

LUNG CANCER

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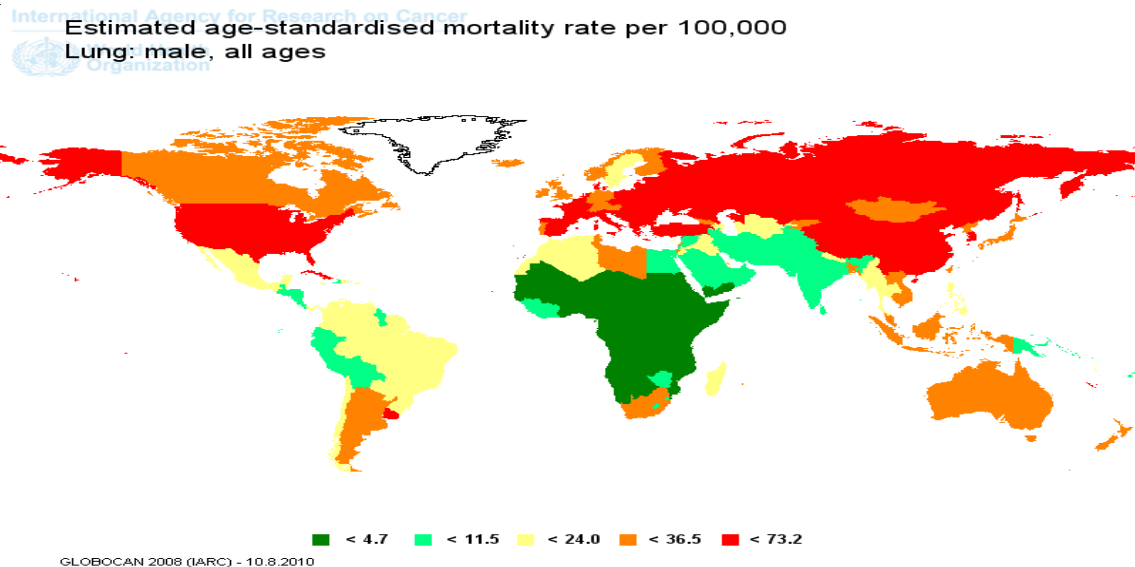
South Asia Network for Chronic Disease

Background

Cancer is the leading cause of death worldwide, it accounted for 7.4 million deaths (around 13% of all deaths) in 2004 (1). About 30% of cancer deaths can be prevented (1). In 2005, cancer killed approximately 826,000 people in India of which 519,000 were under the age of 70 (2). Lung cancer is among the five main types of cancer leading to overall cancer mortality contributing about 1.3 million deaths/year globally(1). Tobacco use is the single most important risk factor for cancer (1). The economic cost of treating four major tobacco related diseases such as cancer, cardiovascular diseases, respiratory diseases and tuberculosis in India is as high as US\$1.7 billion (3).

Globally, lung cancers (including trachea and bronchus cancers) are the most common cause of death from cancer among men (4,5). This is also the case in five of the seven regional groupings including South East Asia (4). The age standardised mortality rate per 100,000 for lung cancer males is shown in Figure 1 (5). In India trachea, bronchus, lung cancers are the most common cancers found in men. At a rate of 85 age-adjusted DALYs per 100,000 population, lung cancer accounts for 7% of total cancer DALYs in India (6).

Figure 1



This chapter will provide a description of lung cancer and its natural history. The distribution, incidence and mortality of lung cancer in India will also be presented. Risk factors, treatment, management and gaps in research for lung cancer will be included. Current policy research programs in India, of lung cancer research will also be reviewed.

Mortality, Incidence and Prevalence associated with Lung cancer.

Globally in Males

- 0.85 million deaths in 2002.
- 29.4 age standardized death rates (world) per 100,000 in 2008.
- 34.0 age standardized incidence rates (world) per 100,000 in 2008.
- One year prevalence of 0.38 million and five year prevalence of 0.93 million in 2002.

Globally in Females

- 0.33 million deaths in 2002.
- 11.0 age standardized death rates (world) per 100,000 in 2008.
- 13.5 age standardized incidence rates (world) per 100,000 in 2008.
- One year prevalence of 0.16 million and five year prevalence of 0.42 million in 2002.

In India for Males

- 58,000 deaths in 2004.
- 549,000 DALYs in 2004
- 9.8 age standardized death rates per 100,000 in 2008.
- 10.9 age standardized incidence rates per 100,000 in 2008.
- One year prevalence of 11,511 and five year prevalence of 27,477 in 2002.

