

Smoking "attributable" mortality in India
Some relevant considerations

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SUMMARY

Gupta (1989) and Notani *et al* (1989) have estimated that at least 630,000 and possibly up to a million deaths occur annually in India as a result of tobacco use. This document casts doubt on the validity of these findings, and independently attempts to estimate “smoking attributable” mortality in India.

Section 1 describes briefly the method by which smoking “attributable” deaths are calculated. Section 2 summarizes in general terms the major problems in obtaining the appropriate data for India needed for these calculations, highlighting the lack of valid and representative data on mortality by cause, on prevalence of smoking, and on relative risk of disease by smoking. In sections 3 to 13 an attempt is made to review appropriate literature in order to obtain information on these.

Numbers of deaths (sections 3 and 4): There are no national data available on deaths by cause. Estimates for 1978 indicate that, of 9 mn deaths annually, 2.5% are from cancer, 7.1% are from cardiovascular disease and 14.6% are from chest diseases, but they do not indicate the proportions of deaths from smoking-related diseases such as coronary heart disease or chronic obstructive lung disease (COLD). Data from the Bombay cancer registry, which may not be representative of India, give some information on the relative frequency of different types of cancer. While rates of cancers of the tongue, mouth, pharynx, oesophagus and larynx are higher in India than in England, rates of lung cancer are much lower, by a factor of 5 or 6, and show no evidence of an increase over time.

Smoking habits (section 5): Although no nationally representative prevalence data are available, it was possible to collect together data from over 30 surveys, most conducted in the course of epidemiological studies. There is wide regional variation, not only in prevalence of smoking, but also in what is smoked (including cigarettes, bidis, chillum, hookah, dhumti and chutta) and in how smoking takes place (conventional and reverse). On average, perhaps about 50% of adult men and 10% of adult women smoke. The proportion who smoke cigarettes is probably no more than about a quarter of these figures.

Smoking and overall mortality (section 6): The data available, from only 3 studies, are

extremely sparse, relating to a very limited number of regions of India. They provide essentially no data on risk relating to smokers of conventional cigarettes and do not take into account any potential confounding variables.

Smoking and lung cancer (section 7): The available data suggest that 5-6% of all cancers are lung cancers, forming about 15,000 deaths annually. The relatively small number of epidemiological studies all show an elevated risk associated with smoking but to quite a varying extent. They suggest that 7,500 - 12,500 of the 15,000 deaths may be attributable to smoking, though other known risk factors, such as burning of biomass fuels, have not been accounted for in the studies.

Smoking and oral cancer (section 8): Data from Bombay suggest that there are perhaps about 40 - 50,000 deaths a year from oral cancer in India. A number of studies indicate that smoking of bidis is associated with about a 5-fold increase in risk, but there is very little evidence on cigarette smoking. Using a relative risk of 5 and a frequency of smoking of 30% implies that about 22,000 - 27,000 oral cancer deaths may be attributable to smoking.

Smoking and oesophageal cancer (section 9): The available data suggest that smoking is associated with about a 3-fold risk. Assuming, based on data from Bombay, that there are about 25,000 deaths a year in India from oesophageal cancer, this implies that about 9,000 deaths may be attributable to smoking.

Smoking and other cancers (section 10): No data were found here, but it is likely anyway that cancers of the lung, oral cavity and oesophagus would form the great majority of smoking-associated cancers.

Smoking and coronary heart disease (section 11): While some studies have reported an association between smoking and heart disease, a greater number have not, so there is great uncertainty as to what an appropriate relative risk estimate would be, all the more so since the studies have generally failed to consider relevant confounding variables. There is also great uncertainty about the number of cardiovascular deaths that are due to coronary heart disease - rheumatic heart disease is a major cause of death in India. Assuming 640,000 cardiovascular deaths, that about 10-25% of these are from coronary heart disease and a relative risk of 1.5 gives

a very tentative estimate of 10,000 - 20,000 deaths.

Smoking and chronic obstructive lung disease (COLD) (section 12): Although many studies have been conducted suggesting that the great majority of cases of chronic bronchitis (as determined by the MRC questionnaire) occurred in smokers, it was not clear this was so for COLD. In one study, 63% of cases of COLD were in lifelong non-smokers, and there is considerable evidence that various factors other than smoking are relevant to the aetiology of lung disease in India. Not only is it difficult to assess the proportion of COLD deaths that are due to smoking, it is also difficult, in the absence of suitable data, to assess the total number of COLD deaths that occur annually. One study reported only 1 in 1,000 hospital admissions are due to chronic bronchitis, but this proportion may not apply to deaths. It is considered impossible, with the data available, to come up with a reliable estimate of smoking-attributed deaths from COLD.

Smoking and other diseases (section 13): No attempt has been made to collect data here. It seems likely that cancer, coronary heart disease and COLD will cover 80% or more of the total deaths associated with smoking in India.

Overall deaths associated with smoking (section 14): Given that COLD deaths associated with smoking are somewhat less than half of cancer deaths associated with smoking, and given deaths from other causes (including vascular diseases other than CHD) are of the same order as deaths from COLD, one can arrive at a tentative overall figure of about 100,000 deaths annually associated with smoking in India. Probably over 75% of these would be associated with smoking of products other than manufactured cigarettes.

The main reasons why this estimate is substantially less than that of Gupta (1989) and of Notani et al (1989) are:

- i) their estimates include chewing as well as smoking;
- ii) they use data on relative risks of mortality derived from 2 studies in specific areas (Ernakulam and Srikakulam) which are highly unrepresentative, in one of which reverse smoking is commonly practised;
- iii) they use a higher smoking relative risk for coronary heart disease than I do;
- iv) they estimate far more total coronary heart disease deaths than I do; and

- v) they assume that COLD deaths associated with smoking form a much larger proportion of total deaths associated with smoking than I do and much higher than Peto et al (1994) have estimated for developed countries.

Overall, it is clear that the published estimates of deaths due to tobacco use in India are highly unreliable as most of the basic data required to make these estimates are missing.

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1. **Calculating smoking "attributable" mortality**

Suppose the proportion of a population who smoke is P . Suppose the risk of a specified cause of disease is R times higher in smokers than in an otherwise comparable group of non-smokers. Then, if, in a given time period, we observe N deaths from the disease, the number "attributable" to smoking can be readily calculated as $A = NP (R-1)/(1+P (R-1))$.

This calculation can be separately applied to subsets of the population (e.g. sex, age, religion) where P and R may vary, with the attributable numbers accumulated over the subsets to give a total for the disease.

The calculation is usually carried out separately for the major diseases associated with smoking with results accumulated to give an overall estimate of smoking "attributable" mortality.

To carry out the calculation requires the following data:

- 1) Estimates of the smoking habit distribution for the population of interest,
- 2) Estimates of number of deaths by cause for the population of interest, and
- 3) Estimates, by cause, of relative risk of death for smokers compared to non-smokers for the population of interest.

Preferably all estimates should be age and sex specific or at least the data on smoking habit distribution should be appropriate to an age group typical of the decedents.

The estimates of relative risk of death should preferably be adjusted for all relevant confounding factors. If this is not the case, one can certainly not describe the calculated results as smoking attributable deaths. At best, they are smoking associated deaths.

2. **Difficulties in obtaining appropriate data for India**

There are a number of major problems in obtaining appropriate data for India from which "attributable" deaths could be calculated. These are outlined below and then discussed further in more detail in sections that follow, which summarize relevant data from the papers that I have been able to obtain.

Deaths by cause. There seem to be few, if any, available national, or even regional, data on numbers of deaths by cause. Estimates of numbers of deaths by cause have to be arrived at by methods which are at best, only approximate.

Smoking habits. There are no available national data on the distribution of smoking habits in India. There are a number of surveys that have been conducted in various regions of India, some more representative than others. These show considerable variation by region, religion and social class in the proportion of men and women who smoke. The situation is made more complex by the many types of products that are smoked, including:

- (i) cigarette,
- (ii) bidi - an Indian form of cheap cigarette made by rolling between the fingers a rectangular dried piece of tendu leaf with tobacco and securing the roll with thread,
- (iii) chilum - a conical clay pipe, the narrow lower end being put to the mouth, sometimes arranged with a small piece of wet cloth, which acts as a filter,
- (iv) hookah - a pipe where the tobacco smoke is filtered through water kept in a special receptacle which sometimes contains aromatic substances,
- (v) dhumti - a kind of cigar made by rolling leaf tobacco inside the leaf of a jackfruit tree,
- (vi) chutta - a kind of cigar made by rolling local tobacco in a sun-dried tobacco leaf.

These may be smoked alone or in combination, different products being associated with different disease risks. The way products are smoked - conventional or reverse - varies markedly by region and is also associated with different disease patterns.

Relative risks. For some diseases that are considered smoking associated based on Western data,

there are very few if any studies that provide relative risk estimates specific for India and the products smoked there. For other diseases relative risk estimates are available or can be calculated from published data. However these are typically based on studies conducted in specific regions of India and results may not be generalizable to other regions where different products are smoked. Relative risk estimates in these studies are often highly variable and are not usually adjusted for potential confounding effects of any factors other than, at most, age and sex, though some studies have tried to disentangle possible associations with smoking and with chewing which is common in some parts of India.

3. **Deaths in India**

Although the WHO, in their World Health Statistics Annual series, do not give detailed data on deaths by cause for India, some relevant information is given. Using the latest report (WHO, 1994) one can find the following data for India (with comparative data for the UK shown alongside).

	<u>India</u>	<u>UK</u>
Population in millions (1994)	918.6	58.1
Distribution by age (1994)		
- 0-14	35.5%	19.5%
15-64	60.0%	65.0%
65+	4.5%	15.5%
Death rate per 1,000 (1991-95)	10.0	11.4
	<u>India</u>	<u>UK</u>
∴ Deaths per year (millions)	about 9.2 million	0.66
Life expectancy at birth (1990-95)	60.4 in both sexes	73.6 M 78.7 F
Cumulative risk of dying by age 5 (per 1,000 live births)	142	9

Sapru *et al* (1983) present data on deaths by broad cause of death for 1978 in selected countries of the world. For India they give the following data:

	<u>Millions of deaths</u>	<u>%</u>
All deaths	9.07	100.0
Cardiovascular disease	0.64	7.1
Chest diseases	1.32	14.6
Cancer	0.23	2.5

Ali and Sisodia (1995) present more recent data on the percentage distribution of deaths by major cause group:

	<u>1974</u> %	<u>1980</u> %	<u>1986</u> %	<u>1992</u> %	<u>1992*</u> million deaths
Coughs/disorders of the respiratory system	20.5	20.0	19.8	19.6	1.80
Diseases of the circulatory system	7.1	8.6	9.0	10.8	0.99

*Assuming a total of 9.2 million deaths for 1992

While they suggest that diseases of the circulatory system have risen somewhat over the period, so that they now total about 1 mn deaths, they do not suggest an increase is occurring in respiratory system disorders. It should be noted that Ali and Sisodia's data, while totalling 100% of deaths from all causes (only selected categories shown above), do not separate out cancer deaths. Presumably, therefore, deaths from lung cancers are included in the group "coughs/disorders of the respiratory system."

It is interesting to note that, though the annual number of deaths from chest disease in India (1.32 mn in 1978, and presumably somewhat more currently) is much more, by a factor of 15 or so, than the corresponding figure for the UK (91.1 thousand in 1983 for diseases of the respiratory system excluding cancer), the annual number of deaths from cancer in India (0.23 mn in 1978) is not vastly greater than the corresponding figure for the UK (0.14 mn in 1993), the

factor here being more like 1.6 or so. The difference for cardiovascular disease is also less great than it is for chest disease (India 0.64 mn for 1978, UK 0.18 mn in 1993).

