

# Bias in relative survival methods when using incorrect life-tables: Lung and bladder cancer by smoking status and ethnicity in New Zealand

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Relative survival and excess mortality approaches are commonly used to estimate and compare net survival from cancer. These approaches are based on the assumption that the underlying (non-cancer) mortality rate of cancer patients is the same as that of the general population. This assumption is likely to be violated particularly in the context of smoking-related cancers. The magnitude of this bias has not been estimated. The objective of this article is to estimate the bias in relative survival ratios (RSRs) and excess mortality rate ratios (EMRRs) from using total population compared to correct subpopulation specific life-tables. Analyses were conducted on 1996–2001 linked census–cancer data (including smoking status) for people with lung and bladder cancer, using sex-specific (standard practice), sex- and ethnic-specific, sex- and smoking-specific and sex-, ethnic- and smoking-specific life-tables. Five-year RSRs using sex-specific life-tables, compared to fully stratified life-tables, were underestimated by 10–25% for current smoking and Māori populations. For example, the current smoker male bladder cancer RSR was 0.700 for sex-specific life-tables, compared to 0.838 for fully stratified life-tables. Similarly, EMRRs comparing current to never smokers and Māori to non-Māori were overestimated using sex-specific life-tables only: modestly only for lung cancer, but markedly for bladder cancer. For example, the EMRR comparing current to never smokers with bladder cancer in a fully adjusted regression model was 1.475 when using sex-specific life-tables only, but reduced to 1.098 when using fully stratified life-tables. Substantial bias can occur when estimating relative cancer survival across subpopulations if non-matching life-tables are used.

Relative survival and excess mortality analyses are commonly used to estimate and compare net survival (or excess mortality) among patients with cancer. Relative survival and excess mortality analyses use overall survival and the total number of deaths, respectively, and then adjust for the expected survival and number of deaths using population life-tables. Relative survival ratios (RSRs) are calculated using the ratio of observed survival among cancer patients to the expected survival in the underlying population. Excess mortality rate modelling is a mirror image of survival analyses and usually undertaken with a Poisson model using the observed minus expected number of deaths as the dependent variable.<sup>1–3</sup>

**Key words:** relative survival, excess mortality, life-tables, lung cancer, bladder cancer, bias

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The key advantages of relative survival and excess mortality rate methods are that error due to incorrect coding of cause of death is avoided, and that one captures cancer-consequent deaths through the difference in observed and expected deaths (or survival).<sup>2</sup> The key disadvantage, however, is that one has to assume that the population life-tables provide accurate estimates of the expected mortality rate or survival for the people developing cancer. In other words, these methods assume that those who develop cancer would have had the same risk of mortality as the general population if they had not developed cancer. This assumption is perhaps most obviously violated for smoking-related cancers. Patients with these cancers are considerably more likely to smoke than the general population, and thus are likely to have a higher background mortality rate than that estimated by the general population because of higher rates of chronic respiratory disease, cardiovascular disease and other chronic diseases among smokers.<sup>4</sup> The calculated relative survival for smoking-related cancers is likely to be underestimated because if general population life-tables are used to estimate the background mortality for these patients they will tend to *underestimate* the non-cancer-related deaths in the cancer patient population, thus *overestimating* the cancer-consequent deaths and *underestimating* the relative survival.

This 'non-comparability bias' is also a problem when these methods are used to *compare* the cancer survival experience between groups (such as between regions and cancer services, or between ethnic and socioeconomic groups<sup>5-8</sup>) who may vary in terms of their background mortality. If, as is often the case, only population life-tables by sex are available to estimate expected mortality and survival, comparisons of sub-population cancer survival will be biased without the use of each sub-population's correct life-table. As 'overall' life-tables are, in effect, weighted towards the majority groups within a population, this bias will be most marked for minority groups where such groups have different mortality experiences to the majority. For example, if ethnic differences in survival are being compared, using overall life-tables may not affect the survival estimates for the majority ethnic group, but may well do so for minority groups.