In India for Females

- 12,500 deaths in 2004.
- 127,000 DALYs in 2004.
- 2.3 age standardized death rates per 100,000 in 2008.
- 2.5 age standardized incidence rates per 100,000 in 2008.
- One year prevalence of 2,646 and five year prevalence of 6,394 in 2002.

Source: WHO, 2009b (6); GLOBOCAN 2002, 2008 database IARC (5)

What is Lung Cancer?

Cancer refers to a class of diseases in which a cell or a group of cells divide and replicate uncontrollably, intrude into adjacent cells and tissues (invasion) and ultimately spread to other parts of the body than the location at which they arose (metastasis) (7). The transformation from a normal cell into a tumour cell is a multistage process, typically a progression from a pre-cancerous lesion to malignant tumours. These changes are the result of the interaction between a person's genetic factors and three categories of external agents, including:

- Physical carcinogens, such as ultraviolet and ionizing radiation.
- Chemical carcinogens, such as asbestos, components of tobacco smoke, aflatoxin (a food contaminant) and arsenic (a drinking water contaminant).
- Biological carcinogens, such as infections from certain viruses, bacteria or parasites (1).

Natural History of Lung Cancer

Most lung cancer starts in the lining of the bronchi, but it can also start in other parts of the lung: including in the windpipe (trachea) and bronchi (singular, bronchus) (8). The American Cancer Society (8) classifies lung cancer into two main subtypes:

- Small Cell Lung Cancer (SCLC)
- Non-Small Cell Lung Cancer (NSCLC)

Small Cell Lung Cancers are also known by Oat Cell Carcinoma and Small Cell Undifferentiated Carcinoma. This cancer often starts in the bronchi near the centre of the chest. Although the cancer cells are small, they can divide quickly, form large tumours, and spread to lymph nodes and other organs throughout the body. Small Cell type accounts for 10% to 15% of all lung cancers (8). Non-Small Cell Lung Cancer has three subtypes. About 8 to 9 out of 10 cases of all lung cancers are the non-small cell type (8). The cells in these sub-types differ in size, shape, and chemical make-up. These three subtypes include:

- Squamous Cell Carcinoma: About 25% to 30% of all lung cancers are this kind. They are linked to smoking and tend to be found in the middle of the lungs, near a bronchus (8).

- Adenocarcinoma: This type accounts for about 40% of lung cancers. It is usually found in the outer part of the lung (8).
- Large-Cell (undifferentiated) Carcinoma: About 10% to 15% of lung cancers are this type. It can start in any part of the lung. It tends to grow and spread quickly, which makes it harder to treat (8).

This distinction is important, because the treatment varies; non-small cell lung carcinoma (NSCLC) is sometimes treated with surgery, while small cell lung carcinoma (SCLC) usually responds better to chemotherapy and radiation (9).

The most common symptoms are shortness of breath, coughing (including coughing up blood), and weight loss (10).

Distribution, prevalence and incidence of Lung cancer in India

Prevalence and incidence of Lung cancer

As of 2002, the 1 year prevalence of lung cancer in India for males was 11,511, and the 5 year prevalence was 27,477 accounting for approximately 3% of global prevalence, and 55% of total prevalence in South Central Asia* (5). For India, the age-adjusted incidence of lung cancer (10.8 per 100,000 men, 47,010 incident cases) is the first relative to that of all other types of cancer in men. The age adjusted incidence of cancer of the lip and oral cavity is 9.8 per 100,000 men (45,445 incident cases) and 8.3 per 100,000 men (36,731 incident cases) for other pharynx respectively (5).

* South central Asia, as per GLOBACAN, IARC, includes Afghanistan, Bangladesh, Bhutan, India, Iran, Kazakhstan, Kyrgyzstan, Nepal, Pakistan, Sri Lanka, Tajikistan, Turkmenistan & Uzbekistan

Regional Variations

Lung cancer is the leading cancer among men in terms of incidence rates in 6 out of the 12 Population Based Cancer Registries (PBCRs) in India (table 1). The age-adjusted

incidence is highest in Kolkata, a metropolitan city in the west, and lowest in Barshi , a rural registry in Maharashtra(11).

