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 stomach, liver, bladder, oral cavity, esophagus, colon, a portion of the solid cancer remainder, and leukemia. Greater improvements in risk estimates for NS's 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, and 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 implement 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-Meyer (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 comparison these deaths were also censored at the time of the work related death. Figure 1B, shows how censoring the work related deaths changes the survival curve. Figure 1C and 1D compares the overall astronaut KM curve to the M and F US average and NS survival estimates. When the work related deaths are included, the survival probability has a dip between ages 30 and 60 that is not seen in the average US population. However when we account for work related deaths, the survival curve is similar to the NS female survival. This improvement over NS male survival could be due to factors such as obesity and socioeconomic factors that are not accounted for in the NS survival.

Because the astronaut survival curve was similar to the NS female survival, when calculating % REID we also compared males using female NS survival estimates and kept the male NS rates the same. Figure 2 shows comparisons for %REID per 1 Sv for multiplicative and mixture models. For lung cancer and all cancers, there are large improvements in %REID for female NS. Using a multiplicative model also improves the %REID for NS. There is less of an improvement in %REID for male NS. For CHD and stroke %REID, the longer survival due to NS cancer improvements creates slightly larger CHD and stroke risks. When M survival is improved further to the NS female survival, there is a larger increase in risk for CHD and stroke. Overall improvements in risk are seen when we account for smoking status.

Sources for radiation risk:

BEIR VII. Washington DS: National Academy of Sciences Press: 2006.

UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes. New York, NY: United Nations; 2008.

Preston DL et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. Radiat Res. 2007; 168: 1-64.

Preston DLet al. Report 13: Solid cancer and noncancer disease mortality: 1950-1997. Radiat. Res. 2003; 160: 381-407.

Furukawa K et al. Radiation and smoking effects on lung cancer incidence among atomic bomb survivors. Radiat Res. 2010; 174: 72-82.

Cucinotta FA, Chappell LJ. Updates to Astronaut Radiation Limits: Radiation Risks for Never-Smokers. Radiat Res. 2011; 176: 102-114.

Cucinotta FA, Kim MY, Chappell LJ. Space Radiation Cancer Risk Projections and Uncertainties – 2010. Houston, TX: NASA TP-2011-216155.

Sources for cancer and mortality rates:

Thun MJ et al. Lung cancer occurrence in never-smokers: an analysis of 13 cohorts and 22 cancer registry studies. PLoS Med. 2008; 5: 1357-1371.

United States Cancer Statistics: 1999 - 2005 Incidence and Mortality, WONDER On-line Database. August 2008. Accessed at http://wonder.cdc.gov.

United States Life Tables, 2005. National Vital Statistics Reports, Vol. 58, No. 10, March 3, 2010.

Worktable 291R. Death rates for 113 selected causes…by 5-year age groups, race and sex: United States, 1999-2005.

Malarcher AM et al. Methodological Issues in Estimating Smoking-attributable Mortality in the U.S. Am J Epidemiol 2000; Vol. 152, No. 6: 573-584.

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.

