IS THE INCREASE IN ADENOCARCINOMA A RESULT OF CHANGES IN CIGARETTE DESIGN?

David Burns and Christy Anderson, UCSD School of Medicine

IS THE INCREASE IN ADENOCARCINOMA A RESULT OF CHANGES IN CIGARETTE DESIGN?

David Burns and Christy Anderson, UCSD School of Medicine

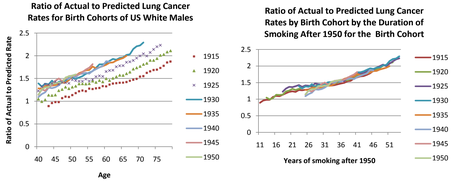
Adenocarcinoma as a percentage of all lung cancer has increased over time and this increase has been attributed to changes in cigarette design. We use five-year birth cohort specific estimates of smoking behaviors and a model of lung cancer risk derived from the ACS CPS I data to estimate the expected rate of lung cancer by birth cohort and compare those estimates to actual US lung cancer mortality by birth cohort. Risk data from CPS I are based on cigarettes smoked prior to 1972, and these risk estimates progressively underestimate actual US lung cancer mortality between 1970 and 2000 culminating in a 50% underestimate. This underestimate can be eliminated by including a simple scaling term for the duration of smoking cigarettes manufactured after the mid 1960s. Birth cohort specific lung cancer incidence by tissue type was examined using the SEER data and the same risk models scaled to the percentage of all lung cancer represented by that type. Squamous cell carcinoma incidence rates by birth cohort were well predicted by the model without any adjustment for cigarettes smoked after the mid 1960s suggesting that there has been no increase in risk of smoking over time for squamous cell. Incidence rates for adenocarcinoma were progressively underestimated suggesting that the risk of smoking for adenocarcinoma has increased dramatically over time. These data suggest that up to one half of current lung cancer occurrence may be attributable to changes in cigarette design and correspondingly that current lung cancer rates might be reduced by up to 50% through regulatory control of cigarette design and composition.

Estimating U.S. Lung Cancer Mortality Rates

A risk equation for white males incorporating terms for CPD, duration of smoking and age using the American Cancer Society Cancer Prevention Study I data collected between the years 1960-72 was applied to 5-year birth cohort specific estimates of smoking behavior to estimate the lung cancer rates for birth cohorts of white males by calendar year.

These estimates underpredict the actual lung cancer mortality for the same birth cohorts and the magnitude of that underestimate increases with advancing calendar year and is different for different cohorts.

The difference between cohorts can be minimized if the ratio of actual to predicted rates is plotted against smoking duration after1950.



Adjusting Estimates of Mortality Rates

The predictive equation is adjusted using two sets of adjustments by the following approach

$$LC = a \cdot \{[NS \cdot LC_{NS}] + [CS \cdot LC_{CS} \cdot (b \cdot S_{CS})] + [FS \cdot LC_{FS} \cdot (b \cdot S_{FS})]\}^{c}$$

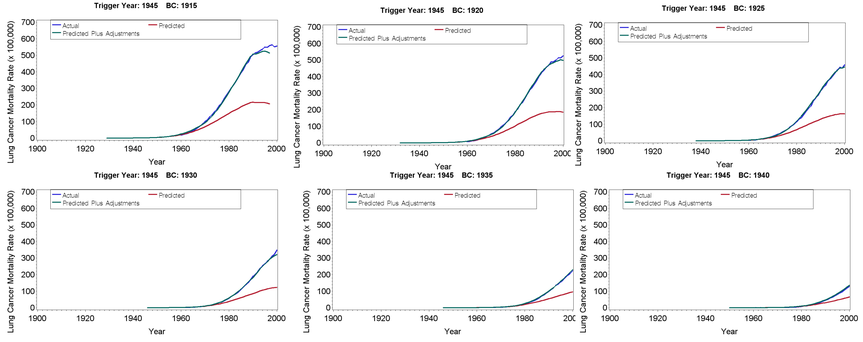
a and c are adjustments for an underestimate due to the CPS I population being healthier than the US population

b is a simple scaling term derived by fitting the predicted rates to the actual U.S. mortality and applied to the number of years (S) after a target year that the population smoked for current (CS) and former smokers (FS)

Only positive adjustments are applied and they begin to increase estimates after 1971 and 26 years duration

a = 0.94, c = 1.085 and b = 0. 038

Predicted, Adjusted and Actual Lung Cancer Mortality Rates



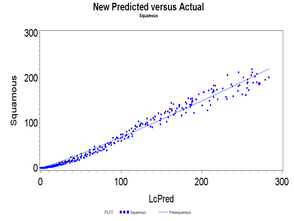
Predicting Lung Cancer Incidence by Cell Type

-The CPS I risk equation without adjustments was fit to birth cohort specific estimates of lung cancer incidence by cell type derived from the SEER data and a new a and c were estimated.

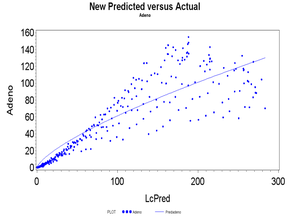
-Squamous cell lung cancer was well estimated but the difference between actual and estimated rates for adenocarcinoma varied by birth cohort and calendar year.

-Adding a scaling term for number of years of smoking after 1950 dramatically improved the fit and removed the variation with calendar year and cohort.

Squamous Cell

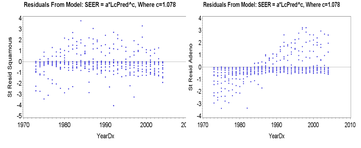


Adenocarcinoma

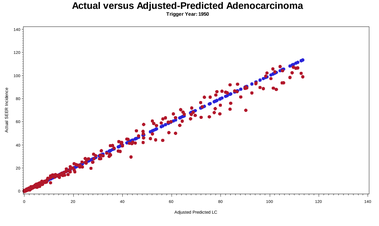


Adjusted Adenocarcinoma Estimates

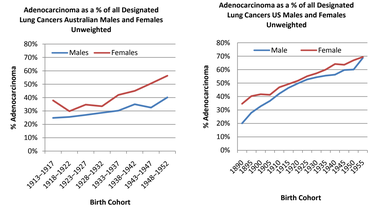
Variance with Age and Calendar Year



Actual versus Adjusted-Predicted Adenocarcinoma



Comparison of the Fraction of Lung Cancer that is Adenocarcinoma by Birth Cohort in the US and Australia



Summary

1) The study provides new evidence that among smokers there has been an increase in the risk of developing lung cancer, controlling for amount and duration of smoking, which has progressively increased in the US over the past four decades.

2) This increase in the risk of lung cancer among smokers coincides with a change in cigarette design over the past five decades.

3) This increase in risk of smoking over time is not evident for squamous cell carcinoma of the lung and is driven largely by changes in the risk of adenocarcinoma. The increase in adenocarcinoma as a proportion of all lung cancers is much less evident in Australia. This suggests that the difference may be caused by a difference in the cigarettes used in the two countries. One major known differences in cigarettes between the two countries is the lower levels of tobacco specific nitrosamines (a lung specific carcinogen for adenocarcinoma) in Australian cigarettes. The increased risk of adenocarcinoma in the US may be explained by the higher levels of tobacco specific nitrosamines in US cigarettes.

4) These observations strongly support the need for regulation of tobacco products, since technology exists to lower nitrosamines in tobacco.