Table 1: Crude & age-adjusted incidence rates per 100,000 population for Lung cancer in 12 PBCRs in India

PBRC	Crude Incidence Rate	Age-Adjusted Incidence Rate
Bangalore	7.3	7.3
Barshi	4.2	1.8
Bhopal	12.0	15.2
Chennai	9.9	11.3
Delhi	9.9	14.0
Mumbai	9.2	12.0
Ahmedabad	9.6	11.4
Karunagappally	18.0	18.6
Kolkata	16.3	18.7
Nagpur	6.5	8.4
Pune	6.8	7.5
Thiruvananthapuram	9.9	9

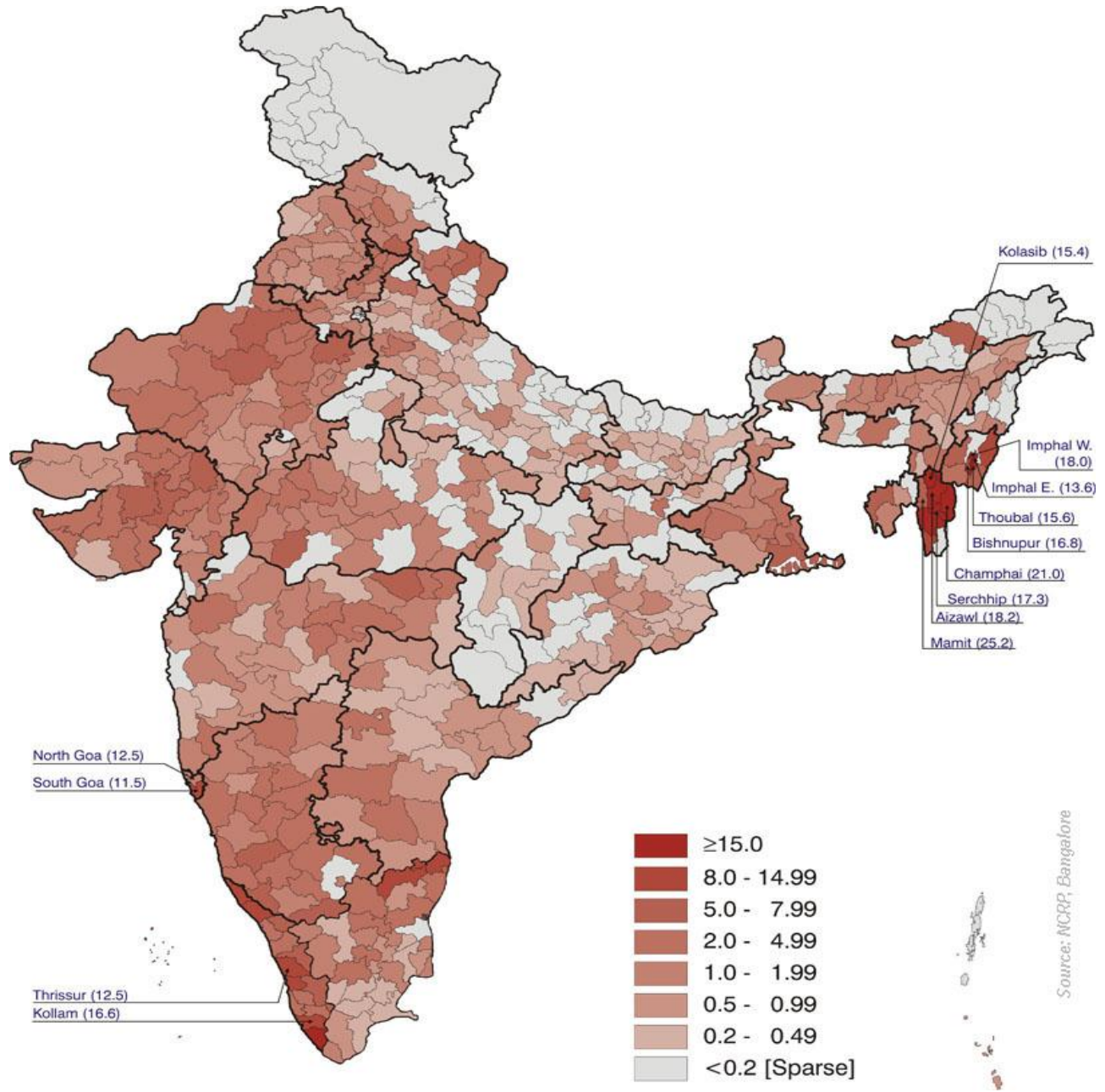
Source: National Cancer Registry Programme and World Health Organisation, Atlas of Cancer in India

Population based cancer registries in the world use age adjusted incidence rates for their unit of analysis. In India, districts are used as a unit of analysis for estimating incidence rates for the National Cancer Registry programme of India. The estimate used is the Minimum Age Adjusted Incidence Rates (MAAR) to allow for the fact that not all institutions within a district are included. The cases are only microscopically confirmed for lung cancer so the actual rates could be higher (11).

The district wise MAAR figures for lung cancer in males (Figure 2) (12) shows that Aizawl in Mizoram State and Imphal in West Manipur State had a highest incidence rate of 18.2 and 18.0/100,000 in India for 2001-2002. This incidence is 1.5 times higher of the urban population of Delhi with an incidence rate of 11.5/100,000. In comparison, the lowest incidence rate is in Barshi based in rural Maharashtra of 1.7/100,000 (Graph 1).

