Sensitivity Analysis of Median Lifetime on Radiation Risks Estimates for Cancer and Circulatory Disease amongst Never-Smokers

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Abstract

Radiation risks are estimated in a competing risk formalism where age or time after exposure estimates of increased risks for cancer and circulatory diseases are folded with a probability to survive to a given age. The survival function, also called the life table, changes with calendar year, gender, smoking status and other demographic variables. An outstanding problem in risk estimation is the method of risk transfer between exposed populations and a second population where risks are to be estimated. Approaches used to transfer risks are based on: 1) Multiplicative risk transfer models - proportional to background disease rates. 2) Additive risk transfer model - risks independent of background rates. In addition, a Mixture model is often considered where the multiplicative and additive transfer assumptions are given weighted contributions. We studied the influence of the survival probability on the risk of exposure induced cancer and circulatory disease morbidity and mortality in the Multiplicative transfer model and the Mixture model. Risks for never-smokers (NS) compared to the average U.S. population are estimated to be reduced between 30% and 60% dependent on model assumptions. Lung cancer is the major contributor to the reduction for NS, with additional contributions from circulatory diseases and cancers of the liver, bladder, oral cavity, esophagus, colon, a portion of the solid cancer remaining, and leukemia. Greater improvements in risk estimates for NS are possible, and would be dependent on improved understanding of risk transfer models, and elucidating the role of space radiation on the various stages of disease formation (e.g. initiation, promotion, progression).

Methods

ESTIMATING RADIATION RISKS:
The cancer radiation risks for never-smokers (NS) were considered by Cucinotta et al (2011) in both a Radiation Research article and a NASA publication. The cancer models considered here transfer the NASA 2010 Risk projection models which include model fits from BEIR VII, UNSCEAR 2006, and Preston (2007). We compare the multiplicative risk transfer models and the mixture model. We have also added coronary heart disease (CHD) and stroke radiation risks as estimated by Preston (2003).

ESTIMATING NEVER-SMOKER (NS) RATES:
US average rates and life tables are available online from the Centers for Disease Control’s website. Thun et al. provides a detailed review of lung cancer rates for NS with estimates (2008). Malarcher et al. provides Age-specific relative risks (RR) for the four leading causes of smoking related deaths; lung cancer, CHD, stroke, and chronic obstructive pulmonary disease (COPD). We can estimate NS rates using the US average rates and these age-specific relative risks. For the less studied cancers, overall RR can be used to estimate the NS rates. The RR estimates used are reported in Table 1. In Figure 3, we compare the estimates provided by Thun to the methods of estimating NS rates using RR. The Non-smoker lung cancer rates reported by Thun et al. and the NS cancer rates estimated using age specific RR risks have similar shapes, but slightly different absolute values. Overall estimates using RR risks approximate the NS rates fairly well with less accuracy at older ages. The survival function for NS will be adjusted using the NS mortality rates for lung cancer, smoking sensitive cancers, CHD, stroke, and COPD.

Discussion

Astronaut Kaplan-Meier (KM) estimates for different demographics of US astronauts and payload specialists (PS) are shown in Figures 1A-B. There was data available for 339 astronauts with 44 deaths, and 23 PS with one death. 296 of the astronauts were male (M) and 40 were female (F). In Figure 1A, you can see that there is no significant differences between M, F, and PS, and all combined data. The low F and PS frequencies provide little power for statistical testing of differences. 18 of the deaths were work related and would not compare well with the average US population. For females, we use 18%, 35%, and 47% of the population.

Table 1. Estimates of relative risks (RR) for never-smokers (NS) compared to US average population for several cancers attributable to smoking, coronary heart disease (CHD), stroke, and chronic obstructive pulmonary disease (COPD). For males, current smokers, former smokers, and NS are estimated at 24%, 40%, and 36% of the population.

Sources for radiation risks:


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Figure 1. Comparison on estimated survivor functions conditional on surviving to age 30. Astronaut survival estimated using Kaplan-Meier estimates. US average and never-smokers (NS) estimates based on US 2005 life tables.

Figure 2. Comparison of %REID per 5y for males and females as a function of age at exposure for mixture model and multiplicative model for the US average population and never-smokers (NS) adjusted population.

Figure 3. Comparison on age-specific cancer incidence per million and mortality rates for the 2005 US average population, recent analysis for never-smokers (NS) by Thun et al, NS rates estimated using relative risks (RR), and NS rates estimated using age-specific RR.

Figure 4. Comparison on estimated survivor functions conditional on surviving to age 30. Astronaut survival estimated using Kaplan-Meier estimates. US average and never-smokers (NS) estimates based on US 2005 life tables.

Figure 5. Comparison of %REID per 5y for males and females as a function of age at exposure for mixture model and multiplicative model for the US average population and never-smokers (NS) adjusted population.

Figure 6. Comparison on age-specific cancer incidence per million and mortality rates for the 2005 US average population, recent analysis for never-smokers (NS) by Thun et al, NS rates estimated using relative risks (RR), and NS rates estimated using age-specific RR.