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# Life at higher elevation linked to lower incidence of lung cancer, study suggests

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Image credit: Wikimedia Commons.

Here's another potential reason to live up in the mountains. Lung cancer rates in both smokers and non-smokers are lower in higher-elevation counties in the western part of the United States, suggesting that oxygen may promote the incidence of lung cancer, according to a new study co-authored by a student at the Perelman School of Medicine at the University of Pennsylvania.

While lung cancer primarily afflicts smokers, 10 to 15 percent of cases arise in nonsmokers and over 80 percent of smokers never develop lung cancer.

Controlling for smoking, education, and numerous other variables associated with higher rates of cancer, the study, published online on

*PeerJ*, has found that for every 1,000-meter rise in elevation, lung cancer incidence in the population living in that area decreased by 7.23 cases per 100,000 individuals. (The 260 counties in 11 western states studied have a median lung cancer rate of 56.8 cases per 100,000 people.) The researchers did not find similar pronounced effects for elevation on colorectal, breast, and prostate cancer, all of which are also prevalent in the United States.

Previous studies have pointed to an inverse relationship between elevation and lung cancer rates, and more recent findings have raised the possibility that incomplete or faulty metabolism of oxygen during normal breathing may lead to cell injury and mutation, including free radical damage, setting the way for lung cancer to develop. The Penn study is the most comprehensive assessment of this relationship, examining data from more than three times as many geographic areas as earlier research and controlling for numerous potential confounding variables previously unaddressed or only partially addressed.

"Lower atmospheric pressure at higher elevations results in less inhaled oxygen, sometimes as much as one-third less than low-elevation areas," says co-author Kamen P. Simeonov, who is studying for a medical degree and a doctorate. "Non-acclimated professional and amateur athletes know this very well. Our study suggests that this factor may explain why lung cancer incidence rates decrease as geographic elevation increases, but not rates for such equally pernicious cancers as colorectal, breast, and prostate."

Simeonov and co-author Daniel Himmelstein, a doctoral candidate in the bioinformatics program at University of California, San Francisco, compared elevation with seven environmental correlates of elevation to see which was the best explanation of lung cancer distribution. Other factors studied include amount of sunlight, precipitation, temperature, and pollution.

For lung cancer, elevation performed by far the best. The second best (radon) was $10^8$ times worse. Sunlight was over $10^{13}$ times worse.

Looking closer at sunlight as an illustration of their approach, Simeonov notes that "Vitamin D synthesis is stimulated by sunlight and we know that the hormonally active form of vitamin D, calcitriol, potentially possesses anti-cancer properties. Hence, a reasonable proposition would be that increased vitamin D synthesis and not elevation per se is the primary explanation for the lower rates of lung cancer at higher elevations."

But sunlight data taken from the CDC Wonder database showed far less association with lung cancer rates than elevation. In fact, of all variables studied, geographic elevation was second only to smoking in terms of significance and effect size as a predictor of lung cancer incidence.

"If our findings are confirmed, the implications for future treatments in a number of areas are significant," says Simeonov. "For example, they add weight to research that has uncovered significant increases in childhood cancers in cases of neonatal oxygen supplementation."

**More information:** Simeonov KP, Himmelstein DS. (2015) "Lung cancer incidence decreases with elevation: evidence for oxygen as an inhaled carcinogen." *PeerJ* 2:e705 dx.doi.org/10.7717/peerj.705

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