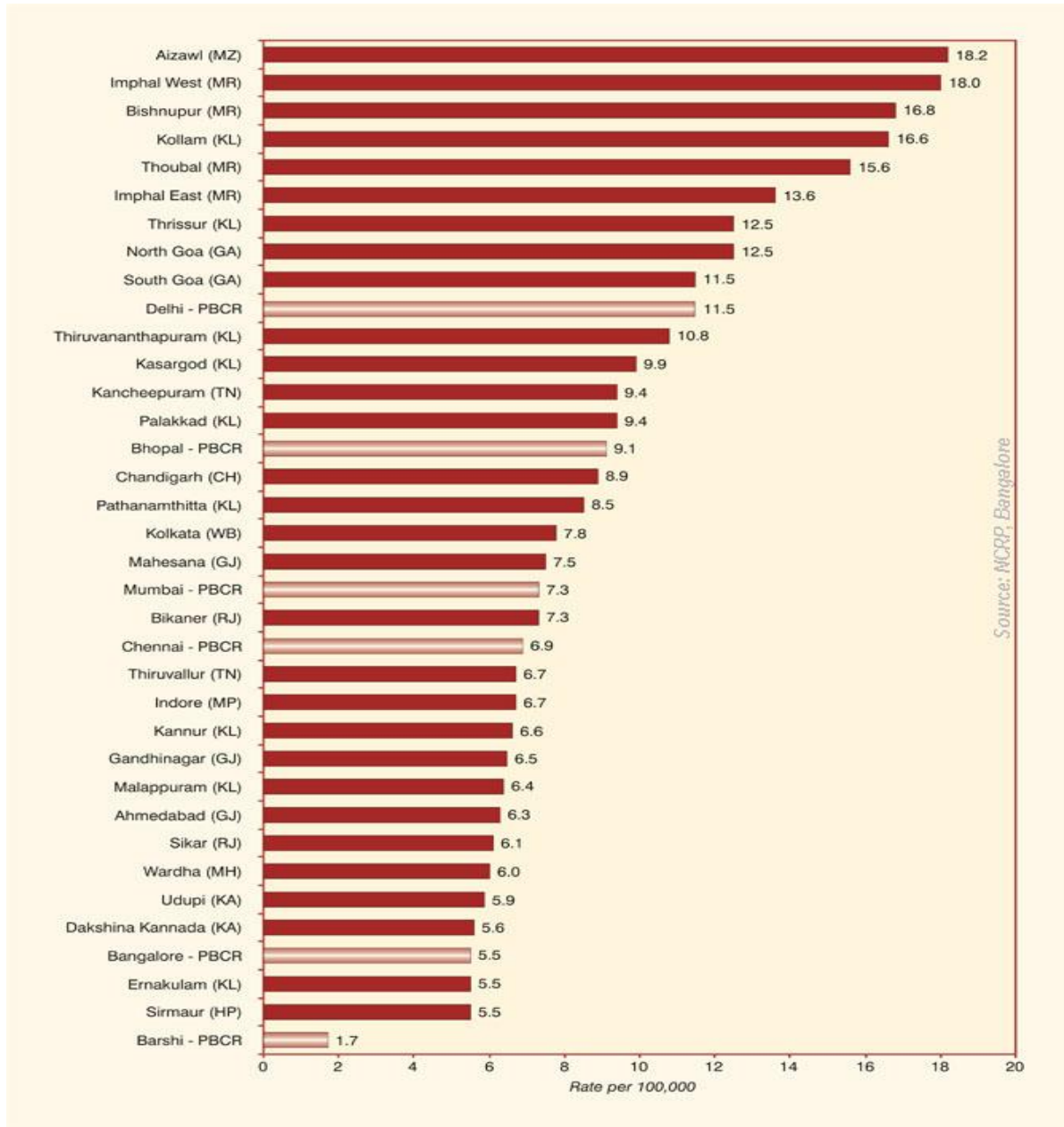
For females, the MAAR in the districts of India for 2001-2002 showed that the incidence of lung cancer was almost ten times more in Aizawl compared to Mumbai (26.2 compared to 2.8/100,000) (Figure3). Imphal West, and East Mizoram State and South Goa also had much higher MAARs than that seen in Mumbai (Graph2) (13) for 2001-2002.

Figure 2: District wise comparisons of Minimum Age Adjusted Incidence Rates with that of Populations Based Cancer Registries under National Cancer Registry Programme (NCRP) for LUNG (ICD-10: C33-C34) – Males.



