A Critical Review of the Theory of Professor P.R.J. Burch

1. Over the last two years Professor P.R.J. Burch of Leeds General Infirmary has had a number of letters published, firstly in the Lancet and more recently in the New Scientist, arguing against the conventional medical view that cigarette smoking causes lung cancer. The letters in the New Scientist, especially, have produced a considerable response and the purpose of this document is to attempt to evaluate the true worth of Burch's theory. For convenience, copies of the most relevant letters are attached.

2. Burch's arguments against the conventional causation theory of lung cancer fall into two main parts, as follows:-

(a) He attempts to show that certain observations are inconsistent with the possibility of smoking causing lung cancer.

(b) He claims that all relevant results can be explained by postulating, firstly, that there is a gene which makes people both more likely to smoke and more likely to contract lung cancer, and secondly, that the standards of diagnosis of lung cancer have changed dramatically during this century.

The next sections of this document deal with his various points in detail.

3. Apparent inconsistencies in the causation theory

3.1 Inhalation

Burch's argument

3.1.1. Burch (2) stated that "from data supplied to him by Hill and Doll, Fisher (E) was able to show that, at a given level of smoking, the incidence of lung cancer among inhalers was 10% lower, on the average, than among non-inhalers. Fisher (E) commented:- It disproves at about the 1 per cent level the hypothesis that inhalers and non-inhalers have the same cancer incidence. Even equality would be a fair knock-out for the theory that smoke in the lung causes cancer."

Comments

3.1.2 Although Burch oversimplifies Doll and Hill's results which in fact show a positive relationship of lung cancer to inhaling at low levels of smoking, and does not mention that Hammond (H) showed a positive relationship to inhaling within each amount smoked, the main force of his argument still remains. On a simple causal hypothesis, one would have expected non-inhaling smokers to have a risk little greater than that of non-smokers. In fact their risk is far greater and much nearer that of inhaling smokers.

3.1.3 There are at least two possible explanations for this finding. Firstly, Davies (C) has suggested that deep inhalers may in fact draw the smoke past the bronchi. Secondly, in all studies reporting associations between lung cancer and inhalation, self-reported inhalation has been used as the index of inhalation. Misreporting of inhalation will tend to reduce the apparent association observed.

Conclusion

3.1.4 So little is known about where smoke constituents are deposited at the various levels of inhalation reported that this argument cannot seriously refute causation, though until more facts are known, it will remain a target of attack for anti-causationists.

3.2 Doctors giving up smoking

Burch's argument

3.2.1 Burch (9) observed that, comparing the lung cancer rates in 1958-61 and 1962-65 of 65 to 84 year old doctors in the Doll and Hill study, lung cancer mortality had increased by 34% despite a number of doctors giving up smoking since the beginning of the study.

Comment

3.2.2 As the lung cancer rate for this age group for all men in England and Wales has increased markedly over the period in question it is more meaningful to assess the effect of giving up smoking by giving the doctor's rates as a proportion of the national rate. Using the full data for the study we have

Lung cancer rates per 1000 men aged 65-84 per year	1954-1957	1958-1961	1962-1965
England and Wales	3.05	3.92	4.81
British Doctors	3.23	2.06	2.82
Ratio $\frac{\text{British Doctors}}{\text{England and Wales}}$	1.06	0.53	0.59

It can be seen that in the earliest period, before many doctors had given up, their lung cancer rate was on a par with the national average. Subsequently it was only about 50% of it. Although there are only 143 deaths of doctors in total in this age group the reduction is highly significant.

Conclusion

3.2.3 The doctors' results, far from undermining causation appear to strengthen the argument. (Though some may doubt the relevance of data on doctors to the whole community at large).

3.3 Evidence from secular changes in the relation of lung cancer rates to age

Burch's arguments

3.3.1 Burch (6) commented on various characteristics of the relationship between age-specific death rates and age. He makes the following claims:

(1) That, under the causal hypothesis, the increase in rates between, say, 1921-25 and 1960-61 for men 50-54 years of age (recorded as a factor of 19) should have been far greater than for those aged 80-84 years of age (recorded as a factor of 58).

