## <u>Commentary</u>

### Exploring the Disparity in Indoor/Outdoor Time and Radon Exposure as Possible Factors Contributing to the Unexpected Increase in Lung Cancer Risk among Non-Smoking Women

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#### ABSTRACT

According to a NIH study, Lung cancer among individuals who have never smoked is more prevalent in women and occurs at an earlier age than in smokers. The rise in lung cancer rates among female non-smokers might be linked to radon inhalation and should be further investigated. Our theory is based on the differences in radon exposure between males and females, which can be attributed to the variations in time spent indoors versus outdoors. Over the past few years, the smoking rates have shown a steady decline in the United States and other developed countries. This decrease in smoking prevalence has led to a new shift in the primary risk factors associated with lung cancer. Although tobacco smoke historically served as the primary cause of lung cancer, the reduction in smoking rates has allowed other risk factors, such as radon exposure, to come to the forefront. Given that women in certain countries, on average, might spend more time indoors compared to men, they are potentially exposed to higher levels of radon. This increased exposure could explain the rising rates of lung cancer among female non-smokers. The theory is still in its nascent stages and requires further research and validation. However, if proven correct, it could significantly alter our understanding of lung cancer risk factors and lead to new prevention. It is therefore crucial to expedite the review and publication of this theory, given its potential implications for public health.

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#### Keywords

Radon; Lung Neoplasms; Smoking; Gender; Women; Indoor/Outdoor Time

#### Introduction

ung cancer is a major health concern, with high mortality rates and a significant number of new cases expected each year [1]. Historically considered a disease predominantly affecting men, recent studies have indicated a rise in lung cancer cases incidence in women, particularly in developed countries. The increasing prevalence of lung cancer in women underlying the importance of raising our understanding of the risk factors and biological mechanisms driving its progression. The current state of knowledge on lung cancer in women focuses on risk factors, epidemiology, and potential molecular mechanisms [2-4]. Some of <sup>2</sup>MVLS College, The University of Glasgow, Glasgow, Scotland, UK

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the main factors that currently are believed to affect the lung cancer risk are as follows:

#### 1. Smoking

Tobacco consumption is recognized as a significant contributor to the occurrence of lung cancer, and as more women have started smoking over the years, the rates of lung cancer in women have increased. In the past, smoking was more common among men, but now the rate of tobacco use among females has been observed to vary, especially in some regions.

#### 2. Passive Smoking

Even if a woman doesn't smoke herself, inhaling secondhand smoke can heighten the likelihood of developing lung cancer. Women who live with smokers or work in environments where smoking is allowed may be at higher risk.

3. Exposure to environmental toxins

Exposure to air pollution can raise the risk of lung cancer, and in some countries, air pollution levels have increased in recent years. Women residing in urban areas with elevated air pollution levels may experience an augmented risk of adverse health consequences.

#### 4. Hormonal factors

Indications suggest that hormonal factors, including menopausal status and hormone replacement therapy usage, may influence lung cancer susceptibility in females. However, further research is warranted in this domain.

5. Genetic susceptibility

Some studies suggest that certain genetic factors may increase the lung cancer risk in women, but more research is needed to fully understand this relationship.

#### The scope of the Problem

The occurrence of lung cancer in never smoker women is on the rise, and the reasons for this are not fully understood. However, some studies suggest that it could be attributed to high degrees of exposure to secondhand smoke, as well as increased exposure to indoor pollutants, including radon, due to women spending more time indoors than men [5-7]. Women, on average, have smaller lungs and a higher percentage of body fat, which can increase the absorption of radon into the body. Additionally, research indicates that most young lung cancer patients are female, often have adenocarcinoma histology, are less likely to be smokers, and frequently present with more advanced disease stages [8-10]. It is important to note that smoking is still considered the main cause of lung cancer, and that non-smokers can also develop lung cancer as a result of exposure to various environmental factors.

#### Concerns Over Unexpected Rise in Risk of Lung Cancer among Non-Smoking Women

According to a NIH study, it has been observed that lung cancer in non-smoking women is more prevalent and tends to occur at an earlier age compared to smokers [2]. Due to the American Lung Association, lung cancer rates for women have increased by 79 percent over the past 44 years, while they have decreased by 43 percent for men. Additionally, more young women than men are now being diagnosed with lung cancer, marking a historic shift in the gender distribution of this disease [11]. However, the majority of these cancers still have unknown causes, although Exposure to environmental risk factors, such as radon, secondhand tobacco smoke, air pollution, asbestos, or previous lung diseases, may account for certain cases of lung cancer. The latest data show that nonsmoking women between the ages of 40 and 79 are more likely to get lung cancer or die from lung cancer than nonsmoking men [12, 13]. The incidence of lung cancer among young people who have never smoked is on the rise. Detecting the risks at an earlier stage is challenging because early-stage lung cancer seldom presents red-flag symptoms [3]. According to Gallup, over the last 20 years, the smoking rate has decreased significantly from 35% to 12%. Nowadays, young adults are more inclined to smoke e-cigarettes and marijuana rather than tobacco. It seems that smoking habits among young adults are