Source: National Cancer Registry Programme and World Health Organisation, Atlas of Cancer in India

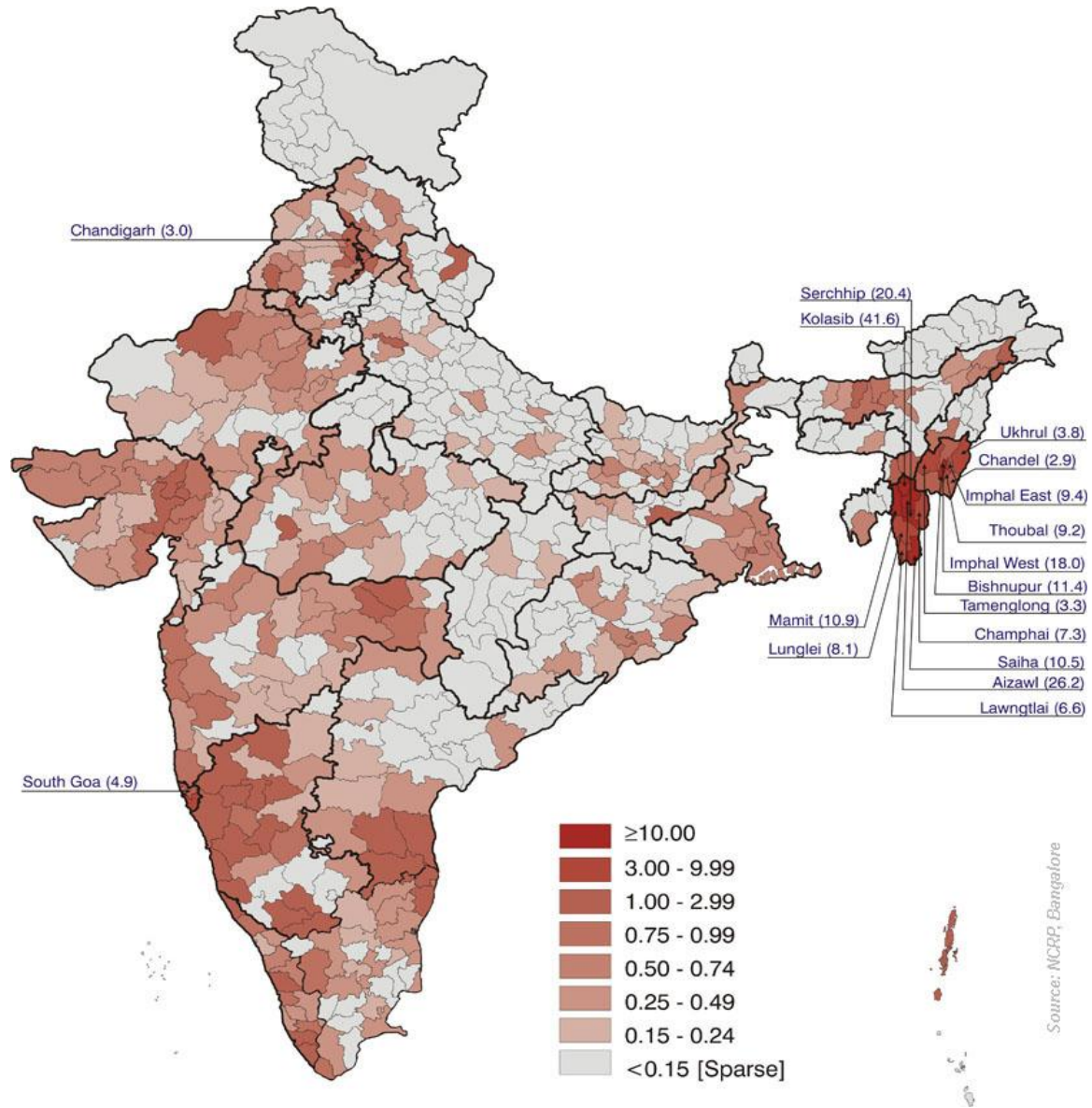
Graph 1: District wise Comparisons of Minimum Age Adjusted Incidence Rates with that of Populations Based Cancer Registries under National Cancer Registry Programme (NCRP) for LUNG(ICD-1: C33 C34)Males.