(2) That the causal hypothesis fails to explain the shape of the relationship between lung cancer rates and age (which he describes as bell-shaped).

(3) That the causal hypothesis fails to explain why the modal age remained almost constant at 65-70 years until 1955 and why it increased after that, when the causal hypothesis would suggest that the predominant increase in death-rates should have occurred in heavy-smoking middle-aged men.

Comments

3.3.2 The expected relationship between age-specific death rates and age under a causal hypothesis depends on the mechanism by which smoking causes lung cancer. No well-defined mechanism has been accepted by smoking causationists so it is not possible to give absolute values for the extent of lung cancer risk for a person of a given age with a given smoking history.

3.3.3 In the Statistical Appendix, details are given of an attempt to fit lung cancer rates to cigarette consumption patterns assuming a mathematical model (the multi-stage model) of carcinogenesis indicated strongly by mouse skin painting experiments. In this model it is assumed that risk is partly due to a "promoting" effect due to recent cigarette consumption levels, and partly to an "initiating" effect which depends on both the number of years of smoking as well as the level of smoking in those years. This analysis also involves assumptions about the distribution of cigarette consumption by age group in years when only the overall cigarette consumption was known.

3.3.4 Despite all the approximations involved in the assumptions the fit to the observed lung cancer rates by 5 year age groups over the last 50 years was reasonably good. The fit was in fact far better than if one assumed that only diagnostic changes in lung cancer rates, equal in each age group, have occurred.

3.3.5 In particular the causal model in the Appendix predicts the bell-shaped nature of the age-pattern of lung cancer, the shift of the mode to higher ages and the greater relative increase in rates at higher ages between 1920 and 1960.

3.3.6 It is, in any case, clear without a detailed examination of the mathematics that Burch is wrong to expect a smaller increase in higher ages on the causal hypothesis. For example, 45 year olds today have similar lifetime smoking histories to 45 year olds of 20 years ago and therefore one would not expect their lung cancer rates to have risen. 70 year olds today however smoked far more in the age range 15-40 (1915-1940) than a 70 year old 20 years ago (1895-1920) and therefore one would expect their lung cancer rates to have risen. In fact 45 year olds rates have changed by 0.9 times in 20 years and 70 year olds by 3.6 times. Thus one would expect, and do find, a <u>greater</u> increase of lung cancer rates in higher ages.

<u>Conclusion</u>

3.3.7. There is no major feature of the relationships between age specific lung cancer rates and age at different years which is unexpected on the causal hypothesis.

3.4 Relationships between lung cancer rates and cigarette consumption in different countries

Burch's argument

3.4.1 Burch (9) comments that in 1960-61 Finland, while having the second highest rate for lung cancer in Europe, has a below-average per capita consumption of cigarettes and deduces that something other than cigarette smoking helps to determine the levels of lung cancer.

Comment

3.4.2 Burch's statement that Finland had a per capita consumption of cigarettes that was below average for Europe in 1960-61 seems not to be true. Beese (B) gives figures for 17 European countries in which Finland comes third highest in consumption. Also Finland for many years had the highest per capita consumption in Europe.

3.4.3 Doll (D) found a significant positive relationship between lung cancer rates in 1952-54 and consumption in 1930. It has not, as far as I know, been suggested by anyone that lung cancer is solely determined by cigarette smoking. Thus one would not expect a perfect correlation in any case, with so many other factors involved in a comparison between countries.

Conclusion

3.4.4 The relevant evidence does not contradict the causation theory.

3.5 Relationship between average age of diagnosis of lung cancer and age at which smoking started

Burch's argument

3.5.1 Burch (6) quoted Passey (L) who found that the average age of diagnosis of lung cancer in 13 men who commenced smoking at an average age of 9 years was 61.4 $\pm$ 2.0 years, and in 14 men who commenced smoking at an average of 30 years was 61.3 $\pm$ 2.4 years. Burch went on to say that this observation tended to reject the hypothesis that smoking precipitated lung cancer.

