

Some analyses of lung cancer rates from CPS-I and CPS-II based on  
published data in NCI Monograph 8

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NCI Smoking and Tobacco Control Monograph No. 8 "Changes in cigarette-related disease risks and their implications for prevention and control" published in 1997 includes a chapter by M J Thun *et al* entitled "Trends in tobacco smoking and mortality from cigarette use in Cancer Prevention Studies I (1959 through 1965) and II (1982 through 1988)". This chapter, no. 4 in the book (pp 305-382) includes a series of appendices giving lung cancer deaths and person-years, separately for CPS I and II, by five year age group, for never smokers and for current cigarette smokers subdivided jointly by number smoked per day (20 or 40) and by duration of smoking (30-34, 35-39, 40-44, 45-49 or 50+ years). Appendices 3 (male) and 4 (female) give data for all races and includes subjects with prevalent cancers at baseline, while appendices 5 (male) and 6 (female) give data for whites excluding subjects with prevalent cancers at baseline. For CPS I, deaths and person-years are calculated for the first 6 years of the study, to make them comparable to CPS II. In both studies, smoking data are as reported at baseline.

The actual chapter makes no real attempt to analyse these data formally. Accordingly, I input the deaths and person-years onto a spreadsheet and tested various hypotheses of interest. For each hypothesis I used the same basic technique, in which the data were divided into strata by the adjustment variables selected, with comparisons being made between levels (i) of interest of the variable of interest by comparing the observed ( $O_i$ ) number of lung cancers at each level with those expected ( $E_i$ ) assuming risk was independent of level.  $O_i$  and  $E_i$  were then accumulated over strata, to give an overall O and E, O/E being an approximate indicator or relative lung cancer risk in the group.

### Differences between CPS I and CPS II (Table 1)

Among never smoking men, there were 80 lung cancers in CPS I and 119 in CPS II in the analysis including all races and prevalent cancers (Table 1a) with risk very similar in the two studies (Relative risk for CPS II/CPS I = 0.96). When the analysis was restricted to whites and prevalent cancers were excluded (Table 1c), the numbers reduced to 74 and 76 in the two studies and the relative risk showed some advantage to CPS II (RR = 0.71).

Among current smoking men, there were 479 cancers in CPS I and 869 in CPS II in the inclusive analysis (Table 1a), with risk increased by a factor 1.41 in CPS II after adjustment for age, amount smoked and duration of smoking. The increase, which was highly statistically significant, was evident in all age groups and at all levels of amount smoked and duration of smoking. In the restricted analysis (Table 1c), numbers reduced to 443 and 734 in the two studies, but the relative risk estimate (RR = 1.38) and general conclusions are little affected.

Among never smoking women, there were 198 lung cancers in CPS I and 305 in CPS II in the inclusive analysis (Table 1b) with risk higher in CPS II by a factor 1.32. In the restricted analysis (Table 1a), numbers reduced to 156 and 192 in the two studies, and the relative risk became smaller, at 1.16.

Among current smoking women, there were only 32 lung cancers in CPS I but 465 in CPS II in the inclusive analysis (Table 1b). After adjustment for age, amount smoked and duration of smoking, risk in CPS II is higher by the large factor of 2.76. This excess is again evident in all age groups at all levels of amount smoked and duration of smoking and, as for males, is highly statistically significant. In the restricted analysis (Table 1d), numbers reduced to 29 and 374 in the two studies, but the relative risk estimate (RR = 2.55) and general conclusions are little affected.

The chapter by Thun et al reports the following conclusions for men based on the data in Appendices 3 to 6:

“Comparisons of cigarettes-per-day, age-, and duration-specific strata reveal modest increases in the lung cancer death rates in CPS-II compared with CPS-I for males of all races who smoked 40 cigarettes per day and when prevalent cancers are included. No consistent difference between the rates for the two studies is noted for the comparison of strata-specific rates of white males who smoked 20 cigarettes per day until they have smoked more than 40 years. The rates for smokers of 20 cigarettes per day who have smoked for 40 to 49 years are substantially higher in CPS-II than in CPS-I for males of all races with prevalent cancers included and for white males with prevalent cancers excluded.”