4. Distribution of cancer by site

The Cancer Registry in Bombay has been providing data for 30 years or more to "Cancer Incidence in Five Continents", volumes of which were first published by UICC and then by IARC. A recent IARC scientific publication by Coleman *et al* (1993) presents data in trends in cancer incidence by site and registry. Table 1 presents data comparing estimates of site-specific rates for 1970 and 1985 in India (Bombay) and in the UK (South Thames). Rates are per 100,000 per year standardized to the age distribution of the world standard population, so are comparable between the two cancer Registries. From this table a number of observations can readily be made:

- (i) Overall cancer incidence rates are, in both sexes, substantially lower in India than in England. For both sexes the Indian rates are 50-60% or so of those in England.
- (ii) The distribution of cancer by site is very different in the two registries. Most notably rates of cancers of the tongue, mouth, pharynx, oesophagus and larynx are much higher in Indian men than women then in English men and women, often by a factor of 5 or more. Cervix cancer rates are also higher in Indian women than in English women, by a factor of about 2. In contrast Indian men and women have a 5 or 6 fold lower risk of lung cancer than English men and women. Rates are also substantially lower in India for cancers of the stomach, colon/rectum, pancreas, breast, corpus uteri, prostate, testis, bladder and kidney and (unsurprisingly) for melanoma.
- (iii) There is no evidence that cancer incidence is rising in India. Rates of lung cancer have changed very little from 1970 to 1985.

5. Smoking habits

A report of a World Health Organization workshop on "Smoking in Developing Countries" held in Sri Lanka in 1981 noted that "India is the third largest producer of tobacco in the world. 80 percent of what is grown is consumed locally, primarily in the form of bidis, hookahs, chuttas, chewing tobacco and snuff. 30 percent of the tobacco is used to produce cigarettes. Annual production is estimated to be 80 billion cigarettes. In comparison, 675 billion bidis are produced each year. Production is rapidly rising: In 1950, production averaged 100 per adult Indian; by the 1970's, this had increased to 190".

The report also noted that "smoking habits in India vary widely by occupation, region, socioeconomic status, religion and many other factors. Cigarette smoking is more prevalent in urban areas, particularly among the young. Urban blue collar workers generally prefer bidis, although some of the younger ones have taken up cigarette smoking. Smokers in rural areas generally use the indigenous forms of tobacco (bidis, chuttas, hookah, etc). Male smokers generally greatly outnumber female smokers, except in the lower classes, few women use tobacco".

The IARC monograph on tobacco smoking (1986) presented a table comparing annual per-head cigarette consumption to 110 countries, ranging from 3117 in Cyprus to 17 in Guinea. India, with a consumption of 141, was 102nd in the list.

Table 2 summarizes data on prevalence of smoking habits from a number of studies. Some of these data come from simple surveys of smoking habits conducted in specific regions, but most come from surveys with a medical interest in mind, either control groups from case-control studies or special surveys to determine prevalence of conditions such as oral cancer/leukoplakia, chronic bronchitis or heart disease. Most of these studies are referred to in later sections of this document.

These data are further summarized in Table 3, which gives percentages of smokers

(regardless of products smoked) in the 34 studies in Table 2. It can be seen that, for females, there is an enormous variability in the percentage of smokers. While 8 of the 20 studies providing data give estimates of 5% or less, with a further 4 in the 6%-12% range, estimates are in the 20%-36% range in 5 studies and in the 64%-91% range in 3 studies. It is notable that, in the studies (4, 19, 21) with very high percentages, reverse smokers formed the great majority of the woman who smoked. Indeed in all 3 of these studies less than 10% of the women smoked cigarettes conventionally. Reverse smoking was also prevalent in 2 other studies (8, 13). Even where reverse smoking was not practised, reported prevalence of cigarette smoking was never more than a few percent, other forms of smoking, such as bidis, dhumtis and chilum explaining the moderate prevalence of women smokers seen in other studies (eg. 10, 13, 22).

For males, percentages are much higher, all the estimates but one in Table 3 lying between 29% and 86%. The higher figures often contain a substantial number of reverse smokers. The median percentage of Indian men who smoke is around 50%, but this estimate must be considered unreliable given the non-representative nature of the locations and populations studied and the variability in the age ranges covered. There appears to be some tendency for percentages of smokers to decrease with time, judging by the fact that high prevalences, of greater than 70% are more commonly evident in earlier than later studies (studies 1-34 are in chronological order of publication). However, again it is difficult to come to a reliable conclusion. Some studies do not give breakdowns by product smoked, but it is clear from the data in Table 2 that the great majority of what is smoked is not cigarettes. Indeed, in many rural populations cigarettes are hardly smoked at all, while in other populations the proportion of men who smoke cigarettes rarely exceeds 20%. Only in studies conducted in large cities, like Bombay (studies 16 and 24), Delhi (14 and 32) and Chandigarh (17), did cigarette smokers form a substantial proportion of total smokers.

It appears not unreasonable, for the purposes of estimating smoking-attributable deaths, to assume that about 30% of Indian adults smoke, i.e. about 50% of men and about 10% of women. The proportion who smoke cigarettes is probably no more than about a quarter of these figures, though this estimate is highly uncertain.

6. Overall mortality

In 1968-1971, Mehta et al (1972) carried out a survey of oral cancer and precancerous lesions in over 100,000 individuals in the Pune district of Maharashtra. In follow-up surveys all the lesion cases and matched controls were re-examined and interviewed four times over an 8-year period. Gupta et al (1980) presents the results of an analysis comparing death rates in men who smoked and men who chewed, there being too few men who did not smoke or chew or women who smoked for analysis. In the control group without leukoplakia, the age adjusted risk of mortality was 1.6 times higher in the smokers, based on 108 deaths in smokers and 241 in chewers. In the group with leukoplakia, the relative risk was 1.9, based on 42 deaths in smokers and 64 in chewers. Presence of leukoplakia was also associated with an increased death rate. Again confounders were not adjusted for, and there was no data on deaths by cause.

Gupta et al (1984a) followed up 10,287 inhabitants of Ernakulam district in Kerala, a south-western state of India, for 10 years and related mortality to tobacco chewing and smoking habits. A total of 746 deaths were reported, 415 in men and 331 in women. Age-adjusted relative risks for, respectively, no habit, smoking habit, chewing habit and mixed habits were 1.0, 1.5*, 1.2 and 1.4* in males and 1.0, 1.1, 1.3* and 1.7 in females (* $p < 0.05$). Very few women smoked so the relative risks for smoking habit and mixed habits are based on very few deaths. No adjustment was made for any potential confounding variables and deaths were not separated by cause of death. 90% of smokers smoked the bidi.

Gupta et al (1984b) followed up 10,169 inhabitants of Srikakulam district in Andhra Pradesh, a Southern state of India, for 10 years and related mortality to tobacco chewing and conventional and reverse smoking habits. A total of 1,432 deaths were reported, 757 in men and 675 in women. Compared to those who had no habit, age-adjusted relative risk of mortality was significantly elevated in both sexes in reverse smokers (of chutta) (RR=1.95 in men, and 1.91 in women) and in men in conventional smokers (of chutta or bidis) (RR=1.77) or in chewers (RR=1.96). Multiple usage was associated with RRs of 1.20 in men and 1.24 in women. Again no adjustment was made for any potential confounding variables and deaths were not separated by cause of death, although it was noted that only 14 of the deaths occurred from oral cancer. 34% of men and 59% of women reverse smoked in this population.

It can be seen that the data on overall mortality are very sparse. They relate to a limited number of regions of India, they provide essentially no data on risk relating to smokers of conventional cigarettes, they do not take into account potential confounding variables (other than chewing) and they do not give relative risks by age. Although all three studies show an increased risk of mortality in smokers, it would not be possible to estimate any sort of reliable figure of total deaths associated with smoking, let alone deaths attributable to smoking, from these figures.

7. Lung Cancer

7.1 Incidence

Data from the Bombay Cancer Registry for 1970 and 1985, (Coleman et al, 1993) summarized in Table 1, shows that lung cancer incidence rates are about 6 times lower than those recorded in England. Lung cancer forms about 12-15% of the total incident cancers in men and about 3% of the total in women in Table 1, but it should be noted that the data of Coleman et al do not cover all cancer types. Data for liver cancer, rare in Western countries but common in some developing countries, are, for example, not given.

Jussawalla and Jain (1979) also confirmed that lung cancer incidence rates were 5-7 times lower than in a number of registries in USA and in Western Europe and that there was no evidence of a trend over time. They also noted that incidence in non-Parsi males was about double that in Parsi males, though incidence in Parsi and non-Parsi females was similar.

Sanghvi (1981) also presented data from the Bombay Cancer Registry. In 1968 to 1972 he stated that the total cancer incidence was 143.1 in men and 121.7 in women, and that the lung cancer incidence was 13.5 in men and 3.1 in women, i.e. lung cancer formed 6.3% of total cancer incidence for the sexes combined.

Behera (1992) pointed out that the Indian National Cancer Registry has, since 1982, been collecting incidence data in 5 regions (Bombay, Madras, Chandigarh, Dibrugar and Trivandrum). In 1986, the combined data showed that lung cancer formed about 8% of all cancers in males and less than 1% in females. He reviewed data from 17 studies showing variation in the recorded male:female ratio of lung cancers, usually in the range 4 to 8. 12 of the studies reported smoker:non-smoker ratios ranging from 1.9 to 7.3, though it should be appreciated these are not relative risks, control data on smoking habits usually not being collected.

The above data suggest that something like 5-6% of all incident cancers are lung cancers. Taken in conjunction with the estimate of deaths from cancer given in section 4, and bearing in mind that the percentage may be somewhat higher for fatal cancers, this suggests that numbers

of lung cancer deaths in India each year are perhaps around 15,000, substantially less than in the UK (33,000 in England and Wales for 1993).

7.2 **Relative risks**

Notani and Sanghvi (1974) carried out a retrospective study at the Tata Memorial Hospital in Bombay involving 520 lung cancer cases and an equal number of age, sex, community matched controls who came to the hospital within the same period and were diagnosed as not having cancer. The cases and controls were similar in regard to income and urban/rural residence. Compared with non-smokers the relative risk of lung cancer was estimated to be 2.45 for all smokers, 2.64 for bidi smokers and 2.23 for cigarette smokers. Risk rose with amount smoked, rising to 5.25 for 30+ bidis per day and to 10.50 for 10+ cigarettes per day. Only 178 of the cases had the radiological diagnosis confirmed by histology or cytology. For confirmed cases, relative risks were 1.88 for all smokers, 2.18 for bidi smokers and 1.67 for cigarette smokers. Results were not presented separately for males and females.

Jussawalla and Jain (1979) compared 792 males with lung cancer with randomly selected controls, matched for age and community, obtained from the voters list of the Greater Bombay Corporation. Compared to non-smokers the relative risk of lung cancer was estimated to be 16.8 for any smoking, 19.3 for bidi smoking and 8.6 for cigarette smokers. Hindu, Moslem and Christian smokers had similar relative risks and a dose-response relationship was found for both bidi and cigarette smokers. Among the 350 histologically confirmed cases relative risks were 14.7 for all smokers, 14.9 for bidi smokers and 10.2 for cigarette smokers. Jussawalla and Jain did not comment on the striking difference between their results and those of Notani and Sanghvi, both studies being conducted in the same city. The difference seems likely to be due to the different choice of controls, it being noteworthy that Notani and Sanghvi had made no attempt to exclude subjects from their controls who had diseases other than cancer that were associated with smoking. [It is interesting to note that IARC (1986), commenting on the "substantially different" estimates of relative risk in the two studies, merely noted that the use of community controls risked "some confounding" by socioeconomic status, as all cases may not have been on the list of registered voters.]

Jindal et al (1987) studied the distribution of age, sex and smoking habits in 480

histologically diagnosed cases of lung cancer in Chandigarh in Northern India. 83% of cases occurred in men and 75% in smokers. Unfortunately, there was no control group so relative risks could not be calculated.

Sankaranarayanan et al (1994) carried out a case-control study in Trivandrum in the state of Kerala in South-West India. This involved 281 male lung cancer patients and 1207 controls selected from visitors and patients' bystanders in the hospital. Extensive dietary questions were asked, with questions also being asked on education, religion and smoking. Though diet was the main interest of the study, negative associations being found with bananas and green vegetables (particularly pumpkins and onions) and positive associations being found with animal protein foods and dairy products, the authors did present results of one analysis relating smoking to risk. The relative risk, adjusted for age, education and religion, rose from 1.0 in never smokers to 22 in smokers of 21-25 pack-years, 44 in smokers of 31-40 pack-years, and 114 in smokers of 61+ pack-years. No attempt was made to adjust relative risks for diet or to separate results by type of product smoked.