Comment

3.5.2 Passey's study was on 496 men, and Burch has followed Passey in selecting data on the 13 men who started smoking youngest and on the 14 who started oldest. Pike and Doll (N) have commented very fully on Passey's complete results. They criticised the use of average age of diagnosis of lung cancer as a misleading statistic. They also calculated the relationship that they would have expected under certain assumptions involving causation between age at starting to smoke and age at death for British doctors smoking 15-24 cigarettes a day. Compared with Passey's results they presented the following table

Passey's (1962) data			British doctors smoking 15-24 cigarettes a day	
Age at starting to smoke	No. of men	Average age at diagnosis (yr.)	Age at starting to smoke (yr.)	Average age at death (yr.)
6 - 14	117	57.9	17	70.5
15 - 19	285	55.9	22	72.0
20 - 24	69	59.6	27	73.5
25 - 41	25	62.0	32	75.0
			37	76.5
			42	78.0

It can be seen that the increase in average age at death with increasing age at starting to smoke is quite small, and that the trend in Passey's results is in the right direction.

The sub-sample of 27 men chosen by Burch is so small that the 0.1 year difference in actual average age for the two groups quoted is not inconsistent with a true difference of 6 years.

3.5.3 There is, in any case, very much better data available on the subject than Passey's. In the Dorn study of smoking and mortality reported by Kahn (K), the relationship found between annual probability of death from lung cancer per 100,000 and age when cigarette smoking began was as follows (numbers of deaths in brackets):

	Age Began Cigarette Smoking			
Age Group	< 15	15-19	20-24	25+
55-64	270(50)	194(214)	115(95)	68(20)
65-74	478(37)	384(165)	268(98)	141(33)

These figures show very clearly that risk of lung cancer is in fact highly dependent on the age of starting to smoke. As a similar trend can be seen when this data is further broken down by level of smoking, this association cannot be explained by an association between level of smoking and age of starting to smoke.

Conclusion

3.5.4 The weight of evidence does nothing to undermine the causation theory.

3.6 Evidence from twin studies

Burch's argument

3.6.1 Burch (1) quotes data from Friberg's 1970 paper (F) on his twin study, and states that "on a formal statistical test, the difference in mortality ratios ("non-exposed and less-exposed"/"smoker and more-exposed") between the sets of monozygotic and dizygotic male twin corroborates the constitutional hypothesis and rejects (at the 1 - 2% level) the causal hypothesis". In (9) Burch comments on the more recent (1973) Friberg paper (G) and states that this "is remarkably consistent with Fisher's constitutional hypothesis and inconsistent with the causal hypothesis of cigarette-associated fatal diseases".

Comments

3.6.2 The basic logic behind a smoking discordant twin study is impeccable. If the constitutional theory holds then, in the case of monozygotic twins, the heavier smoker will die first from lung cancer as often as the lighter smoker, whereas for dizygotic twins, on the other hand, the heavier smoker will die first more often. If the causal theory holds then, for both types of twins the heavier smoker will die first more often.

3.6.3 Having agreed with Burch that twin studies are a valid method of settling the argument, it is necessary to check his conclusions based on Friberg's work.

3.6.4 Firstly, we present Friberg's results, given below as numbers of first deaths of smoking discordant twin pairs.

	MALE				FEMALE			
	Dizygotic		Monozygotic		Dizygotic		Monozygotic	
	Less Exp.	More Exp.	Less Exp.	More Exp.	Less Exp.	More Exp.	Less Exp.	More Exp.
Deaths from all causes								
Up to 1970	13	34	14	9	18	20	4	6
1971-1973	18	21	4	9	13	22	9	8
Up to 1973	31	55	18	18	31	42	13	14
Deaths from lung cancer only								
Up to 1973	1	7	1	1	0	1	0	0

The first line of figures corresponds to Friberg's 1970 paper, the third to the 1973 paper and the second to the difference.