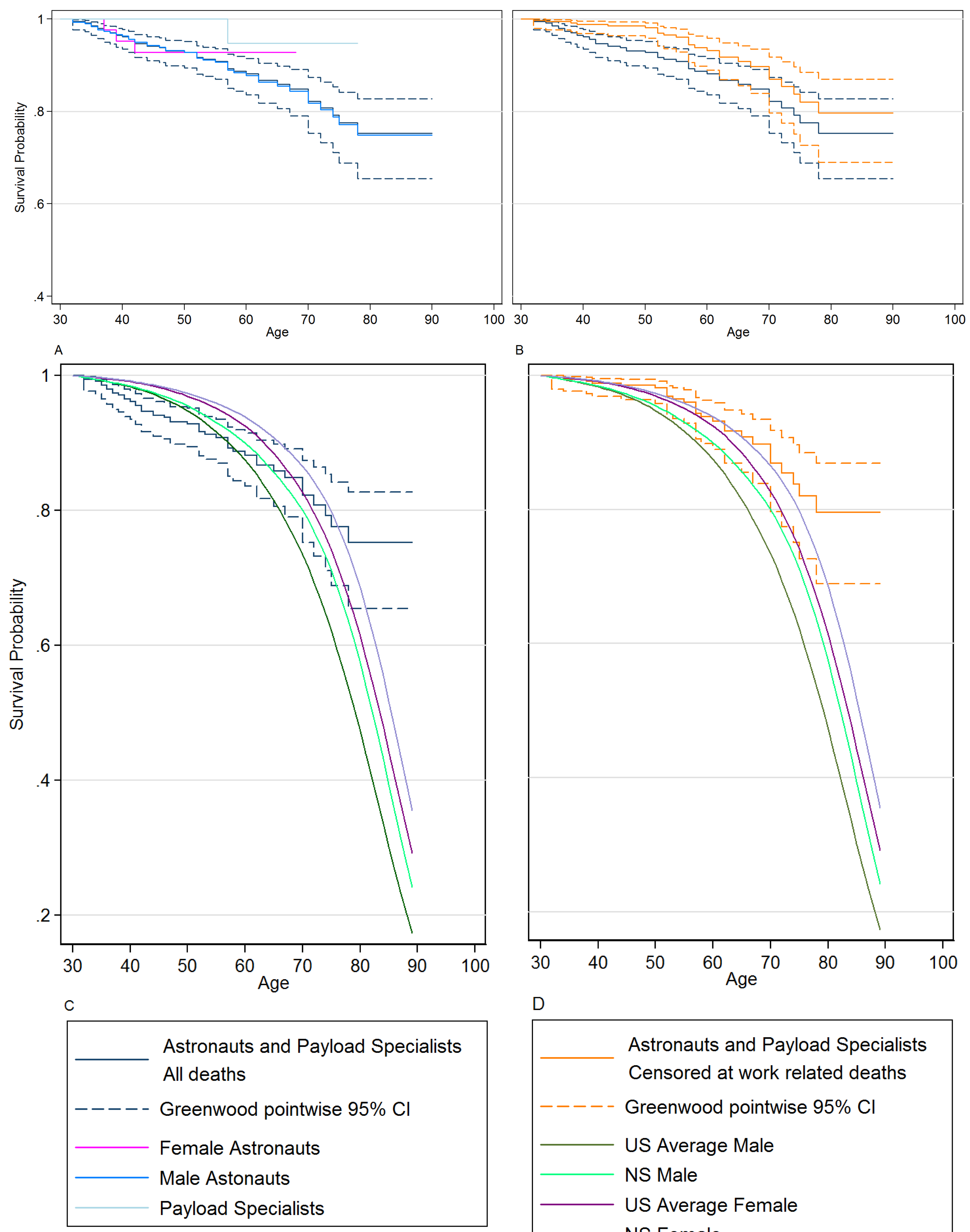


Figure 2. Comparison of %REID per Sv for males and females as a function of age at exposure for mixture model and multiplicative