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Derivation of Background Mortality by Smoking and Obesity in Cancer Simulation Models

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Abstract

BACKGROUNDS—Simulation models designed to evaluate cancer prevention strategies make assumptions on background mortality—the competing risk of death from causes other than the cancer being studied. Researchers often use the U.S. lifetables and assume homogeneous other-cause mortality rates. However, this can lead to bias because common risk factors such as smoking and obesity also predispose individuals for deaths from other causes such as cardiovascular disease.

METHODS—We obtained calendar year-, age- and sex-specific other-cause mortality rates by removing deaths due to a specific cancer from U.S. all-cause life tables. Prevalence across 12 risk factor groups (3 smoking (never, past, and current smoker) and 4 body mass index (BMI) categories (<25, 25-30, 30-35, 35+ kg/m²) were estimated from national surveys (National Health and Nutrition Examination Surveys (NHANES) 1971-2004). Using NHANES linked-mortality data, we estimated hazard ratios for death by BMI/smoking using a Poisson regression model. Finally, we combined these results to create 12 sets of BMI and smoking-specific other-cause life tables for U.S. adults aged 40 and older that can be used in simulation models of lung, colorectal, or breast cancer.

RESULTS—We found substantial differences in background mortality when accounting for BMI and smoking. Ignoring the heterogeneity in background mortality in cancer simulation models can lead to underestimation of competing risk of deaths for higher risk individuals (e.g. male, 60-year old, white obese smokers) by as high as 45%.

CONCLUSION—Not properly accounting for competing risks of death may introduce bias when using simulation modeling to evaluate population health strategies for prevention, screening, or

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treatment. Further research is warranted on how these biases may impact cancer screening strategies targeted to high-risk individuals.

INTRODUCTION

Mathematical models are increasingly used to quantify the contribution of risk factor trends and potential impacts of preventive strategies on cancer outcomes.^{1,2} These models typically simulate the natural history of cancer initiation, progression, and death (both from cancer and non-cancer causes). Explicit assumptions are required on competing risks when simulating the population dying from causes other than the specific cancer of interest.

Many cancer modelers use life tables of all-cause mortality to approximate background mortality, despite the fact that certain cancers can be substantial contributors to all-cause mortality. For example, for an average 60-year-old adult in the United States, cancers of the lung, breast, and colorectum are responsible for approximately 13%, 7% (women), and 3% of mortality, respectively (National Center for Health Statistics). Not deducting them from all-cause mortality can thus result in significant double-counting. Furthermore, very few cancer models estimate differential other-cause mortality by risk factors. Because several very prevalent risk factors for these cancers, such as obesity and cigarette smoking, are also strong predictors of other diseases, background mortality rates need to be estimated as a function of one's risk factor profile.

The issue of competing mortality risks in cancer simulation models has been previously addressed for breast cancer³ and for lung cancer.^{4,5} Rosenberg et al. described the process to remove breast cancer mortality from all-cause cohort life tables obtained from the Berkeley Mortality Database. They found that the largest decrease in mortality after removing breast cancer as a cause of death is at age 40, and the impact is larger among women born in more recent years. Several lung cancer models consider differential background mortality by smoking history, finding other-cause mortality, especially from coronary heart diseases, among current smokers to be several folds greater than never smokers, and such differences in relative risks are more profound in younger ages than in older ages.^{4,5}

Accounting for risk-factor-specific background mortality has implications on the conclusions of cancer models designed to evaluate preventive or screening programs. For example, a postmenopausal breast cancer prevention model may simulate in detail the processes through which obese women have greater risk than women of normal weight to develop, and eventually die from, breast cancer; and the model can project how an obesity prevention program reduces the population's mortality risk from breast cancer. Another example could be the use of a colorectal cancer model to evaluate whether high-risk individuals (e.g. severely obese smokers) should be more aggressively screened⁶. It may seem obvious that intensifying cancer screening on these adults would provide greater health gains than screening lower-risk individuals. However, because the same risk factors lead to higher background deaths from other causes (e.g. lung cancer, stroke and heart diseases), the optimal screening schedule conditional on behavioral risk factors is not always straightforward.

