

# Vitamin D, Vitamin A and Lung Cancer Mortality

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The cause of lung cancer in persons who have never smoked remains uncertain. Yet, vitamin D may reduce lung cancer mortality due to its ability to inhibit cell proliferation and promote cell differentiation and apoptosis. Normal respiratory epithelial cells have high levels of the vitamin D receptor and of the enzyme involved in forming active vitamin D; however, these are dysregulated in malignant lung tissues.

Vitamin A (retinol) is involved in vitamin D-regulated gene transcription but excess dietary levels can interrupt this process. Thus, Ting-Yuan David Cheng and Marian Neuhauser of the Public Health Sciences Division recently set out to investigate the association between serum 25-hydroxyvitamin D, the accepted biomarker of vitamin D status, and death from lung cancer, while taking into account smoking status, circulating levels of vitamin A, and vitamin A/ $\beta$ -carotene supplement use.

In a nationally representative sample of 16,693 men and women from the Third National Health and Nutrition Examination Survey, the authors observed an inverse association between serum vitamin D and lung cancer mortality among non-smokers, despite no overall association between serum vitamin D and lung cancer mortality. Serum vitamin D  $\geq 44$  nmol/L vs.  $< 44$  nmol/L was associated with a 47-69% reduced risk of lung cancer mortality [former/never smokers: Hazard Ratio (HR) 0.53, 95% Confidence Interval (CI) 0.31-0.91; distant-former (quit  $\geq 20$  years)/never smokers: HR 0.31, 95% CI 0.13-0.77]. Additionally, vitamin A appeared to diminish the inverse association between vitamin D and lung cancer mortality, such that the beneficial effect of serum vitamin D  $\geq 44$  nmol/L was not seen among individuals with excess circulating vitamin A (serum retinyl esters  $\geq 7.0$   $\mu\text{g/dL}$  or ratio of retinyl esters to retinol  $\geq 0.08$ ) or among vitamin A/ $\beta$ -carotene supplement users, although statistical tests to confirm effect modification by vitamin A were not conclusive.

In this study, the difference between non-smokers with high versus low serum vitamin D translated into a lower lung cancer mortality rate by 581 per 10,000. Yet, 29% of this nationally-representative sample had excess circulating vitamin A. Thus, if the observed antagonistic actions of excess vitamin A and vitamin A/ $\beta$ -carotene supplement use reflect the true underlying etiology, the associations between elevated vitamin D levels and reduced lung cancer mortality may have been even greater in those with normal levels of vitamin A.

Further research to determine the exact level of vitamin A intake that reduces the anti-carcinogenic actions of vitamin D are needed and will be important for understanding the true nature of the associations between vitamin D and lung cancer development and progression.

[Cheng TY, Neuhouser ML](#). (2012). Serum 25-hydroxyvitamin D, vitamin A, and lung cancer mortality in the US population: a potential nutrient-nutrient interaction. *Cancer Causes Control*. 23:1557-1565.