There has been little empiric work on the bias that is likely to be introduced if inaccurate life tables are used in relative survival or excess mortality methods. Dickman *et al.* calculated relative survival estimates by social class for ten cancers sites and compared estimates using general population and social class-specific life-tables.<sup>9</sup> They found that general population life-tables overestimated social class differences, with the difference between the methods being largest when the rate of deaths from non-cancer causes was high. These authors commented that there was likely to be additional bias for smoking-related cancers, but they were unable to adjust background mortality for smoking status. Sarfati *et al.* similarly demonstrated that Māori-specific relative colon cancer survival was underestimated when general population life-tables were used compared to ethnic-specific tables.<sup>2</sup> To date, there has been little or no empirical analysis of the impact of using smoking adjusted life-tables to assess the impact of these biases. The primary reason for this is that the necessary population level smoking data linked to mortality data are rarely, if ever, available.

In New Zealand, smoking questions were included in the 1996 national population census, as well as questions relating to ethnicity and income. We have linked these census data with mortality data, enabling us to calculate life-tables for combinations of sex, ethnicity, income and smoking status.<sup>10,11</sup> This puts New Zealand in the unique position of being able to empirically assess the magnitude of the bias associated with the use of incorrect life tables in relative survival and excess mortality analyses.

The monitoring and analysis of ethnic inequalities in health is important. Māori, the indigenous population comprising about 15% of the total New Zealand population, have a life expectancy about 8 years less than non-Māori.<sup>12</sup> Some of the ethnic inequalities in health arise due to varying survival from disease once diagnosed, including cancer.<sup>7,13</sup> Similar ethnic and socioeconomic inequalities in cancer have been described internationally.<sup>14-20</sup> The accurate quantification of ethnic and socioeconomic inequalities in cancer survival requires the use of ethnic and socioeconomic specific life-tables.

This article, therefore, has two objectives. The first is to quantify the magnitude of bias arising in relative survival analyses from the use of incorrect life-tables. We focus on lung and bladder cancer, both smoking-related cancers and cancers with higher incidence (and worse survival for lung cancer at least) among Māori. We use the life-tables described above, and parallel linked census and New Zealand cancer registration (NZCR) data,<sup>21,22</sup> to address this first objective. We calculate 5-year RSRs for current and never smokers, and Māori and non-Māori for lung and bladder cancer, varying the utilisation of incorrect (*i.e.*, just sex specific) to fully correct life-tables (*i.e.*, sex-, ethnic- and smoking-specific life-tables).

The second objective of this article is to quantify the magnitude of bias in the excess mortality rate ratios (EMRR) comparing current to never smokers, and Māori to non-Māori, for the same two cancers. This objective not only explores the impact of using incorrect life-tables to estimate each strata's expected mortality, but the additional (if any) impact of adjusting in the regression modelling for the covariates of sex, age, ethnicity and smoking status that may confound (or mediate) the association of ethnicity or smoking status with cancer survival itself.

## Material and Methods

### Data

*Linked census and cancer records.* Ethnicity is often misclassified on health data compared to 'gold standard' census data.<sup>23</sup> We, therefore, used linked cancer registration data for 1996–2001 to the 1996 census (which also asked about smoking status) as our base cancer population. The 1996 census and 1996–2001 NZCR data (including mortality follow-up to 2006) were anonymously and probabilistically linked using common variables for geocode, sex, date of birth, ethnicity and country of birth (further details of methods are available elsewhere).<sup>24</sup> Across all cancers, 80% of eligible cancer records were successfully linked to a census record, with at least 95% of linkages estimated to be true linkages.

Adults aged 25–99 at diagnosis who had a primary trachea, bronchus and lung cancer (ICD codes C33–C34) or a primary bladder cancer (ICD code C67), registered in the NZCR between March 6, 1996 and March 6, 2001, and who did not have a death certificate only registration or zero survival time (*i.e.*, 660 and 50 such cases of lung and bladder cancer excluded) were included in the study. The numbers of eligible cancers, linked cancers and cancers with data on both ethnicity and smoking status are listed in Table 1.

