

## Technical Appendix

### Methods

Multi-state life tables were used to determine remaining Health-adjusted life expectancy (HALE)<sup>1,2</sup> of Australian adults aged 35 to 80 years of age in the year 2000 divided amongst mutually exclusive groups defined by tobacco use: (i) Lifelong never smokers and non-snus users; (ii) Current smokers in the year 2000 who continue to smoke; (iii) Current smokers in the year 2000 who quit all tobacco use; (iv) Current smokers in the year 2000 who switch to snus; and (v) Never smokers in the year 2000 who become lifelong snus users. Changes in tobacco use, e.g. quitting all tobacco use or starting to use snus, are assumed to be instantaneous in the year 2000 with no further changes in tobacco use after this year. The model was constructed in Microsoft Excel.

### Mortality rates by smoking status in the year 2000

As there is no direct source of Australian mortality rates stratified by smoking status (never, former, or current smokers), we first estimated tobacco-attributable mortality rates for smokers and former smokers combined, for the causes listed in Table 1.

**Table 1: Tobacco-related causes of mortality in model<sup>3</sup>**

<b>Cause</b>	<b>ICD-10 code</b>
Ischemic heart disease	I20-I25
Arterial disease	I70-I79
Stroke	I60-I69, G45
Other CVD	I26,I27.1,I28,I43-45,I47.0- I47.1,I47.9,I48,I49.1-.9,I51.0- I51.4,I52,I77-I84,I86-I97,I98.1-I98.8,I99
Lung cancer	C33-C34
Upper aerodigestive cancer	C00-C14
Pancreas cancer	C25
Bladder cancer	C67
Kidney cancer	C64-C66,C68
Chronic obstructive pulmonary disease	I27.0,I27.8-I27.9;J40-J44
Other respiratory disease	J30-J39,J47-J99

Tobacco-attributable lung cancer rates were estimated as the difference between age-and-sex specific lung cancer mortality rates in the Australian population from the Australian Bureau of Statistics (ABS), and lung cancer mortality rates in never smokers from the American Cancer Society Cancer Prevention Study II (CPS-II) – the largest recent cohort study of tobacco exposure and associated health outcomes.<sup>4</sup>

For other tobacco-related cancers and chronic obstructive pulmonary disease (COPD) we calculated the smoking impact ratio (SIR; Equation 1), an artificial compound prevalence measure of accumulated past exposure to cigarette smoking in a population relative to the CPS-II population.<sup>5</sup> The SIR represents the proportion of equivalent lifelong smokers from CPS-II in the population of interest.

**Equation 1:**

$$SIR = \frac{C_{LC} - N_{LC}}{S_{LC} - N_{LC}}$$

Where:

$C_{LC}$  is the age-sex-specific lung-cancer mortality rate in the Australian population for the year 2000 from ABS;

$N_{LC}$  is the age-sex-specific lung-cancer mortality rate of never-smokers from CPS-II; and

$S_{LC}$  is the age-sex-specific lung cancer mortality rate of lifelong smokers from CPS-II.

The SIR was used instead of current prevalence in a population attributable fraction (PAF; Equation 2) with relative risks from CPS-II (Table 2) to determine the fraction of age-sex-cause-specific mortality rates in the Australian population in the year 2000 that is attributable to smoking. For all other conditions the prevalence of smoking a year prior to the baseline was used, assuming a short lag between exposure and outcomes.<sup>6</sup>

**Equation 2:**

$$PAF = \frac{p(RR - 1)}{p(RR - 1) + 1}$$

Where:

$p$  is prevalence (SIR for COPD, cancers); and

$RR$  is the relative risk in smokers versus the never smokers (from CPS-II; Table 2)

**Table 2: Relative risks (RR) of tobacco related disease (other than lung cancer) in lifelong smokers compared to never smokers from the American Cancer Society Cancer Prevention Study II (CPS-II)<sup>7</sup>**

Tobacco Related Disease	Relative Risk (95% Confidence Interval)	
	Males	Females
Upper aerodigestive tract	8.1 (5.7-11.7)	6.0 (4.3-8.5)
Pancreas cancer	2.2 (1.7-2.8)	2.2 (1.8-2.8)
Urinary bladder cancer	3.0 (2.1-4.3)	2.4 (1.5-4.1)
Kidney, other urinary cancer	2.5 (1.8-3.6)	1.5 (1.0-2.1)
Ischemic heart disease		
35-64 years	2.6 (2.4-2.9)	3.2 (2.8-3.6)
65+ years	1.5 (1.3-1.6)	1.7 (1.6-1.9)
Stroke		
35-64 years	2.4 (1.8-3.0)	3.8 (3.1-4.7)
65+ years	1.5 (1.2-1.8)	1.6 (1.4-1.9)
Arterial disease	3.9 (3.1-4.9)	3.8 (3.1-4.8)
Other CVD	1.8 (1.6-2.0)	1.7 (1.5-1.9)
Chronic obstructive pulmonary disease	10.8 (8.4-13.9)	12.3 (9.9-15.2)
Other respiratory disease	1.9 (1.5-2.4)	2.2 (1.7-2.8)

The fraction of current mortality rates attributable to tobacco calculated above is a function of accumulated risk from past as well as current (year 2000) exposure and therefore includes risk attributable to those who currently smoke as well as those who are former smokers. To determine the proportion of the tobacco attributable mortality rate in current smokers only, we used information on self-reported years since quitting in former smokers from The Australian Diabetes, Obesity and Lifestyle Study (AusDIAB),<sup>8</sup> along with estimates of risk reversal following smoking cessation to apportion the tobacco attributable mortality rate between current and former smokers (Equation 3). Relative risks of lung cancer, COPD and CVD in former smokers compared to current smokers by year since quitting were derived by fitting a Weibull distribution to the CPS-II estimates of risk reversal<sup>9</sup> (Figures 1 to 3). We assumed that risk reversal values for lung cancer were applicable to lung, upper aerodigestive, pancreatic, bladder and kidney cancer; and that risk reversal values for CVD also applied to respiratory disease other than COPD.<sup>10</sup>

**Equation 3:**

$$AF_{CS} = \frac{p_{CS}}{(p_{FS} \times RR_{FS} + p_{CS})}$$

Where:

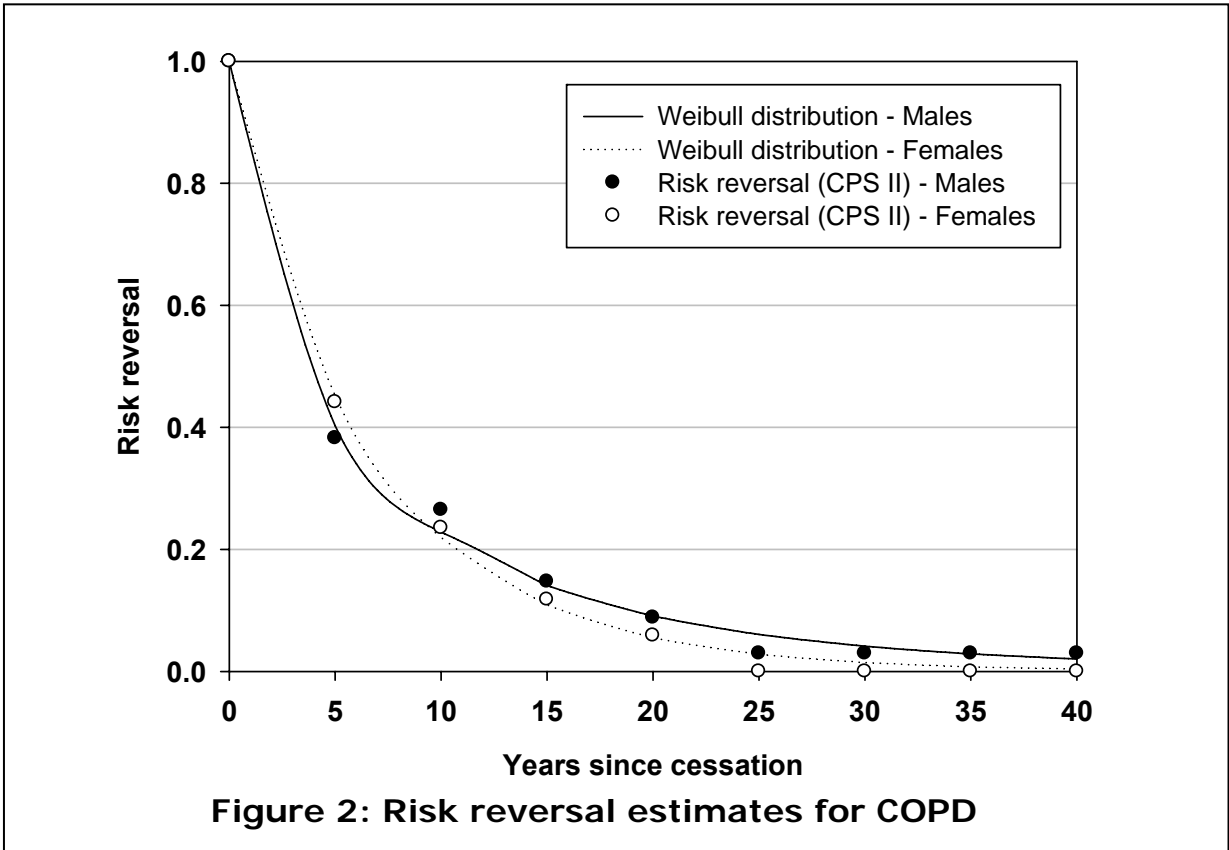
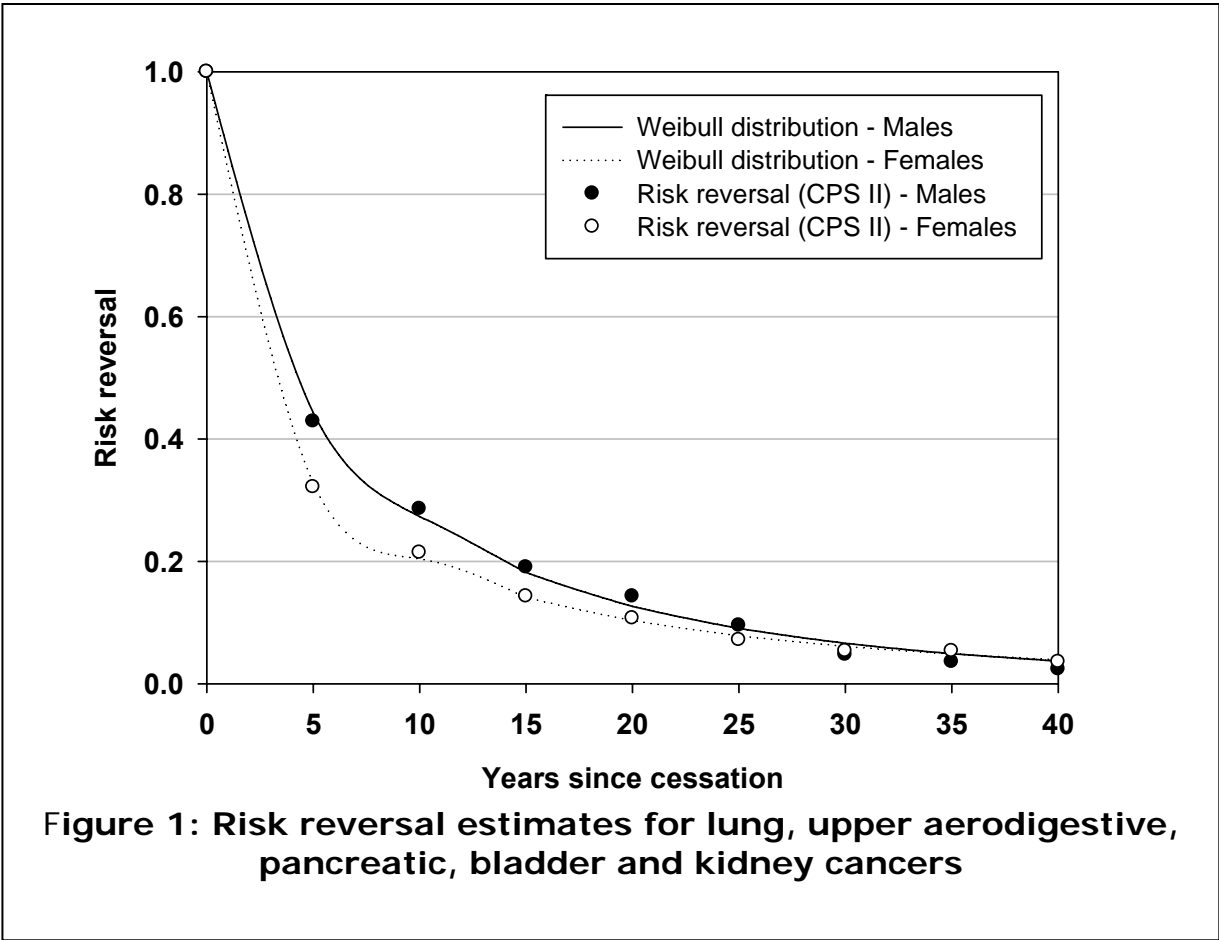
$AF_{CS}$  is the proportion of the tobacco attributable fraction due to current smokers;

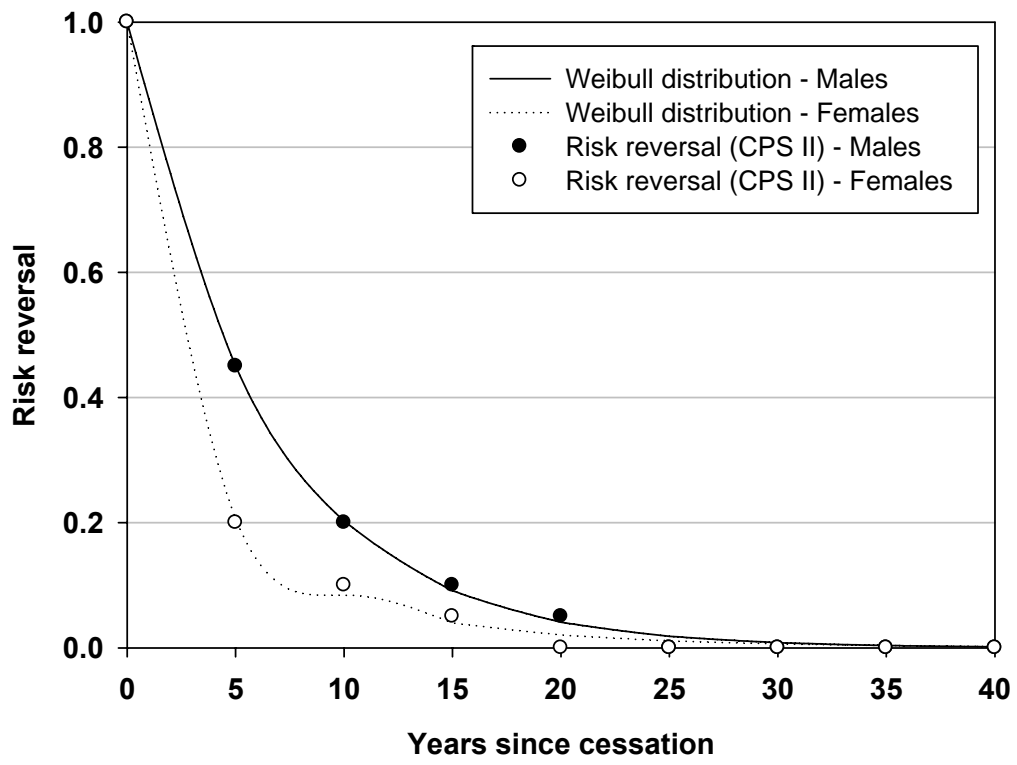
$p_{CS}$  is the prevalence of current smokers;

$p_{FS}$  is the prevalence of former smokers; and

$RR_{FS}$  is the average relative risk of tobacco attributable mortality in former smokers compared to current smokers based on reported years since quitting smoking.

The proportion of current tobacco attributable mortality due to current smokers by cause is shown in Table 3.