In this study, we describe the methods to derive other-cause life tables by body mass index (BMI) and smoking status, two main risk factors shared by cancer and non-cancer deaths. We derive both cross-sectional and cohort lifetables by BMI and smoking status for all causes of death, and for all causes other than lung, breast, and colorectal cancer. The cross-sectional lifetables are derived for each year from 1970-2003, and the cohort lifetables are derived for each year of birth between 1886 to 1963, although for each cohort they are left truncated prior to 1970 and right truncated in 2003 or at age 85 (whichever comes first). The

lifetables with one cause of death removed represent the mortality experience in the absence of a specific cause of death, while disease specific models produce deaths in the absence of other cause deaths. Taken together they produce a complete mortality experience, and we discuss the use of these improved risk factor specific life lifetables in the context of lung, breast, and colorectal cancer simulation models.

METHODS

Overview

Figure 1 summarizes the analytic processes involved in the construction of other-cause life tables. We begin from a series of U.S. cross-sectional, annual life tables from 1970 to 2003 from the National Center for Health Statistics (NCHS), a common source for disease modelers to obtain age-, sex-, and race-specific mortality rate estimates. We then estimated corresponding mortality rates in the absence of a specific cancer (Step 2), including breast, colorectal and lung cancers. From the National Health and Nutrition Examination Surveys (NHANES), we estimated the prevalence for twelve categories of BMI (normal weight defined as: $<25 \text{ kg/m}^2$, overweight: $25\text{--}29.9 \text{ kg/m}^2$, obese: $30\text{--}34.9 \text{ kg/m}^2$, or very obese $\geq 35 \text{ kg/m}^2$) and smoking status (never-, former-, and current-smoker) in the U.S., by race, sex, and age (Step 3). Underweight ($<18.5\%$) represents an extremely small proportion of the population and therefore combined with the normal weight category. In Step 4, we estimated the relative risk of NHANES subjects dying from causes other than the specific cancer in each risk factor category, using normal weight non-smoker as the reference category. Finally, we combined information obtained from previous steps to estimate other-cause lifetables by risk factor category. These resulting other-cause lifetables for a particular cancer contain annual age-specific mortality rates as a function of race (all, white, black), sex, calendar year, smoking status and BMI—for example, the mortality rate from causes other than breast cancer at age 55 to age 56 for a white, normal-weight female smoker in 1972. Because most deaths that are attributable to smoking or BMI (e.g. cancer, cardiovascular, and respiratory diseases) usually occur at middle age, we assume other-cause mortality does not differ by BMI and smoking before age 40 and after age 85, similar to the assumptions made in Rosenberg et al.⁵

Removing cancer from all-cause life tables (Steps 1 & 2)

The NCHS life tables contain annual mortality rates from all causes in each year for single-year age groups for ages 40–84 years. The central mortality rate (denoted as m_x for age x to $x+1$) was calculated by taking the number of deaths divided by the census population:

$$m_x = d_x / L_x,$$

where d_x are the number of deaths between age x to $x+1$ and L_x is the average population at age x . We obtained cause-specific mortality rates for breast, lung and colorectal cancer (generically denoted as $m_{x,c}$, c =type of cancer) by sex and race (all, white, black) for calendar years 1970–2003 from NCHS and the National Cancer Institute. Assuming the overall hazard of death is the sum of the hazard rates of cancer (C) and non-cancer (NC, which denotes causes other than the cancer indicated) causes, we subsequently estimated the other-cause mortality rates ($m_{x,NC}$) by subtracting mortality for a specific cancer ($m_{x,C}$) from all-cause mortality rates (m_x):

$$m_{x,NC} = m_x - m_{x,C}.$$

Trend analysis of joint distribution of BMI and smoking (Step 3)

Based on NHANES I (1970-1975), II (1976-1980), III (1988-1994), and the continuous, biannual NHANES 1999-2000, 2000-2001, 2003-2004, we estimated the prevalence proportions of U.S. population for each of the 12 risk factor categories for a given race, sex, calendar year and age (denoted as $p_1, p_2, \dots, p_{12}$ where $\sum p_i = 1$). In NHANES, a current smoker is defined as someone who smoked at least 100 cigarettes in his lifetime and is currently smoking; a former smoker is defined as someone who smoked at least 100 cigarettes in his lifetime but is not currently smoking; a never smoker is defined as someone who has not smoked 100 cigarettes in his lifetime. BMI is calculated (by NHANES) as one's weight in kilograms divided by height in meters squared. Sample design and data collection protocols have been previously published and are available online at <http://www.cdc.gov/nchs/about/major/nhanes/datalink.htm>.