The 1996 census used a two-step question approach to elicit smoking status: (i) 'Do you smoke cigarettes regularly (*i.e.*, one or more per day)?', with instructions to not count pipes, cigars or cigarettos; and for those answering 'no', (ii) 'Have you ever been a regular smoker of one or more cigarettes per day?'. Smoking status was categorised into current smokers, ex-smokers and never smokers. Survival and mortality analyses are presented for current and never smokers

**Table 1.** Number of lung and bladder cancer patients diagnosed 1991–1996 by various data set restrictions

	Lung				Bladder			
	Male		Female		Male		Female	
	N	%	N	%	N	%	N	%
Eligible cancer registrations (excluding death certificate only)	4,465	100	2,761	100	2,002	100	736	100
Linked to census record	3,855	86	2,478	90	1,539	77	624	85
Linked to census with non-missing ethnicity	3,180	71	2,064	75	1,500	75	591	80
Linked to census with non-missing ethnicity and smoking status	3,051	68	1,977	72	1,449	72	558	76

only, due to the difficulty of interpreting ex-smoker results in the absence of data on time since quitting. The census ethnicity variable was self-identified, and coded as Māori (any response) and non-Māori.

**Expected mortality—life-tables.** Four population-mortality life-tables were used in our study. The first life-table data set used was the official period New Zealand Life-Table for 1995–1997 that was stratified by single year of age (0–100) and sex ([www.stats.govt.nz](http://www.stats.govt.nz)). These official life-tables were used to generate three additional sets of life-tables for the socio-demographic factors of interest: (i) ethnic-specific (*i.e.*, Māori and non-Māori); (ii) smoking-specific (*i.e.*, never smoker, current smoker and ex-smoker); and (iii) ethnic by smoking-specific life-tables (six levels). These three sets of life-tables were created by combining the official life-tables with: (i) the proportionate distribution of the total population by subpopulation (*e.g.*, smoking prevalence); and (ii) estimates of the differences in subpopulation mortality rates [from the New Zealand Census-Mortality Study (NZCMS), a census-mortality record linkage study ([www.uow.otago.ac.nz/nzcms-info.html](http://www.uow.otago.ac.nz/nzcms-info.html)<sup>10,12,25,26</sup>)]. Due to the large variations in mortality by both smoking and ethnicity, male period life expectancy at birth ranged from 63.8 for Māori current smokers to 78.3 for non-Māori never smokers, and for females from 69.5 to 82.2 years, respectively. Further detail on how these life-tables were derived is published elsewhere.<sup>11</sup>

## Analyses

**Relative survival.** We calculated 5-year RSRs using each of the four population mortality life-tables: (i) sex-specific only; (ii) sex- and ethnic-specific; (iii) sex- and smoking-specific; and (iv) sex-, ethnic- and smoking-specific life-tables. Age-standardised RSRs were calculated using the diagnosed population's age distribution as the external standard, using four age groups (25–54, 55–64, 65–74 and 75–99 years). This method can become unstable with sparse data and differential

background mortality rates between sub-population, and result in wide confidence intervals. Hence, as a sensitivity analysis, we also used internal age-standardisation weights,<sup>27</sup> summarised in Web Annex Table 1. This method allows valid comparisons for the different use of life-tables within a given sub-population, but not necessarily valid comparisons between sub-populations (*e.g.*, current and never smokers) due to varying background mortality rates that influence the weighting.<sup>28</sup> All analyses were undertaken in the Statistics New Zealand data laboratory Wellington using Stata software version 10<sup>29</sup> using relative survival (including standardisation extensions) and generalised linear models commands.

**Excess mortality rate modelling.** The excess mortality rate is the difference between the mortality rate of the cancer populations and the background population mortality rates. It is relatively simple to use Poisson regression modelling of excess mortality rates adjusted for multiple covariates.<sup>1</sup> Three sets of models were run, adjusting for different sets of covariates: (i) sex, age group and ethnicity; (ii) sex, age group and smoking status; and (iii) all of sex, age group, ethnicity and smoking status. Each of these three sets of models was run four times, using the four sets of population mortality life-tables described above. Due to sparse data, each regression model included five annual follow-up intervals. Interaction terms were specified for age group by annual follow-up intervals to allow for commonly observed higher initial excess mortality for older people early in follow-up (65–74, first year; 75–99, first year; 65–74, second year; 75–99, second year; all other age-by-year combinations as the reference). EMRRs comparing, current and ex- to never smokers, and Māori to non-Māori, are presented.

For excess mortality rate regressions (and the internally age-standardised RSRs in Web Annex Table 1), it should be noted that the 95% confidence intervals may be wide due to small numbers (*i.e.*, Māori for both cancers, and never smokers for lung cancer). However, the purpose of this article is to determine systematic shifts in effect sizes from varying life-tables and covariates in the models, with models conducted on the same samples, meaning that our primary interest is on the central estimates—not the random error driven by the sample sizes.