Percentage attributable risks of lung cancer can be estimated from the 3 studies providing relative risk data, as follows:

Notani and Sanghvi	-	Bombay	47.0%
Jussawalla and Jain	-	Bombay	76.4%
Sankaranarayanan	-	Trivandrum	83.6%

Applying these percentages to the estimated number of lung cancer deaths occurring each year in India would give numbers of lung cancer deaths associated with smoking of order 7,500-12,500. Of course this is most unreliable, given the limited areas covered and the wide variation in smoking habits by area.

7.3 **Other causes of lung cancer**

Behera (1992) cited results of various studies showing that in areas where biomass fuels are used for cooking, exposure to benzo(a)pyrene is equivalent to smoking about 20 packs of cigarettes per day. It is notable that cooking habits have never been considered as a potential confounding variable in studies of smoking and lung cancer. Indeed none of the epidemiological studies relating smoking to lung cancer have made any serious attempt to take potential confounding variables into account. Even the dietary study of Sankaranarayanan et al (1994) did not attempt to adjust relative risks associated with smoking for dietary variables.

8. Oral and pharyngeal lesions

8.1 Cancer

Sanghvi *et al* (1955) conducted a case-control study in Bombay involving 730 male and 110 female patients with cancer of the upper alimentary tract and 288 male and 112 female control patients without cancer. From the data presented broken down by sex, smoking and chewing it is possible to estimate relative risks (95% CIs) for men, adjusted for chewing, as follows:

	<u>RR (95% CIs)</u>
Buccal mucosa	0.64 (0.38-1.09)
Oral cavity (other)	1.72 (1.02-2.90)
Oesophagus	2.05 (1.01-4.14)
Hypopharynx	3.24 (1.76-5.98)
Base of tongue	5.30 (2.78-10.1)
Oropharynx	5.74 (2.22-14.8)
All upper alimentary tract	2.52 (1.77-3.58)

The relative risk in men for all upper alimentary tract cancer for chewing, adjusted for smoking, could be estimated as 2.32 (1.74-3.10). In women, relative risks for all upper alimentary cancer could be calculated as 2.90 (1.00-8.42) for smoking and 5.30 (2.88-9.72) for chewing. Adjustment for the potential confounding factors of community, age and occupation did not affect the general conclusion that “the habit of chewing was associated with cancer of the oral cavity; that the combined habit of smoking and chewing was associated with cancer of the hypopharynx and base of the tongue; and that only smoking was associated with cancer of the oropharynx and oesophagus.”

Hirayama (1966) carried out an investigation of the epidemiology of oral and pharyngeal cancer in several different countries and localities in Central and South-East Asia. He concluded that there was strong supportive evidence for an association with the habit of chewing tobacco, but a less marked association with smoking, the drinking of alcohol, and vegetarian dietary customs. Age-adjusted mortality from oral cancer was noted to be higher in Bombay (2.5 per

100,000) than in westernized countries (range 0.4-2.0) and rising. The proportion of all cancer due to oral cavity cancer was found to vary widely in India, from 9.8% in Calcutta and 11% in Vellore to 68% Mainpuri and 76% in Nanyur. In Bombay, this proportion increased markedly with decreased social class. Combined results from a case-control study conducted in India and Ceylon showed that tobacco chewing was associated with a significantly increased risk of cancer of the lip, cheek, gingiva and anterior tongue, but that tobacco smoking was associated mainly with an increased risk of the posterior tongue and the rest of the oropharynx (where relative risks were in the range 4 to 6).

Wahi (1966) reported the results of a study on oral and oropharyngeal cancer conducted in Mainpuri District, a rural district 75 miles from Agra. Among never smokers, 126 oral cancers were seen in an estimated population of 206,800, a rate of 0.61 per 1,000. Among occasional smokers and daily smokers, rates were 0.85 and 1.60 per 1,000 based on 10 and 210 cases respectively. Rates were 3.60 in bidi smokers, 0.76 in smokers of chilum, and 1.85 in smokers of hookah. Detailed results were presented showing the joint relationship of smoking, chewing and alcohol drinking to prevalence of oral cancer. It was clear, see table below, that the association was much more strongly with chewing tobacco, particularly Mainpuri tobacco (which is a ready-made mixture of finely cut betel nut, slaked lime and tobacco), than with smoking.

		<u>Males</u>	<u>Females</u>
Non-chewers of tobacco	- non-smokers	0.50	0.07
	- smokers	0.64	0.25
Chewers of Mainpuri tobacco	- non-smokers	4.00	6.38
	- smokers	7.88	13.04
Chewers of other kinds of tobacco	- non-smokers	0.81	0.74
	- smokers	1.68	3.42

(prevalence rates per 1,000 are shown for non-drinkers)

Jussawalla and Deshpande (1971) compared tobacco chewing and smoking habits in Bombay in a study involving 2,005 cases of oral cavity, pharynx, oesophagus and larynx cancer and 2,005 age/sex/religion matched controls from the voters' list. Compared with those who neither smoked nor chewed, relative risks of all the types of cancers combined were 4.1 for

chewing only, 5.6 for smoking only and 15.7 for smoking and chewing. For oral cavity cancer these relative risks were 6.0, 2.8 and 10.1, for oropharyngeal cancer they were 3.3, 11.8 and 31.7, while for larynx cancer they were 4.6, 7.7 and 20.1. Compared with those who did not smoke, relative risks of all the types of cancers combined were 5.7 for bidi only smokers and only 1.2 for cigarette only smokers. Only for oropharyngeal cancer was risk significantly elevated in cigarette only smokers and then the relative risk, 2.3, was much lower than it was for bidi only smokers, 14.1.

Carcinoma of the hard palate is a very unusual cancer in most countries. It is quite common in the Visakhapatnam area of India and Reddy *et al* (1971) and Ramulu and Reddy (1972) describe the results of a study conducted there showing a strong association of reverse smoking with this cancer. Among controls without oral cancer and aged over 20 attending the out-patient department of the hospital, reverse chutta smoking was reported in 6.6% of 883 men and in 7.2% of 886 women. Among the cases of carcinoma of the palate, reverse chutta smoking was reported in 78% of the 18 men and 100% of the 46 women. Reverse smoking was also associated with a clearly increased risk of oral cancers of other sites, being reported in 28% of the 29 men and 86% of the 7 women. Reddy *et al* concluded that reverse smoking of chuttas is of great significance, especially in the cases of carcinoma of the hard palate, but that the ordinary method of smoking chuttas does not seem to be of great significance, while cigarette and bidi smoking are of no significance at all. Chewing was uncommon in this population.

Reddy (1974), describes the results of a further study, conducted at King George Hospital Visakhapatnam, which serves the Visakhapatnam and Srikakulam districts of the east coast of India. The study involved 600 patients with carcinomas of the oral cavity and oropharynx, admitted in 1970-73, and 600 healthy hospital visitor population controls matched on age, sex, economic status, education, occupation, religion and area of residence. Compared with subjects with no smoking habits, relative risks (and 95% CIs) could be estimated from the data presented, as shown in the table below. The strikingly high risk of oral cancer, particularly of the hard palate, in relation to reverse chutta smoking is well illustrated, though it is clear that ordinary smoking of chuttas is also associated with increased risks.

Hard palate cancer

Other oral cancer

	<u>Males</u>	<u>Females</u>	<u>Males</u>	<u>Females</u>
Reverse smoking of chuttas	96.1(12.1-764)	226.0(54.6-940)	10.5(4.7-23.5)	12.4(5.5-28.1)
Ordinary smoking of chuttas	12.0(1.5-97.7)	32.5(6.0-178)	6.3(2.9-13.5)	5.6(1.4-21.5)
Other smoking habits	0.0	-	2.9(1.3-6.4)	-
No habit	1.0	1.0	1.0	1.0

Reddy *et al* (1975), in a further study based on patients from the same hospital, compared 520 new cases of cancer of the oral cavity, pharynx, larynx and oesophagus admitted in 1972 to 1974 and 520 controls, defined and matched as in the previous paper (with which there may be some overlap). Compared with all those who did not reverse smoke, reverse smokers had an 8.5-fold increased risk of oral cavity cancer and a 19.5-fold increased risk of hard palate cancer. Smokers of cigarettes were found to have five times lower risk than non-cigarette smokers, but as the latter group included reverse and conventional chutta smokers and bidi smokers, this finding was uninterpretable.

Notani and Sanghvi (1976) described the results of a study of oral cancer conducted in males in Bombay involving 214 cases and 230 undefined controls. The paper mainly concerned diet, but relative risk estimates of 1.99 for smoking only, 3.93 for chewing only and 4.34 for chewing and smoking, compared to those with neither habit, were calculated. The relative risk for smoking alone was not statistically significant, but the other two were ($p < 0.01$, $p < 0.001$).

Jayant (1977) attempted to assess the evidence then available to determine whether the association of smoking and chewing with oral and pharyngeal cancers was causal. He concluded that chewing a quid containing tobacco and bidi smoking could be taken to be causally associated with these cancers, but study was required to assess possible effects of chewing betel quid without tobacco. He estimated, using the data of Jussawalla and Deshpande (1971), for Bombay, that 70% of oral cavity cancer would have been avoided had the habits of smoking and chewing not existed in the population.

Notani and Jayant (1987) carried out a case-control study involving 819 cases of oral cavity, pharynx, oesophagus or larynx cancer attending the Tata Memorial Hospital in Bombay between 1976 and 1984. All were male Hindus from the State of Maharashtra. There were two sex/community matched control groups, one hospital patients without cancer, the other obtained

from electoral rolls. The authors reported relative risks (95% CI) as follows:

	<u>Oral cavity</u>	<u>Pharynx</u>	<u>Larynx</u>
No habit	1.0	1.0	1.0
Chewers only	3.9 (2.1-7.1)	2.3 (1.2-4.4)	1.8 (0.6-5.1)
Smokers only	5.2 (2.8-9.8)	4.2 (2.2-8.0)	6.8 (2.6-17.4)
Chewers and smokers	7.6 (3.5-16.8)	5.0 (2.4-10.7)	7.7 (2.4-25.0)

86% of the smokers smoked bidis. No habit includes those smoking or chewing up to twice a day. The study mainly concerned possible effects of diet on cancer, negative associations being reported with vegetable and fish consumption and positive associations with fat and chili consumption. No attempt was made to see whether any of the association of smoking or chewing with the cancers studied could be explained by confounding due to diet.

Using the same database, Notani (1988) investigated the joint relationship of smoking, chewing and alcohol consumption on oral cavity, pharynx and oesophageal cancer. Adjusted odds ratios for smoking were noted to be 4.7 for oral cavity cancer and 4.5 for pharyngeal cancer.

Sankaranarayanan *et al* (1989) carried out a case-control study in Kerala, Southern India involving 185 cases of gingival cancer and 895 hospital-based controls for whom head and neck malignancies had been excluded. A stepwise multiple logistic regression analysis showed that the main factor associated with gingival cancer risk in men was pan-tobacco chewing, with relative risks rising to 13.2 for ≥ 10 times per day. Significant or near significant associations were also seen for bidi smoking (relative risk of just over 2), alcohol drinking and snuff use. Cigarette smoking was not associated with an increased risk.

The evidence on oral cavity cancer is far more abundant than is the case for lung cancer. Generally it is quite consistent in showing that both tobacco chewing and tobacco smoking are associated with an increased risk of oral cancer. However, the evidence on tobacco smoking mainly relates to the smoking of bidis, for which relative risks of order 5 have been reported by a number of authors, and also to the reverse smoking of chuttas, which clearly massively increases risk of carcinoma of the hard palate. There is very little evidence on cigarette smoking

specifically - indeed the only study separating this out (Jussawalla and Deshpande, 1971) reported a relative risk of only 1.2. It is also noticeable that alcohol consumption, a known risk factor for oral cavity cancer, has rarely been considered in these studies.

It is difficult enough to get any sort of accurate figure on the total number of oral cavity cancer deaths a year in India, since incidence varies widely from region to region and national data are not available. It is even more difficult to allocate these deaths to the various chewing and smoking habits practised in India.

The evidence from Bombay in Table 1 suggests that about 20% of all cancer deaths in India are cancers of the tongue, mouth, pharynx or larynx, implying that there are perhaps 40-50,000 such deaths a year in India. Assuming a relative risk of 5 for smoking and a frequency of smoking of 30% would imply around 22-27,000 oral cancer deaths were associated with smoking, with the great majority of these deaths associated with smoking products other than conventional cigarettes.