Source: National Cancer Registry Programme and World Health Organisation, Atlas of Cancer in India

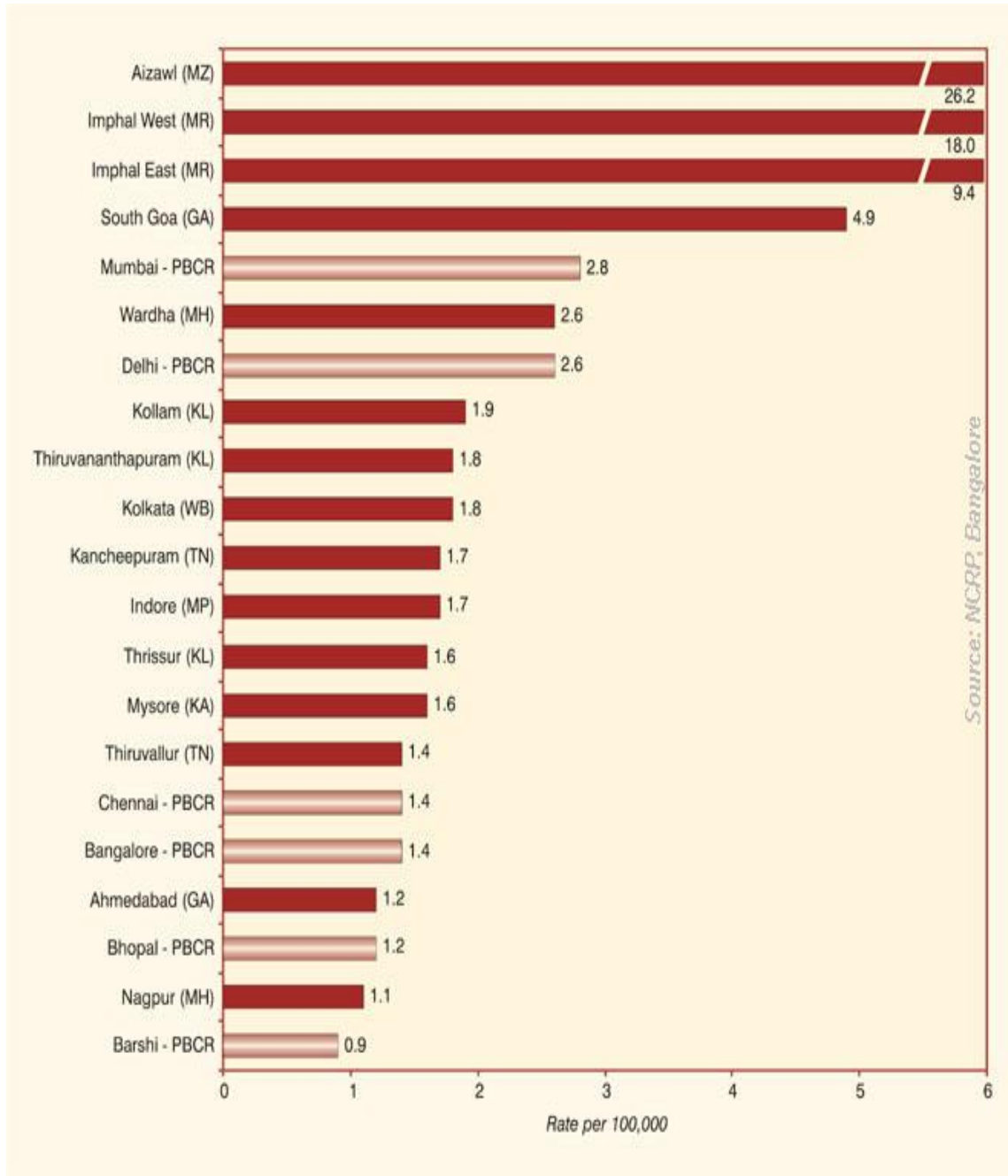
Figure 3: District wise Minimum Age Adjusted Incidence Rate Per 100,000

LUNG (ICD-10: C33-C34) – Females.



Source: National Cancer Registry Programme and World Health organisation, Atlas of Cancer in India

Graph 2: District wise Comparisons of Minimum Age Adjusted Incidence Rates with that of Population Based Cancer Registries under National Cancer Registry Programme (NCRP) LUNG (ICD-10: C33-C34) - Females.



Source: National Cancer Registry Programme and World Health Organisation, Atlas of Cancer in India

Lung cancer and Demographic Status

A review of 32 Indian studies conducted by Behera and Balamugesh in 2004, (14) provides valuable data on the prevalence on lung cancer over two time periods: 1958-1985 and 1986 -2001(Table 2). Increases in lung cancer rate were predominantly observed among farmers, but lung cancer remained predominantly a disease of males with a male to female ratio of 6.7:1.5 and 5.7:1. The mean age was 54.6 years in males and 52.8 years in females which has remained the same over the years (15). Small Cell Carcinoma type was predominant than Non Cell Carcinoma with a ratio 2.5:1 and 2.7:1.