model for the US average population and never-smokers (NS) adjusted population.

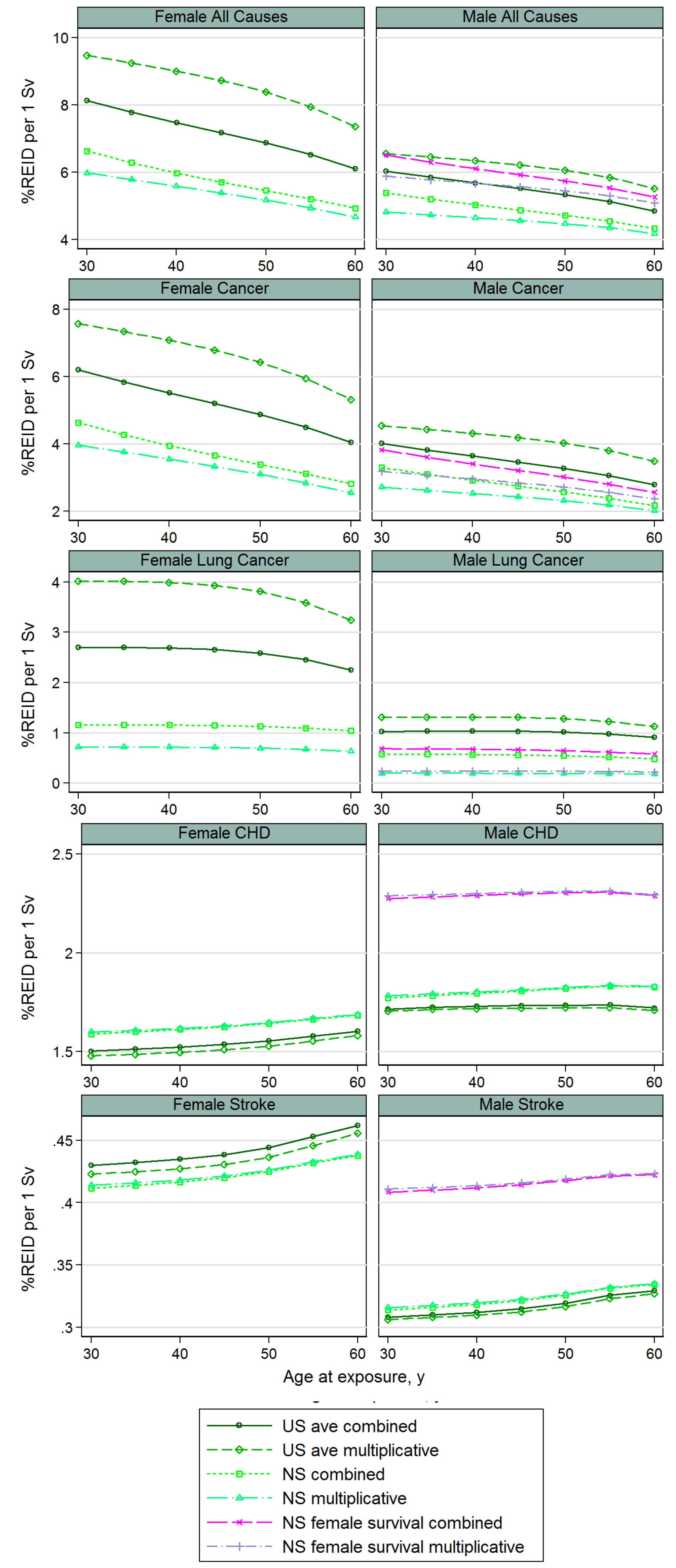
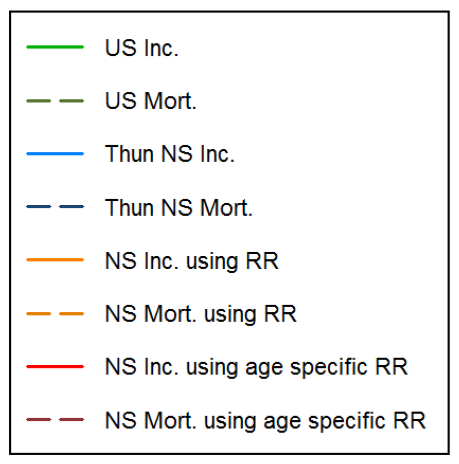