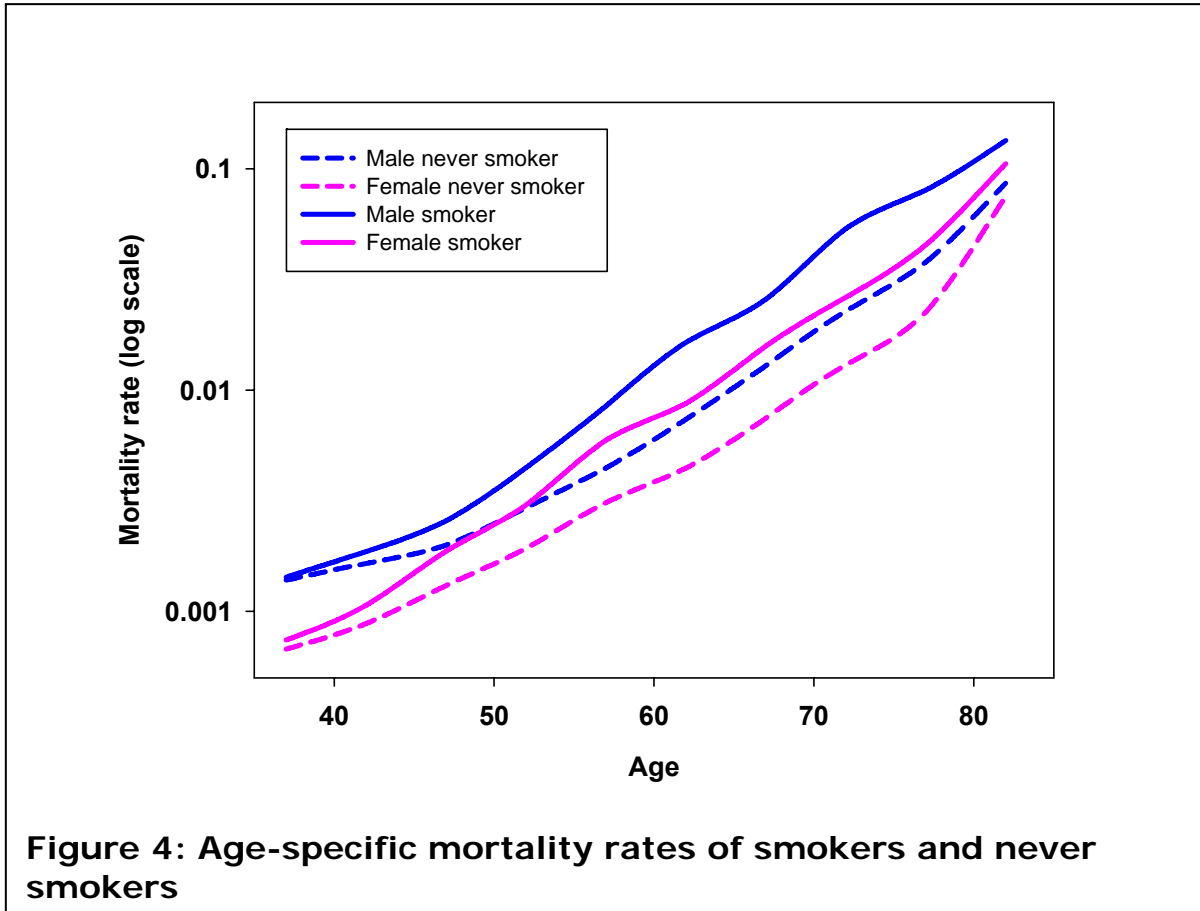


**Figure 3: Risk reversal estimates for CVD and Respiratory Disease other than COPD**

**Table 3: Proportion of tobacco attributable mortality that is attributable to current smokers, by age, sex and cause**

Cause of mortality	Smoking attributable age-specific mortality rate									
	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84
<b>Males</b>										
Lung cancer	83%	74%	78%	75%	66%	63%	63%	51%	42%	42%
Upper aerodigestive cancer	83%	74%	78%	75%	66%	63%	63%	51%	42%	42%
Pancreas cancer	83%	74%	78%	75%	66%	63%	63%	51%	42%	42%
Kidney cancer	83%	74%	78%	75%	66%	63%	63%	51%	42%	42%
Bladder cancer	83%	74%	78%	75%	66%	63%	63%	51%	42%	42%
Ischemic heart disease	86%	79%	83%	83%	75%	73%	73%	71%	57%	58%
Stroke	86%	79%	83%	83%	75%	73%	73%	71%	57%	58%
Arterial disease	86%	79%	83%	83%	75%	73%	73%	71%	57%	58%
Other CVD	86%	79%	83%	83%	75%	73%	73%	71%	57%	58%
COPD	85%	77%	81%	79%	71%	69%	68%	58%	46%	46%
Other respiratory disease	86%	79%	83%	83%	75%	73%	73%	71%	57%	58%
<b>Females</b>										
Lung cancer	79%	76%	80%	80%	69%	80%	56%	63%	49%	67%
Upper aerodigestive cancer	79%	76%	80%	80%	69%	80%	56%	63%	49%	67%
Pancreas cancer	79%	76%	80%	80%	69%	80%	56%	63%	49%	67%
Kidney cancer	79%	76%	80%	80%	69%	80%	56%	63%	49%	67%
Bladder cancer	79%	76%	80%	80%	69%	80%	56%	63%	49%	67%
Ischemic heart disease	88%	88%	91%	93%	86%	91%	76%	86%	78%	89%
Stroke	88%	88%	91%	93%	86%	91%	76%	86%	78%	89%
Arterial disease	88%	88%	91%	93%	86%	91%	76%	86%	78%	89%
Other CVD	88%	88%	91%	93%	86%	91%	76%	86%	78%	89%
COPD	76%	74%	81%	84%	70%	81%	57%	71%	58%	77%
Other respiratory disease	88%	88%	91%	93%	86%	91%	76%	86%	78%	89%

Using prevalence of current and never smokers, cause-specific mortality rates and attributable fractions derived above, age-sex-specific mortality rates from all causes for never smokers and current smokers are shown in Figure 4.



### Mortality risk following smoking cessation

For smokers who quit all tobacco use in each age group in the year 2000, the mortality rate at successive ages was determined by the addition of the all-cause mortality rate of never-smokers and summing across all tobacco-related causes the product of the risk reversal estimates by years since quitting (Figure 1 to 3) and the tobacco attributable mortality rates in current smokers.

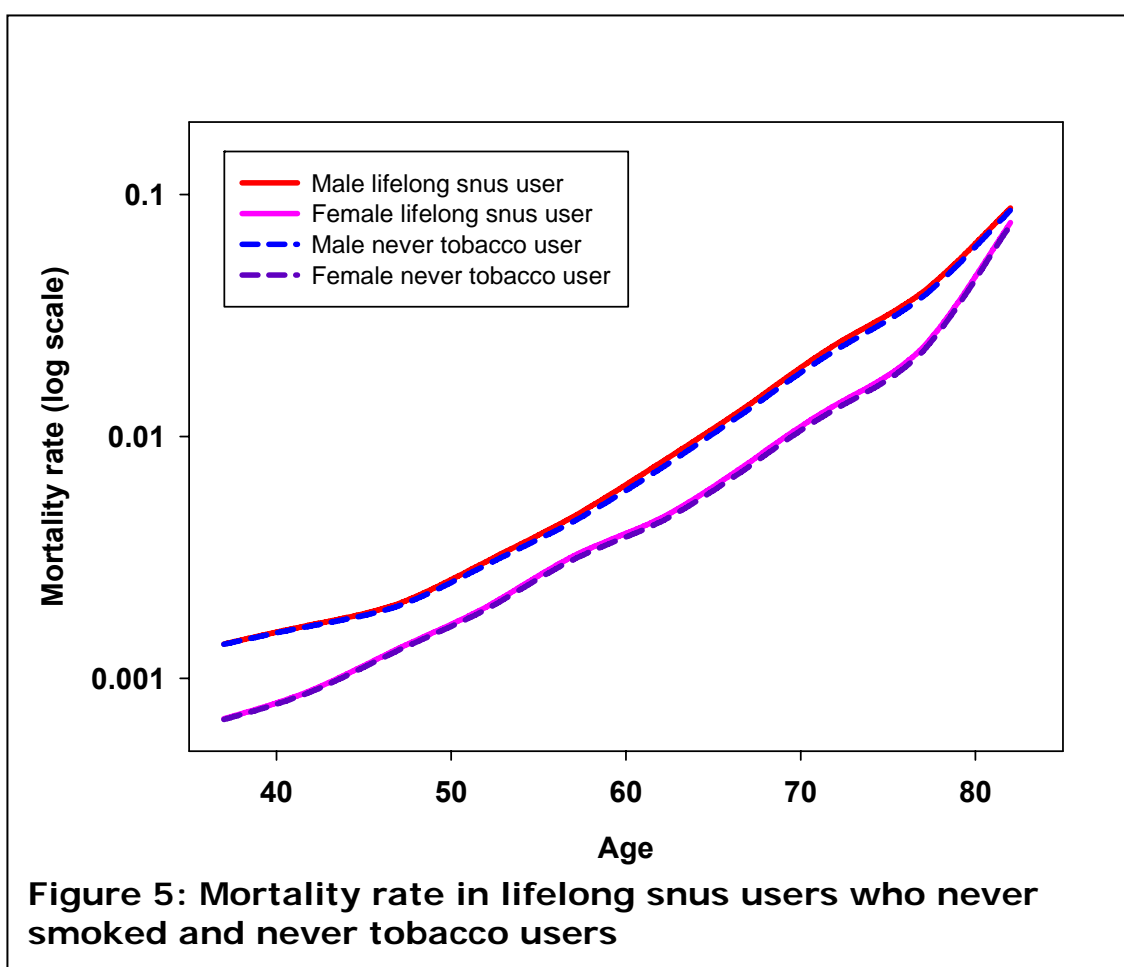
### Mortality risk associated with lifelong snus use