We fit generalized logit models to estimate smoothed prevalence estimates of smoking and BMI, adjusted for race, age and calendar year (as continuous variable). Higher order (squared or cubed) terms for the linear independent variables, age and year, were included in the model if they were statistically significance at two-sided $p=0.05$ levels. Separate models were fitted for men and women. We adjusted for the stratified multi-stage cluster survey design and applied sample weights from NHANES using the MULTLOG procedure (SUDAAN 10.0, Research Triangle Institute).

Relative mortality risks of risk factors (Step 4)

The effect of smoking status and BMI on other-cause mortality was estimated using the NHANES linked mortality data, which contain vital statistics records of NHANES I, II, and III respondents through 2002. The primary underlying cause of death was identified using ICD-9 codes (lung cancer: 162.3-162.9, breast cancer: 174, and colorectal cancer (153-154). We made the following exclusions: (1) Death from a specific cancer cause (e.g. breast cancer); (2) women who were pregnant at baseline; (3) deaths and person time that occur after 15 years since the baseline date of the survey, and (4) deaths and person time that occur within 3 years since baseline. Condition (3) was applied because risk factor status was only assessed at baseline and may likely have changed after 15 years. Condition (4) was applied to address potential effects of reverse causality, that the BMI and smoking status was a result of the possible illness underlying the subjects' death briefly after the survey, rather than risk factors.⁷

Using normal-weight never smokers as the reference category, relative risks for other-cause death ($RR_{x,NC,i}$, $i=2-12$) were estimated based on a Poisson regression method using the SAS LOGLINK procedure (Appendix). This method uses counts of deaths as the dependent variable, total person years as offset, and age, race, BMI, and smoking status as independent variables. Theoretically, this methods produces instantaneous rate ratios which were used to approximate relative risks. In our final model, the inclusion of a calendar year effect produced unstable estimates and therefore it was dropped from the model. To flexibly accommodate the nonlinear relationship between BMI and mortality as well as between age and mortality, we modeled continuous BMI and age (using mid-points of BMI and age categories) using restricted cubic regression splines with five knots set at the 5th, 25th, 50th, 75th and 95th percentiles of the BMI and age values.⁸

Solving for risk factor-specific other cause mortality rates (Step 5)

Assuming the population-wide other-cause mortality rate ($m_{x,NC}$) is a weighted average of group-specific mortality rates, we link all three components from steps 2-4 in the following equation:

$$m_{x,NC} = \sum_{i=1}^{12} p_{x,i} \times m_{x,NC,i}$$

where $p_{x,i}$ is the prevalence proportions for risk factor group i , at age x , in a particular year from Step 3, and $m_{x,NC,i}$ is the other-cause mortality rate for group i at age x in the same year. In addition, as the absolute mortality rate for risk factor groups 2 to 12 can be estimated as a multiple of the reference group ($i=1$, normal weight never smokers), then $m_{x,NC,i} = m_{x,NC,1} \cdot RR_{x,NC,i}$, where $RR_{x,NC,i}$ is the relative risk of being in risk factor group i ($i=2, 3, \dots, 12$) dying from other causes, compared to normal weight never smokers. Combining the two equations, we can solve for group-specific mortality rate estimates as:

$$m_{x,NC,1} = \frac{m_{x,NC}}{\sum_{i=1}^{12} p_{x,i} \times RR_{x,NC,i}}, \quad \text{and } m_{x,NC,i} = m_{x,NC,1} \cdot RR_{x,NC,i} \text{ where } i=2, 3, \dots, 12.$$

Converting rates to probabilities

We assumed an exponential relationship between central mortality rate and probability of dying within the same year, essentially assuming constant hazard rate within the year.⁹ Therefore, in the absence of competing cancer causes, for example, under a hypothetical scenario in which cancer is eradicated, deaths will be entirely due to non-cancer causes and can be written as: $q_{x,NC,i} = 1 - \exp(-m_{x,NC,i})$ for risk factor group $i=1-12$. Lifetables as a function of risk factors in the absence of cancer are used in conjunction with the cancer simulation models (which produce death from cancer in the absence of other cause death) to simulate the age and cause of death as the earlier of the two latent death times.

Transforming cross-sectional to birth-cohort lifetables

Many models simulate actual birth cohorts rather than a hypothetical or synthetic cohort estimated using cross-sectional data. Assuming no differential mortality prior to age 40, the cross-sectional lifetables from 1970-2003 were rearranged by corresponding age and calendar year to form lifetables for each birth cohort born between 1886 and 1963, with the lifetables left truncated in 1970 and right truncated at age 85 or 2003, whichever comes first. Because of the assumption of no differential mortality prior to age 40, for birth cohorts born from 1930 to 1969, the portion of the 12 smoking by BMI lifetables prior to 1970 are not stratified and therefore can be filled in with a common lifetable that are not dependent on prevalences and relative risks derived from 1970 and after from NHANES. Only starting age at 40 do these common lifetables split into their 12 risk strata specific tables.