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transitioning from tobacco to e-cigarettes [14]. Given this consideration, we believe that the reduction in smoking rates has allowed other risk factors, such as radon exposure, to come to the forefront. Lung cancer stands as the foremost cause of cancer-related fatalities globally. While the majority of lung cancer cases are associated with a history of tobacco smoking, approximately 10% to 20% of individuals diagnosed with lung cancer have never smoked [15]. Exposure to radon is a recognized cause of lung cancer, and recent studies suggest that even at low concentrations, inhaling radon poses a risk of developing lung cancer [16].

#### The Key Issue of the Differences in Indoor/ Outdoor Time between Men and Women

It is worth investigating the potential role of high concentrations of radon as women spend more time indoors. A recent survey reveals that on average, women spend only 25 minutes outside per day, underscoring the need for further investigation into potential health risks associated with prolonged indoor exposure. Women are more likely to spend time indoors due to work commitments, childcare responsibilities, and household chores. The study also found that women who spend more time outside tend to have better health and well-being. There are several possible reasons why women spend more time indoors. One reason is that women tend to take on more unpaid childcare and domestic work, leaving them with less leisure time and fewer opportunities to earn in the marketplace. Another factor is the normalization of intensive parenting, with individuals placing high value on maximizing time spent actively engaging with their children. Additionally, women may feel less safe than men when spending time outdoors, which could lead them to spend more time indoors [17, 18].

## The Link between Indoor/Outdoor Time and Radon Inhalation

Radon, a colorless and odorless radioactive gas, is naturally generated through the decay of uranium in soil and rock. It has the potential to infiltrate buildings through foundation cracks and can amass to hazardous concentrations, particularly in regions with inadequate ventilation and high background radiation areas. Long-term exposure to radon can cause lung cancer, and women who spend most of their time indoors may be at a higher risk. It is concerning to note that the reason behind the rise in lung cancer cases in women could be linked to spending more time indoors and exposure to radon. According to a survey, the average woman spends only a few tens of minutes outside per day, and they spend more time indoors, especially in poorly ventilated areas, which can raise the risk of lung cancer [19].

Spending more time indoors and exposure to even low concentrations of radon have been identified as potential risk factors for lung cancer, and there is some evidence to suggest that they may contribute to the increasing rates of lung cancer in women. It is worth noting that besides the key factor of exposure to radon, other indoor air pollutants such as tobacco smoke, cooking fumes, and cleaning chemicals can also be involved in unexpected rise in of the occurrence lung cancer risk in women who do not smoke [20].

# The Importance of Studies on lung cancer conducted in regions prone to radon exposure

Ramsar, a city on the northern coast of Iran, is known for having some of the highest levels of naturally occurring background radiation in the world. The Talesh Mahalleh district in Ramsar is recognized as one of the most radioactive inhabited areas on Earth, primarily due to its proximity to hot springs and the utilization of building materials sourced from these springs. The effective dose equivalents in very high background radiation areas (VHBRAs) of Ramsar, particularly in Talesh Mahalleh, radiation levels exceed the radiation dose limits recommended by the International Commission on Radiological Protection (ICRP) for radiation workers by several times. adon, a naturally occurring radioactive gas, is generated through the decay process of uranium

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present in soil, rock, and water sources. In certain regions of Ramsar, radon levels can reach up to 3700 Becquerels per cubic meter. Radon is the second most significant contributor to lung cancer after tobacco smoking. Despite this, there is a notable absence of comprehensive data on the incidence of radon-related lung cancers in Iran. The maximum recorded indoor radon concentrations in Ramsar are not explicitly mentioned in the provided search results. However, it is clear that Ramsar is a radon-prone area due to its high levels of naturally occurring background radiation and in certain regions of Ramsar, maximum radon levels can reach up to 31,000 Becquerels per cubic meter. There are currently no national radon regulations or mitigation strategies in Iran. However, the National Radiation Protection Department of the Iranian Nuclear Regulatory Authority is responsible for radiation protection and safety in the country. Moreover, there is a scarcity of comprehensive data regarding the prevalence of radon-induced lung cancers in Iran. Lung cancer studies in radon prone areas such as Ramsar, can shed more light on the dark corners of unexpected rise in risk of lung cancer in women who do not smoke [21-24].