It is clear from the chapter that they have looked at the data separately by strata and have not tried to aggregate the CPS II/CPS I differences to form broader conclusions. Elsewhere in the chapter they state that “there were too few deaths among women in CPS-I for meaningful comparison” which is true when considering one stratum at a time, but not true when considering the total data.

#### Risk by age (Table 2)

Table 2 summarises relative risks by 5 year age group, after adjustment for amount smoked. In men in both surveys, risk rises steadily with age and is around 10 times higher at age 75+ than at age 50-54. In women, numbers of lung cancers are rather low in CPS I. In CPS II, a rise in risk with age is seen, but is weaker than for men, with risk at age 75+ only about 3 times higher than at age 50-54.

#### Risk by amount smoked (Table 3)

For males in both surveys and for women in CPS II, risk in 40/day smokers was about 50% higher than that in 20/day smokers after adjustment for age and duration of smoking. For women in CPS I, the risk in 40/day smokers was estimated to be about 3 times that in 20/day smokers. However, this estimate is highly variable, due to the small numbers of deaths in currently smoking women in CPS I.

### Risk by duration of smoking (Tables 4 and 5)

In Table 4, risks are adjusted for age and amount smoked. Where numbers of deaths were adequate (males in CPS I and CPS II, women in CPS II), a moderate trend towards increasing risk with increasing duration was seen, with risk about 50% higher in the highest duration group (50+ years) compared to the lowest group (30-34 years).

In Table 5, risks are adjusted for amount smoked but not for age, following the suggestion that duration, not age, is most relevant to lung cancer. The strength of the relationships between lung cancer risk and duration markedly increased, especially in males, but were not quite as strong as those seen with age in Table 2. Whether this reflects a true effect of age, given duration, is not clear. A major problem is that age is measured much more accurately than duration.

### Risk by sex (Table 6)

It has been suggested that women are more susceptible to the effects of smoking than are men. The results in Table 6 for both surveys do not indicate this. Among current smokers, after adjustment for age, duration and amount smoked, the relative risk for females/males were 0.39 in CPS I and 0.65 in CPS II, both highly significant differences. Among never smokers, risk was also lower in women, but not so markedly, with the age-adjusted relative risk 0.61 in CPS I and 0.83 in CPS II. (These analyses were only conducted for the inclusive population as excluding non-whites and prevalent cancers generally made little difference.)

### Comment

The data in Appendices 3-6 are limited by the fact that smokers of amounts other than exactly 20 or 40/day are ignored so that many lung cancers in smokers are not included, so losing considerable power. The data would also have been better cast by age, amount smoked and age of starting to smoke, to allow a clearer analysis avoiding the intrinsic strong correlation between duration and age. However, as is apparent from this document, some relevant conclusions can be reached without recourse to the raw data.

**Fuller details**

The analyses summarised here are available as Quattro Pro 9 spreadsheet files for those who wish to have copies (T:\pnlee/thunapp3.QPW, thunapp4.QPW, thunapp5.QPW, thunapp6.QPW, thunapp34.QPW, thunapp34B.QPW).

Table 1Comparison of interest : Lung cancer risk for CPS II v CPS I(a) Males : all races; including prevalent cancers