Mortality from lung cancer, oral cancer and heart disease attributable to snus use was based on estimates of a panel of international experts<sup>11</sup> (Table 4). We conservatively assumed that the panel's estimate for heart disease mortality in snus users also applied to mortality due to stroke, arterial disease and other cardiovascular diseases. We also assumed that their estimate for oral cancer mortality applied to all upper aerodigestive cancers, and cancer of the pancreas, bladder and kidney. No excess mortality from COPD or other respiratory diseases for snus users was included.<sup>12</sup>

**Table 4: Relative risk of tobacco attributable mortality in snus users who have never smoked compared to current smokers**

Mortality due to:	Relative risk	
	35-49 year olds	≥ 50 year olds
all CVDs (including coronary heart disease, stroke and arterial disease)	0.10	0.10
upper aerodigestive, pancreatic, bladder and renal cancer	0.15	0.30
Lung cancer	0.02	0.034

These values were applied to the cause-specific tobacco-attributable mortality rate in current smokers to obtain the mortality rate attributable to snus in lifelong users who had previously never smoked. Figure 5 shows total mortality rates from all causes in never smokers compared to lifelong snus users.



### Mortality risk associated with smokers who switch to snus

Current smokers who switch to snus were assumed to have the same excess mortality as smokers who quit tobacco entirely (i.e. based on risk reversal estimates from CPS-II) and the excess mortality associated with using snus combined in a multiplicative formula (Equation 5).



**Equation 5:**

$$M_{CS \rightarrow Sn} = M_{CS} (1 - (1 - RR_{FS})(1 - RR_{Sn}))$$

Where:

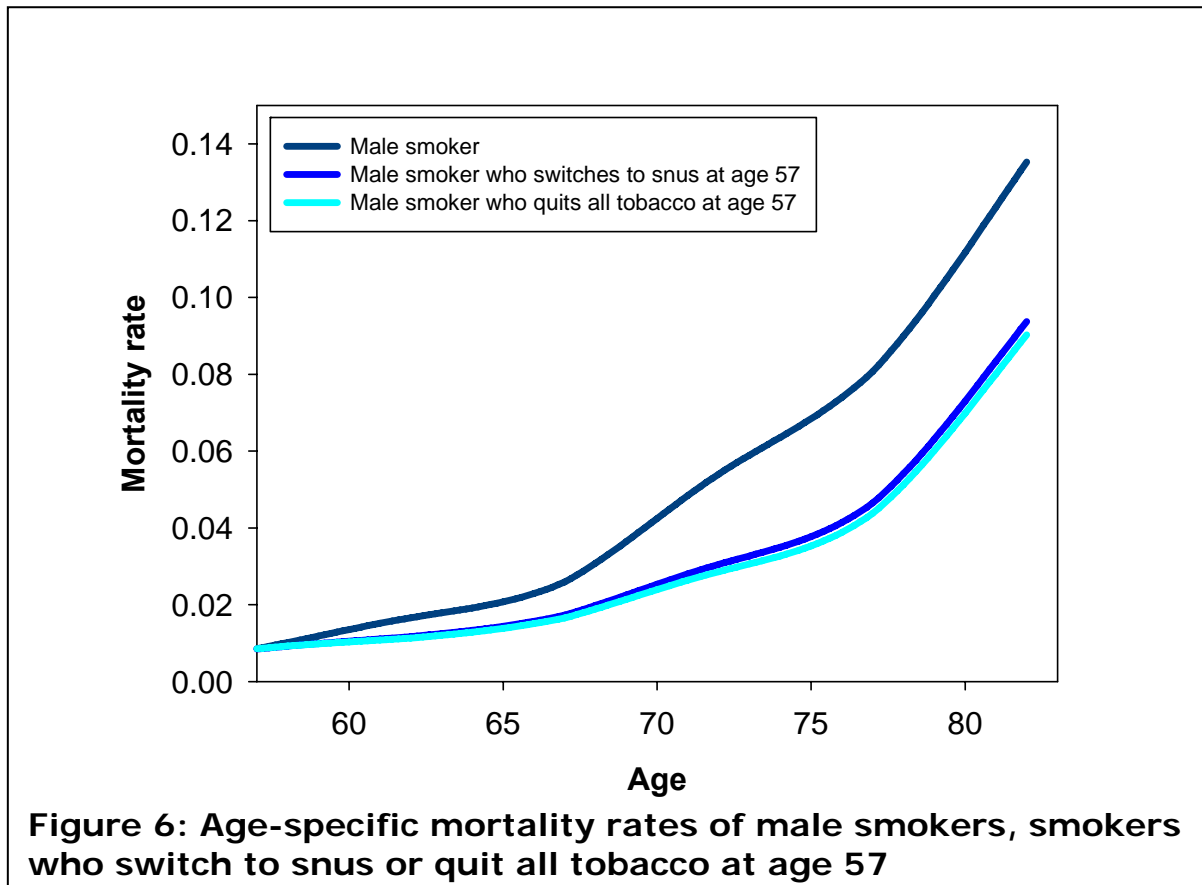
$M_{CS \rightarrow Sn}$  is the excess mortality rate in current smokers who switch to snus;

$M_{CS}$  is the tobacco attributable mortality rate in current smokers;

