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Title: Bone mineral density is associated with the risk of non-small cell lung cancer, the HUNT study

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Body: Background: The overall survival in lung cancer is poor. The highest survival has been observed for cancers diagnosed in early stages, so early identification of patients at risk is important. Estrogen receptors have been found in non-small cell lung cancer. This may indicate that estrogen promote carcinogenesis. Estrogen level is associated with bone mineral density (BMD). Hence, BMD might be used as surrogate measure of long term estrogen exposure. Aim: To investigate whether low BMD is associated with lower risk for lung cancer. Method: We analyzed data from a cohort study, the Nord-Trøndelag Health Study (HUNT-study) linked to the Norwegian Cancer Registry. 18156 subjects underwent bone densitometry of the forearm. The results were reported as z-scores and categorized into tertiles. All analyses were stratified by sex. Body mass index (BMI), lung function and smoking were tested as confounders in logistic regression models. BMI and lung function changed the odds ratio less than 10% and were not included in the final model. Results: 72% of the 18156 participants were females. In the low z-score group we found more ever smokers (P < 0.001), but no difference in age and sex distribution between the three z-score groups. In all 194 cases with non-small cell lung cancer were identified. Among these 56 % were females, 87% were ever smokers and the mean age was 72 ± 11 years. In men, low compared to high z-score was associated with a higher risk of lung cancer, OR 3.3 (95% CI: 1.85-5.99) and adjusted for smoking OR 2.93 (95% CI: 1.62-5.31). In women no association with BMD was seen. Conclusion: Low bone mineral density is associated with a higher risk of lung cancer, in men, but not in women.