RESULTS

Proportion mortality due to other causes

Cancer deaths constitute a varying proportion of all-cause mortality rate depending on type of cancer, age, sex, race, and calendar period (Table 1), depicting a changing picture in competing causes. Breast cancer represents 11% of all female deaths at age 40 in 1970, while lung cancer represents 13% of deaths in 2000 at age 60 for both men and women. Colorectal cancer contributes a smaller amount to overall deaths, between 1 and 5% depending on age, race, and year. In general, the absolute death rates for breast (in women), colorectal, and lung cancer increases by age, but the relative share of these causes in overall mortality is often greater at younger ages, e.g. lung cancer contribute to 13% deaths in men

at age 60 vs. 7% at age 80, and breast cancer contributes to close to 10% of overall deaths among women at age 40. Contrasting the death rate composition at age 60 in 1970 and 2000, the absolute breast cancer rate declined in white women (79 to 60 per 100,000) but increased in black women (65 to 81 per 100,000). However, for both black and white women, breast cancer has become proportionally more important as a cause of deaths over time.

Trends in risk factors

The US population showed a decline in cigarette smoking and a concurrent increase in obesity. These concurrent trends, for example, result in an expansion of the highest risk group (current smoker, BMI ≥ 35), especially among women. The joint distribution (Figure 2) between the two risk factors therefore shows a mixed trend in risk over time, and a different pattern in risk factor mix across race-sex groups.

Relative risks of smoking and BMI on deaths from other causes

Smoothed relative risks at ages 40 to 85 were estimated for deaths from all causes, deaths from causes other than breast cancer, deaths from causes other than lung cancer, and deaths from causes other than colorectal cancer. Table 2 showed the relative risk estimates at age 65, the age generally with high cancer burden for the three cancers, for all 12 risk factor groups, by causes of death.

Resulting lifetables and survival

We constructed 12 lifetables by race and sex for each of the smoking and BMI combinations. The lifetables were constructed for all causes of death, as well as causes other than breast cancer, causes other than lung cancer, and causes other than colorectal cancer. Figure 3 demonstrates the resulting life expectancy estimates for cohorts at age 40 using the all-cause lifetables (assuming the same age- and sex-specific mortality rates after age 85), benchmarked by the overall U.S. lifetables. Other cause-specific life tables are available upon request. These tables were also rearranged by birth cohorts. For example, Figure 4 shows non-breast cancer mortality probability from age 40 to 75 for women born in 1945. The clear separation of the mortality curves demonstrated the potential bias one may introduce by assuming homogenous background mortality. In addition, these results also suggest that, although smoking is not an important risk factor for breast cancer, ignoring the impact of smoking on background mortality in breast cancer simulation models will overestimate competing mortality among never smokers and underestimate competing mortality among current smokers.

More specifically, Table 3 exemplifies how different assumptions for background mortality can result in underestimation or overestimation of competing risks of death. For instance, in models of breast cancer, one may use age-specific, all-cause mortality rates from the U.S. lifetables, which result in 147/100,000 for 40-year-olds and 812/100,000 for 60 year-old women (also appeared in Table 1). If such a model were used to evaluate cancer control strategies, it will underestimate background mortality rate for very obese, current smokers by 58% (147/100,000 vs. 347/100,000) among 40-year-olds and by 61% (812/100,000 vs. 2,086/100,000) among 60 year olds. On the other hand, such model would overestimate background mortality for the normal weight, never smokers by 134% (147/100,000 vs. 63/100,000) among 40-year-olds and by 113% (812/100,000 vs. 381/100,000) among 60 year olds. Similar bias, though of varying magnitude, occurs for modeling colorectal cancer and lung cancer and in race-specific groups (Table 3).

DISCUSSION

Population lifetables are often used to simulate the age of death from causes other than the cancer of interest. Typically, the processes of developing cancer and of dying from other causes are simulated independently: a model may generate times to death from cancer and to death from other causes, and the individual is assumed to die of the cause and age of the younger of the two. Using all-cause life tables for background mortality may be a good approximation to other-cause life tables if the specific cancer cause comprises only a small proportion of overall mortality, and if the specific risk factor modification(s) being studied has little impact on other-cause mortality. However, if the cancer being modeled is responsible for a significant portion of deaths of the population and shares certain prevalent risk factors as its competing causes of deaths (such as heart diseases), such approach is likely to result in substantial bias.

