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Lung Cancer Attributable to Environmental Risk Factors

To the Editor:

We read with interest the article by Wang and colleagues regarding a great attempt to develop and validate a prediction model for the risk of lung cancer for never- and ever-smokers (1). The huge database ensured the degree of credibility of the model. Moreover, the covariates selected by the authors were accessible in real-world practice, which augmented the functionality of the model. We appreciate the valuable contribution of the study that could benefit both never- and ever-smokers. However, there were two covariates that should be further discussed to enhance the accuracy of the model.

First, air pollution makes a great impact on the risk of lung cancer and could be included in the model. Both the review article by Cheng and colleagues and the editorial by Christiani highlighted the huge effect of different air pollutants on lung cancer, especially particulate matter 2.5 (2, 3); therefore, excluding the factor of air pollution might affect the validity of the model. We noticed that the authors mentioned the lack of data on air pollution, so we would like to offer a method of air pollution evaluation by taking the disparity of provinces into consideration. There were studies that analyzed the spatial association between air pollution and lung cancer incidence in China (4, 5) which demonstrated that the different status of air pollution in different provinces can possibly affect the incidence of lung cancer. We suppose that the authors could analyze the air pollution disparity of the eight provinces included in the database and make a connection to the lung cancer rate.

Second, dietary factors could be further explored in the article. The authors mentioned the dietary intake of fresh vegetables as a risk factor while illustrating the China National Lung Cancer Screening criteria. However, the authors did not include dietary factors in the model, nor did they clarify the reason why they excluded it. We found a large cohort study using data from the UK Biobank that delineated the association between diet and lung cancer (6). The article indicated that a high intake of fruits, vegetables, breakfast cereals, and dietary fiber could lower the risk of lung cancer. Although the correlation between diet and lung cancer might be conflicting, it is a rising issue. We suggest that the authors should consider more about common dietary factors in the analysis.

Above all, the study demonstrates the possibility of constructing a screening model for lung cancer with a large database, which takes into account both accuracy and functionality. The authors also emphasized the growing rate of lung cancer of never-smokers and designed this model to draw the attention of health policy makers. Further analysis and validation through covariates such as air pollution and diet could refine the model and contribute to the health care of people at risk for lung cancer. ■

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Ya-Yu Lee*
Chia-Chin Wu*
Yih-Jyh Lee*
Chung Shan Medical University
Taichung, Taiwan

Cho-Han Chiang
Mount Auburn Hospital
Boston, Massachusetts

Kevin Sheng-Kai Ma‡
Massachusetts General Hospital
Boston, Massachusetts

Harvard T. H. Chan School of Public Health
Boston, Massachusetts

and

University of Pennsylvania
Philadelphia, Pennsylvania

James Cheng-Chung Wei‡
Chung Shan Medical University
Taichung, Taiwan

Chung Shan Medical University Hospital
Taichung, Taiwan

and

China Medical University
Taichung, Taiwan

*These authors contributed equally to this work.
‡Corresponding authors (e-mail: kevinshengkaima@g.harvard.edu and jccwei@gmail.com).

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Reply to *Lee et al.*

From the Authors:

We thank Lee and colleagues for their interest in our publication, which developed and validated risk models of lung cancer for never- and ever-smokers in China (1), and we wish to respond to the main topics addressed in their letter to the editor.

As the authors noted, the impact of air pollution and dietary factors on lung cancer incidence is of considerable public health importance. A previous comparative assessment showed that particulate matter 2.5 was one of the modifiable risk factors of lung cancer and accounted for 14.4% of the total attributable cancer deaths in mainland China (2). There is also an existing meta-analysis that showed that several fruits and vegetables containing carotenoids and other phytochemicals may provide protection from lung cancer (3). However, these two variables were generally excluded from the prediction of individualized lung cancer risks. We searched the PubMed database without date restrictions for the development and validation of prediction models for lung cancer that could be used in lung cancer screening programs before November 24, 2021. A total of 53 studies were identified as reporting risk predictions of lung cancer. Among these studies, none included air pollution, and only one study considered dietary factors on the basis of a case-control study design (4). The difficulties in accurately measuring these variables at the individual level and the limited improvement in model performance by these variables may be the possible explanations.

In our study, the reason for not including the two variables in the prediction models was due to the difficulties in accurately measuring the actual exposure of the two variables at the individual level. For the variable of air pollution, using overall environment across each province to represent the individual-level exposure is a potential option. However, individuals within the same community but who vary in age, sex, occupation, living condition, and other unmeasured characteristics may have different exposures to the air pollution. Individual reporting of exposure to severe air pollution (binary) was available in our study, but individual perception of pollution is subjective and hard to evaluate using a uniform standard. The addition of this variable did not substantially increase the area under the receiver operating characteristic curve of the prediction model for both never-smokers (0.697 [95% confidence interval, 0.681–0.713] vs. 0.701 [0.685–0.716]) and ever-smokers (0.723 [0.704–0.743] vs. 0.724 [0.704–0.743]).

For the variable of dietary factors, the data on vegetable consumption, including the intake frequency and amount (never, $<$2.5 kg/wk, or $\geqslant$2.5 kg/wk), were collected at the cohort entry by self-report. Studies have shown that relying on one measure of the dietary factors from the questionnaire-based survey may not be accurate enough to infer an association (5, 6). Moreover, our questionnaire collected the intake from 2 years before the survey to the time of survey, which may not be the etiologically relevant exposure period. *Post hoc* analyses found that the area under the receiver operating characteristic curve did not significantly increase after considering the variable of dietary factors for both never-smokers (0.697 [0.681–0.713] vs. 0.700 [0.684–0.715]) and ever-smokers (0.723 [0.704–0.743] vs. 0.725 [0.706–0.744]).

Finally, we appreciate the suggestions that the authors provided, as they are of great help to us. It is undoubtedly important to continue improving the measurement of environmental and dietary variables, such as obtaining sequential information on environmental and nutritional exposures during the life period before lung cancer occurs, and possibly using instruments such as a portable detector for particulate matter 2.5 or food diaries to ascertain individual-level exposure information (7). We will consider updating our prediction models with the addition of these two variables when accurate measurements at the individual level are available. ■

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Fei Wang, Ph.D.
Ni Li, Ph.D.*‡
Jie He, Ph.D.‡
Chinese Academy of Medical Sciences and Peking Union Medical College
Beijing, China

On behalf of all the authors

*Corresponding author (e-mail: nli@cicams.ac.cn).
‡Co-senior authors.

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