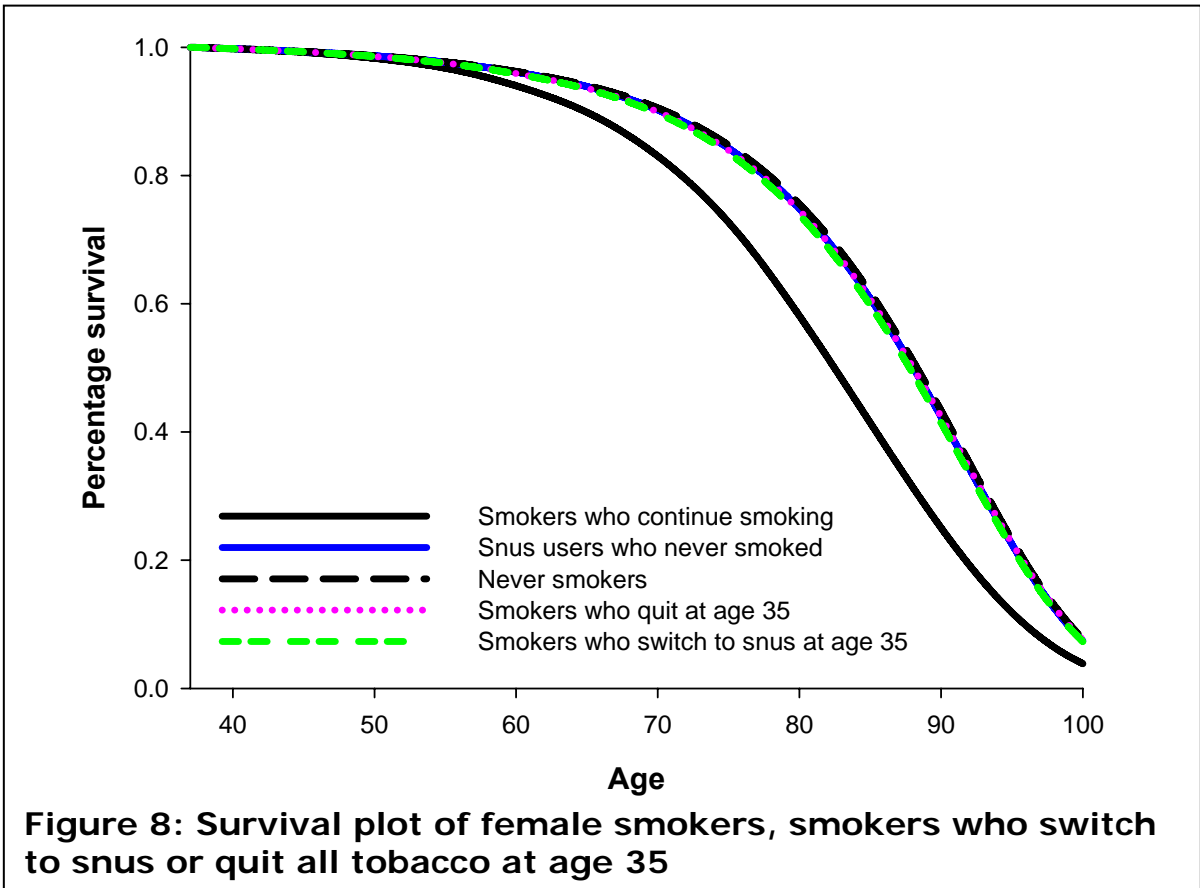
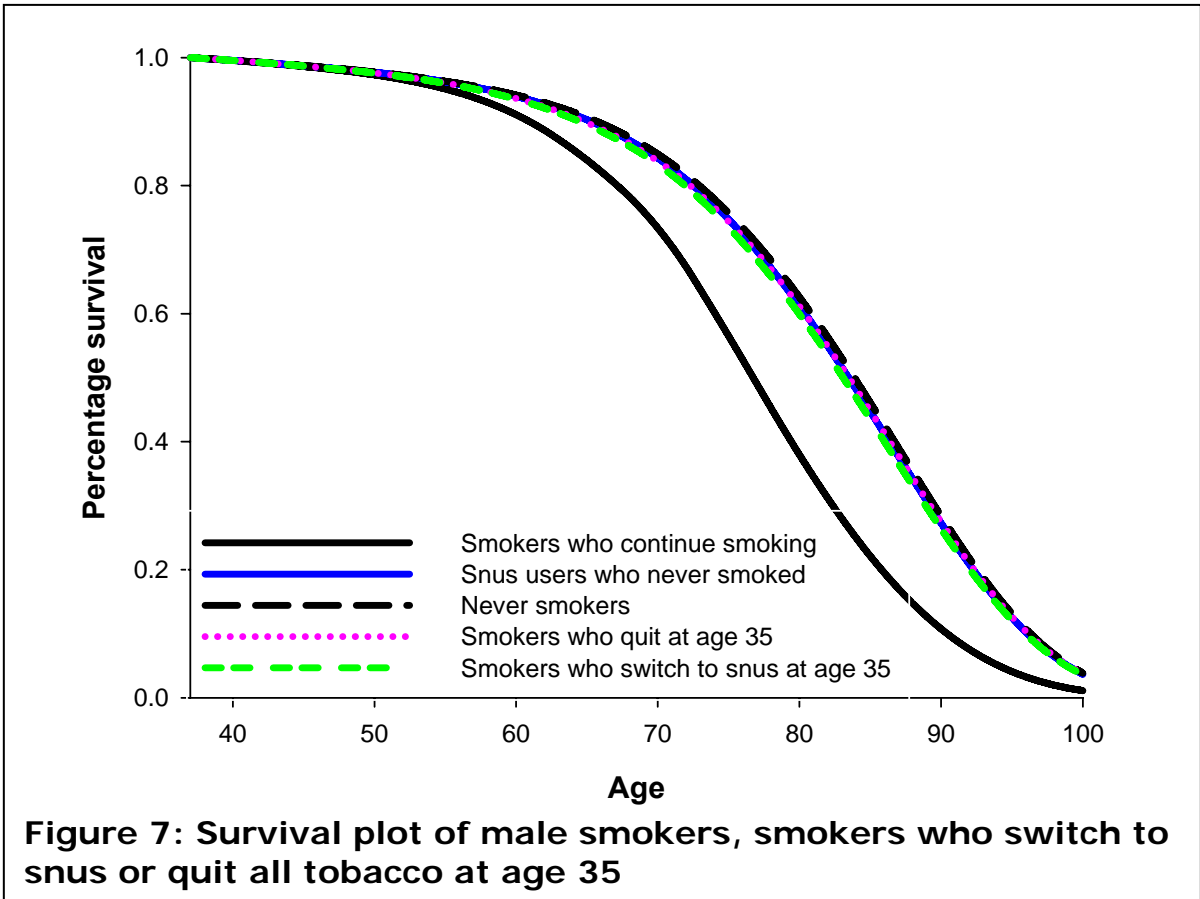
$RR_{FS}$  is the relative risk of tobacco attributable mortality in former smokers compared to current smokers based on years since quitting (Figure 1 to 3); and