In our paper, we described the methods of deriving nationally-representative, BMI- and smoking-specific mortality rates from competing causes of deaths. The primary purpose of deriving these other-cause life tables is to inform population-based simulation models of a cancer that share common risk factors with background mortality. For the cancer types demonstrated in this analysis, especially breast and colorectal cancers, the assumption of homogenous background mortality was previously used because of a lack of risk specific lifetables. If a factor elevates the risk of death from other cause death but not the cancer (e.g. smoking and breast cancer), then naively using lifetables which do not include smoking status in a simulation models will overestimate the breast cancer deaths and underestimate other cause deaths for current smokers. If the factor elevates the risk of death from both causes (e.g. smoking and lung cancer), then the direction of the bias depends on the relative and absolute levels of cancer versus other-cause mortality rates for each level of the risk factor.

The issue of competing mortality risks in cancer simulation models has been previously addressed by McMahon and colleagues.⁴ They applied a Bayesian evidence-synthesis approach to estimate the other-cause mortality rate, by smoking status, over 1987-1995 to lung cancer simulation models. They used the National Health Interview Survey linked to the National Death Index – similar to our NHANES-linked mortality data—to fit cause-specific hazard models for lung cancer, heart disease, and all causes of death. The strength of their Bayesian approach lies in the handling of uncertainty but at the cost of extensive distributional and model assumptions. More recently, Stewart and colleagues¹⁰ forecasted the joint effect of increasing obesity and reducing smoking on US life expectancy and quality-adjusted life expectancy. Several methodological components of their approach are similar to our study. Using a four-part forecasting model, they combined projections on all-cause mortality rates, prevalence proportions, and relative risks to calculate the mortality rates for 16 BMI and smoking groups. They projected that, between 2005 and 2020, increases in the remaining life expectancy of a typical 18-year-old are held back by 0.71 years or 0.91 quality-adjusted years. These results led the authors to the conclusion that, if obesity trend continues, the negative effect on health can outweigh the positive effect from the population-level decline in cigarette smoking.

Complex simulation models are increasingly being used for understanding the epidemiology and forming and evaluating cancer control strategies. The Cancer Intervention and Surveillance Modeling Network (CISNET) represents a collection of such examples. CISNET is a consortium of investigators sponsored by the National Cancer Institute that use statistical modeling to improve our understanding of cancer control interventions in prevention, screening, and treatment and their effects on population trends in incidence and mortality. It is expected that other-cause life tables described here will be integrated with

other inputs on cancer-specific mortality, risk factors for incident cancers, and other epidemiological inputs in the modeling framework. Accounting for the differential mortality from competing risks in these cancer models allows researchers to evaluate novel cancer screening strategies otherwise difficult to study. For example, investigators from the MISCAN-colon group incorporated the non-CRC mortality risks by obesity and smoking to examine the cost-effectiveness of targeting obese smokers for intensified colorectal cancer screening⁶. Their preliminary findings suggest that the effects on optimal screening schedules of using an average life table or a risk factor specific life table in obese current-smokers are considerable. The effect of obesity and smoking on increasing background mortality somewhat offset the benefit of more intensive screening obese or current smokers who are at higher risk of developing colorectal cancer. Ignoring the impact of risk factors on background mortality will therefore result in overestimation of the benefit of intensified screening among obese current smokers.

Compared to previous studies of similar objectives, our approach has several strengths. We used the same nationally representative data source (NHANES) to derive the prevalence of risk factors and to estimate the corresponding relative risks of mortality. We made no parametric assumptions about the functional forms of the mortality curves by using a semi-parametric, Poisson regression approach in estimating the relative risks. Sampling weights were also used in all steps of estimation, rendering representative estimates for the US population.