#### Conclusion

Spending more time indoors and exposure to even low concentrations of radon have been identified as potential risk factors for lung cancer, and there is some evidence to suggest that they may contribute to the increasing rates of lung cancer in women. The average woman spends only a few tens of minutes outside per day, and they spend more time indoors, especially in poorly ventilated areas, which can increase the lung cancer risk. As the rates of lung cancer in women continue to rise, it's important to take steps to address these potential risk factors. This may include improving ventilation in buildings, testing for radon in homes and workplaces, and encouraging women to spend more time outdoors and away from sources of indoor air pollution. It's important to note that the relationship between indoor air quality and lung cancer is complex, and many other factors may also contribute to the increasing rates of lung cancer in women. More research is needed to fully understand the role of indoor air pollution, radon, and other risk factors in the development of lung cancer. It's also essential to raise Awareness regarding the risks associated with lung cancer and the importance of early detection and treatment. By addressing these issues, we can help reduce the burden of lung cancer on women.

#### Authors' Contribution

A. Safari, SAR. Mortazavi, L. Sihver, and A. Ghadimi-Moghadam conceptualized the idea. M. Haghani and SMJ. Mortazavi assisted in data collection. A. Safari, SAR. Mortazavi and A. Ghadimi-Moghadam have equally contributed to this work. All authors assisted in drafting, revising and finalizing the manuscript. L. Sihver edited, revised and submitted the manuscript.

#### **Conflict of Interest**

SMJ. Mortazavi and L. Sihver, as the Editorial Board Members, were not involved in the peer-review and decision-making processes for this manuscript.

#### References

- Schabath MB, Cote ML. Cancer Progress and Priorities: Lung Cancer. *Cancer Epidemiol Biomarkers Prev.* 2019;**28**(10):1563-79. doi: 10.1158/1055-9965.EPI-19-0221. PubMed PMID: 31575553. PubMed PMCID: PMC6777859.
- Jemal A, Miller KD, Ma J, Siegel RL, Fedewa SA, Islami F, et al. Higher Lung Cancer Incidence in Young Women than Young Men in the United States. *N Engl J Med.* 2018;**378**(21):1999-2009. doi: 10.1056/NEJMoa1715907. PubMed PMID: 29791813. PubMed PMCID: PMC7717174.
- Fidler-Benaoudia MM, Torre LA, Bray F, Ferlay J, Jemal A. Lung cancer incidence in young women vs. young men: A systematic analysis in 40 countries. *Int J Cancer*. 2020;**147**(3):811-9. doi: 10.1002/ijc.32809. PubMed PMID: 32020598.
- 4. Khazaei Z, Sohrabivafa M, Momenabadi V,

Moayed L, Goodarzi E. Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide prostate cancers and their relationship with the human development index. *Advances in Human Biology*. 2019;**9**(3):245-50. doi: 10.4103/2321-8568.262891.

- 5. Lee YS. Gender differences in physical activity and walking among older adults. *J Women Aging*. 2005;**17**(1-2):55-70. doi: 10.1300/ J074v17n01\_05. PubMed PMID: 15914419.
- 6. Bonsang E, Van Soest A. Time devoted to home production and retirement in couples: a panel data analysis. *Labour Economics.* 2020;**65**:101810. doi: 10.1016/j.labeco.2020.101810.
- Lee S. Falls associated with indoor and outdoor environmental hazards among communitydwelling older adults between men and women. *BMC Geriatr.* 2021;**21**(1):547. doi: 10.1186/ s12877-021-02499-x. PubMed PMID: 34641812. PubMed PMCID: PMC8507100.
- Lortet-Tieulent J, Soerjomataram I, Ferlay J, Rutherford M, Weiderpass E, Bray F. International trends in lung cancer incidence by histological subtype: adenocarcinoma stabilizing in men but still increasing in women. *Lung Cancer.* 2014;**84**(1):13-22. doi: 10.1016/j.lungcan.2014.01.009. PubMed PMID: 24524818.
- Meza R, Meernik C, Jeon J, Cote ML. Lung cancer incidence trends by gender, race and histology in the United States, 1973-2010. *PLoS One.* 2015;**10**(3):e0121323. doi: 10.1371/journal.pone.0121323. PubMed PMID: 25822850. PubMed PMCID: PMC4379166.
- Chapman AM, Sun KY, Ruestow P, Cowan DM, Madl AK. Lung cancer mutation profile of EGFR, ALK, and KRAS: Meta-analysis and comparison of never and ever smokers. *Lung Cancer*. 2016;**102**:122-34. doi: 10.1016/j.lung-can.2016.10.010. PubMed PMID: 27987580.
- 11. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. SEER cancer statistics review, 1975–2018. *National Cancer Institute*. 2021:1-25.
- Titan AL, Baiu I, Liou D, Lui NS, Berry M, Shrager J, Backhus L. Eligibility for Lung Cancer Screening Among Women Receiving Screening for Breast Cancer. JAMA Netw Open. 2022;5(9):e2233840. doi: 10.1001/jamanetworkopen.2022.33840. PubMed PMID: 36178692. PubMed PMCID: PMC9526079.
- 13. Toh CK, Ong WS, Lim WT, Tan DS, Ng QS,

