Environmental emissions, public health and lung cancer risk

Recent coverage of diesel emissions and the installation of defeat devices in the motor industry have been primarily centred on the economic impact on car sales for manufacturers and second hand values for owners. More importantly and largely ignored in the press coverage, diesel exhaust particulate phase is implicated as a lung carcinogen, classified as an International Agency for Research on Cancer (IARC) category 1 carcinogen in 2012. However, IARC evaluation does not provide information regarding the degree of exposure or the public health risk in general. Insights into the exposure–response (lung cancer) relationship can be gleaned from two analyses of a large mining study published in 2012 [1, 2]. On this basis, this journal suggests that there may be public health questions to be considered regarding lung cancer risk.

The most informative study on lung cancer risk from diesel emissions is a cohort of United States miners, which formed the basis for a mortality study and a case–control study, both published in 2012 [1, 2]. In the case–control study, Silverman et al. observed increasing lung cancer risk with increasing diesel exhaust exposure, measured by respirable elemental carbon (REC), considered the best index, in 12 315 workers in eight mining facilities [2]. Risk of lung cancer was three times greater (odds ratio 3.2) in workers exposed to heavy exposure compared with those workers in the lowest quartile of REC exposure, with an exposure–response relationship observed after adjustment for confounding lung cancer risk factors such as smoking. The authors proposed a continuous model of exposure and lung cancer risk, with a steep slope at lower exposures that plateaus at higher exposure levels. These studies may have environmental health implications for urban dwellers, since the environmental exposures to average REC levels in the 2–6 µg/m³ range during a lifetime in polluted cities would approximate to lower exposure levels in this study with a 50% increased lung cancer risk. Median REC values in one of London’s busiest shopping streets, Oxford Street, have been estimated to be 7.5 µg/m³ [3].

Silverman et al. concluded:

Thus, if the diesel exhaust/lung cancer relation is causal, the public health burden of the carcinogenicity of inhaled diesel exhaust in workers and in populations of urban areas with high levels of diesel exposure may be substantial.

Similarly, Attfield et al. analysing the same cohort found increased lung cancer mortality associated with diesel exhaust exposure in workers exposed to exhaust underground, with exposure–response relationship documented [1]. There was clear evidence of this relationship for the lower exposure range particularly, with a plateau at higher exposures.

In an accompanying editorial to the two papers of the mining study in 2012, Lesley Rushton justifiably predicted a fall in environmental exposures due to the impact of legislation applying to new engines to conform to European Union (EU)’s stringent emission standards. http://www.dieselnet.com/standards/eu/ld.php#stds for the EU [4]. Dr Rushton concluded that

These results indicate that stringent occupational and particularly environmental standards for diesel engine exhaust should be set and compliance ensured to have an impact on health outcomes.

Both analyses concluded that even lower exposure levels conferred an increased risk. Despite residual uncertainties, the steep exposure response relationship observed in both analyses at lower exposures suggests the worrying possibility that even small rises in elemental carbon concentrations may have an effect on lung cancer risk. While the size of the effect is small when compared with smoking, the number of people at risk to low exposure levels over prolonged periods of time is large, particularly when the inexorable rise in diesel vehicles over the last decade is considered (UK estimates: 1994 7.4% of all vehicles to 31% in 2011 data from the Department for Transport).

Indeed, in a meta-regression of lung cancer mortality using relative risks from three occupational cohort studies, including the United States miners cohort, published in 2014, the authors concluded that based on occupational and environmental exposure levels in the workplace and outdoor air, 6% of annual lung cancer deaths may be due to diesel exhaust exposure [5].

Because of the latency in lung carcinogenesis, the available results from studies of diesel-exposed populations refer to exposure circumstances prevalent two or more decades ago; the impact of contemporaneous environmental exposures will not be evident for some time. Although the number of diesel cars has increased, the technology of diesel engines has changed in recent years, and emissions of potential carcinogens have decreased, as long as engines are properly operated and maintained and results from emission analyses can be believed. A decade ago, many believed in the potential environmental benefits of diesel engines. If the impact on public health of these ‘modern’ diesel engines is expected to be lower, direct evidence is lacking and prospective studies should be encouraged. In light of the increasing concerns over environmental emissions in general together with advances in genomic technologies to decipher environmental mutational signatures in cancer genomes, this journal argues that efforts to quantify the incidence of
never-smoking lung cancer and its underlying pathogenesis are urgently required. While the incidence of smoking-related lung cancer continues to decline in most industrialized countries, the incidence of lung cancer among never smokers remains stable. As a consequence, the proportion of lung cancers in never smokers is increasing [6, 7].

In summary, the two parallel phenomena of diesel emissions and lung cancer risk and a growing perception that lung cancer in never smokers is a rising problem relative to smoking-associated lung cancer may warrant detailed investigation of mutational processes, seeking carcinogenic exposure traces, in cancer genomes of these tumours, in order to explore this matter further. The impact of defeat devices in some diesel vehicles may not be simply an economic problem with no public health consequences. At a population level, environmental carcinogenic exposures and contributing factors to never-smoking lung cancer require deeper investigation [8].

*Annals of Oncology* is actively seeking submissions in the area of environmental exposures and cancer risk and work shedding light on this complex but important public health issue.

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**Guidelines for endometrial cancer management: finding order amid the uncertainties**

In the January 2016 issue of *Annals of Oncology*, Colombo et al. [1] published a comprehensive set of clinical guidelines for the diagnosis, evaluation, and management of carcinomas of the endometrium. Forty participating experts tackled these topics in a thoughtful, methodical way and have produced a document that will undoubtedly be an extremely valuable resource for practicing clinicians. Although the authors state that no systematic literature review was performed for this project, it is clear that the participants had a thorough knowledge of the relevant data. Their discussion reflects a balanced and insightful analysis of the literature and, to my knowledge, there are no major gaps in their citations.

Although many of the topics addressed in these guidelines have been subjects of heated controversy, the authors have achieved a remarkable degree of consensus. Better than 90% agreement was achieved in all but one of their recommendations—the only exception was the 73% support for performance of staging lymphadenectomy in patients who have deeply invasive grade 3 cancers. However, the high level of consensus achieved in the development of these guidelines should not be misconstrued to suggest that all or even most of the important questions have been answered. Many of the authors’ recommendations are worded as suggestions or options, making room for considerable leeway in the application of suggested treatments. The discussion, particularly where it relates to the indications for adjuvant treatments, clearly reflects the uncertainties that continue to surround many of the issues addressed in this document.

In fact, the authors’ method of scoring both the level of evidence and the strength of each recommendation highlights, as perhaps nothing else has, the paucity of high-quality data available to guide us in the management of patients with endometrial cancer. Remarkably, of the more than 100 recommendations made in this document, only two—the suggested use of minimally invasive surgery for low and intermediate risk endometrial cancer and the recommendation to withhold any adjuvant treatment from patients with very low-risk disease—were scored as grade A recommendations backed by level I evidence. Of the 31 recommendations regarding adjuvant treatment, 60% were scored as only grade B or C recommendations based on level III or IV evidence; the admonition not to over treat low-risk disease was the only strong (grade A) recommendation made about any question regarding adjuvant treatment.

This situation reflects the particular challenges of endometrial cancer as a subject for investigation. Although endometrial