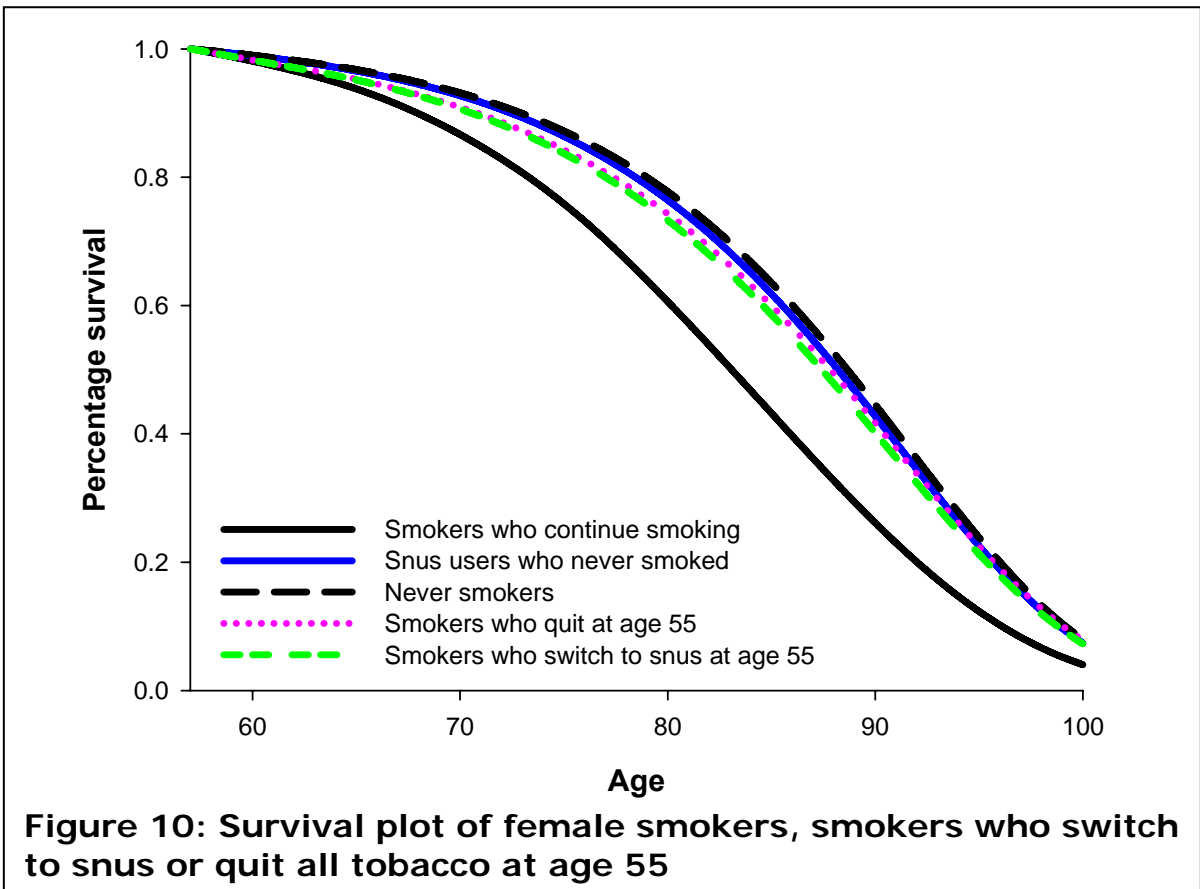
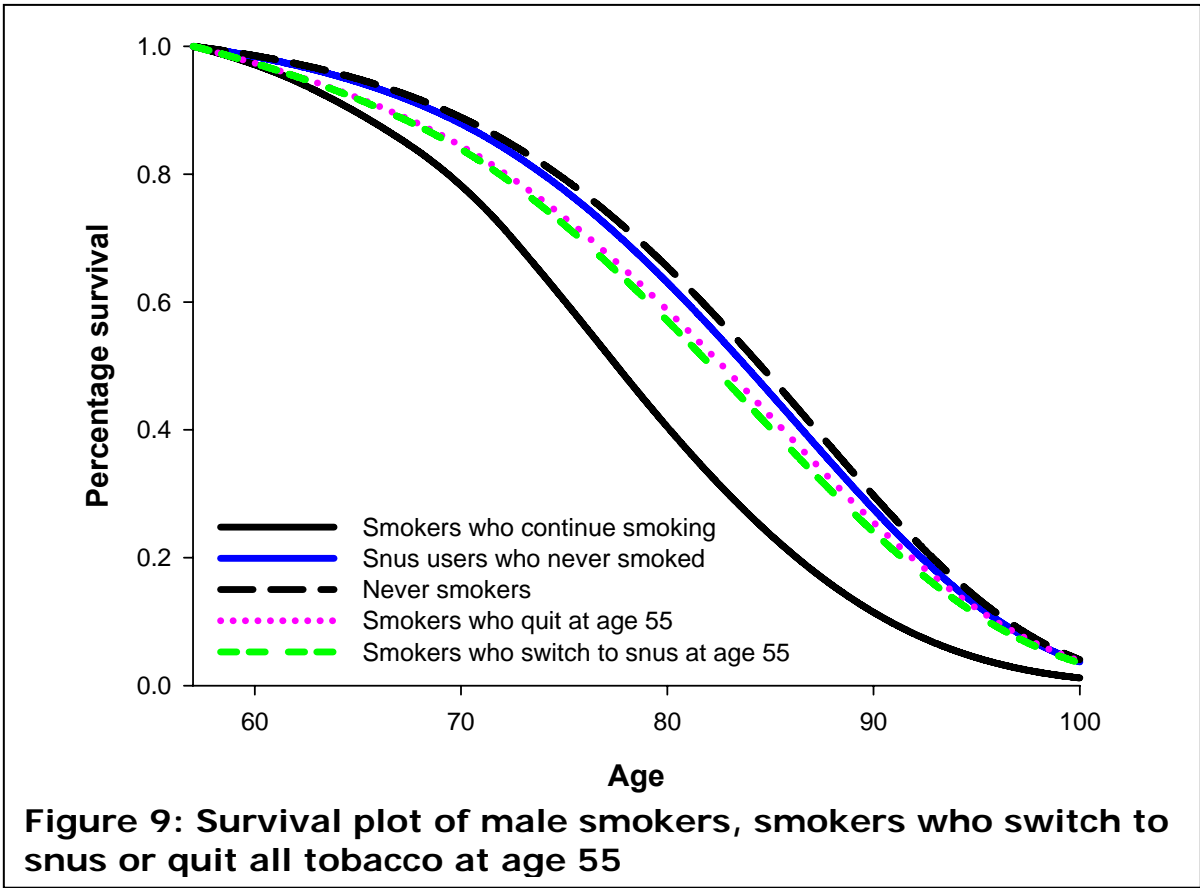
$RR_{Sn}$  is the relative risk of tobacco attributable mortality in snus users who never smoked compared to current smokers (Table 4).

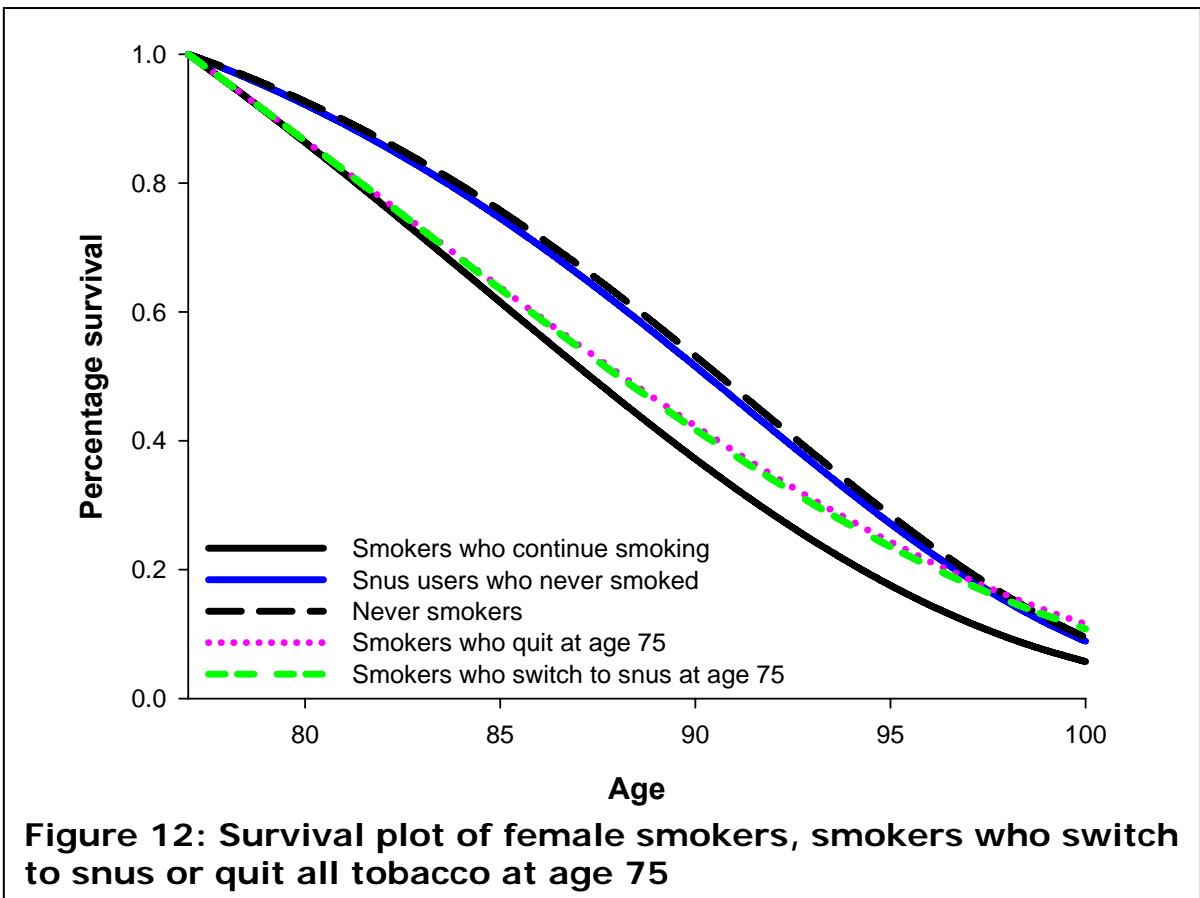
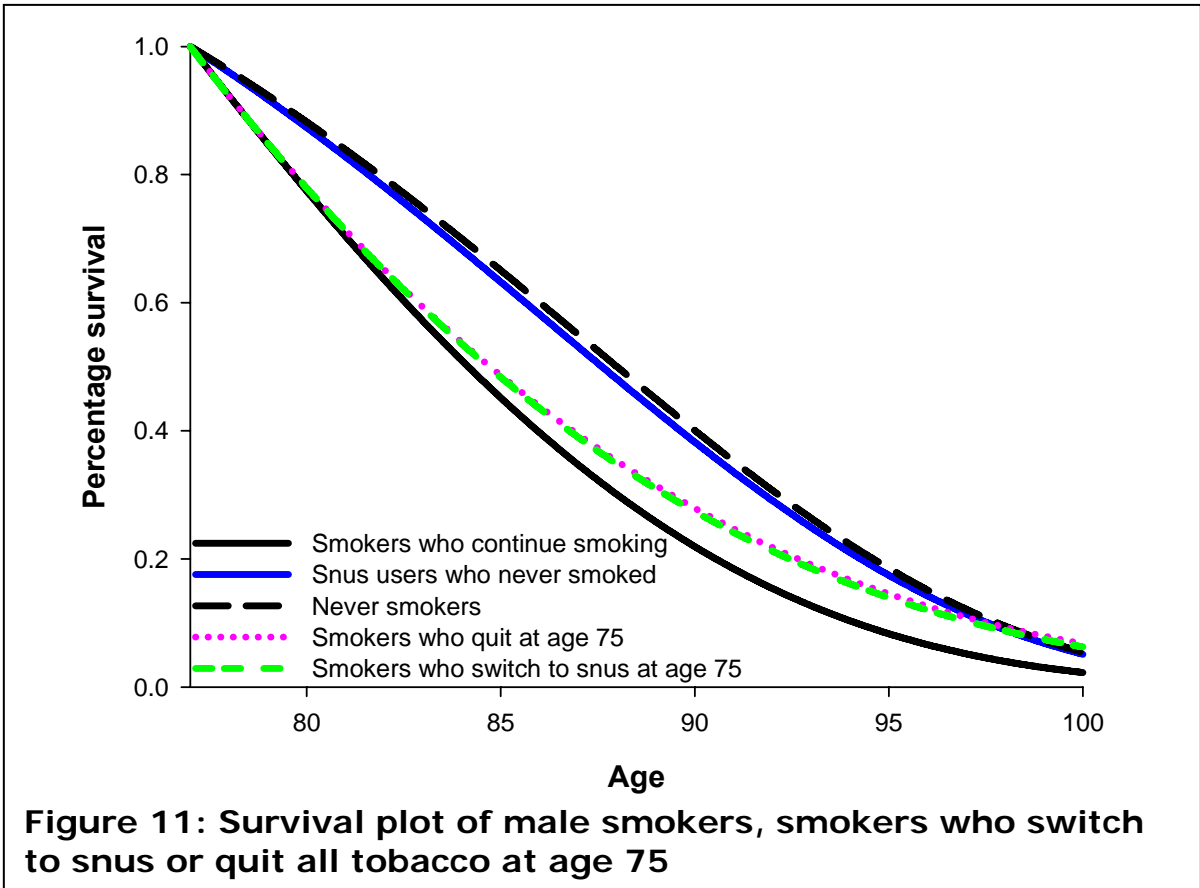
Figure 6 shows age-specific mortality rates from all causes in a current male smoker who continues to smoke, a male smoker who quits tobacco use altogether at age 57 and a male smoker who switches to snus at age 57.