3.6.5 It should be emphasised, before considering the statistical significance of these figures, that Burch uses for his arguments only the results for all causes of death. Inasmuch as he is putting forward a theory explaining lung cancer death rates this is not really logical. It is clear, of course, that there are far too few lung cancer deaths so far in Friberg's study to critically test between the causal and constitutional hypotheses. However, if it could be shown that smoking had no relation to death rates in monozygotic twins it would be very important as it would suggest that observed associations of smoking with all causes of death are not due to a causal effect of smoking. (Presumably Burch would propose a generalized constitutional theory.) Thus it is worth looking at Burch's arguments as given in 3.6.1.

3.6.6 It is clear that the latest data for deaths from all causes is consistent with a generalized constitutional hypothesis. For both sexes the numbers of deaths in monozygotic twins is virtually independent of level of exposure. What is not clear, however, is that the latest data is inconsistent with the causal hypothesis. Neither comparisons of the ratio of more exposed : less exposed for the two zygosites for both sexes together ($p = 0.2$) nor separately (Male $p = 0.2$, Female $p = 0.8$) give a statistically significantly difference. Thus Burch is quite wrong to say that the 1973 results are inconsistent with the causal hypothesis.

3.6.7 Burch is correct in his analysis of the 1970 results but the subsequent deaths tend to suggest that the excess of deaths of less exposed over more exposed in the male monozygotics may have been a chance finding.

3.6.8 It will probably be 10 years before the numbers of deaths in Friberg's study settle the question one way or the other and even then data on lung cancer deaths will be very sparse.

3.6.9 If Friberg's deaths had all been ten times larger then the causal theory, as such, would become untenable. Burch's suggestion (1) to put the issue beyond reasonable doubt by further surveys would seem worth very serious thought therefore. The outcome of such surveys may well be to show that observed death rates may be due to both smoking and genetic factors. In that case it would still be valuable to know the relative contributions of these two components.

Conclusion

3.6.10 Although Friberg's latest data does not significantly refute the causal theory, it is so suggestively in the direction predicted by the constitutional theory that reasonable doubt must still remain and further studies are strongly indicated.

The constitutional theory

4. Introduction

4.1 Having considered the various points put up by Burch against the causation theory, the merits of the constitutional theory are now considered. In Section 4.2, the arguments put up by Burch in favour of the constitutional theory are examined and in Section 4.3, criticisms of the theory by other authors are considered.

4.2 Burch's arguments in favour of the constitutional theory

Friberg's results are Burch's main argument in favour of the constitutional theory. A second argument he puts up is Tokuhata's (R) result that the frequency of smokers among the first-degree relatives of non-smoking lung cancer probands is higher than among the corresponding relatives of non-smoking matched controls. Investigation of the data reveals that in fact there were only 11 lung cancer probands who did not smoke and 64 matched controls. Although the frequency of smokers (40%) among all relatives of the lung cancer probands was in fact significantly higher than the frequency of smokers (31%) among all relatives of the controls this only proved there was either a genetic factor or a common environmental factor or both. Comparing the frequency of smoking of one relative per proband with that of a corresponding relative of the matched control would have allowed testing of only the genetic factor but the numbers in this case would have been far too small for statistical significance. Thus Tokuhata's results do not really provide any relevant information.

4.3 Arguments against the constitutional theory

The possibility that the rise in observed lung cancer rates is due to changes in diagnosis

4.3.1 Burch (7) claimed that the whole of the rise in observed lung cancer rates is due to artefacts in the diagnosis and/or recording of lung cancer. He quoted Rosenblatt's (P) findings that lung cancer was over diagnosed by about a factor of two between about 1960 and 1971.