## Results

Table 1 lists the number of eligible cancers that were linked to a census record, and that had complete data. The percentage of eligible cancers with complete data ranged from 68% for male lung cancer to 76% for female bladder cancer, and the number of incident cancers from 558 for female bladder cancer to 3,051 for male lung cancer.

Table 2 summarises the cumulative number of deaths during 5 years of follow-up (which largely determines the statistical precision of the excess mortality rate models) by sex and cancer, and further by ethnicity and smoking status. Numbers are sparse for Māori bladder cancer, as well as for lung cancer cases who were never smokers.

**Table 2.** Number of cancer registrations and cumulative number of deaths at 5 years following registration for lung and bladder cancer patients diagnosed 1996–2001 with follow-up to 2006, by sex, ethnicity and smoking status<sup>1</sup>

	Māori				Non-Māori			
	All	Current	Ex	Never	All	Current	Ex	Never
<i>Number of lung and bladder cancer patients (linked to census with non-missing data)</i>								
<b>Lung</b>								
Males	342	219	69	54	2,679	1,053	1,299	327
Females	345	219	66	60	1,620	669	528	423
<b>Bladder</b>								
Males	42	15	12	15	1,404	285	717	402
Females	21	12	6	–	540	96	135	309
<i>Cumulative number of deaths 5 years following cancer registration</i>								
<b>Lung</b>								
Males	327	216	60	51	2,463	984	1,200	279
Females	321	207	60	54	1,497	603	471	423
<b>Bladder</b>								
Males	24	3	9	12	603	111	318	174
Females	9	6	–	–	252	45	57	150

<sup>1</sup>Counts of patients 5 and below are marked as ‘–’ for suppressed due to confidentiality provisions from using linked census–cancer data. All numbers are random rounded to a near multiple of 3 as per SNZ confidentiality requirements. Note, though, that exact data were used to calculate RSRs and EMRRs.

**Relative survival ratios.** Table 3 summarises the 5-year RSRs for lung and bladder cancer, by smoking status and ethnicity, and for the four varying life-tables used to estimate expected survival. For male cancers, current smoker survival is worse than never smoker survival for lung cancer, and Māori survival is worse than non-Māori survival for both cancers. However, there are some major shifts in the RSRs depending on which life-table is used. Considering the Māori and non-Māori RSRs for bladder cancer (Table 3), moving from just using sex-specific life-tables to sex- and ethnic-specific life-tables, the Māori RSR increases by 19.3% from 0.539 to 0.643 (due to now allowing for the higher background mortality among Māori) and the non-Māori RSR decreases modestly. Similarly, considering the current and never smoker RSRs, moving from just using sex-specific life-tables to sex- and smoking-specific life-tables, the current smoker RSR increases by 20.6% from 0.700 to 0.844 (due to now allowing for the higher background mortality among smokers) and the never smoker RSR decreases by 6.6% from 0.726 to 0.678.

For male lung cancer, the RSRs are much lower than for bladder cancer due to high mortality from lung cancer, limiting the impact of incorrect life-tables in absolute terms. Nevertheless, there are notable relative increases in the Māori RSR when moving from a sex- to sex- and ethnic-specific life-table, and likewise for current smokers when moving from sex- to sex- and smoking-specific life-tables.

Similar patterns of shifts in RSRs with varying life tables to those described above for males are present for females (Table 3).

There are modest shifts in RSRs by ethnicity when moving from sex-specific to smoking-specific life-tables, and *vice versa* in RSRs by smoking status when moving from sex-specific to ethnic-specific life-tables. This is because Māori are more likely to smoke, meaning using ethnic-specific life-tables partly address differences in smoker-related differences in background mortality, and using smoking-specific life-tables partly address differences in ethnic-related differences in background mortality.

The total impact of using fully stratified life-tables, compared to sex-specific only life-tables, is that the absolute gap in RSRs between: Māori and non-Māori for lung cancer is modestly reduced; Māori and non-Māori for bladder cancer is approximately halved; current and never smokers for lung cancer is modestly reduced; and current and never smokers for bladder is largely reduced (females) or reversed (males).

Using internal age standardisation weights found similar patterns (Web Annex Table 1).