| <u>Subset</u>        | <u>Adjustment variables</u> | <u>CPS I</u> |          | <u>CPS II</u> |          | <u>R</u> |
|----------------------|-----------------------------|--------------|----------|---------------|----------|----------|
|                      |                             | <u>O</u>     | <u>E</u> | <u>O</u>      | <u>E</u> |          |
| Never smokers        | Age                         | 80           | 78.24    | 119           | 120.76   | 0.96     |
| Current smokers      |                             |              |          |               |          |          |
| 20/day               | Age, duration               | 358          | 443.04   | 539           | 453.96   | 1.47     |
| 40/day               | Age, duration               | 121          | 145.96   | 330           | 305.04   | 1.30     |
| Duration 30-34 years | Age, amount                 | 70           | 81.93    | 64            | 52.07    | 1.44     |
| Duration 35-39 years | Age, amount                 | 112          | 129.32   | 123           | 105.68   | 1.34     |
| Duration 40-44 years | Age, amount                 | 126          | 152.40   | 221           | 194.66   | 1.37     |
| Duration 45-49 years | Age, amount                 | 84           | 98.70    | 147           | 132.30   | 1.31     |
| Duration 50-54 years | Age, amount                 | 87           | 126.65   | 314           | 274.35   | 1.67     |
| Age 50-54            | Duration, amount            | 62           | 72.63    | 55            | 44.37    | 1.45     |
| 55-59                | Duration, amount            | 110          | 126.93   | 125           | 108.07   | 1.33     |
| 60-64                | Duration, amount            | 127          | 138.79   | 183           | 171.21   | 1.17     |
| 65-69                | Duration, amount            | 103          | 133.14   | 226           | 195.86   | 1.49     |
| 70-74                | Duration, amount            | 44           | 70.69    | 164           | 137.31   | 1.92     |
| 75-79                | Duration, amount            | 29           | 36.98    | 90            | 82.02    | 1.40     |
| 80-84                | Duration, amount            | 4            | 8.91     | 23            | 18.09    | 2.83     |
| 85+                  | Duration, amount            | 0            | 0.92     | 3             | 2.08     | ∞        |
| All                  | Age, duration, amount       | 479          | 589.00   | 869           | 758.00   | 1.41     |

Table 1Comparison of interest : Lung cancer risk for CPS II v CPS I(b) Females : all races; including prevalent cancers

| <u>Subset</u>        | <u>Adjustment variables</u> | <u>CPS I</u> |          | <u>CPS II</u> |          | <u>R</u> |
|----------------------|-----------------------------|--------------|----------|---------------|----------|----------|
|                      |                             | <u>O</u>     | <u>E</u> | <u>O</u>      | <u>E</u> |          |
| Never smokers        | Age                         | 198          | 232.31   | 305           | 270.69   | 1.32     |
| Current smokers      |                             |              |          |               |          |          |
| 20/day               | Age, duration               | 24           | 65.96    | 344           | 302.04   | 3.13     |
| 40/day               | Age, duration               | 8            | 13.40    | 121           | 115.60   | 1.75     |
| Duration 30-34 years | Age, amount                 | 18           | 35.30    | 71            | 53.70    | 2.59     |
| Duration 35-39 years | Age, amount                 | 7            | 24.26    | 98            | 80.74    | 4.25     |
| Duration 40-44 years | Age, amount                 | 5            | 12.40    | 123           | 115.60   | 2.64     |
| Duration 45-49 years | Age, amount                 | 1            | 4.25     | 80            | 76.75    | 4.43     |
| Duration 50-54 years | Age, amount                 | 1            | 3.14     | 93            | 90.86    | 3.21     |
| Age 50-54            | Duration, amount            | 10           | 16.75    | 35            | 28.25    | 2.08     |
| 55-59                | Duration, amount            | 6            | 20.22    | 71            | 56.78    | 4.21     |
| 60-64                | Duration, amount            | 7            | 18.91    | 112           | 100.09   | 3.02     |
| 65-69                | Duration, amount            | 9            | 13.48    | 118           | 113.53   | 1.56     |
| 70-74                | Duration, amount            | 0            | 4.90     | 72            | 67.10    | ∞        |
| 75-79                | Duration, amount            | 0            | 4.25     | 42            | 37.75    | ∞        |
| 80-84                | Duration, amount            | 0            | 0.77     | 12            | 11.23    | ∞        |
| 85+                  | Duration, amount            | 0            | 0.09     | 3             | 2.91     | ∞        |
| All                  | Age, duration, amount       | 32           | 79.36    | 465           | 417.64   | 2.76     |

