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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disclosure
PB has consulted on diesel exhaust and lung cancer for EMA (2013–2014) and MARG (2012), two industry-based organizations. All remaining authors have declared no conflicts of interest.

references

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
Cancer is the most common gynecologic malignancy diagnosed in developed countries, most patients with the disease are curable with hysterectomy alone and therefore derive no benefit from adjuvant treatments. That said, an important subset are either diagnosed with extrauterine disease or have cancers whose local features predict a high risk of recurrence. In general, most of these recurrences occur in patients who have two, three or more local risk factors of high-grade disease, high-risk histology, deep myometrial invasion, large tumor size, or lymphovascular space invasion [2, 3]. Although patients with multiple high-risk features are the ones most likely to benefit from additional treatment, they have generally been under-represented in trials evaluating the benefit of adjuvant radiation and chemotherapy. Randomized trials have clearly demonstrated that the risks of adjuvant treatment are not justified for low-risk cancers but have, unfortunately, generally been underpowered to permit any useful conclusions about the value of adjuvant therapies for higher risk disease.

High-risk endometrial cancers also vary considerably in their patterns of disease recurrence. Patients with cancers that disseminate hematogenously or intraperitoneally are unlikely to benefit from adjuvant regional radiation. However, many endometrial cancers progress with predominantly locoregional disease; retrospective studies demonstrate that these cancers can often be cured with adjuvant radiation alone, indicating that regional metastases are not necessarily harbingers of hematogenous dissemination. Retrospective studies suggest that radiation is a critical component of the curative treatment of stage IIIC endometrioid cancers [4, 5]. Unfortunately, trials that evaluate treatment of ‘advanced endometrial cancer’ too often fail to differentiate patients with locoregionally confined disease from those with evidence of wider dissemination. Such studies can produce confusing results and may fail to identify subsets that benefit from regional treatment.

Ultimately, much more study will be needed before clinicians can be confident that they understand how to best use adjuvant treatments in the management of endometrial cancer. However, in the meantime, guidelines such as the one included in this issue and the recently published ASTRO guidelines [6] help to bring order to a complex and often confusing literature and provide an invaluable framework for clinical decision making.

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