Figure 3. Comparison on age-specific cancer incidence and mortality rates for the 2005 US average population, recent analysis for never-smokers (NS) by Thun et al, NS rates estimated using relative risks (RR), and NS rates estimated using age-specific RR.



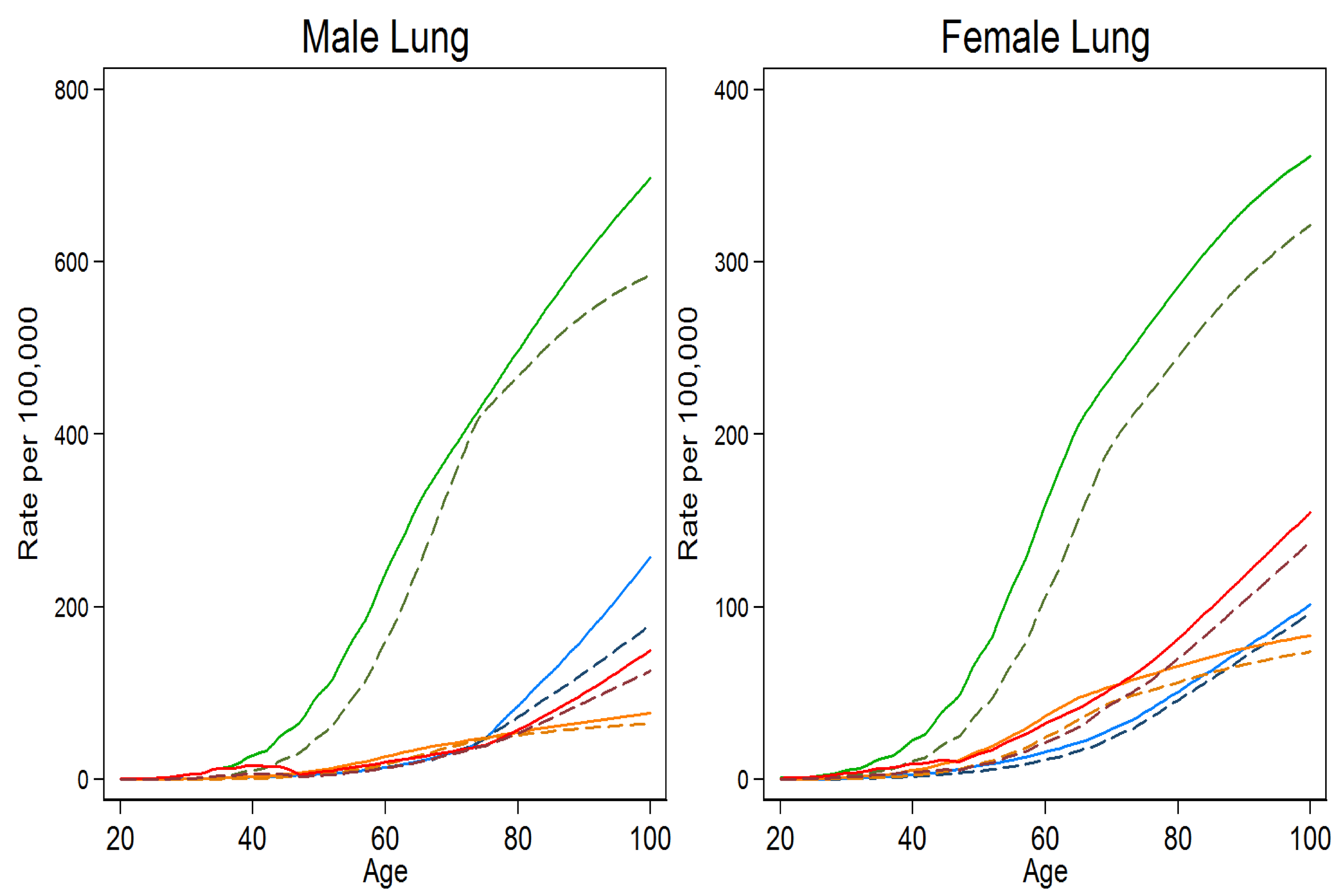


Table 1. Estimates of relative risks (RRs) for never-smokers (NS) compared to US average population for several cancers attributable to smoking, coronary heart disease (CHD), stroke, and chronic obstructive pulmonary disease (COPD). For males, current smokers, former smokers, and NS are estimated at 24%, 40%, and 36% of the population. For females, we use 18%, 35%, and 47% of the population.

Males	RR-Smoker	RR-Former	RR-NS	RR(NS/US)
Esophagus	6.76	4.46	1	0.27
Stomach	1.96	1.47	1	0.71
Bladder	3.27	2.09	1	0.50
Oral Cavity	10.89	3.4	1	0.23
Liver	2.25	1.75	1	0.63
Colon	1.19	1.21	1	0.89
Leukemia	2	1.5	1	0.69
Remainder	4	2.5	1	0.43
Lung cancer				
35-59	27.21	11.09	1	0.09
60-69	30.71	11.25	1	0.08
70-79	27.23	9.43	1	0.09
80+	13.4	6.55	1	0.16
Age-adjusted	23.26	8.7	1	0.11
CHD				
35-59	3.36	1.99	1	0.51
60-69	2.06	1.44	1	0.70
70-79	1.49	1.19	1	0.84
80+	1.23	1.04	1	0.93
Age-adjusted	2.68	1.72	1	0.59
Stroke				
35-59	3.64	1.12	1	0.59
60-69	2.48	1.19	1	0.70
70-79	1.77	1.15	1	0.80
80+	1.09	0.81	1	1.06
Age-adjusted	2.97	1.12	1	0.66
COPD				
50-69	13.57	11.18	1	0.12
70+	9.76	7.43	1	0.18
Age-adjusted	12.4	10	1	0.14

Females	RR-Smoker	RR-Former	RR-NS	RR(NS)/US
Esophagus	7.75	2.79	1	0.35
Stomach	1.36	1.32	1	0.85
Bladder	2.22	1.89	1	0.65
Oral Cavity	5.08	2.29	1	0.46
Liver	2.25	1.75	1	0.67
Colon	1.28	1.23	1	0.88
Leukemia	2	1.5	1	0.74
Remainder	4	2.5	1	0.48
Lung cancer				
35-59	14.77	4.53	1	0.21
60-69	14.7	5.05	1	0.20
70-79	11.28	4.5	1	0.25
80+	7.31	2.95	1	0.35
Age-adjusted	12.69	4.53	1	0.23
CHD				
35-59	3.61	1.61	1	0.59
60-69	2.43	1.14	1	0.77
70-79	1.63	1.18	1	0.85
80+	1.34	0.99	1	0.95
Age-adjusted	2.7	1.38	1	0.69
Stroke				
35-59	6.34	1.33	1	0.48
60-69	2.64	1.22	1	0.73
70-79	2.22	1.22	1	0.77
80+	0.59	0.75	1	1.19
Age-adjusted	3.82	1.23	1	0.63
COPD				
50-69	12.29	8.26	1	0.18
70+	8.92	5.94	1	0.24
Age-adjusted	10.96	7.34	1	0.20