8.2 Oral leukoplakia

In view of the high incidence of oral cancer in India, there have been quite a number of studies conducted in which prevalence of the pre-cancerous condition oral leukoplakia has been determined in relatively large populations, and linked to tobacco smoking and to chewing habits. For example:

- (i) Pindborg et al (1967), in a large-scale dental survey conducted in Lucknow in the State of Uttar-Pradesh involving 10,000 patients, reported a prevalence of 3.28%, with prevalence being far higher among users of tobacco and betel-nut than among non-users.
- (ii) Mehta et al (1969), in a similar study in Bhavnagar in the State of Gujarat, reported a prevalence of 1.7% in 10,071 persons studied. Prevalence was far higher in smokers than in non-smokers or those who only chewed tobacco.
- (iii) Mehta et al (1972), in a follow-up study of 3,674 Bombay policemen, found that the 10 year incidence rate was 2.8%. Prevalence was commoner, and more persistent, among smokers than among chewers.
- (iv) Bhonsle et al (1976), in a survey of 5,449 villagers in Goa, reported a prevalence of leukoplakia of 1.6%. Again it was seen almost exclusively in smokers.
- (v) Gupta et al (1984c), in a survey of 12,213 tobacco users in Ernakulam in the State of Kerala, reported a stronger dose-response relationship with smoking than with chewing.
- (vi) Van der Eb et al (1993), in a study of 480 persons in Andhra Pradesh, where reverse chutta smoking is widely practised, reported leukoplakia of the palate in 13%. Prevalence of palatal lesions was much higher in reverse than in conventional smokers.

None of these studies showed any relationship of oral leukoplakia to the smoking of conventional cigarettes, generally being carried out in rural regions where such smoking was rare.

9. Oesophageal cancer

As noted in Table 1 incidence of oesophageal cancer in the Bombay registry is substantially higher than in the UK, by a factor of 2-3 for men and 3-5 for women.

Paymaster *et al* (1968), who also noted that the frequency of cancer of the oesophagus is very high in India, compared the frequency of smoking and pan-chewing in 741 male and 278 female cancer cases and in 821 male and 493 female controls with no cancer taken from the Tata Memorial Hospital in Bombay. The cases and controls were found to have a similar distribution of age and religion. From these data the following relative risks can be estimated.

	<u>Males</u>	<u>Females</u>
No habit	1.00	1.00
Chewing only	1.91	2.48
Smoking only	2.45	2.44
Chewing & Smoking	3.09	3.64

Jussawalla and Deshpande (1971), in their case-control study conducted in Bombay (see section 9.1) reported a relative risk of oesophageal cancer for smokers of 2.1.

Jussawalla (1981), reviewing evidence on oesophageal cancer in India, noted the high incidence rates in India, with both males and females affected equally. He concluded that bidi smoking, pan chewing with or without tobacco, and alcohol drinking are the factors strongly associated with oesophageal cancer in Bombay. He presented relative risks from a case-control study involving 649 cases and 649 age/sex/religion matched general population controls. Relative risks for men were 5.3 for smoking bidis only, 2.7 for smoking cigarettes alone, 31.1 for smoking bidis and chewing pan, and 51.4 for smoking cigarettes and chewing pan.

Notani and Jayant (1987), in their case-control study in Bombay referred to in section 9.1, reported relative risks (95% CI) of 1.0 for non-smokers/chewers, 1.5 (0.8-2.8) for chewers only, 3.2 (1.8-5.9) for smokers only, 3.3 (1.6-6.9) for chewers and smokers.

Notani (1988), in their detailed analysis of the joint effect of smoking, chewing and alcohol on risk of cancers of the upper alimentary tract, based on the Bombay case-control study

referred to in section (9.1), estimated that smoking was associated with a relative risk of 4.0 for oesophageal cancer.

The evidence summarized above suggests that smoking is associated with a 2-4 fold increased risk of oesophageal cancer, though there is relatively little data on risk by type of cigarette. The data in Table 1, from Bombay, suggest that 10% of cancer deaths in India might be due to oesophageal cancer, ie. about 25,000 deaths in total. Assuming 30% smoke and a relative risk of 3 would imply about 9,000 deaths associated with smoking. Again these estimates are very rough.

10. Other cancers

At the time of writing I am not aware of any study which has estimated the risks associated with smoking for other types of cancer. No such data are given in IARC's (1986) monograph on tobacco smoking. Of the other commoner types of cancer in India, cancers of the breast, stomach, colon-rectum and ovary are little if at all smoking associated in Western studies. Cervix cancer is, but this is generally thought to be an artifact due to an association of smoking with sexual habits, the true cause agent being the sexually transmitted human papilloma virus. Restricting attention to the lung, oral cavity and oesophagus would certainly pick up the great majority of the smoking-associated cancers.

11. Coronary heart disease

Datey *et al* (1965) noted that 3.3% of hospital admissions to the KEM Hospital in Bombay in 1952 and 1956 were due to heart disease. Of the 3,456 heart disease cases, 22.5% were from rheumatic heart disease, 18.3% from hypertensive heart disease, 14.9% from arteriosclerotic heart disease and 13.0% from cor pulmonale. Total incidence and relative frequency of the different types of heart disease did not vary by religious group. They cited results from studies in Agra, Lucknow, Delhi, Madras, Calcutta and the Himachal Hills showing a higher percentage of rheumatic heart disease among heart disease cases (31.5 to 50.6%). Proportions with hypertensive and arteriosclerotic heart disease are noted to be lower than those from Western countries. Smoking habits were not considered in this paper.

Naik *et al* (1966) noted that the ideal way of evaluating the prevalence of CHD was from a cross-sectional study of the population. However, they were not able to carry out such a study, merely observing that, over the period 1961-63, 3.8% of total medical admissions to Osmania General Hospital in Hyderabad were from CHD. The proportion among total cardiac cases was 18.8%. They cited results from a number of other studies, conducted in Madras, Bombay, Lucknow, Delhi, Amritsar, Simla, Calcutta and Agra, all showing that CHD formed between 10% and 23% of cardiac cases except for Simla (in the Himalayan hills) where it formed only 6%. In their own study the proportion of medical admissions due to CHD was higher in men (4.9%) than in women (2.1%). Risk factors were not considered.

Bhargava *et al* (1966) noted that 4.1% of hospital admissions to the PBM Group of Hospitals in Bikaner, Rajasthan between 1945 and 1964 were due to heart disease. Of the 3,722 heart disease cases, 2,541 were men and 1,208 women. Percentages of cases from rheumatic heart disease were 32.0% and 34.3% in 1945-54 and 1955-64. For coronary artery disease the corresponding figures were 11.8% and 14.8%, while for hypertensive disease they were 19.3% and 20.8%. Smoking habits were not considered.

Vytilingham *et al* (1966) studied hospital admissions to the CMC Hospital in Vellore, South India between 1955 and 1965. Of the total number of 34,837, 10,276 (29.5%) were diagnosed as having organic heart disease, 15.3% of which (1,572) were classified as having

coronary artery disease. It is unclear why the figure of 29.5% was so much higher than the figures of 3 or 4% reported in the previous papers. Possibly it was because this concerned admissions diagnosed as having heart disease rather than as admissions due to heart disease. In a sample of 1,200 cases of ischaemic heart disease, 1,016 of which were men, it was noted that 60% gave a history of smoking. The authors noted that the incidence of 60% corresponded roughly to the number of smokers in the general population, though no specific control data were cited. If this is true, it does not indicate any association of smoking with ischaemic heart disease in this population.

Malhotra (1967) described the results of a study of CHD deaths occurring in men aged 18-55 serving on the eight zonal railways in different parts of India. Over the five year period 1958-1962, 679 CHD deaths occurred amongst a total of 1.15 mn employees. Mortality rates in the quinquennium varied from 20 per 100,000 employees in the Northern Railway zones to 135 in the Southern zones. The per capita sale of cigarettes was noted to be eight times higher in the Punjab (north) than in Madras (south) though the incidence of CHD was seven times more in Madras than in the Punjab. The author noted that his data did not take into account other smoking habits and tobacco chewing, but concluded that there was "nothing" in his study "to suggest cause and effect between smoking and ischaemic heart disease".

Sarvotham and Berry (1968) carried out a prevalence survey of CHD in Chandigarh in Northern India involving all 2,030 persons above age 30. Diagnosis was based on a history of myocardial infarction or angina pectoris or defined ECG abnormalities. In both sexes the prevalence rates were noted to be similar to those reported in a study by Epstein in Tecumseh in Michigan. Smoking habits were not recorded.

Bahl (1968), in a study conducted in Delhi, noted a higher prevalence of IHD, whether considered as a proportion of total admissions (6.5%) or of cardiac admissions (37.2%) than reported by Naik et al (1966) in his study in Hyderabad or in the studies he reviewed.

Bansal et al (1970) compared 100 well documented cases of ischaemic heart disease with 100 sex/age matched ophthalmology controls in a study conducted in Delhi. The number of smokers in the cases, 38, and in the controls, 39, was very similar. However, the distribution of

type of smoking was very different in the two groups, with cigarette, bidi and hookah smokers forming, respectively, 30, 5 and 3 of the cases, and 15, 8 and 16 of the controls. Heavier smokers (>10 cigarettes or bidis per day) were also more common in cases, 20, than controls, 6.

Sinha (1970), in a review editorial, pointed out that, though the proportion of cardiac cases with IHD was found to vary from 6% to 23%, higher proportions, of around 40%, were reported when attention was restricted to upper income groups. He referred to Keys' well-known seven countries study (1970) as providing evidence that heavy smoking is a factor in IHD and cited a study by Banerjea (1958) as finding that 64.4% of CHD cases were either heavy or moderately heavy smokers.

Gupta and Malhotra (1975) found that the prevalence of CHD was about two-and-a-half times more common in the urban population of Rohtak town than in the rural population of Dighal village, in Haryana. They reported finding no appreciable difference in the prevalence of CHD between smokers and non-smokers, either in the town or the village.

Mukerjee (1975) noted that rheumatic heart disease formed a larger proportion of total heart disease in India than did ischaemic heart disease.

Chinniah and Yavagal (1979) studied 100 patients with acute myocardial infarction aged 24-40 from South India. 94 were men and 6 women. 76 were smokers (37 bidi, 36 cigarettes, and 3 ex-smokers). Smoking was noted to be the commonest risk factor in these cases. No attempt was made to collect control data.

Sapru (1983), based on literature available at the time, estimated that 2.5% of the total Indian population aged 40+ are likely to suffer from coronary artery disease, forming 3.42 million out of a total of 136.9 million. He noted that, even amongst people from the poor socioeconomic groups, almost all individuals have atherosclerosis of the coronary arteries after the age of 40. He referred to a survey conducted by the Registrar General of India which found that cardiovascular diseases accounted for 5.1% of all deaths in the rural community in 1979.

Jayant et al (1983) described what was referred to as the first case-control study in India aiming at studying the relationship of CHD to different types of tobacco used. The cases were 185 patients from the Cardiothoracic Unit of a Bombay hospital. Controls, matched for age, religion and community care from either the general population or for age 58+ from the Orthopaedic Unit. Compared with non-smokers/non-chewers, relative risks could be calculated as 3.1 for bidi smokers/non-chewers, 2.5 for cigarette smokers/non-chewers, 1.0 for non-smokers/tobacco chewers, and 2.8 for those with mixed habit. Ignoring chewing, smoking was associated with a relative risk of 2.7 ($p < 0.001$) with no significant difference by product smoked.

Jajoo et al (1988) carried out a survey of the prevalence of CHD in 2,433 members of an asymptomatic rural community aged 30 years or more living near Sevagram, Western India. The overall prevalence was 14.8 per 1,000 adults, being higher in women (20.09) than in men (10.46). Among the 1,338 men, prevalence was no higher in the 339 bidi smokers (8.9%) than in the 999 non-bidi smokers (11.0%). The authors concluded that "while modifications of risk factors and primary prevention of CHD will continue to be a focus of considerable interest and concern, we believe that such attempts are uncalled for in this rural community around Sevagram."

Chadha et al (1990) carried out a community based survey of CHD on a random sample of 13,723 adults aged 25-64 in Delhi. The overall prevalence was 31.9 per 1,000 adults. The prevalence of smoking was, respectively, 36.5%, 34.9% and 36.7% in men who were diagnosed as CHD on clinical history, who had silent CHD and who were CHD free. The corresponding prevalences for women were 5.9%, 10.9% and 3.8%. The authors concluded that "smoking did not show evidence of association with CHD".