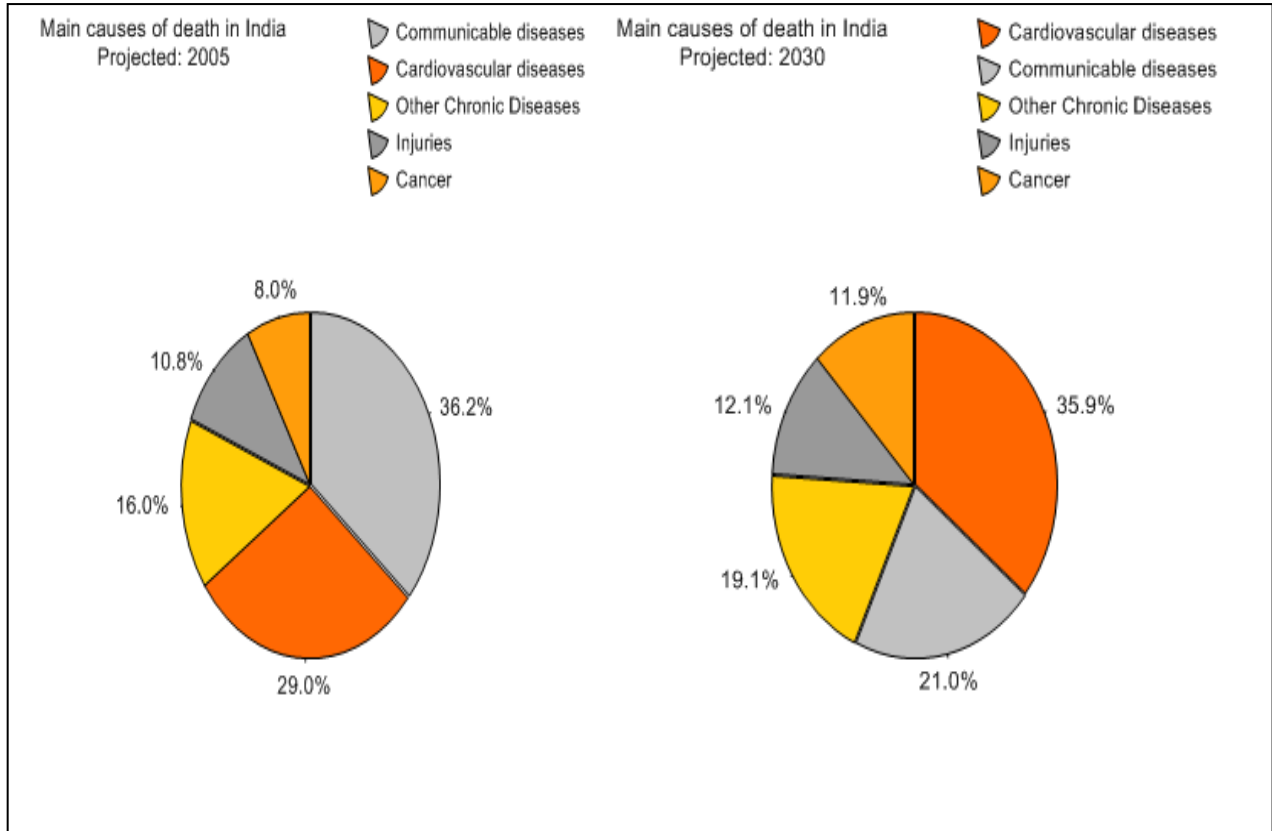
Table 2: Summary of demographic data of lung cancer reported from Indian studies (14)

Details	1958-1985	1986-2001
Total cases	1735	2973
M:F	6.67:1.5	5.76:1
Mean age(years)	52.16	54.6
SM:NS	2.5:1	2.7:1
Urban: Rural	19.6-81.6	18.4-80.4
Occupation		
Farmers		13.9-48%
Labourers		21.0-27.3%
Clerks/Teachers		16.7%
Businessmen		21.3%
Housewives		8.0-14.7%
Others		23%
Religion		
Hindus		75.1%
Muslims		18.9%
Christians		5.9%

Burden of Lung cancer in India

Projection estimates from the WHO has shown that by the year 2030, cancer will account for (12%) of death in India (Figure 4). Currently lung cancer is the fourth largest cause of cancer mortality in India after cancers of the cervix anduteri, breast, lip and oral accounting for nearly 8% of all cancer related deaths in the country (5). Among males, it is the leading cause of cancer mortality, accounting for 13% of all cancer deaths (5).