4.3.2 There are two reasons why this explanation does not impress. One is the sheer magnitude of the increase which for all men is nearly 100-fold since before the first world war. The second is the differencesin the size of the increase for the different age-groups. One would have expected that any improvement in diagnosis would have multiplied the rates by a similar amount for each age group (with the possible exception of the very old). In fact since 1930 the following increases in male lung cancer rates have been seen in England and Wales.

(a) 40 year olds increased by 3.4 by 1945 then fairly static
(b) 50 year olds increased by 8.2 by 1955 then fairly static
(c) 60 year olds increased by 17 by 1965 then fairly static
(d) 70 year olds increased steadily until 1970, final factor 28.

This is inconsistent with the above expectation. In fact in the statistical Appendix it is shown that the assumption that only diagnostic changes in lung cancer rate, equal in each age-group, have occurred fits the data very much worse than the assumption that only cigarette-related changes have occurred.

4.3.3 Heasman and Lipworth (J) in a survey conducted in 75 hospitals in 1959 found that, of 450 cases of lung cancer diagnosed by the clinician, only 253 were confirmed by autopsy. However, they also found 281 cases at autopsy not diagnosed. The total extent of underdiagnosis could therefore be computed at 16%. Even since 1959 observed lung cancer rates in the over 70's have risen by more than 50%. Is there now overdiagnosis? A repeat study would be of interest.

The artificiality of the theory

4.3.4 Doll (D) puts forward this criticism as follows. "In the absence of adequate twin data, Fisher's hypothesis remains unattractive. It requires us to postulate not only that the same genes determine susceptibility to lung cancer and the desire to smoke (in itself an odd thing for a few specific gene products to do) but that both effects are neatly correlated over a wide range of values, from less than five to more than 40 cigarettes a day, and over different ages at starting to smoke and at stopping".

4.3.5 It certainly seems not an unreasonable point of view to think it odd that a few specific gene products should determine susceptibility to lung cancer and the desire to smoke. However, if this is so, as Fisher (E) pointed out it is only a natural corollary of the theory that there will be a correlation between lung cancer rate and level of smoking, age at starting or age at stopping. Thus although Doll perhaps has a point, it is not so strong as he claims.

5. General conclusions

5.1 When considered in detail, none of Burch's attempts to prove inconsistencies in the causation theory are valid.

5.2 His alternative suggestion, the constitutional theory, is an artificial concept, it necessitates postulating that diagnostic standards have increased a hundred fold and it leaves unexplained the great differences observed in the rates of lung cancer increase for different age groups.

5.3 The only evidence in favour of Burch's argument lies in Friberg's work, which is suggestive but is based on numbers too small for statistical significance. Although it would be of great value to do a twin study on sufficient numbers to determine the relative contributions of smoking and genetic constitution to lung cancer at the moment one can only conclude that the causation theory is to be definitely preferred to the constitutional theory.

P.N.L.
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STATISTICAL APPENDIX

1. In 1954, Armitage and Doll (A) suggested a possible theory of carcinogenesis. They supposed a simplified situation in which

a) there are a large and constant number of cells at risk, N;

b) that for cancer to occur one cell must undergo k successive transformations;

c) that the transition probability b_i, of a cell which has already undergone i - 1 transformations, undergoing the ith one in the next interval of time is small and constant;

and showed that under these conditions (multistage hypotheses) the cancer incidence rate, I, at age t would be given by

$$I = \frac{b_1 b_2 b_3 \ldots b_k}{(k-1)!} t^{k-1} = \text{constant} \times \text{age}^{k-1}$$

They pointed out that, for many human cancers, including lung cancer, the cancer incidence rate did indeed approximate a power function of age over a considerable age range.

2. Pike (M) later suggested that a model of this sort may be suitable for the analysis and interpretation of mouse skin painting experiments. Many experiments carried out at Harrogate in which smoke condensates or fractions or combinations of fractions were so tested gave results which obeyed the equation of paragraph 1. These experiments further suggested that two of the transition probabilities were affected by the treatments in a simple dose related fashion.