Chadha et al (1992) carried out a study of CHD in 1,317 Gujaratis aged 25-64 in Delhi. The overall prevalence was 25.1 per 1,000 adults. The proportion of smokers was no higher in those with a clinical history of CHD (23%) or in those with silent CHD (12%) than in those who were CHD free (23%). The authors concluded that "smoking did not seem to play a major role as a single risk factor for CHD".

Gopinath et al (1992) carried out a community based study of CHD in a random sample

of 13,723 adults aged 25-64 in urban Delhi. Based on a sample of 5,621 of those with no symptoms of CHD, 1.4% had definite and 5.3% had probable CHD based on ECG evidence. Of those with definite or probable CHD, 35% of men and 11% of women smoked. No comparable percentages of smokers were reported for men and women without CHD detected by ECG.

Raman Kutty *et al* (1992) carried out a survey in rural Thiruvananthapuram district in Kerala state involving 1,253 individuals aged 25+. Prevalence rates per 1,000 were 36 for ECG changes suggestive of CHD, 48 for angina determined by the Rose questionnaire, 14 for definitive evidence of CHD and 74 for possible evidence of CHD. 42-54% of men in each group smoked, but no attempt was made to relate smoking to prevalence of CHD.

Gupta *et al* (1994) studied educational status, CHD and coronary risk factor prevalence in 3,148 residents aged over 20 in rural Rajasthan in Western India. 3.4% of men and 3.7% of women were diagnosed as having CHD based on ECG abnormalities, the Rose questionnaire or a documented history of angina or infarction. Current or past smoking was reported in 51% of men and 5% of women, but again no attempt was made to relate smoking to the prevalence of CHD.

Singh *et al* (1994) carried out a population survey of 162 rural and 152 urban subjects aged 26-65 in Moradabad, North India. Prevalence of coronary artery disease (based on WHO criteria) was higher in urban subjects, 8.6%, than in rural subjects, 3.0%. Prevalence of smoking, defined as smoking >15 cigarettes or bidi per day or smoking hookah >15 times/day was comparable in the urban and rural subjects (20.5% vs. 20.0%). The relationship of smoking to coronary artery disease was not presented.

Begom and Singh (1995) carried out a survey of the prevalence of CHD in a sample of 235 men and 225 women sampled from the urban population of Trivandrum in Kerala state in Southern India. The prevalence of coronary artery disease was 17.4% in men and 10.2% in women. The authors presented data showing that prevalence of CHD was 4.4% among the 315 non-smokers, 62.4% among the 32 ex-smokers and 26.6% among the 113 current cigarette smokers. Unfortunately these results were not separated by sex, the frequency of tobacco consumption differing greatly between the two sexes (men 44.6%, women 3.5%). The authors

compared the findings of this survey in South India with the urban subjects of the previous study (which was based on similar methodology) conducted in North India. The authors noted that prevalence of diabetes, glucose intolerance, hypertension, hypercholesterolemia and hypertriglyceridemia were similar in both sexes in North and South Indians, but that the prevalence of smoking in South Indians was higher. However, the authors stated that it was clear (though no supporting analysis was presented) that these risk factors could not explain the higher prevalence of coronary artery disease among South Indians (which was incorrectly stated to be statistically significant).

Gupta et al (1995) carried out a cross-sectional study in three villages in Rajasthan and six wards in Jaipur involving a total of 1,963 women. The prevalence of CHD, as diagnosed by history and ECG, was 10.5% in urban and 3.7% in rural women. Although smoking was also more common in the urban women, the age-adjusted prevalence of CHD was not significantly associated with smoking.

Gopinath et al (1995) carried out a survey of CHD on a random urban sample of 13,560 adults of different ethnic groups in Delhi. The prevalence rate of CHD on a clinical basis per 1000 adults was the highest in Sikhs (47.3), lowest in Muslims (22.8) and intermediate in Hindus (31.8) and Christians (31.2). The Sikhs also had the highest prevalence rate of myocardial infarct and angina pectoris. Prevalence rates were not presented in relation to smoking, but it was noted that the prevalence of smoking was lowest in Sikhs (0.9%), highest in Muslims (20.1%) and intermediate in Hindus (15.0%) and Christians (12.5%), i.e. in the opposite direction to the pattern of prevalences for CHD.

A number of studies have shown that Indian migrants have a high risk of coronary disease. For example:

- (i) Balarajan et al (1984) compared mortality by cause among migrants to England and Wales from the Indian subcontinent with that expected from the cause distribution for England and Wales. Although deaths from lung cancer in the migrants formed a smaller proportion of total deaths than seen in England and Wales as a whole, deaths from coronary heart disease were proportionately more common, by about 20%, in both sexes. The excess was evident in all ethnic groups.

- (ii) Beckles *et al* (1986) carried out a prospective study of a community living in Port of Spain, Trinidad. By comparison with adults of African descent, age-adjusted relative risks of death from all causes and from cardiovascular diseases were significantly increased in those of Indian origin (by 1.5 and 2.6 respectively). The difference could not be explained by differences in smoking habits or other coronary risk factors.
- (iii) Bhatnagar *et al* (1995) compared coronary risk factors in a randomly selected group of 247 migrants of Punjabi origin from India living in West London and 117 of their siblings living in the Punjab. The West London cohort had significantly higher body mass index, blood pressure, glucose, apolipoprotein B and total serum cholesterol and lower high-density lipoprotein cholesterol. Smoking habits were not determined.

A recent editorial in the BMJ (Gupta *et al*, 1995) reviews the evidence that "irrespective of regional, cultural, and religious differences, immigrant South Asians all share a significantly higher mortality from coronary heart disease than the indigenous white population." A commentary in the Lancet on the paper by Bhatnagar *et al* (1995) considered that established risk factors for heart disease do not explain the increased CHD of migrant Asians. As compared with the indigenous UK population, "their serum total cholesterol concentration is about the same or even lower" and "there is no apparent excess of hypertension or smoking."

The evidence from Indian data of a role of smoking in coronary heart disease is very limited indeed. Indeed a number of studies (Chadha *et al*, 1990; Chadha *et al*, 1992; Gupta *et al*, 1995) reported no association of smoking with non-hospitalized CHD prevalence, and the case-control study of Bansal *et al*, (1970) showed no very clear relationship either. Malhotra (1967) also found no relationship, in his study of railway workers, and contrasted the much greater incidence of CHD in Madras (then the Punjab) with the much lower sales of cigarettes there, and Vytillingham *et al* (1966) stated the percentage of smokers in hospital admissions from CHD in Vellore was similar to that in the general population. Singh (1995), commenting on a study in Delhi by Gopinath *et al* (1995) which had shown that "the wide variations in prevalence rates of CHD in different ethnic groups cannot be explained satisfactorily on the basis of conventional risk factors," stated that "we agree that smoking does not appear to be associated with CHD in Indians." The only studies reporting an association of smoking with CHD were the case-control study by Jayant *et al* (1981) in Bombay (which cited a relative risk of 2.7, $p < 0.001$,

but took no account of potential confounding factors other than chewing tobacco) and the prevalence study of Begom and Singh (1995) in Trivandrum (which reported a strong association in an analysis which did not even separate results by sex, let alone adjust for potential confounding variables).

It would be impossible from these data to obtain any sort of reliable estimate for India of the relative risk associated with smoking. It is also difficult to come up with a reliable estimate of numbers of coronary heart disease deaths. The data of Sapru et al (1983) tell us that in 1978 there were approximately 640,000 deaths from cardiovascular disease, but the proportion of deaths from coronary heart disease is not clear. The data reviewed by Naik et al (1960) showed that rheumatic heart disease, which I believe is not associated with smoking, is the main form of heart disease, and that coronary heart disease formed about 15% or so of total heart disease admissions. This percentage may be out of date, since there is evidence that urbanization and westernization is associated with an increase in deaths. Also, being a percentage of admissions, it need not necessarily apply to deaths.

Given 640,000 cardiovascular deaths, given 30% of the population smoke and given various possible estimates of the proportion of cardiovascular deaths due to coronary heart disease and of the relative risk associated with smoking, one can, as in the table below estimate coronary heart disease deaths associated with smoking.

Estimated CHD deaths (thousands) associated with smoking

Proportion of CVD deaths that are CHD	Relative risk			
	<u>1.5</u>	<u>2.0</u>	<u>2.5</u>	<u>3.0</u>
10%	8.3	14.8	19.9	24.0
15%	12.5	22.2	29.8	36.0
20%	16.7	29.5	39.7	48.0
25%	20.9	36.9	49.7	60.0

Western data normally suggest a relative risk around 2.0 or somewhat less. This would suggest estimates in the range 20-30,000 might seem not unreasonable. However, this takes no account of the fact that, as noted above, a number of studies report no association between smoking and CHD. Furthermore, coronary heart disease is highly multifactorial, and the studies considered have generally taken little or no account of potential confounding variables. In view of these points a lower estimate in the range 10-20,000 might be more reasonable. In any event, it must be considered most unclear what an appropriate estimate of deaths due to smoking actually is.

This uncertainty is reflected by a recent article (Bonita and Beaglehole, 1994) which noted that “very little is known about the prevalence and incidence of cardiovascular diseases in developing countries, less of the trends in disease occurrence over time, and even less of the reasons for the variations in occurrence of disease by time and place. In particular, we have no idea how much of the ‘emerging epidemic’ of cardiovascular disease in developing countries is merely a reflection of the ageing of the population.”

12. Chronic obstructive lung disease (COLD)

Saha and Jain (1970) studied the clinical and pathophysiological features of 50 men in Delhi with chronic non-specific respiratory disease and compared these with those reported for London and Chicago by Fletcher. The authors noted close similarities in the clinical, radiological and physiological features of the disease in the three groups. However, they pointed out that, whereas almost all of the London and Chicago groups had smoked, 16% of the Delhi group reported lifelong non-smoking; suggesting that factors in addition to smoking may be responsible for causing this condition in Delhi.

Saha and Jain (1973) later reported results of 3 years follow-up of these men. At that time, 11 were known to have died. 8 of the deaths were among the 17 patients who reported currently smoking 20 or more cigarettes a day at the start of the study, whereas none were among the 19 patients who were non-smokers or were smokers of less than 10 cigarettes a day.

Malik (1974) compared prevalence of chronic bronchitis in 65 non-smokers, 78 bidi smokers and 55 cigarette smokers in a study of working men in Chandigarh, in Northern India. Based on clinical diagnoses using the (Medical Research Council) MRC questionnaire, chronic bronchitis was diagnosed in 3% of non-smokers, 35% of bidi smokers and 45% of cigarette smokers. Prevalence was related to amount and duration of smoking. Based on objective measurements, forced expiratory volume in one second as a proportion of forced vital capacity (FEV_1 / FVC) and maximal mid-expiratory flow rate (MMEFR) were abnormal in, respectively, 3% and 6% of non-smokers, 14% and 32% of bidi smokers, and 24% and 45% of cigarette smokers. FEV_1 / FVC and MMEFR were related to amount and duration of cigarette but not bidi smoking.

Purohit and Sharma (1974) carried out a survey of the prevalence of chronic bronchitis (MRC) in 374 persons aged 60+ living in 29 villages in Naila in southern Jaipur. The prevalence of chronic bronchitis was noted to be 70.0%, higher in males (85.9%) than in females (50.1%), and to rise with age. Prevalence of chronic bronchitis was higher in smokers than in non-smokers, both in males (87.0% vs. 79.3%) and in females (74.1% vs. 37.6%). Tobacco was consumed mainly in the form of smoking through earthen pipes (chilum).

Thiruvengadam et al (1974) studied 79,301 hospital admissions from 3 teaching hospitals in Tamilnadu, 2 in Madras and 1 in Vellore. Only 130 (0.16%) were recorded as being from chronic bronchitis and scrutiny of their case records revealed that in fact only 70 actually had the condition. All of 30 subjects examined in detail at one of the hospitals proved to be smokers, 23 of bidis, 6 of cigarettes and 1 of cigars. 17 of the 30 smokers were classified as smoking heavily. No control data were available for comparison.

