline the importance of the imposition of regulations on air pollution levels, she suggests.

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