Our analysis does have several key limitations. First, we made associations between individuals' risk factor status surveyed at baseline and future mortality. Because there are no follow up interviews between the survey date and the time of death or assumed last-follow-up date, smoking and BMI status likely have changed over time. Generally speaking, BMI later in life is likely to be greater than baseline, and a substantial number of smokers at baseline may have quit smoking to become former smokers. As a result, we included only person-time and event counts up to 15 years from baseline, to partially address this issue. Misclassification would nonetheless remain in the direction of an underestimate of obesity and overestimate of current smokers at the time of death. This misclassification would not likely occur for never smokers (since very few people start smoking past the age of 25). Second, although we excluded events and person time less than three years since baseline, it is possible that there is residual effect from reverse causality. However, some argued that there is no evidence for reverse causation in the relationship between BMI and mortality.¹¹ Nonetheless previous discussions on this topic¹²⁻¹⁵ have guided us to adopt this range of exclusion. Third, our estimates are constrained by available sample sizes, which led to greater uncertainty in groups with fewer observations available, such as older ages, blacks, and deaths among younger ages. As for the small portion of linked mortality data had missing information on the cause of death, we had to assume they are missing at random. Fourth, there exists measurement error with regards to using BMI as a proxy for body fat, although measured BMI in NHANES is highly correlated with body fat.¹⁶ BMI also does not fully capture the mortality benefit from increasing physical activity or improving diet, both may improve survival independent of weight status. In addition, smoking status was based on self-report and thus subject to reporting bias. Fifth, our approach made no inference on the possible lag time between a behavioral change (e.g. quitting smoking) and survival benefit. Users who simulate a life history of smoking status and BMI over the life course need to assume when to switch between the 12 lifetables derived here. Certainly a person who just quit smoking 2 years ago has other-cause mortality closer to that of a current smoker than that of a former smoker. However, mortality may fall rather quickly after risk factor changes in a population, for instance, following a smoking ban in public places.¹⁷ Finally, we did not include calendar effects in our final model for estimating relative risks for mortality from smoking and BMI in order to result in more stable

estimates. However there may exist secular trends on the magnitude of how excess adiposity and smoking affect mortality, especially from cardiovascular diseases. The effect is likely in the direction of smaller increase in mortality risks from BMI and smoking in more recent years. Although there are regional variations in life expectancy and the impact of smoking and BMI and life expectancy, we did not take this into account because the publicly available NHANES do not include such geographical indicators, and the simulation models these lifetables are derived as inputs for do not include regional specifications.

In conclusion, prevalent risk factors which are strong predictors of competing mortality should be considered for constructing lifetables that are used in cancer simulation models. Ignoring differential other-cause mortality, even if the risk factor is not related to the cancer under investigation (e.g. smoking and breast cancer) can result in substantial biases. These biases can have influence over the conclusions on the optimal cancer screening strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Analytic Steps in the Construction of Other-cause Life Tables by Smoking and BMI

Figure 2. Trends in smoking and obesity, by race and sex

Estimated proportion of never smoker (green), former smoker (orange) and current smokers (grey) as well as not overweight (BMI <25, not shaded), overweight (BMI 25-29.9, dotted), obese (BMI 30-34.9, solid grey), and very obese (BMI ≥35, cross-hatched) in the United States, 1970-2000. The proportions are estimated using National Health and Nutrition Examination Surveys (NHANES) 1971-2004.

Panel 1: White Male

Panel 2: White Female

Panel 3: Black Male

Panel 4: Black Female

Panel (a) White Males

Panel (b) White Females

Panel (c) Black Males

Panel (d) Black Females

Figure 3.

Predicted remaining life expectancy at age 40, by BMI and smoking status, and from U.S. lifetables 1970-2003

Y-axis label: Remaining life expectancy at age 40 (years)

Footnote: Estimated from cross-sectional, annual life tables (National Center for Health Statistics, http://www.cdc.gov/nchs/products/life_tables.htm). Mortality rates after age 85 are assumed to be the same across all smoking and BMI categories.

Figure 4.
 Estimated annual probability of death from causes other than breast cancer for cohorts born in 1945, by age, body mass index, and smoking status
 Y axis represents the estimated annual probability of dying from non-breast cancer causes for women born in 1945, in 100,000. The x-axis represents age from 40 to 75 years.
 Columns represent all women, white women, and black women.