Table 1

Comparison of interest : Lung cancer risk for CPS II v CPS I(c) Males : Whites; excluding prevalent cancers

| <u>Subset</u>        | <u>Adjustment variables</u> | <u>CPS I</u> |          | <u>CPS II</u> |          | <u>R</u> |
|----------------------|-----------------------------|--------------|----------|---------------|----------|----------|
|                      |                             | <u>O</u>     | <u>E</u> | <u>O</u>      | <u>E</u> |          |
| Never smokers        | Age                         | 74           | 61.40    | 76            | 88.60    | 0.71     |
| <hr/>                |                             |              |          |               |          |          |
| Current smokers      |                             |              |          |               |          |          |
| 20/day               | Age, duration               | 329          | 399.34   | 446           | 375.66   | 1.44     |
| 40/day               | Age, duration               | 114          | 135.05   | 288           | 266.95   | 1.28     |
| Duration 30-34 years | Age, amount                 | 68           | 76.19    | 54            | 45.81    | 1.32     |
| Duration 35-39 years | Age, amount                 | 102          | 118.27   | 110           | 93.73    | 1.36     |
| Duration 40-44 years | Age, amount                 | 117          | 135.50   | 183           | 164.50   | 1.29     |
| Duration 45-49 years | Age, amount                 | 77           | 91.34    | 129           | 114.66   | 1.33     |
| Duration 50-54 years | Age, amount                 | 79           | 113.09   | 258           | 223.91   | 1.65     |
| Age 50-54            | Duration, amount            | 56           | 65.24    | 48            | 38.76    | 1.44     |
| 55-59                | Duration, amount            | 105          | 114.89   | 104           | 94.11    | 1.21     |
| 60-64                | Duration, amount            | 113          | 125.50   | 158           | 145.50   | 1.21     |
| 65-69                | Duration, amount            | 101          | 124.12   | 193           | 169.88   | 1.40     |
| 70-74                | Duration, amount            | 41           | 64.38    | 137           | 113.63   | 1.89     |
| 75-79                | Duration, amount            | 23           | 31.29    | 73            | 64.71    | 1.53     |
| 80-84                | Duration, amount            | 4            | 8.59     | 20            | 15.41    | 2.79     |
| 85+                  | Duration, amount            | 0            | 0.39     | 1             | 0.61     | ∞        |
| All                  | Age, duration, amount       | 443          | 534.39   | 734           | 642.61   | 1.38     |



Table 1

Comparison of interest : Lung cancer risk for CPS II v CPS I(d) Females : Whites; excluding prevalent cancers

| <u>Subset</u>        | <u>Adjustment variables</u> | <u>CPS I</u> |          | <u>CPS II</u> |          | <u>R</u> |
|----------------------|-----------------------------|--------------|----------|---------------|----------|----------|
|                      |                             | <u>O</u>     | <u>E</u> | <u>O</u>      | <u>E</u> |          |
| Never smokers        | Age                         | 156          | 168.54   | 192           | 179.46   | 1.16     |
| Current smokers      |                             |              |          |               |          |          |
| 20/day               | Age, duration               | 21           | 54.64    | 270           | 236.36   | 2.97     |
| 40/day               | Age, duration               | 8            | 11.92    | 104           | 100.08   | 1.55     |
| Duration 30-34 years | Age, amount                 | 17           | 30.00    | 57            | 44.00    | 2.29     |
| Duration 35-39 years | Age, amount                 | 5            | 19.90    | 78            | 63.10    | 4.92     |
| Duration 40-44 years | Age, amount                 | 5            | 10.74    | 99            | 93.26    | 2.28     |
| Duration 45-49 years | Age, amount                 | 1            | 3.58     | 69            | 66.42    | 3.72     |
| Duration 50-54 years | Age, amount                 | 1            | 2.33     | 71            | 69.67    | 2.38     |
| Age 50-54            | Duration, amount            | 10           | 14.68    | 27            | 22.32    | 1.78     |
| 55-59                | Duration, amount            | 6            | 17.34    | 59            | 47.66    | 3.58     |
| 60-64                | Duration, amount            | 6            | 15.65    | 89            | 79.35    | 2.93     |
| 65-69                | Duration, amount            | 7            | 11.04    | 96            | 91.96    | 1.65     |
| 70-74                | Duration, amount            | 0            | 4.28     | 59            | 54.72    | ∞        |
| 75-79                | Duration, amount            | 0            | 3.18     | 34            | 30.82    | ∞        |
| 80-84                | Duration, amount            | 0            | 0.35     | 7             | 6.65     | ∞        |
| 85+                  | Duration, amount            | 0            | 0.04     | 3             | 2.96     | ∞        |
| All                  | Age, duration, amount       | 29           | 66.57    | 374           | 336.43   | 2.55     |