Bhattacharyya et al (1975) carried out a survey of the prevalence of chronic bronchitis (MRC definition) in 1140 persons aged 30+ living in 5 villages near Lucknow. The prevalence of chronic bronchitis was noted to be 5.7%, somewhat higher in males (6.7%) than in females (4.5%), and to rise with age, to 10.6% in those aged 70%. None of this population smoked cigarettes, most smoking bidi or hookah. The prevalence of chronic bronchitis was similar in smokers (4.4%) and in non-smokers (4.2%) but much higher in ex-smokers (25.0%) suggesting that many of these people gave up smoking because of the bronchitis. Prevalence was 4 times higher (11.8%) in heavy smokers (15 grms + a day) than in light smokers (2.6%).

Joshi et al (1975) studied 473 male industrial workers aged 17-64 in Ludhiana in North-West India. The prevalence of chronic bronchitis (MRC) was estimated as 12.5%, with little variation by age after 25 years old. Prevalence was much higher in smokers (20.5%) than in non-smokers (3.9%). No attempt was made to relate prevalence to cigarette consumption as no subject smoked more than 20 cigarettes per day. FEV_{1.0} was also noted to be significantly lower in smokers than in non-smokers, given age.

Malik (1977) reported the results of two studies of males attending sick friends or relatives conducted in Chandigarh in Northern India. In the first study, simple chronic bronchitis (MRC) was seen in 10.8% of 185 bidi smokers and in 3.1% of 1182 non-smokers, with chronic airways obstruction seen in 5.4% of bidi smokers and in 0.5% of non-smokers. In the second study, the ratio of FEV₁/FVC was less than 70% in 17% of 121 bidi smokers and in 3.4% of 88 closely matched non-smokers.

Radha et al (1977) carried out a random sample of 505 households in a selected area of Delhi. Overall 2098 subjects aged 3 or over were surveyed, of whom 67 (3.2%) had chronic

bronchitis (MRC). Prevalence was higher in men (4.2%) than in women (2.1%) and rose to 12.6% in subjects aged 60+. Only one woman smoked. In men, prevalence was higher in those who had ever smoked (8.0%) than in those who had never smoked (4.4%). In smokers, prevalence rose with pack-years of consumption, to 15.3% in the highest category (>8). The prevalence was higher in smokers of bidi (8.3%) or combinations (15.7%) than in smokers of cigarettes (6.0%).

Malik and Singh (1978) screened 278 male farmers belonging to a village near Bhiwani, North India, for the presence of chronic respiratory disease of non-specific origin. Among the 197 smokers (all of hookah or bidi) 16% had simple chronic bronchitis (MRC) and 5.6% had chronic bronchitis with associated airways obstruction. Prevalences were not given for the 81 non-smokers, but it was noted that respiratory symptoms were much less common than in the smokers.

Kinare *et al* (1981) studied lung sections from 163 cases of sudden death occurring in Bombay. Emphysema was noted to be present in 68.7% of cases. This frequency was noted to be comparable to that in other developed countries. Smoking was not studied.

Nigam *et al* (1982) carried out a house-to-house survey for chronic bronchitis in adults residing in a rural community of Jhansi in Uttar Pradesh. Out of 1424 individuals examined clinically, 92 (6.5%) had chronic bronchitis (MRC). Prevalence of chronic bronchitis was higher in men (8.1%) than in women (4.5%) and rose with age, to 10.3% in the 70+ age group. Prevalence of chronic bronchitis was 4.6% in non-smokers, 6.1% in smokers and 24.1% in ex-smokers. Among current smokers, prevalence was higher in heavy smokers (10.1%) than in light smokers (3.4%). Prevalence was higher in chilum/hookah smokers (8.5%) than in bidi smokers (4.6%) or cigarette smokers (4.3%).

Malik (1982) estimated the prevalence of chronic bronchitis (MRC) in 3,228 men and 1,772 women in Chandigarh. Evidence of chronic bronchitis with or without airways obstruction was seen in 4.2% of non-smokers, 14.1% of cigarette smokers, 16.6% of bidi smokers, 40.9% of hookah smokers and 17.7% of mixed smokers. Evidence of chronic bronchitis with airways obstruction was seen in 0.5%, 2.6%, 2.4%, 16.4% and 9.4% in the same

five groups. The higher chronic bronchitis rate in smokers was evident at all age groups and was related to extent and duration of smoking.

Malik *et al* (1983) carried out a study in 150 men and 100 women in the village of Gopalpur in Orissa State. Chronic bronchitis (MRC) with and without airways obstruction was seen in 32.7% of reverse chutta smokers (who formed 45% of the population of the village), with prevalence increasing sharply with duration of smoking.

Behera and Malik (1984) studied 169 men and 205 women of the Telgu community in the coastal village of Gopalpur and Cuttack city in Orissa. Among 225 reverse chutta smokers, chronic bronchitis (MRC) was diagnosed in 33.3% of men and 32.7% of women, as against only 1.7% in 59 non-smokers. In reverse smokers prevalence increased with duration of smoking to 49% in those who had smoked for 41 years or more. Reverse smokers also showed lower FEV₁ than non-smokers.

Malik and Kashyap (1986) studied the prevalence of chronic respiratory diseases in 304 men and 142 women aged 18 to 80 living in the rural hills of Shimla in Himachal Pradesh. Prevalence of simple chronic bronchitis (MRC) was 14.5% in men and 8.5% in women, with prevalence of evidence of airways obstruction seen in an additional 7.2% of men and 10.5% of women. In smokers (predominantly of bidis) prevalence was higher than in non-smokers; for simple chronic bronchitis 21.2% vs. 4.2% in men and 25.0% vs. 0.9% in women; and for airways obstruction 10.8% vs. 1.6% in men and 27.5% vs. 3.9% in women. Among smokers prevalences rose with increasing smoking. For overall chronic bronchitis (including airways obstruction), the prevalence was 58.2% in men and 90.0% in women in the highest category (>300 cig/bidi years) vs. 11.1% in men and 7.1% in women in the lowest category (1-100 cig/bidi years).

Malik and Behera (1986) compared the prevalence of chronic bronchitis (MRC) in 2372 non-smokers of a total sample of 2825 men and women from a rural population, Mullanpur village. Prevalence was markedly higher in the rural population (males 4.1%, females 5.0%) than in the urban population (males 0.9%, females 1.6%).

Kamat and Doshi (1987) studied 4129 subjects in 3 urban communities in Bombay with

different pollutant profiles together with a rural control. At the start of the study, prevalence of chronic bronchitis (standardized for age, sex, smoking and family income) was 5.0% in the rural area and 4.5%, 4.5% and 2.3% in the high, medium and lower pollution urban areas. In a multiple regression analysis conducted separately in each area, a correlation was seen between severity of chest symptoms and both occupation and smoking. Respiratory symptoms in the urban areas were strongly correlated with the levels of SO₂, NO₂ and SPM. From a considerable number of additional analyses the authors concluded that "our data from studies done over 1977-82 in Bombay reveal a large cardiorespiratory morbidity and mortality attributable to the prevailing air pollution levels."

Jindal (1993) reported some findings from 10 year follow-up of the subjects in Chandigarh and Mullanpur considered by Malik and Behera (1986). The overall percent prevalences of symptomatic subjects seen in 1990 were similar to those observed in 1980. Amongst male smokers, the prevalences were 6.9% and 8.3% in the follow-up study compared to 5.6% and 6.8% in the initial study for, respectively, simple chronic bronchitis (MRC) and chronic bronchitis with airways obstruction. In asymptomatic subjects, the mean change in peak expiratory flow rate did not differ significantly between smokers and non-smokers in men aged less than 40 years, but the decline was significantly greater in smokers in men aged above 40 years of age initially. Those with an initial airways obstruction deteriorated significantly more than those with normal initial PEFr.

Qureshi (1994) carried out a study of 155 men and 131 women from a Gujjar village and of 136 men and 138 women from a non-Gujjar village, both in the Kashmir valley. The Gujjar villagers have lower socio-economic status and spend much of their time in single-room hutments with poor ventilation, burning firewood for cooking and heating purposes. In both villages the entire population aged 15+ was screened. The prevalence of chronic bronchitis in Gujjars was 8.4% in men and 12.2% in women; in non-Gujjars it was 6.6% in men and 3.6% in women. The prevalence was higher in smokers than in non-smokers in both Gujjars (16.4% vs. 8.4%) and non-Gujjars (8.8% vs. 2.5%). The excess prevalence in Gujjars, given smoking habits, was considered to be due to the increased time they spend near unventilated fireplaces, evidence being presented that prevalence rose sharply with average time spent there.

Ray *et al* (1995) carried out a survey with follow-ups over a 5 year period in a total of 9946 residents aged 30+ of four rural villages in Tamil Nadu. At the end of the period 328 patients were diagnosed to have COLDF. The overall prevalence rate was noted to be 3.3%, higher in males, 4.1%, than in females, 2.6%. The rate rose with age up to 60-69, after which it declined. Smoking habits were only obtained for those with COLDF, so prevalence by smoking could not be calculated. However it was noted that all of the 130 females with COLDF denied ever having smoked, as did 76 of the 198 males. Of the 122 male smokers with COLDF, 106 were bidi smokers, while the other 16 smoked cigarettes. 44 were heavy smokers, 68 light smokers and 10 ex-smokers.

The great majority of the studies described in this section concern the prevalence of chronic bronchitis as defined by the MRC questionnaire. In a number of studies prevalence was reported to be in the range 1 to 4% for non-smokers and substantially increased in smokers. In these studies prevalences in the range 20%-45% were noted in relation to reverse chutta smoking (Malik *et al*, 1983; Behera and Malik, 1984), hookah smoking (Malik, 1982), bidi smoking (Malik 1974; Malik and Kashyap 1986) and cigarette smoking (Malik 1974; Joshi *et al*, 1975), and between 10 and 20% in relating to bidi smoking (Malik, 1977; Malik, 1982) and cigarette smoking (Malik, 1982). There are however, some studies showing different patterns. These include the study of Purohit and Sharma (1974) which reported prevalences as high as 79% in male and 38% in female non-smokers (though rates were higher in smokers of chillum, 87% and 74% respectively), the study of Radha *et al* (1977) which only reported an 8% prevalence in male smokers, and the studies of Bhattacharyya *et al* (1975) and Nigam *et al* (1982) which reported similar prevalences of about 4-6% in current and non-smokers (but much higher rates in ex-smokers).

Although most of the studies of MRC chronic bronchitis prevalence suggested that the great majority of cases were in smokers, it was not clear that this was so for COLDF. In the study by Ray *et al* (1995), 76 out of 198 (38%) males with COLDF and 100% of the 130 females with COLDF denied ever having smoked, as did 16% of the 50 cases of chronic non-specific lung disease investigated by Saha and Jain (1970). A number of studies pointed to the relevance of other factors in the aetiology of lung disease in India, including burning firewood for cooking and heating purposes in poorly ventilated hutments (Qureshi, 1994), air pollution (Kamat and

Doshi, 1987) and factors associated with rural living (Malik and Behera, 1986).

None of the studies provide any very useful information on the role of smoking in mortality from lung diseases. The only study of deaths was that by Saha and Jain (1973) and that study only concerned 11 deaths in those who had diagnosed lung disease at the start of follow-up.

Nor do they provide any useful information on the frequency of death from COLD. The study of Thiruvengadam et al (1974) is of some interest in that it investigated hospital admissions, finding that only about 0.1% of a large sample of admissions from 3 teaching hospitals were from chronic bronchitis subsequently confirmed to be so. This figure of 0.1% contrasts very sharply with the percentage of deaths in India from all chest diseases given by Sapru et al (1983) as 14.6%.

Based on this material it seems virtually impossible to estimate the number of deaths per year from COLD that are attributable to smoking. A major problem is that there seem to be no good data on the total number of deaths from COLD. The 1978 estimate of Sapru et al (1983) of 1.32 mn is clearly a very considerable overestimate as it is for “all chest diseases” and includes deaths from diseases such as pneumonia and influenza (many of which occur in children anyway) and possibly from respiratory tuberculosis. Equally, arriving at a figure of about 10,000 COLD deaths, by applying the 0.1% figure given by Thiruvengadam et al (1974) for the ratio of bronchitis admissions to all admissions to the total number of deaths in India, could well be a substantial underestimate, since many sufferers from COLD may not be admitted to hospital. The fact that these two estimates are so far apart does not help in coming to a reliable figure.