**Excess mortality rate ratios.** EMRRs extend and complement the RSR patterns in two ways: by allowing an examination of relative differences on the mortality rate scale (as opposed to cumulative survival proportion scale), allowing greater understanding of the public health impact of subpopulation differences; and by allowing simultaneous covariate adjustment for sex, age, ethnicity and smoking status (as opposed to the RSRs above that could present ethnic and smoking results by sex and standardised by age, but not mutually adjusted for both ethnicity and smoking status due to the limitations of stratification).

Table 4 summarises the EMRRs for current compared to never smokers, and Māori compared to non-Māori, using all

**Table 3.** Five-year RSRs for lung and bladder cancer patients by sex, and by ethnicity and smoking status, using varying life-tables for expected mortality—using the initial population distribution (smoking and ethnic groups combined) by age as the direct standard<sup>1</sup>

Smoking status	Males			Females		
	Current smoker	Never smoker	Difference	Current smoker	Never smoker	Difference
<b>Lung cancer</b>						
a. Sex specific	0.062	0.155	0.094	0.087	0.145	0.059
b. Sex and ethnic specific (% change c.f. a)	0.062 (0.0%)	0.156 (0.6%)	0.094	0.088 (1.1%)	0.147 (1.4%)	0.059
c. Sex and smoking specific (% change c.f. a)	0.071 (14.5%)	0.147 (−5.2%)	0.076	0.098 (12.6%)	0.143 (−1.4%)	0.045
d. Sex, ethnic and smoking-specific (% change c.f. a)	0.071 (14.5%)	0.147 (−5.2%)	0.077	0.098 (12.6%)	0.144 (−0.7%)	0.046
<b>Bladder cancer</b>						
a. Sex specific	0.700 (0.546, 0.840)	0.726	0.026	0.559	0.707	0.148
b. Sex and ethnic specific (% change c.f. a)	0.700 (0.0%)	0.726 (0.0%)	0.027	0.560 (0.2%)	0.710 (0.4%)	0.145
c. Sex and smoking specific (% change c.f. a)	0.844 (20.6%)	0.678 (−6.6%)	−0.166	0.639 (14.3%)	0.692 (−2.1%)	0.053
d. Sex, ethnic and smoking specific (% change c.f. a)	0.838 (19.7%)	0.676 (−6.9%)	−0.161	0.636 (13.8%)	0.690 (−2.4%)	0.054
Ethnicity	Māori	Non-Māori	Difference	Māori	Non-Māori	Difference
<b>Lung cancer</b>						
a. Sex specific	0.038	0.098	0.061	0.061	0.119	0.058
b. Sex and ethnic specific (% change c.f. a)	0.045 (18.4%)	0.098 (0.0%)	0.053	0.070 (14.8%)	0.118 (−0.8%)	0.048
c. Sex and smoking specific (% change c.f. a)	0.041 (7.9%)	0.104 (6.1%)	0.063	0.064 (4.9%)	0.124 (4.2%)	0.060
d. Sex, ethnic and smoking specific (% change c.f. a)	0.048 (26.3%)	0.103 (5.1%)	0.055	0.074 (21.3%)	0.123 (3.4%)	0.049
<b>Bladder cancer</b>						
a. Sex specific	0.539	0.747	0.208	0.436	0.676	0.239
b. Sex and ethnic specific (% change c.f. a)	0.643 (19.3%)	0.743 (−0.5%)	0.100	0.485 (11.2%)	0.672 (−0.6%)	0.187
c. Sex and smoking specific (% change c.f. a)	0.557 (3.3%)	0.780 (4.4%)	0.221	0.463 (6.2%)	0.691 (2.2%)	0.228
d. Sex, ethnic and smoking specific (% change c.f. a)	0.660 (22.4%)	0.773 (3.5%)	0.114	0.527 (20.9%)	0.687 (1.6%)	0.160

<sup>1</sup>Using the initial cancer population as the standard ensures comparability between ethnic and smoking groups. However, estimates may become unstable due to different age structures and background mortality rates between populations. Web Annex Table 1 summarises the same results using internal age weights as per Brenner *et al.*<sup>27</sup> which allows more robust comparisons down columns (but invalid across rows), and gives valid confidence intervals. The pattern of findings with respect to the research questions addressed in this article is similar in Table 3 to those in Web Annex Table 1.

four life-table options to estimate expected mortality, and for covariate adjustments for just sex, age, smoking or ethnicity (Models 1 and 2, respectively), and mutually for both smoking status and ethnicity (Model 3).