Figures 7 to 12 show survival plots of a cohort of smokers aged 35, 55 and 75 who continue to smoke, snus users aged 35, 55 and 75, smokers who quit tobacco use altogether at ages 35, 55 and 75 and smokers who switch to snus at ages 35, 55 and 75.



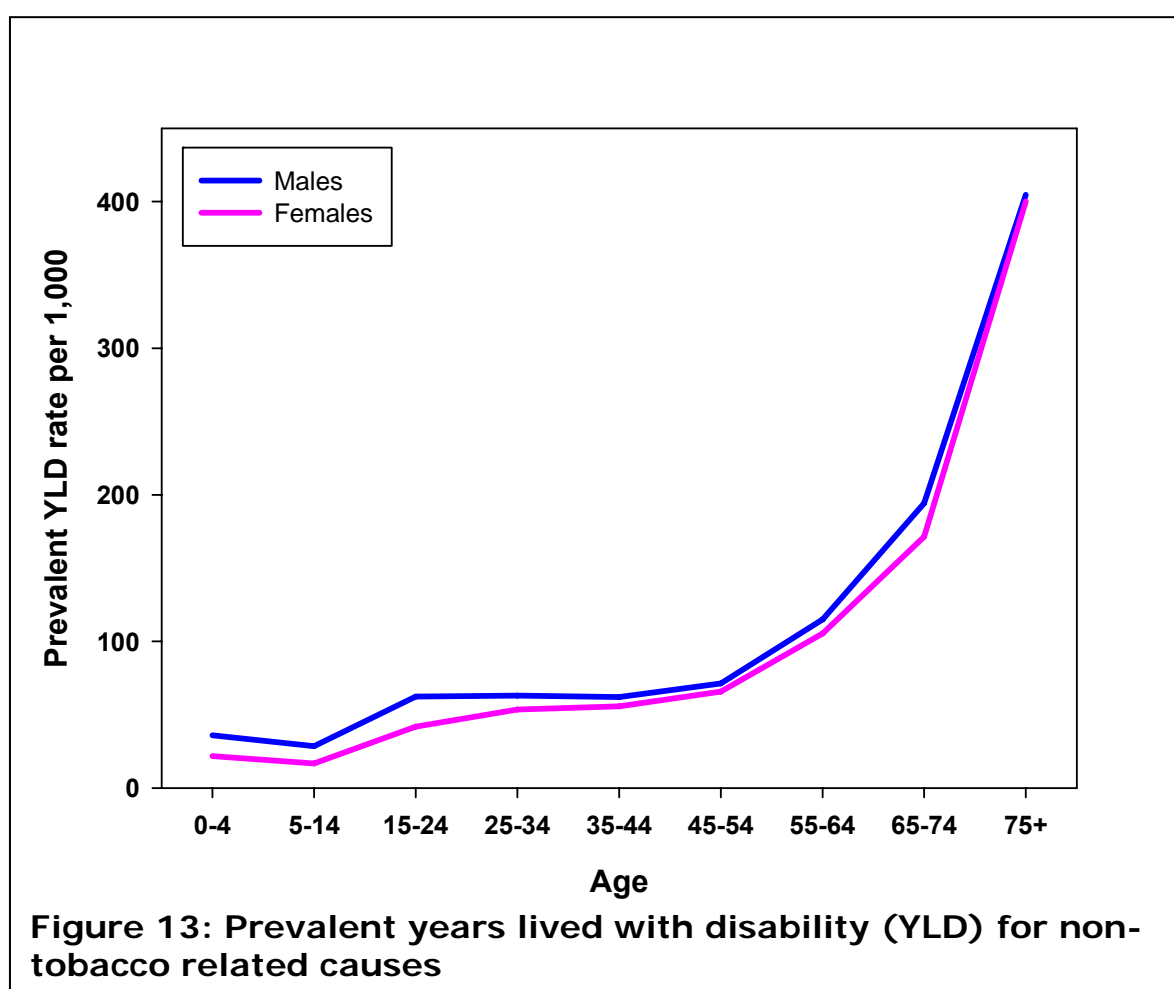




## Health adjusted life expectancy (HALE) by smoking status

Life tables, using the mortality rates in Figure 4, with the appropriate adjustments for stopping smoking or starting to use snus, were used to determine the remaining life-expectancy for different sex and 5-year age (ages 35 to 80) cohorts by smoking status. We assume that age-specific mortality rates by smoking status in the year 2000 are applicable to future cohorts as they age. Given that current smokers in Australia have similar ages of initiation, and thus exposure time (the main determinant of tobacco risk), this assumption is likely to hold reasonably well.