3. In the human context one requirement that is clearly not satisfied in the model, is the constancy of those transition probabilities which are related to smoking, as the number of cigarettes smoked varies with age. In a mouse experiment carried out in Harrogate in which the treatment was discontinued

after a time it was found that the relationship between incidence rate and time could be predicted by adapting the equation to take account of the change in transition probabilities. It therefore seemed reasonable to attempt to fit such a modified model to the human situation.

4. If assumption c) of paragraph 1 is altered so that b_i, instead of being a constant, is a function of age, the relationship between incidence rate and age, T, can be shown to be given by the multiple integral:

$$I = b_k \int_0^T b_{k-1} \int_0^{U_{k-1}} b_{k-2} \cdots\cdots \int_0^{U_3} b_2 \int_0^{U_2} b_1 du_1 du_2 \ldots . du_{k-1}$$

5. Theoretically, b_i may depend on any factor associated with observed lung cancer rates, cigarette consumption, air pollution, diagnostic standards etc. In the first attempt at fitting lung cancer rates to the model let us assume that <u>only</u> cigarette consumption has an effect on the value of one or more of these transition probabilities. Let us further assume that, for the stages on which cigarettes are postulated to have an effect, the transition probability at time t is given by

$$b_i(t) = O_i + \alpha_i C(t)$$

where O_i is the "background" probability in the absence of cigarettes, assumed constant, C(t) is the consumption level at age t and α_i is a constant (which measures the relative effect of unit consumption of cigarettes to background).

6. A computer program was therefore written in which, given

a) the consumption level at each age,

b) the number of stages of cancer, k,

c) which stages are affected by cigarettes, and

d) the ratio α_i/O_i for each affected stage

the relationship between incidence rate and age could be calculated.

7. This program was applied to lung cancer rates in England and Wales for the period 1920 to 1970 (in steps of 5 years) and for the age groups 35-39, 40-44 , ... up to 80-84.

8. Consumption levels were estimated from Todd (Q) by assuming, for years where this information was unavailable, that the total consumption at all ages could be divided into separate age groups in the same proportion as for years where this information was available.

9. Various permutations of the possibilities outlined in 6b) , c) and d) have been tested so far. Although this work is not yet complete a reasonably good fit to the data can be obtained by assuming a 6 stage process in which the 1st and 5th stages are affected by cigarettes.

10. Table 1 shows the lung cancer rates observed (with numbers of deaths in brackets) together with those predicted by the model in this case. It can be seen

1) That the magnitude of the lung cancer increase over the years is of the right order.

2) That the shape of the relationship between lung cancer rate is of the right order.

3) That the mode is in about the right place, shifting to the right with increasing years.

11. There are areas of misfit of this model, however. The rates predicted at the very old age group (80-84) are consistently higher than those observed. This could be due perhaps to diagnosis of lung cancer being poorer in the

very old. Also in 1970, predicted rates are rather higher in nearly every age group than observed rates. This could be explained perhaps by reduced air pollution or by reduced tar per cigarette.

12. The model does not fit the data exactly. One did not expect it would. The model itself is only approximate, and takes no account of changes in air-pollution, in diagnosis standards or in tar yields per cigarette. However, the results from Table 1 unequivocally show that there is no reason to doubt that changes in lung cancer rates are consistent with changes in cigarette consumption.

13. It is of interest to note that a further model was fitted in which the "standard of diagnosis" was allowed to vary from year to year. This improved the fit, as adding extra parameters always will, but not a great deal. No real indication of any trend in the parameter "standard of diagnosis" was found , only slight fluctuations. It should be noted, however, that this fitted parameter, though it would be affected by true changes in diagnostic standards could also be affected by other factors, such as changes in air-pollution levels (if air-pollution affected the final stage of the cancer process).

14. The next stage is to consider whether Burch's hypotheses fit the observed lung cancer rates. Burch has postulated

a) that true lung cancer rates depend on age by a fixed relationship that is independent of time and

b) that diagnostic standards account for the variation in observed lung cancer rates.

