

## Peer Review File

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### Reviewer A

The short manuscript from Kim et al. detailed the risk levels associated with family history of lung and other cancers amongst those enrolled in the KoGES registries. There are additional limitations that the authors may consider listing, including the limited pathology data available. For example, risk factors for small cell, and different types of non-small cell carcinoma, especially when further broken by different driver mutations, are known to be different. This may well extend to any familial/genetic component of lung cancer pathogenesis. Nonetheless, the message conveyed is delivered in a clear and concise manner. Thank you for the opportunity to review this manuscript.

**Response (R).** Thank you for carefully reviewing our manuscript. As the reviewer mentioned, we added a limitation regarding the lack of available data on lung cancer pathology.

*Page 6, line 109–111*

*“...Moreover, important characteristics of lung cancer, such as its pathology and types like primary, recurrent, and metastatic lung cancer, could not be assessed due to the lack of available data.”*

## Reviewer B

This study investigated whether having a family history of cancer (both lung and non-lung) in first-degree relatives increased the risk of developing lung cancer using data from the Korean Genome and Epidemiology Study (KoGES). The authors showed that having a family history of cancer was associated with an increased risk of developing lung cancer. In subgroup analysis, the authors found that family histories of lung cancer and multiple cancers were associated with increased risks of lung cancer among females and never-smokers. The findings of this study suggest that individuals with a family history of cancer may benefit from personalized lung cancer screening strategies.

**Response (R).** We truly appreciate the reviewer's dedication to enhancing the quality of our manuscript.

My comments and questions are as follows.

1. Page 3 Lines 26-27: The authors mentioned several studies but only cited one article. Are some references missing here?

**(R1).** We appreciate your valuable comments. We added additional references accordingly.

*Page 3, line 26–27*

*“Several studies have indicated a potential link between a family history of cancer, particularly lung cancer, and an increased risk of developing lung cancer (1-3).”*

*Page 7, line 115–123*

*“1. Lin H, Huang YS, Yan HH, Yang XN, Zhong WZ, Ye HW, et al. A family history of cancer and lung cancer risk in never-smokers: A clinic-based case-control study. Lung Cancer. 2015;89(2):94-8.*

*2. Cannon-Albright LA, Carr SR, Akerley W. Population-Based Relative Risks for Lung Cancer Based on Complete Family History of Lung Cancer. J Thorac Oncol. 2019;14(7):1184-91.*

*3. Cassidy A, Balsan J, Vesin A, Wu X, Liloglou T, Brambilla C, et al. Cancer diagnosis in first-degree relatives and non-small cell lung cancer risk: results from a multi-centre case-control study in Europe. Eur J Cancer. 2009;45(17):3047-53.”*

2. In the KoGES study, did the lung cancer outcome include all types of lung cancers (e.g., primary lung cancer, recurrent lung cancer, and metastatic lung cancer) or just primary lung cancer?

**(R2).** Thank you for your insightful comments. We acknowledge that types of lung cancer are very important factors in our study. However, our dataset unfortunately did not include information

on these types. We added this point in the limitation section.

*Page 6, line 109–111*

*“...Moreover, important characteristics of lung cancer, such as its pathology and types like primary, recurrent, and metastatic lung cancer, could not be assessed due to the lack of available data.”*

3. What is the distribution of the outcome variable (i.e., how many study participants developed and did not develop lung cancer)?

**(R3).** Thank you for your thoughtful comments. We added the distribution of the outcome variable in the result section.

*Page 4, line 61–66*

*“Out of the total, there were 135 (0.1%) cases of lung cancer, distributed as 9 out of 4,555 (0.2%) in those with a family history of lung cancer, 32 out of 23,155 (0.2%) in those with a family history of other cancers, 34 out of 24,471 (0.2%) in those with a family history of single cancer, and 7 out of 3,239 (0.2%) in those with a family history of multiple cancers. Among individuals without any family history of cancer, there were 94 cases of lung cancer out of 103,424 (0.1%).”*

4. In the adjusted analysis, the authors mentioned age and sex were covariates. Have the authors considered also adjusting for smoking status (i.e., current, former, never) in the analyses for the total population and gender subgroups?

**(R4).** Thank you for your insightful comments. To explore a larger study population, we adjusted the age and sex since there were missing values in smoking status. Following your suggestion, we have now also adjusted for smoking status (categorized as current, former, or never smokers) by excluding participants with missing values in smoking status.

*Page 4, line 52–53*

*“Age, sex, and smoking status (current, former, and never) were used as covariates.”*

5. I would suggest replacing ‘gender’ with ‘sex’ throughout the text because gender is socially constructed while sex is biologically determined.

**(R5).** We agree with your opinion. We changed the gender to the sex throughout the manuscript.

*Page 4, line 52–53*

*“Age, sex, and smoking status (current, former, and never) were used as covariates.”*