Remaining life-expectancy was adjusted for severity-weighted disability due to both tobacco related and non-tobacco related causes. Non-tobacco related disability was applied as a function of age (Figure 13) and was determined from the Australian Burden of Disease Study.<sup>3</sup>



To account for disability attributable to tobacco-related causes, a ratio of prevalent years lived with disability (YLD) to death for each cause in the year 2000<sup>3</sup> was used as an average population estimate of smoking-related disability proportionate to each death (Table 5).

**Table 5: Ratio of prevalent years lived with disability to death for tobacco-related causes in the year 2000 from the Australian Burden of Disease Study**

Cause	Males					Females				
	35-44	45-54	55-64	65-74	75+	35-44	45-54	55-64	65-74	75+
Lung Ca	0.9	1.3	1.4	1.0	0.7	2.5	1.9	1.9	1.2	0.7
UA Ca	4.2	0.8	0.5	0.3	0.3	5.4	1.2	1.2	0.5	0.2
Pancreas Ca	0.4	0.7	0.6	0.4	0.3	0.9	0.9	0.8	0.4	0.3
Bladder Ca		6.2	3.4	3.6	6.6		1.3	2.5	3.9	2.3
Kidney Ca	0.8	1.4	2.9	4.6	2.6		3.4	3.4	3.3	1.9
COPD		59.8	30.6	6.8	2.0		54.4	14.8	5.3	3.5
IHD	1.1	0.9	0.7	0.4	0.1	3.8	2.5	2.2	0.8	0.2
Stroke	29.2	17.0	13.4	8.9	3.0	77.8	49.8	23.6	13.9	2.4
Arterial disease		75.8	54.4	15.3	1.2		45.8	48.7	25.6	1.2
Other CVD	6.1	5.4	4.6	2.5	1.5	9.1	5.7	4.0	2.6	1.6
Other resp	159.7	162.4	42.4	32.1	20.4	316.2	272.1	135.9	51.4	10.9

Ca Cancer; UA Upper Aerodigestive; COPD Chronic obstructive pulmonary disease; CVD Cardiovascular disease; IHD Ischemic heart disease; resp dis Respiratory disease

### Uncertainty assumptions

Uncertainty intervals provide a range of values within which the true value of a parameter is likely to fall. Table 6 summarises the assumptions for each of the variables that were used to calculate the expected health adjusted life expectancies for each tobacco use category examined. Tables 2, 7 and 8 provide the point estimates and uncertainty intervals for each of these variables. The impact of uncertainty in these values on the main outcome measures was estimated by Monte-Carlo simulation (2000 iterations) using @RISK (Palisade Corporation).

**Table 6: Uncertainty Assumptions and Distributions**

Parameter	Uncertainty	Type of Distribution	Reference
Relative risk of lung cancer, upper aerodigestive cancer, pancreatic cancer, kidney cancer, bladder cancer, ischemic heart disease, stroke, arterial disease, other CVD, COPD, and other respiratory mortality in smokers compared to never smokers	95% confidence interval (Table 2)	Triangular	7
Tobacco-attributable mortality in snus users who never smoked compared to smokers	+/- 25% (Table 7)	Triangular	Assumption
Ratio of years lost due to disability to number of deaths for tobacco attributable disease	+/- 25% (Table 8)	Triangular	Assumption

**Table 7: Uncertainty estimates of tobacco-attributable mortality in snus users who never smoked compared to smokers**

Cause	Age	
	35-49	≥ 50
Ischemic heart disease, stroke, arterial disease & other CVD	0.10 (0.08 - 0.13)	0.10 (0.08 - 0.13)
Upper aerodigestive, pancreas, bladder and kidney cancer	0.15 (0.11 - 0.19)	0.30 (0.23 - 0.38)
Lung cancer	0.02 (0.02 - 0.03)	0.03 (0.03 - 0.04)

**Table 8: Uncertainty Interval for ratio of years lost due to disability to number of deaths for tobacco attributable disease**

Cause	Age				
	35-44	45-54	55-64	65-74	75+
<b>Males</b>					
Lung Ca	0.9 (0.7-1.1)	1.3 (1.0-1.6)	1.4 (1.0-1.7)	1.0 (0.8-1.3)	0.7 (0.5-0.9)
UA Ca	4.2 (3.2-5.3)	0.8 (0.6-1.0)	0.5 (0.3-0.6)	0.3 (0.2-0.4)	0.3 (0.2-0.4)
Pancreas Ca	0.4 (0.3-0.4)	0.7 (0.5-0.9)	0.6 (0.4-0.7)	0.4 (0.3-0.5)	0.3 (0.3-0.4)
Bladder Ca	0.0 (0.0-0.0)	6.2 (4.6-7.7)	3.4 (2.5-4.2)	3.6 (2.7-4.5)	6.6 (4.9-8.2)
Kidney Ca	0.8 (0.6-1.0)	1.4 (1.1-1.8)	2.9 (2.2-3.6)	4.6 (3.5-5.8)	2.6 (2.0-3.3)
COPD	0.0 (0.0-0.0)	59.8 (44.9-74.8)	30.6 (23.0-38.3)	6.8 (5.1-8.5)	2.0 (1.5-2.5)
IHD	1.1 (0.8-1.4)	0.9 (0.6-1.1)	0.7 (0.5-0.8)	0.4 (0.3-0.5)	0.1 (0.1-0.2)
Stroke	29.2 (21.9-36.5)	17.0 (12.7-21.2)	13.4 (10.1-16.8)	8.9 (6.7-11.2)	3.0 (2.3-3.8)
Arterial	0.0 (0.0-0.0)	75.8 (56.8-94.7)	54.4 (40.8-68.1)	15.3 (11.5-19.1)	1.2 (0.9-1.5)
Other CVD	6.1 (4.6-7.6)	5.4 (4.0-6.7)	4.6 (3.4-5.7)	2.5 (1.8-3.1)	1.5 (1.1-1.9)
Other resp dis	160 (120-200)	162 (122-203)	42.4 (31.8-53.0)	32.1 (24.1-40.1)	20.4 (15.3-25.5)
<b>Females</b>					
Lung Ca	2.5 (1.9-3.2)	1.9 (1.4-2.4)	1.9 (1.4-2.4)	1.2 (0.9-1.5)	0.7 (0.5-0.8)
UA Ca	5.4 (4.0-6.7)	1.2 (0.9-1.5)	1.2 (0.9-1.5)	0.5 (0.4-0.6)	0.2 (0.1-0.2)
Pancreas Ca	0.9 (0.7-1.1)	0.9 (0.7-1.1)	0.8 (0.6-0.9)	0.4 (0.3-0.5)	0.3 (0.2-0.3)
Bladder Ca	0.0 (0.0-0.0)	1.3 (1.0-1.6)	2.5 (1.9-3.1)	3.9 (2.9-4.9)	2.3 (1.7-2.9)
Kidney Ca	0.0 (0.0-0.0)	3.4 (2.6-4.3)	3.4 (2.6-4.3)	3.3 (2.5-4.1)	1.9 (1.4-2.3)
COPD	0.0 (0.0-0.0)	54.4 (40.8-68.0)	14.8 (11.1-18.5)	5.3 (4.0-6.6)	3.5 (2.6-4.4)
IHD	3.8 (2.8-4.7)	2.5 (1.9-3.2)	2.2 (1.6-2.7)	0.8 (0.6-1.0)	0.2 (0.1-0.2)
Stroke	77.8 (58.4-97.3)	49.8 (37.3-62.2)	23.6 (17.7-29.5)	13.9 (10.4-17.4)	2.4 (1.8-3.0)
Arterial	0.0 (0.0-0.0)	45.8 (34.4-57.3)	48.7 (36.5-60.9)	25.6 (19.2-32.0)	1.2 (0.9-1.5)
Other CVD	9.1 (6.8-11.4)	5.7 (4.3-7.2)	4.0 (3.0-5.1)	2.6 (1.9-3.2)	1.6 (1.2-2.0)
Other resp dis	316 (237-395)	272 (204-340)	136 (102-170)	51.4 (38.6-64.3)	10.9 (8.1-13.6)

*Ca Cancer; UA Upper Aerodigestive; COPD Chronic obstructive pulmonary disease; CVD Cardiovascular disease; IHD Ischemic heart disease; resp dis Respiratory disease*

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