Table 1

All-cause, breast cancer, lung cancer, and colorectal cancer mortality rates (per 100,000), by age, sex, and race, 1970 vs. 2000

Sex	Age	All-cause Mortality Rate			Breast Cancer			Lung Cancer			Colorectal Cancer		
		40	60	80	40	60	80	40	60	80	40	60	80
Year 1970													
Male	All races	403 (100%)	2,373 (100%)	11,003 (100%)	-	-	-	17 (4%)	198 (8%)	316 (3%)	4 (1%)	60 (3%)	256 (2%)
	White only	342 (100%)	2,293 (100%)	11,112 (100%)	-	-	-	16 (5%)	196 (9%)	321 (3%)	4 (1%)	60 (3%)	261 (2%)
	Black only	1,018 (100%)	3,449 (100%)	10,954 (100%)	-	-	-	33 (3%)	239 (7%)	265 (2%)	5 (1%)	58 (2%)	192 (2%)
Female	All races	232 (100%)	1,119 (100%)	7,208 (100%)	22 (9%)	78 (7%)	130 (2%)	6 (3%)	37 (3%)	52 (1%)	4 (2%)	48 (4%)	201 (3%)
	White only	191 (100%)	1,034 (100%)	7,241 (100%)	21 (11%)	79 (5%)	132 (2%)	6 (3%)	37 (4%)	53 (1%)	4 (2%)	47 (5%)	205 (3%)
	Black only	556 (100%)	2,118 (100%)	7,482 (100%)	26 (5%)	65 (3%)	101 (1%)	10 (2%)	33 (2%)	49 (1%)	6 (1%)	59 (3%)	142 (2%)
Year 2000													
Male	All races	259 (100%)	1,311 (100%)	7,410 (100%)	-	-	-	8 (3%)	167 (13%)	537 (7%)	4 (1%)	43 (3%)	191 (3%)
	White only	235 (100%)	1,231 (100%)	7,374 (100%)	-	-	-	7 (3%)	164 (13%)	537 (7%)	3 (1%)	41 (3%)	188 (3%)
	Black only	461 (100%)	2,287 (100%)	8,913 (100%)	-	-	-	15 (3%)	236 (10%)	626 (7%)	6 (1%)	66 (3%)	261 (3%)
Female	All races	147 (100%)	812 (100%)	5,178 (100%)	13 (9%)	61 (7%)	133 (3%)	6 (4%)	100 (12%)	264 (5%)	3 (2%)	28 (3%)	133 (3%)
	White only	128 (100%)	767 (100%)	5,130 (100%)	12 (9%)	60 (8%)	134 (3%)	6 (5%)	103 (13%)	272 (5%)	3 (2%)	27 (3%)	131 (3%)
	Black only	279 (100%)	1,269 (100%)	6,338 (100%)	22 (8%)	81 (6%)	142 (2%)	8 (3%)	102 (8%)	216 (3%)	5 (2%)	43 (3%)	171 (3%)

Data source: National Center for Health Statistics. All-cause mortality rates were based on vital statistics reports for single ages; cancer mortality rates were smoothed across 5-year age groups.

Table 2

Relative risk estimates at age 65

Sex	Smoking	BMI*	All-cause Mortality			Causes other than Breast Cancer			Causes other than Lung Cancer			Causes other than Colorectal Cancer		
			All Races	White	Black	All Races	White	Black	All Races	White	Black	All Races	White	Black
Male	Never	<25	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
		25-29.9	0.85	0.85	0.89	0.85	0.86	0.86	0.85	0.86	0.86	0.84	0.84	0.89
		30-34.9	1.30	1.30	1.09	1.33	1.35	1.08	1.33	1.35	1.08	1.29	1.29	1.09
		35+	1.81	1.76	1.55	1.87	1.81	1.55	1.87	1.81	1.55	1.82	1.76	1.57
	Past	<25	1.60	1.73	1.17	1.54	1.08	0.70	1.54	1.08	0.70	1.60	1.74	1.13
		25-29.9	1.26	1.36	0.96	1.16	0.82	0.52	1.16	0.82	0.52	1.28	1.38	0.95
		30-34.9	1.74	1.88	1.06	1.73	1.23	0.63	1.73	1.23	0.63	1.73	1.88	1.03
		35+	2.23	2.40	1.43	2.23	1.57	0.87	2.23	1.57	0.87	2.16	2.35	1.36
	Current	<25	2.56	2.70	2.00	2.21	1.87	1.39	2.21	1.87	1.39	2.58	2.74	1.98
		25-29.9	2.21	2.33	1.81	1.99	1.71	1.26	1.99	1.71	1.26	2.20	2.33	1.79
		30-34.9	3.27	3.44	2.14	2.98	2.54	1.51	2.98	2.54	1.51	3.28	3.47	2.12
		35+	4.17	4.28	2.81	3.86	3.19	2.02	3.86	3.19	2.02	4.25	4.39	2.83
Female	Never	<25	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
		25-29.9	1.26	1.29	0.82	1.29	1.33	0.88	1.27	1.31	0.84	1.26	1.29	0.87
		30-34.9	1.74	1.72	1.10	1.78	1.78	1.16	1.79	1.76	1.14	1.79	1.77	1.18
		35+	2.38	2.46	1.39	2.53	2.63	1.47	2.47	2.55	1.45	2.48	2.55	1.49
	Past	<25	1.15	1.18	1.17	1.23	1.27	1.20	1.06	0.94	0.93	1.19	1.21	1.25
		25-29.9	1.63	1.73	1.10	1.75	1.87	1.17	1.55	1.42	0.90	1.66	1.75	1.22
		30-34.9	2.18	2.26	1.45	2.21	2.33	1.44	2.18	1.96	1.26	2.25	2.33	1.61
		35+	2.66	2.83	1.59	2.76	2.98	1.58	2.61	2.40	1.35	2.75	2.91	1.75
	Current	<25	2.26	2.25	1.78	2.44	2.45	1.83	1.99	1.84	1.48	2.33	2.34	1.77
		25-29.9	2.44	2.64	1.33	2.63	2.87	1.41	2.21	2.21	1.14	2.49	2.69	1.38
		30-34.9	3.26	3.44	1.75	3.54	3.79	1.84	3.02	2.96	1.54	3.38	3.60	1.82
		35+	4.64	5.14	2.29	5.25	5.95	2.48	4.57	4.68	2.14	4.86	5.45	2.41