As it seems likely that any change in diagnostic standards would be approximately the same in each age-group the best approach seemed to compute predicted rates assuming this approximation is exact and see how this fitted the data.

15. Table 2 gives details, therefore, of fitting the relationship

$$I(a,y) = D(y)\ R(a)$$

to the data where I (a, y) is the observed incidence rate at age a in year y, D (y) is the diagnosis factor at year y and R (a) is the age-dependent factor at age a. R (a) has in fact been calculated as that factor which best fits the data, rather than assuming a specific mathematical relationship between R (a) and age as Burch in fact does.

16. The fit of Table 2 is very significantly worse than the fit of Table 1. In the younger age-groups the rate is consistently under-estimated at the beginning of the period and over-estimated at the end, and in the older age-groups the reverse is true. This is not surprising when one considers that, in the 40-44 year old group rates have risen by a factor of about 10 over the period whereas in the 70-74 year old group they have risen by about 100. The consitutional theory, as presented by Burch, therefore, can only be accepted if one is prepared to believe that standards of diagnosis have altered very differently in different age-groups. Until evidence is presented to demonstrate this, a priori unlikely fact, Burch's explanation for the observed variations in lung cancer rates remains more than unconvincing.

17. Summing up, we have handicapped the causal hypothesis by not allowing for diagnostic changes or changes in air pollution and have helped Burch's hypotheses by not restricting the constant shape of the age-rate relationship to be of a particular mathematical form. Nevertheless, we have found that the causal hypothesis fits the data very much better than Burch's hypothesis.

TABLE 1

Lung Cancer Rates Observed (O) (and Numbers of Deaths N), together with
Lung Cancer Rates Predicted (P) on a Model Involving ONLY Past Cigarette Smoking History

YEAR		AGE GROUP 35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84
1920	O (N)	1.1(14)	1.8(22)	2.8(27)	4.5(40)	8.4(62)	8.1(47)	9.3(39)	6.4(18)	4.1(6)	6.6(4)
	P	1.6	2.7	3.8	4.9	6.3	7.5	8.5	9.4	10.4	10.2
1925	O (N)	2.4(30)	2.6(32)	5.4(62)	5.8(63)	10.3(87)	11.1(76)	13.5(64)	12.7(41)	10.3(17)	2.7(2)
	P	2.3	4.5	6.9	8.8	10.6	12.0	13.1	13.9	15.0	14.8
1930	O (N)	3.3(42)	6.8(81)	10.0(120)	15.1(165)	20.2(203)	22.6(169)	19.7(112)	24.1(83)	14.0(28)	14.5(11)
	P	3.5	7.3	12.2	16.6	19.9	21.2	21.8	21.8	22.6	21.3
1935	O (N)	6.8(94)	9.9(124)	22.2(265)	32.6(365)	44.9(463)	46.2(398)	45.9(295)	43.9(185)	30.7(71)	24.5(24)
	P	5.0	10.7	19.2	28.7	36.4	39.0	38.4	36.4	35.6	32.3
1940	O (N)	8.3(124)	19.6(253)	33.6(401)	51.1(586)	70.9(746)	84.0(774)	73.3(531)	68.4(333)	55.2(143)	39.1(43)
	P	6.8	16.1	29.7	47.0	64.7	73.2	72.4	66.3	61.9	52.7
1945	O (N)	9.8(120)	23.2(319)	46.9(596)	71.4(827)	107.8(1158)	126.8(1186)	123.6(954)	91.8(512)	72.4(233)	52.9(73)
	P	8.7	21.7	43.7	71.5	103.9	127.1	132.8	123.0	111.8	92.0
1950	O (N)	8.2(138)	24.9(421)	58.5(894)	110.1(1423)	160.0(1741)	210.6(2001)	214.2(1679)	187.3(1116)	140.5(524)	103.0(174
	P	9.8	24.2	51.5	92.1	140.2	176.4	187.2	182.8	167.6	144.3
1955	O (N)	8.4(123)	25.6(417)	58.4(949)	123.6(1826)	222.2(2628)	292.9(2829)	335.2(2631)	325.5(1940)	257.9(993)	167.2(316
	P	11.4	29.0	59.6	109.8	179.9	245.1	262.0	259.2	251.3	214.0
1960	O (N)	8.7(143)	23.8(344)	58.1(937)	122.6(1918)	233.9(3244)	358.3(3812)	427.6(3476)	437.0(2622)	399.8(1579)	271.1(545
	P	13.0	34.1	71.9	130.0	217.1	314.7	372.8	371.2	368.1	329.1
1965	O (N)	9.0(137)	22.1(369)	55.6(804)	119.9(1858)	226.0(3308)	373.6(4685)	522.8(4632)	540.7(3347)	503.6(1974)	394.7(81
	P	11.7	35.0	77.6	145.1	242.2	363.0	482.0	529.8	534.4	488.3
1970	O (N)	6.5(96)	21.4(322)	51.4(837)	110.0(1526)	223.1(3240)	368.8(4846)	535.4(5568)	670.6(4453)	646.9(2607)	519.6(10
	P	9.7	33.4	79.0	157.8	261.3	399.1	558.8	659.2	698.3	691.9