Focusing on the impacts of using different life-tables for lung cancer, the reduction in the current:never smoker EMRR when moving from sex-specific to smoking-specific life-tables is 1.279–1.236 (15%). Moving from sex-specific to sex- and ethnic-specific life-tables results in a small reduction of the Māori:non-Māori EMRR from 1.380 to 1.353 (a 7% reduction treating 1.0 as the null). Regarding bladder cancer,

smoking and ethnic EMRRs essentially reduce to the null when using the appropriate life-tables.

Figure 1 shows selected EMRRs from Table 4. For smoking EMRRs, the 'best' estimate is that fully adjusted for background mortality rates, and fully adjusting for all covariates (ethnicity is prior to smoking in a casual model, and hence a confounder). For lung cancer, both the use of correct life-tables and the full covariate adjustment make modest contributions to the change from the crudest EMRR of 1.279 (sex-only life-tables, sex and age covariate adjustment) to the 'best' EMRR of 1.216 (full life-tables and covariate

**Table 4.** Excess rate ratios (RRs; 95% confidence intervals) for lung and bladder cancer patients diagnosed 1996–2001 with follow-up to 2006, for: Maori compared to non-Māori; current compared to never smokers

Cancer and life-tables used to estimate expected mortality	Current compared to never smokers	Māori compared to non-Māori
<i>Lung cancer</i>		
<b>Model 1 (adjusted for sex, age and ethnicity)</b>		
Sex specific		1.380 (1.264, 1.505)
Sex and ethnic specific		1.353 (1.238, 1.478)
Sex and smoking specific		1.382 (1.265, 1.509)
Sex, ethnic and smoking specific		1.355 (1.240, 1.482)
<b>Model 2 (adjusted for sex, age and smoking status)</b>		
Sex specific	1.279 (1.170, 1.399)	
Sex and ethnic specific	1.279 (1.169, 1.394)	
Sex and smoking specific	1.236 (1.131, 1.362)	
Sex, ethnic and smoking specific	1.237 (1.131, 1.330)	
<b>Model 3 (adjusted for sex, age, ethnicity and smoking status)</b>		
Sex specific	1.256 (1.149, 1.374)	1.351 (1.237, 1.475)
Sex and ethnic specific	1.254 (1.149, 1.375)	1.325 (1.212, 1.449)
Sex and smoking specific	1.214 (1.100, 1.327)	1.356 (1.242, 1.483)
Sex, ethnic and smoking specific	1.216 (1.111, 1.330)	1.330 (1.216, 1.455)
<i>Bladder cancer</i>		
<b>Model 1 (adjusted for sex, age and ethnicity)</b>		
Sex specific		1.314 (0.738, 2.340)
Sex and ethnic specific		0.925 (0.439, 1.952)
Sex and smoking specific		1.224 (0.651, 2.302)
Sex, ethnic and smoking specific		0.862 (0.385, 1.929)
<b>Model 2 (adjusted for sex, age and smoking status)</b>		
Sex specific	1.485 (1.114, 1.979)	
Sex and ethnic specific	1.477 (1.109, 1.968)	
Sex and smoking specific	1.089 (0.801, 1.481)	
Sex, ethnic and smoking specific	1.092 (0.805, 1.482)	
<b>Model 3 (adjusted for sex, age, ethnicity and smoking status)</b>		
Sex specific	1.475 (1.106, 1.966)	1.266 (0.716, 2.239)
Sex and ethnic specific	1.476 (1.109, 1.965)	0.921 (0.452, 1.876)
Sex and smoking specific	1.083 (0.796, 1.473)	1.253 (0.681, 2.303)
Sex, ethnic and smoking specific	1.098 (0.810, 1.487)	0.861 (0.388, 1.910)

adjustment). However, the impacts for bladder cancer are more substantive, with a shift from the crudest EMRR of 1.485 to the best EMRR of 1.098, almost entirely due to using the full life-tables.