Even were a reliable figure of total deaths from COLD available, it is also highly unclear what proportion of deaths should be attributed to smoking. In Western countries COLD deaths rarely occur in non-smokers and one can attribute most such deaths to smoking with reasonable confidence. Evidence from studies noted above, particularly that by Ray et al (1995) in which 206 out of 328 (63%) occurred in lifelong non-smokers, suggests the situation is not so simple in India. This is supported by a recent editorial on indoor air pollution in India (Smith, 1996) which noted that “chronic lung disease and cor pulmonale are killers of adult Indian women,

even though relatively few smoke tobacco.” Because of all these points I will not attempt to provide an estimate of COLD deaths due to smoking.

13. Other diseases

I have not attempted to collect together any data for other diseases. Estimates of deaths associated with smoking for developed countries (Peto et al, 1994) indicate that 25% are from lung cancer, 13% from other cancer, 35% from vascular disease, 17% from respiratory disease and 10% from other causes. It seems likely that consideration of cancer, coronary heart disease and COLD will cover 80% or more of the total deaths associated with smoking in India.

14. Estimating overall deaths associated with smoking - a comparison of my estimates with those of Gupta (1989) and Notani et al (1989)

In the preceding sections, I have attempted to make estimates of the number of deaths associated with smoking for various diseases. These estimates are limited in many ways - inter alia by absence of reliable data on number of deaths by cause, by the lack of good national data on the distribution of smoking habits in India, and by the paucity of relative risk data and by the fact that it applies only to specific areas and usually takes no account of confounding by other risk factors - and should be viewed as highly approximate. These estimates are as follows:

<u>Cause of death</u>	<u>Deaths associated with smoking (thousands)</u>
Lung cancer	7.5 - 12.5
Oral/pharynx/larynx cancer	22 - 27
Oesophageal cancer	about 9
Coronary heart disease	10 - 20
COLD	??
Other causes	??

Given, in developed countries, COLD deaths associated with smoking are somewhat less than a half cancer deaths associated with smoking, and given deaths from other causes (including vascular diseases other than CHD) are of the same order as deaths from COLD, one can very tentatively substitute about 20 thousand for each of the ?? in the table. This would bring the total up to about 100,000. The majority, probably over 75%, of these deaths would be associated with the smoking of products other than manufactured cigarettes.

It is of interest to compare these findings with estimates made by Gupta (1989) and by Notani et al (1989) at a UICC Workshop.

Gupta estimates that, in India, at least 630,000 deaths, and possibly up to a million, are caused annually by tobacco use. These estimates are based on the following assumptions:

1. About 2.76mn deaths in men, and 2.3mn deaths in women occur among individuals aged 15+.

2. Tobacco is used by 60% to 80% of men and 15% to 67% of women.
3. The relative risk of mortality for tobacco users ranges from 1.4 - 1.9 for men and from 1.3 - 1.5 for women.

The attached figure of 630,000 comes from the minimum estimates of tobacco use frequency and relative risk.

The main problems with these estimates are as follows:

- (a) Tobacco use is defined as including smoking and chewing, with no attempt made to separate out deaths associated with smoking, let alone with smoking specifically of manufactured cigarettes.
- (b) The estimates of relative risk of mortality of users vs. non-users are derived only from 2 studies in specific areas (Ernakulam in Kerala, and Srikakulam in Andhra Pradesh) which are highly unrepresentative of India as a whole. In one of these areas reverse smoking is commonly practised, which makes it very untypical.
- (c) No attempt has been made to take into account statistical variability of the estimates of relative risk from these studies.
- (d) One study, conducted in Pune, is referred to, but this study does not give any estimates of relative risk of users to non-users.
- (e) The relative risk estimates are not adjusted for any potential confounding variables. They are thus, at best, estimates of deaths associated with smoking, not due to smoking. Although this procedure can be criticised, Peto et al (1994) halved the percentage excess risk associated with specific causes in calculating deaths associated with smoking to developed countries to attempt to take account of potential confounding. Such a procedure would clearly substantially reduce estimates.

Notani et al (1989) again do not attempt to separate out chewing and smoking. For 1986 they include the following mortality estimates:

<u>Cause of Death</u>	<u>Total deaths (000's)</u>	<u>Deaths due to tobacco (000's)</u>
Cancer	110	69
CHD	450	101
Stroke	150	27
COLD	350	157
Total for 4 causes	1060	354
Total for all causes	5000	629

Points to note about these estimates are as follows:

- (i) The total of 629,000 for all causes is the same as the 630,000 calculated by Gupta (1989) and calculated in the same way. Gupta, and the authors of the Notani paper, were all members of the same Working Group on the subject.
- (ii) Notani's estimate of 69,000 cancer deaths due to tobacco is based on 39,000 (out of 54,000) deaths from cancer of the oral cavity, pharynx and larynx, 11,000 (out of 30,000) deaths from cancer of the oesophagus and 9,000 (out of 26,000) deaths from cancer of the lung. The difference from my estimate of about 40-50,000 deaths due to cancer arises partly from the fact that they estimate more deaths from cancer in the first place, and partly from the fact that they are including deaths associated with chewing which certainly increases the numbers of cancers of the oral cavity. It should be noted that the paper does not actually state what relative risk estimates they used in their attributable risk calculations.
- (iv) Notani's estimate of 101,000 CHD deaths (stated to be due to smoking not chewing) is stated to be based on a relative risk of 2. Given the deaths form 22% of the total, this implies that 29% of the population smokes, which is not unreasonable. One major reason for the difference between my estimate of 10-20,000 deaths associated with smoking and theirs of 101,000 lies in the relative risk assumed. As I noted in section 11, a number of Indian studies have found no association between smoking and CHD and the value of 2 used by Notani, based on Western data, may well be an overestimate. Another major difference arises from the number of CHD deaths assumed. They estimate 450,000, I estimated 100-130,000. My estimate was based on an estimate of 640,000 for total cardiovascular disease deaths in 1978, and evidence that CHD formed perhaps 15-20% of all cardiovascular disease, with rheumatic heart disease forming a major proportion

of deaths. Their estimate of 450,000 comes from the Registrar General's report in 1983, which I have not yet seen, which states that 4.6% of all deaths in the country are due to "heart attacks". The basis for this estimate needs to be looked at. In any event, it is important to note, particularly for CHD, that confounding factors have not been taken into account.

- (v) Notani's estimate of 27,000 stroke deaths stated to be due to smoking is particularly weakly based. There are no Indian specific relative risk estimates that I am aware of, and the total number of deaths estimated is open to considerable doubt.
- (vi) Notani's estimate of 157,000 COLD deaths stated to be due to smoking forms quite a large proportion of the total for the 4 causes considered. However it seems clear from section 12 that there is in fact very little reliable evidence on which to base such an estimate. If the estimate were valid, it would imply that the relative importance of COLD, as a cause of death, as compared to CHD, cancer and stroke, is much more important in India than in developed countries. Thus we have

	India		Developed countries 1990	
	(Notani et al, 1989)		(Peto et al, 1994)	
	<u>N</u>	<u>%</u>	<u>N</u>	<u>%</u>
Cancers of mouth, pharynx, larynx, lung, oesophagus	110	10	677	14
CHD	450	42	2309	47
Stroke	150	14	1470	30
<u>COLD</u>	<u>350</u>	<u>33</u>	<u>435</u>	<u>9</u>
Total	<u>1060</u>	<u>100</u>	<u>4891</u>	<u>100</u>

Even if it is actually true that COLD deaths are as frequent as this, it is far from clear that smoking is responsible for such a high proportion of the deaths. Whatever is causing the high frequency of COLD, if it exists, may not be smoking at all. It seems to me that one needs serious epidemiological studies in a number of centres to determine incidence of COLD and all risk factors associated with it before one can start making any sort of estimates for COLD deaths associated with or due to smoking.

In summary, it is clear that the published estimates of deaths due to tobacco use in India are highly unreliable as most of the basic data required to make these estimates are missing.

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TABLE 1
Comparison of cancer incidence rates in India and in the UK

	India (Bombay)				UK (South Thames)			
	Males		Females		Males		Females	
	1970	1985	1970	1985	1970	1985	1970	1985
1. Lip	0.6	0.6	-	-	1.3	0.8	-	-
2. Tongue	24.3	14.9	7.0	5.4	1.4	1.9	0.8	0.9
3. Mouth	12.8	12.1	11.8	9.1	1.9	2.0	1.1	1.1
4. Pharynx	28.8	24.1	7.8	5.9	3.6	3.0	2.1	1.3
5. Oesophagus	26.5	21.0	21.4	16.9	7.9	11.5	4.1	5.2
6. Stomach	16.4	13.1	10.2	8.7	34.6	25.1	13.7	9.3
7. Colon and Rectum	13.7	10.8	10.0	9.5	45.3	47.6	39.3	39.5
8. Pancreas	3.6	4.5	1.7	2.8	14.1	14.7	8.2	9.4
9. Larynx	27.3	16.9	-	-	7.1	6.9	-	-
10. Lung	25.1	27.7	6.2	6.2	150.7	118.9	31.6	42.1
11. Bone	1.2	0.9	1.3	0.7	1.3	1.0	0.9	0.8
12. Melanoma	0.4	0.4	0.4	0.4	2.9	6.5	5.6	10.9
13. Breast	-	-	41.1	51.3	-	-	104.3	119.6
14. Cervix Uteri	-	-	50.0	42.1	-	-	28.5	21.7
15. Corpus Uteri	-	-	3.1	4.7	-	-	17.3	18.2
16. Ovary	-	-	9.1	12.4	-	-	24.2	25.6
17. Prostate	7.7	9.2	-	-	22.2	32.4	-	-
18. Testis	0.8	1.2	-	-	4.5	5.3	-	-
19. Bladder	4.6	6.2	1.6	1.6	35.9	35.4	7.7	9.1
20. Kidney	2.2	2.2	1.2	1.2	8.4	10.7	3.5	4.7
21. Thyroid	1.4	1.4	3.1	3.1	1.0	1.2	2.3	2.8
22. Non-Hodgkin Lymphoma	3.2	5.2	2.6	4.0	5.7	14.7	3.8	9.8
23. Hodgkin's Disease	1.0	1.1	0.7	0.7	3.5	3.8	2.3	2.3
24. Multiple Myeloma	0.8	1.4	0.9	2.0	3.8	5.6	2.9	3.6
25. Leukaemia	3.4	4.5	3.8	3.8	8.0	8.4	5.5	5.5
26. TOTAL*	205.8	179.4	195.0	192.5	365.1	357.4	309.7	343.4
% Lung	12.2	15.4	3.2	3.2	41.3	33.3	10.2	12.3
% Upper aerodigestive (1-5, 9)	58.5	49.9	24.6	19.4	6.4	7.3	2.6	2.5

*Of all the cancers (1-25) for which Coleman *et al* (1993) provided data.