Kanesvaran R, et al. A Decade of Never-smokers Among Lung Cancer Patients-Increasing Trend and Improved Survival. *Clin Lung Cancer.* 2018;**19**(5):e539-50. doi: 10.1016/j. cllc.2018.03.013. PubMed PMID: 29627315.

- 14. Jones JM. Cigarette Smoking Rates Down Sharply Among U.S. Young Adults. News; 2022.
- Bryant A, Cerfolio RJ. Differences in epidemiology, histology, and survival between cigarette smokers and never-smokers who develop nonsmall cell lung cancer. *Chest.* 2007;**132**(1):185-92. doi: 10.1378/chest.07-0442. PubMed PMID: 17573517.
- Lorenzo-González M, Torres-Durán M, Barbosa-Lorenzo R, Provencio-Pulla M, Barros-Dios JM, Ruano-Ravina A. Radon exposure: a major cause of lung cancer. *Expert Rev Respir Med.* 2019;**13**(9):839-50. doi: 10.1080/17476348.2019.1645599. PubMed PMID: 31318276.
- Beyer KMM, Szabo A, Hoormann K, Stolley M. Time spent outdoors, activity levels, and chronic disease among American adults. *J Behav Med.* 2018;**41**(4):494-503. doi: 10.1007/s10865-018-9911-1. PubMed PMID: 29383535. PubMed PM-CID: PMC6031452.
- Yuen HK, Jenkins GR. Factors associated with changes in subjective well-being immediately after urban park visit. *Int J Environ Health Res.* 2020;**30**(2):134-45. doi: 10.1080/09603123.2019.1577368. PubMed PMID: 30757907.
- Gökmen A, Gökmen IG, Hung YT. Radon pollution control. In: Advanced Air and Noise Pollution Control. Totowa, New Jersey: Humana Press Inc; 2005. p. 335-57.
- Somsunun K, Prapamontol T, Pothirat C, Liwsrisakun C, Pongnikorn D, Fongmoon D, et al. Estimation of lung cancer deaths attributable to indoor radon exposure in upper northern Thailand. *Sci Rep.* 2022;**12**(1):5169. doi: 10.1038/ s41598-022-09122-y. PubMed PMID: 35338199. PubMed PMCID: PMC8956686.
- Abbasi S, Mortazavi SAR, Mortazavi SMJ. Martian Residents: Mass Media and Ramsar High Background Radiation Areas. *J Biomed Phys Eng.* 2019;9(4):483-6. doi: 10.31661/jbpe. v0i0.1138. PubMed PMID: 31531302. PubMed PMCID: PMC6709356.
- 22. Mortazavi SMJ, Mortazavi Gh, Mortazavi SAR, Paknahad M. Is Induction of Anomalies in Lym-

phocytes of the Residents of High Background Radiation Areas Associated with Increased Cancer Risk? *J Biomed Phys Eng.* 2019;**9**(3):367-72. doi: 10.31661/jbpe.v9i3Jun.654. PubMed PMID: 31341882. PubMed PMCID: PMC6613150.

23. Mortazavi SMJ, Jamali F, Moradgholi J, Mehdizadeh AR, Faghihi R, Mehdizadeh S, et al. Investigation of the Efficacy of Damp-Proof Montmorillonite Nanoclay for Radon Reduction Strategies in Radon Prone Areas of Ramsar. *J Biomed Phys Eng.* 2013;**3**(1):25-8.

 Haghani M, Mortazavi SMJ, Faghihi R, Mehdizadeh S, Moradgholi J, Darvish L, et al. Nanomaterial containing wall paints can increase radon concentration in houses located in radon prone areas. *J Biomed Phys Eng.* 2013;3(3):105-8. PubMed PMID: 25505754. PubMed PMCID: PMC4204498.