Table 2

Comparison of interest : Lung cancer relative risk (number of deaths) by age(among current smokers, adjusted for amount smoked)

| <u>Age</u>                                   | <u>Males</u> |               | <u>Females</u> |               |
|--|--------------|---------------|----------------|---------------|
|  | <u>CPS I</u> | <u>CPS II</u> | <u>CPS I</u>   | <u>CPS II</u> |
| <u>All races including prevalent cancers</u> |              |               |                |               |
| 50-54  | 1.00 (62)    | 1.00 (55)     | 1.00 (10)      | 1.00 (35)     |
| 55-59  | 1.73 (110)   | 1.27 (125)    | 0.76 (6)       | 0.72 (71)     |
| 60-64  | 3.26 (127)   | 2.12 (183)    | 1.70 (7)       | 1.28 (112)    |
| 65-69  | 5.08 (103)   | 3.99 (226)    | 4.42 (9)       | 1.98 (118)    |
| 70-74  | 5.32 (44)    | 5.38 (164)    | 0.00 (0)       | 2.24 (72)     |
| 75+  | 10.00 (33)   | 8.07 (116)    | 0.00 (0)       | 3.34 (57)     |
| <u>Whites excluding prevalent cancers</u>    |              |               |                |               |
| 50-54  | 1.00 (56)    | 1.00 (48)     | 1.00 (10)      | 1.00 (27)     |
| 55-59  | 1.83 (105)   | 1.27 (104)    | 0.77 (6)       | 0.67 (59)     |
| 60-64  | 3.22 (113)   | 2.23 (158)    | 1.49 (6)       | 1.17 (89)     |
| 65-69  | 5.59 (101)   | 4.18 (193)    | 3.63 (7)       | 1.88 (96)     |
| 70-74  | 5.63 (41)    | 5.66 (137)    | 0.00 (0)       | 2.17 (59)     |
| 75+  | 9.34 (27)    | 8.39 (94)     | 0.00 (0)       | 3.07 (44)     |

Table 3

Comparison of interest : Lung cancer risk by amount smoked(among current smokers, adjusted for age and duration)

| <u>Study</u> | <u>Sex</u> | <u>Blacks and prevalent<br/>cancers included?</u> | <u>20/day</u> |          | <u>40/day</u> |          | <u>R</u> |
|--------------|------------|---|---------------|----------|---------------|----------|----------|
|              |            |   | <u>O</u>      | <u>E</u> | <u>O</u>      | <u>E</u> |          |
| CPS I        | Male       | Yes   | 358           | 391.84   | 121           | 87.16    | 1.52     |
|              |            | No  | 329           | 361.71   | 114           | 81.29    | 1.54     |
|              | Female     | Yes   | 24            | 28.84    | 8             | 3.16     | 3.05     |
|              |            | No  | 21            | 26.16    | 8             | 2.84     | 3.51     |
| CPS II       | Male       | Yes   | 539           | 600.25   | 330           | 268.75   | 1.37     |
|              |            | No  | 446           | 498.59   | 288           | 235.41   | 1.37     |
|              | Female     | Yes   | 344           | 376.23   | 121           | 88.77    | 1.49     |
|              |            | No  | 270           | 301.94   | 104           | 72.06    | 1.61     |

Table 4Comparison of interest : Lung cancer relative risk (number of deaths) by duration(among current smokers, adjusted for age and amount smoked)