For ethnic EMRRs, the 'best' estimate is that fully adjusted for background mortality rate variations (*i.e.*, using the full sex-, ethnic- and smoking-specific life-tables), and that adjusted for the covariates sex and age that potentially confound the ethnicity–survival association (*i.e.*, the total effect of ethnicity on lung cancer survival, before considering the mediator of smoking). This 'best total effect' is the third column for each of lung and bladder cancer in Figure 1a. For lung cancer, this 'best total effect' ethnic EMRR is only

slightly different in absolute terms from that estimated using sex-only specific life-tables. But for bladder cancer, there is a substantial decrease in the ethnic EMRR, due principally to the use of correct life-tables. Additional adjustment for smoking estimates the direct effect of ethnicity on survival, independent of pathways through smoking. For both bladder and lung cancer, there was little shift in the EMRR with this additional mediator adjustment.

## Discussion

Our study provides quantification of bias in relative survival and excess mortality, arising from incorrect life-tables used to allow for background mortality. We find that using the

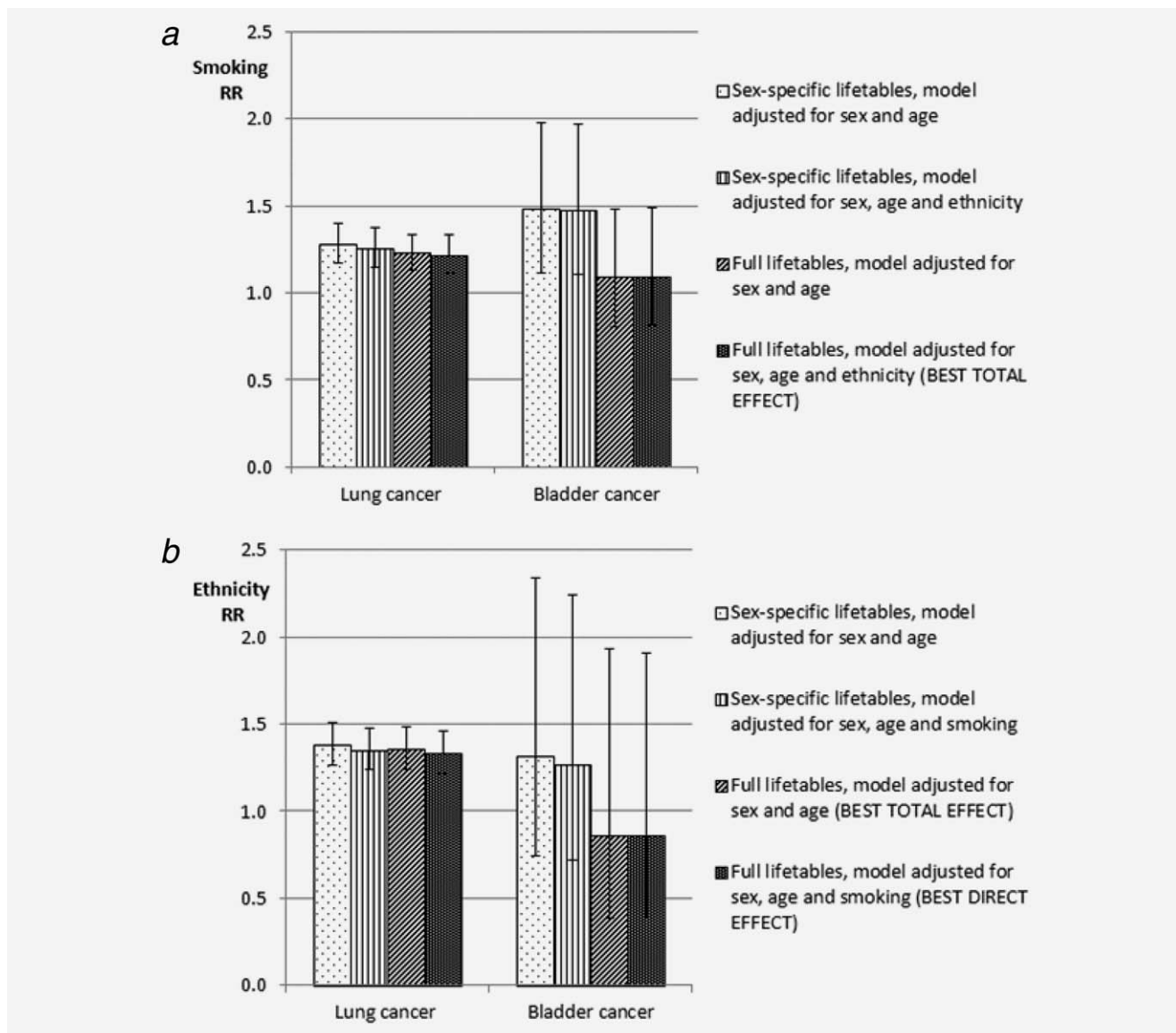


Figure 1. EMRRs by life-tables used [sex specific only; sex-, ethnic and smoking-specific life-tables ("Full")] and covariates included in excess mortality rate model [sex and age (model 2); plus either smoking or ethnicity (model 3)], for males and females combined. (a) RRs for current compared to never smokers, for lung and bladder cancer. (b) RRs for Māori compared to non-Māori for lung and bladder cancer.

incorrect sub-population life-tables for groups with higher mortality (*i.e.*, current smokers and Māori compared to total New Zealand population) results in underestimates of relative survival. Current smoker RSRs were underestimated by 10–20% when not using smoking-specific life-tables, and Māori RSRs were underestimated by up to 20% for lung and bladder cancer when incorrectly using sex-specific life-tables compared to ethnic-specific life-tables (and more so when additionally using smoking-specific life-tables). Similarly, EMRRs comparing smokers to non-smokers were overestimated when not using smoking status-specific life-tables—more notably for bladder cancer than lung cancer. The EMRRs comparing Māori to non-Māori were overestimated if ethnic-specific life-tables were not used. Some life-tables (*i.e.*, ethnic-

specific life-tables) may partly capture the differences in background mortality by other characteristics (*e.g.*, smoking) when they are correlated in the general population. For the empiric examples examined in this article at least, bias from incorrect use of life-tables was more important than incomplete adjustment for covariates in excess mortality rate modelling. Moreover, adjusting for covariates of smoking status and ethnicity, without correct use of life-tables to first estimate expected mortality, did not notably 'fix' the bias due to inappropriate life-tables. Rather, using appropriate and correct life-tables was the most important step in reducing bias in the excess mortality rate modelling.