TABLE 2

Lung Cancer Rates Observed (O), together with those Predicted (P) assuming that ONLY Diagnostic Changes, Constant in each Age Group, occur

YEAR		AGE GROUP 35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84
1920	O	1.1	1.8	2.8	4.5	8.4	8.1	9.3	6.4	4.1	6.6
	P	0.4	0.9	2.0	3.8	6.6	9.6	11.9	12.4	11.1	8.5
1925	O	2.4	2.6	5.4	5.8	10.3	11.1	13.5	12.7	10.3	2.7
	P	0.5	1.3	2.9	5.6	9.7	14.1	17.5	18.2	16.4	12.6
1930	O	3.3	6.8	10.0	15.1	20.2	22.6	19.7	24.1	14.0	14.5
	P	1.0	2.5	5.6	10.8	18.7	27.2	33.8	35.2	31.6	24.1
1935	O	6.8	9.9	22.2	32.6	44.9	46.2	45.9	43.9	30.7	24.5
	P	2.0	5.2	11.4	21.9	38.0	55.4	68.7	71.7	64.3	49.1
1940	O	8.3	10.6	33.6	51.1	70.9	84.0	73.3	68.4	55.2	39.1
	P	3.3	8.2	18.2	35.0	60.7	88.5	109.8	114.6	102.8	78.4
1945	O	9.8	23.2	46.9	71.4	107.8	126.8	123.6	91.8	72.4	52.9
	P	4.7	11.7	25.9	49.9	86.5	122.8	156.4 -	163.3	146.4	111.7
1950	O	8.2	24.0	58.5	140.1	160.0	210.6	214.2	187.3	140.5	103.0
	P	7.4	18.6	41.0	78.9	136.9	199.5	247.5	258.3	231.6	176.7
1955	O	8.4	25.6	58.4	123.6	222.2	292.9	335.2	325.5	257.9	167.2
	P	10.3	25.9	57.2	110.1	191.1	318.7	345.5	360.6	323.3	246.7
1960	O	8.7	23.8	58.1	122.6	233.9	358.3	427.6	437.0	399.8	271.1
	P	12.3	31.0	68.5	131.9	228.9	323.5	413.8	431.9	387.2	295.4
1965	O	9.0	22.1	55.6	119.9	226.0	373.6	522.8	540.7	503.6	394.7
	P	13.7	34.5	76.1	146.5	254.2	370.5	459.7	479.8	430.2	328.2
1970	O	6.5	21.4	51.4	110.0	223.1	368.8	535.4	670.6	646.9	519.6
	P	14.7	36.9	81.6	157.0	272.4	397.0	492.6	514.1	461.0	351.7

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