| <u>Duration of smoking</u>                   | <u>Males</u> |               | <u>Females</u> |               |
|--|--------------|---------------|----------------|---------------|
|  | <u>CPS I</u> | <u>CPS II</u> | <u>CPS I</u>   | <u>CPS II</u> |
| <u>All races including prevalent cancers</u> |              |               |                |               |
| 30-34  | 1.00 (70)    | 1.00 (64)     | 1.00 (18)      | 1.00 (71)     |
| 35-39  | 1.29 (112)   | 1.22 (123)    | 0.87 (7)       | 1.19 (98)     |
| 40-44  | 1.45 (126)   | 1.45 (221)    | 1.63 (5)       | 1.29 (123)    |
| 45-49  | 1.48 (84)    | 1.26 (147)    | 1.06 (1)       | 1.33 (80)     |
| 50+  | 1.64 (87)    | 1.57 (314)    | 4.34 (1)       | 1.53 (93)     |
| <u>Whites excluding prevalent cancers</u>    |              |               |                |               |
| 30-34  | 1.00 (68)    | 1.00 (54)     | 1.00 (17)      | 1.00 (57)     |
| 35-39  | 1.21 (102)   | 1.28 (110)    | 0.68 (5)       | 1.17 (78)     |
| 40-44  | 1.38 (117)   | 1.41 (183)    | 1.91 (5)       | 1.30 (99)     |
| 45-49  | 1.38 (77)    | 1.28 (129)    | 1.39 (1)       | 1.42 (69)     |
| 50+  | 1.58 (79)    | 1.56 (258)    | 5.87 (1)       | 1.48 (71)     |

Table 5

Comparison of interest : Lung cancer relative risk (number of deaths) by duration(among current smokers, adjusted for amount smoked only)

| <u>Duration of smoking</u>                   | <u>Males</u> |               | <u>Females</u> |               |
|--|--------------|---------------|----------------|---------------|
|  | <u>CPS I</u> | <u>CPS II</u> | <u>CPS I</u>   | <u>CPS II</u> |
| <u>All races including prevalent cancers</u> |              |               |                |               |
| 30-34  | 1.00 (70)    | 1.00 (64)     | 1.00 (18)      | 1.00 (71)     |
| 35-39  | 1.80 (112)   | 1.30 (123)    | 0.98 (7)       | 0.87 (98)     |
| 40-44  | 3.16 (126)   | 2.40 (221)    | 2.58 (5)       | 1.39 (123)    |
| 45-49  | 4.64 (84)    | 3.07 (147)    | 2.16 (1)       | 1.88 (80)     |
| 50+  | 7.20 (87)    | 5.96 (314)    | 4.62 (1)       | 2.77 (93)     |
| <u>Whites excluding prevalent cancers</u>    |              |               |                |               |
| 30-34  | 1.00 (68)    | 1.00 (54)     | 1.00 (17)      | 1.00 (57)     |
| 35-39  | 1.70 (102)   | 1.30 (110)    | 0.74 (5)       | 0.82 (78)     |
| 40-44  | 3.04 (117)   | 2.26 (183)    | 2.75 (5)       | 1.36 (99)     |
| 45-49  | 4.45 (77)    | 3.07 (129)    | 2.52 (1)       | 1.99 (69)     |
| 50+  | 6.94 (79)    | 5.77 (258)    | 5.16 (1)       | 2.64 (71)     |

Table 6Comparison of interest : Lung cancer risk for females v males(all races, including prevalent cancers)

| <u>Study</u> | <u>Subset</u>   | <u>Adjustment variables</u> | <u>Males</u> |          | <u>Females</u> |          | <u>R</u> |
|--------------|-----------------|-----------------------------|--------------|----------|----------------|----------|----------|
|              |                 |                             | <u>O</u>     | <u>E</u> | <u>O</u>       | <u>E</u> |          |
| CPS I        | Never smokers   | Age                         | 80           | 55.26    | 198            | 222.74   | 0.61     |
|              | Current smokers |                             |              |          |                |          |          |
|              | 20/day          | Age, duration               | 358          | 318.99   | 24             | 63.01    | 0.34     |
|              | 40/day          | Age, duration               | 121          | 116.63   | 8              | 12.37    | 0.62     |
|              | All             | Age, duration, amount       | 479          | 435.62   | 32             | 75.38    | 0.39     |
| CPS II       | Never smokers   | Age                         | 119          | 103.57   | 305            | 320.43   | 0.83     |
|              | Current smokers |                             |              |          |                |          |          |
|              | 20/day          | Age, duration               | 539          | 437.92   | 344            | 445.08   | 0.63     |
|              | 40/day          | Age, duration               | 330          | 295.48   | 121            | 155.52   | 0.70     |
|              | All             | Age, duration, amount       | 869          | 733.40   | 465            | 600.60   | 0.65     |