

European Respiratory Society Annual Congress 2012

Abstract Number: 7096

Publication Number: 1636

Abstract Group: 11.1. Lung Cancer

Keyword 1: Lung cancer / Oncology **Keyword 2:** No keyword **Keyword 3:** No keyword

Title: Interval lung cancers not detected on screening chest x-rays: How are they different?

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Body: Background: The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial provides us an opportunity to describe interval lung cancers not detected by screening chest x-ray (CXR) compared to screen-detected cancers. Methods: Participants were screened with CXR at baseline and annually for two (never smokers) or three (ever smokers) more years. Putative interval cancers were those with a negative CXR screen but with a diagnosis of lung cancer within 12 months. Screen-detected cancers were those with a positive CXR and diagnosed within 12 months. Potential interval cancers were re-reviewed to determine whether lung cancer was missed and probably present during the initial interpretation or whether the lesion was a “true interval” cancer. Results: 77,445 participants were randomized to the intervention arm with 70,633 screened. Of 5,227 positive screens from any screening round, 298 resulted in screen-detected lung cancers; 152 had potential interval cancers with 128 CXR available for re-review. Cancer was probably present in 45/128 (35.2%) at time of screening; 83 (64.8%) were “true interval” cancers. Compared to screen-detected cancers, true interval cancers were more common among males, persons with <12 years education and those with a history of smoking. True interval lung cancers were more advanced stage IV (31.0% vs. 16.7%, p<0.007), more often small cell, 27.7% vs. 7.4%, and less often adenocarcinoma, 25.3%

vs. 56.4% ($p < 0.0001$), and less likely to be in the right upper lobe, 16.9% vs. 36.2% ($p < 0.001$). Conclusion: True interval lung cancers differ from CXR-screen-detected cancers with regard to demographic variables, stage, cell type and location.