There is inconsistent use of sub-population background mortality life-tables in cancer patient's survival studies,

examining ethnic and socioeconomic differences in cancer patient's survival. For instance in the United States, the application of ethnic-specific life-tables has been cited in the studies examining non-Hodgkin lymphoma and anal cancer survival.<sup>16,17,30</sup> However, the use of ethnic-specific life-tables was not documented for other similar studies for prostate and lung cancers.<sup>18–20</sup> Socioeconomic-specific population mortality life-tables are increasingly applied in relative survival studies such as overall trends in cancer survival in England and Wales, breast cancer survival in New Zealand and colon cancer survival in Sweden.<sup>14,15,31,32</sup>

To our knowledge, this is the most comprehensive empiric examination, to date, of the magnitude of non-comparability bias inherent in relative survival and excess mortality analyses. However, there are limitations in the analyses presented in this article. First, the number of cancers (and more importantly deaths) arising among Māori and never smokers (especially for bladder cancer) were few, making confidence intervals about many of the EMRRs wide. However, this article assessed systematic bias. As we are not sampling a different population with each re-estimate the confidence intervals are not particularly relevant, and shifts in the central estimates can be interpreted with reasonable confidence. Second, the results are (somewhat) specific to the New Zealand context. That said, smoking-related mortality has obvious generalisability across countries, and for social groups with differences of about 8 years in life expectancy in other countries, one

might expect similar biases to that shown in this article for Māori compared to non-Māori. Third, there are some limitations with the New Zealand data including incomplete linkage of cancer records to census data (approximately 20% not linked). However, it would take a very different set of associations among this 20% of unlinked records compared to the 80% linked for selection bias to be problematic.

The key recommendation arising from this empiric article, and consistent with theoretical expectation, is that it is critical to use sub-population life-tables for estimating relative survival when those sub-populations have marked variation in background mortality rates. However, often only sex-specific life-tables are used. In the absence of subpopulation-specific life-tables for a given analysis, researchers should consider sensitivity analyses about their key findings, such as using a derived life-table that more accurately reflects their cancer population's background mortality experience.

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