* BMI: body mass index, defined as weight in kilograms divided by height in meters squared (kg/m^2). BMI is modeled as a continuous variable in our Poisson regression model using the midpoints of each category.

Table 3

Competing mortality rates (per 100,000 annually) for very obese current smokers and for normal weight never smokers (all races) in 2000, under different assumptions, for models of lung cancer, breast cancer, or colorectal cancer.

Assumptions on Competing Mortality Rate		For Models of Lung Cancer		For Models of Breast Cancer	For Models of Colorectal Cancer	
		Men	Women	Women	Men	Women
ALL RACES						
	Use 2000 all-cause U.S. life table	259	147	147	259	147
	Use 2000 all-cause U.S. life table, minus cancer	251	141	134	255	144
Age 40	Use derived other-cause mortality specific for normal weight, never smokers	145	73	63	140	71
	Use derived other-cause mortality specific for very obese, current smokers	606	346	347	632	352
Age 60	Use 2000 all-cause U.S. life table	1,311	812	812	1,311	812
	Use 2000 all-cause U.S. life table, minus cancer	1,145	712	752	1,269	784
	Use derived other-cause mortality specific for normal weight, never smokers	700	389	381	744	410
	Use derived other-cause mortality specific for very obese, current smokers	2,869	1,831	2,086	3,312	2,033
WHITE						
	Use 2000 all-cause U.S. life table	235	128	128	235	128
	Use 2000 all-cause U.S. life table, minus cancer	228	122	116	232	125
Age 40	Use derived other-cause mortality specific for normal weight, never smokers	155	66	53	164	90
	Use derived other-cause mortality specific for very obese, current smokers	531	321	332	491	223
Age 60	Use 2000 all-cause U.S. life table	1,231	767	767	1,231	767
	Use 2000 all-cause U.S. life table, minus cancer	1,064	667	708	1,190	740
	Use derived other-cause mortality specific for normal weight, never smokers	810	382	349	936	554
	Use derived other-cause mortality specific for very obese, current smokers	2,729	1,838	2,164	2,766	1,360
BLACK						
	Use 2000 all-cause U.S. life table	461	279	279	461	279
	Use 2000 all-cause U.S. life table, minus cancer	453	273	257	454	275
Age 40	Use derived other-cause mortality specific for normal weight, never smokers	381	207	176	225	115
	Use derived other-cause mortality specific for very obese, current smokers	830	459	459	1,046	641
Age 60	Use 2000 all-cause U.S. life table	2,287	1,269	1,269	2,287	1,269
	Use 2000 all-cause U.S. life table, minus cancer	2,120	1,169	1,188	2,221	1,226
	Use derived other-cause mortality specific for normal weight, never smokers	2,004	928	845	1,129	539

Assumptions on Competing Mortality Rate	For Models of Lung Cancer		For Models of Breast Cancer	For Models of Colorectal Cancer	
Use derived other-cause mortality specific for very obese, current smokers	4,292	2,040	2,186	5,174	2,997