TABLE 2
Prevalence of smoking in various Indian surveys

Author, location, sample and sample size (N)	Prevalence of smoking (%)			
		<u>Males + Females</u>		
		<u>Chew*</u>	<u>Do not chew</u>	
			<u>Total</u>	
1. Pindborg <i>et al</i> (1967) Lucknow Survey of villages N = 10,000	No smoking	12.2	67.0	79.2
	Bidi only	3.0	8.9	11.9
	Cigarettes only	1.5	3.3	4.8
	Chilum only	0.1	0.2	0.3
	Hookah only	0.5	1.0	1.5
	Mixed smoking habits	0.6	1.8	2.5
	(*tobacco, pan with tobacco, or pan without tobacco)			
		<u>Males</u>	<u>Females</u>	
2. Paymaster <i>et al</i> (1968) Bombay Hospital controls N = 1,314	No habit	23	58	
	Chew only	20	36	
	Smoke only	31	5	
	Chew and smoke	26	1	
		<u>Males + Females</u>		
3. Mehta <i>et al</i> (1969) Bhavnagar Survey of villages N = 10,071	No habit	67.7		
	Bidi smoking	20.2		
	Hookah smoking	5.5		
	Other smoking or mixed	6.6		
		<u>Males</u>	<u>Females</u>	
4. Pindborg <i>et al</i> (1971) Srikakulam Random sample, 15+ N = 10,169	No habit	19	33	
	Conventional smoking	30	2	
	Reverse smoking	35	59	
	Chewing	4	3	
	Multiple usage	12	3	
		<u>Males</u>	<u>Females</u>	
5. Reddy <i>et al</i> (1971) Visakhapatnam Hospital controls N = 1,769	No smoking	21.2	90.6	
	Chutta - ordinary	22.8	2.2	
	Chutta - reverse	6.6	7.2	
	Cigarettes	27.6		
	Bidis	15.7		
	Mixed smoking	6.1		
		<u>Males -</u>	<u>1959</u>	<u>1969</u>
6. Mehta <i>et al</i> (1972) Bombay Policemen followed up N = 3,674	No habits	23.0	14.5	
	Bidi smoking	16.9	17.8	
	Cigarette smoking	5.4	9.1	
	Chewing habits	43.1	47.0	
	Mixed habits	11.5	11.6	

TABLE 2 (continued)
Prevalence of smoking in various Indian surveys

Author, location, sample and sample size (N)	Prevalence of smoking (%)				
		<u>Males</u>			
7. Bhowan <i>et al</i> (1973) Rajasthan Professional men N = 1,742	Non-smokers	58			
	Smokers	42			
		<u>Males</u>		<u>Females</u>	
8. Reddy (1974) Visakhapatnam and Srikakulam Hospital visitors N = 600	No smoking	21.5		64.4	
	Chutta - ordinary	26.5		6.0	
	Chutta - reverse	16.2		29.5	
	Other smoking habits	35.8		0.0	
		<u>Males + Females</u>			
9. Notani and Sanghvi (1974) Bombay Hospital controls N = 519	Non-smokers	39			
	Bidi	44			
	Cigarette	11			
	Mixed smoking	6			
		<u>Males</u>		<u>Females</u>	
10. Purohit and Sharma (1974) Jaipur villages N = 374	Non-smokers	14.0		65.3	
	Smokers (mainly chilum)	86.0		34.7	
		<u>Males + Females</u>			
11. Bhattacharyya <i>et al</i> (1975) Lucknow villages N = 1140	Non-smokers	47.7			
	Ex-smokers	6.7			
	Smokers	5.0			
	- Chilum	12.4			
	- Hookah	28.2			
	- Bidi	28.2			
		<u>Males</u>			
12. Joshi <i>et al</i> (1975) Ludhiana Industrial workers N = 473	Non-smokers	48.4			
	Smokers	51.6			
		<u>Males</u>		<u>Females</u>	
13. Bhonsle <i>et al</i> (1976) Goa Survey of villages N = 5,449		<u>Hindus</u>	<u>Christians</u>	<u>Hindus</u>	<u>Christians</u>
	No habits	26	48	46	66
	Bidi smoking	59	32	12	9
	Dhumti smoking	<1	11	0	19
	Reverse dhumti smoking	0	1	0	3
	Other smoking	5	7	9	<1
	Chewing	4	<1	41	1
	Mixed habits	6	1	2	2

TABLE 2 (continued 2)
Prevalence of smoking in various Indian surveys

Author, location, sample and sample size (N)	Prevalence of smoking (%)					
14. Radha <u>et al</u> Delhi Random sample of an area	Never smoked	<u>Males</u>		<u>Females</u>		
	Ever smoked	56.3		99.9		
	- Bidi	43.7		0.1		
	- Cigarette	10.2				
	- Hookah	26.3				
	- Combinations	1.0				
		6.2				
15. Malik and Singh (1978) Bhiwani Farmers N = 278	Non-smokers	<u>Males</u>				
	Smokers	29.1				
	- Hookah	70.9				
	- Bidi	35.3				
	- Hookah and bidi	20.1				
		15.1				
16. Jussawalla and Jain (1979) Bombay Population controls N = 792	Non-smokers	<u>Males</u> -	<u>Hindus</u>	<u>Muslims</u>	<u>Christians</u>	<u>Total</u>
	Bidi		84	76	49	79
	Cigarette		10	13	9	11
	Mixed smokers		6	10	39	10
			0	1	3	8
17. Malik (1982) Chandigarh Relatives or friends of patients N = 5,000	Non-smokers	<u>Males</u>		<u>Females</u>		
	Smokers	67		99.6		
	- Cigarettes	33		0.4		
	- Bidis	18				
	- Hookah	10				
	- Mixed	2				
	Smokers - 15-34	3				
	- 35-54	30				
	- 55+	38				
		35				
18. Nigam <u>et al</u> (1982) Jhansi House-to-house survey N = 1424	Non-smokers	<u>Males</u>		<u>Females</u>		<u>Total</u>
	Ex-smokers	14.8		86.0		47.3
	Smokers	11.9		2.0		7.4
	- Cigarette	73.3		12.0		45.4
	- Bidi					3.2
	- Hookah/Chilum					27.3
						14.9
19. Malik <u>et al</u> (1983) Godalpur Adults N = 250	Non-smokers	<u>Males</u>		<u>Females</u>		
	Reverse chutta	27		19		
	Regular chutta	27		72		
	Mixed	14		3		
		32		6		

TABLE 2 (continued 3)
Prevalence of smoking in various Indian surveys

Author, location, sample and sample size (N)		Prevalence of smoking (%)			
20. Gupta <i>et al</i> (1984a) Ernakulam Random sample, aged 15+ N = 10,287	No habit	<u>Males</u>		<u>Females</u>	
	Smoke	18.8		61.1	
	Chew	45.5		0.7	
	Smoke and chew	13.7		37.7	
		22.0		0.5	
21. Behera and Malik (1984) Gopalpur , Cuttack N = 374 Telgu community	Non-smokers	23.7		9.3	
	Reverse smokers	30.2		84.9	
	Chutta smoked normally	12.4		2.4	
	Reverse and normal	29.0		3.4	
	Mixed products	4.7		0.0	
22. Malik and Kashyap (1986) Shimla Screening of rural sample N = 446	Non-smokers	39.5		71.8	
	Smokers (mainly bidi)	60.5		28.2	
23. Malik and Behera (1986) Chandigarh, Mullanpur Survey of city block and village N = 2825, 1556		<u>Males + females</u>			
		<u>Chandigarh</u>		<u>Mullanpur</u>	
	Non-smokers	84.2		75.3	
Smokers	15.8		24.7		
24. Kamat and Doshi Bombay 3 urban areas, 1 rural area N = 2077	<u>Males</u>	High pollution	Medium Pollution	Low Pollution	Rural
	Non-smoker	78.6	79.2	83.3	84.4
	Ex-smoker	6.3	3.2	2.4	1.2
	Cigarette	13.2	13.3	14.7	5.6
	Bidi	1.9	4.3	0.6	8.8
25. Masironi and Rothwell (1988) Not stated Survey in 1984 Sample size not given		<u>Males</u>		<u>Females</u>	
	Non-smokers	48		97	
	Smokers	52		3	
26. Jajoo <i>et al</i> (1988) Central India Survey of villages N = 1,338		<u>Males</u>			
	Non-smoker of bidis			75	
	Smoker of bidis			25	
27. Sankaranayanan <i>et al</i> (1989) Kerala Hospital controls N = 546		<u>Males</u>			
	Non-smokers			49	
	Smokers			51	
	- Cigarettes			8	
	- Bidis			26	
	- Bidis and cigarettes			16	

TABLE 2 (continued 4)
Prevalence of smoking in various Indian surveys

Author, location, sample and sample size (N)		Prevalence of smoking (%)				
28. Sarkar <i>et al</i> (1990)		<u>Males</u>	<u>Females</u>	<u>Males + Females</u>		
Chandigarh	Non-smokers	52	94	59		
Doctors	Smokers*	48	3	41		
N = 218	Smokers - 20-29			44		
	- 30-39			40		
	- 40+			36		
	(*69 of 90 smokers were current smokers. All but one smoked cigarettes.)					
29. Raman Kutty <i>et al</i> (1993)			<u>Males</u>	<u>Females</u>		
Thiruvananthapuram	Smokers - 25-34		42	0.4		
Survey of 25+ population	35-44		48	0.0		
N = 1,253	45-54		53	1.1		
	55-64		51	0.0		
	65+		54	2.5		
30. Jindal (1987)		<u>Males</u>		<u>Females</u>		
As study 23		<u>Chandigarh</u>	<u>Mullanpur</u>	<u>Chandigarh</u>	<u>Mullanpur</u>	
	Non-smoker	69.4	57.4	99.0	79.7	
	Smokers	30.6	42.6	1.0	20.3	
31. Gupta <i>et al</i> (1994)				<u>Males</u>	<u>Females</u>	
Rajasthan	Never smoked			49	95	
Survey of villages	Ever smoked			51	5	
N = 1,982						
32. Bhattacharjee <i>et al</i> (1994)				<u>Males</u>		
Delhi			<u><31</u>	<u>31-40</u>	<u>41-50</u>	
Urban flat dwellers	Non-smokers		87	70	62	
N = 508	Smokers		13	30	38	
	(Ex-smokers)		11			
	- daily					
	- daily cigarette					
	- daily bidi					
	- daily unstated					
33. Qureshi (1994)		<u>Males and females combined</u>				
Kashmir valley		<u>Gujjar</u>		<u>Non-Gujjar</u>		
2 village	Non-smokers	78.7		58.4		
N = 286 and 274	Smokers	21.3		41.6		
34. Gupta <i>et al</i> (1995)				<u>Females</u>		
Rajasthan and Jaipur			<u>Urban</u>	<u>Rural</u>	<u>Total</u>	
Survey in villages, wards	Non-smokers		81	95	90	
N = 1,963	Smokers		19	5	10	
35. Gopinath <i>et al</i> (1995)		<u>Males and females combined</u>				
Delhi		<u>Hindus</u>	<u>Muslims</u>	<u>Sikhs</u>	<u>Christians</u>	
Random urban sample	Non-smokers	85.0	79.9	99.1	87.5	
N = 13,560	Smokers	15.0	20.1	0.9	12.5	
					<u>Total</u>	
					85.7	
					14.3	

TABLE 3
Prevalence of smoking in various Indian surveys*

Study No	Location	Population	Males	Females	Males+** Females
1.	Lucknow	Village			20.8
2.	Bombay	Hospital controls	57	6	(31.5)
3.	Bhavnagar	Village			32.3
	Srikakulam	Random sample, 15+	77	64	(70.5)
5.	Visakhaptnam	Hospital Controls	78.8	9.4	(44.1)
6.	Bombay	Policemen	33.8/38.5		
7.	Rajasthan	Professional men	42		
8.	Visakhaptnam/Srikakulam	Hospital visitors	78.5	35.6	57.8
9.	Bombay	Hospital controls			61.0
10.	Jaipur	Villages	86.0	34.7	63.1
11.	Lucknow	Villages			45.6
12.	Ludhiana	Industrial workers	51.6		
13.	Goa	Villages-Hindus	70	23	(46.5)
		- Christians	52	33	(42.5)
14.	Delhi	Random sample, 15+	43.7	0.1	(21.9)
15.	Bhiwani	Farmers	70.9		
16.	Bombay	Population controls	29		
17.	Chandigarh	Relatives/friends of patients	33	0.4	(16.7)
18.	Jhansi	Rural community	73.3	12.0	45.3
19.	Godalpur	Adults	73	81	(77)
20.	Ernakulam	Random sample, 15+	67.5	1.2	(34.4)
21.	Godalpur, Cuttack	Telgu community	76.3	90.7	84.2
22.	Shimla	Rural sample	60.5	28.2	50.2
23. }	Chandigarh	City block	30.6	1.0	15.8
30. }	Mullanpur	Village	42.6	20.3	24.7
24.	Bombay	Urban areas	16.0		
		Rural area	14.4		
25.	?	?	52	3	(27.5)
26.	Central India	Villages	25		
27.	Kerala	Hospital controls	51		
28.	Chandigarh	Doctors	48	3	41
29.	Thiruvananthapuram	Survey, 25+	42-54	0.4-2.5	(21.2-28.2)
31.	Rajasthan	Villages	51	5	(28)
32.	Delhi	Flat dwellers	32		
33.	Kashmir	Gujjar village			21.3
		non-Gujjar village			41.6
34.	Rajasthan/Jaipur	Villages/wards		10	
35.	Delhi	Urban sample			14.3

* See Table 2 for further details

** Bracketed numbers are averages of data for two sexes