Figure 4: Main Cause of Deaths in India during 2005 and Projection Estimates for 2030(2)

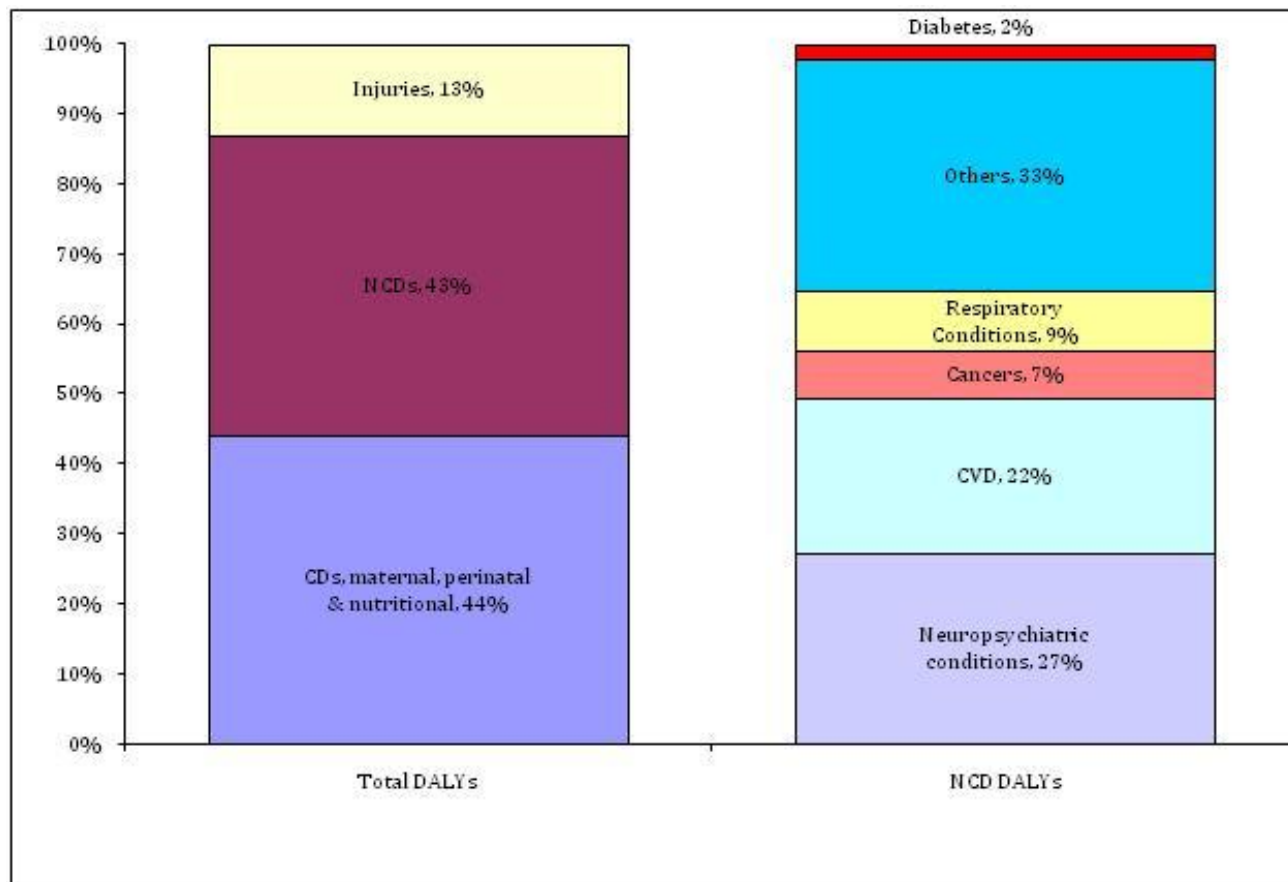


Source: WHO Infobase

Economic burden of lung cancer

Cancers overall rank third in cause of mortality (14%) and 7% of Disability Adjusted life years (DALYs) in India (Graph 3) (16). The years of life lost (YLL) due to cancer in 2004 were 13,96,508 for males and 16,17,787 for females for India (17). At a rate of 85 age-adjusted DALYs per 100,000 population, lung cancer accounts for 7% of total cancer DALYs in India (6).

Graph 3: Pattern of overall Disability Adjusted Life Years (DALYs) and NCD related DALYs in India, 2004(16).



Lung cancer and risk factors

Smoking

Smoking is the most important contributory factor in the causation of lung cancer (18, 19). In India, smoking of tobacco is mainly in the form of bidi, followed by cigarette, hukah, chillum and chutta (20). Bidis accounts for three quarter (77%) of the market of smoking tobacco and 48% of the whole tobacco market (21,22). According to National Family Health Survey (NFHS)-3 carried out during 2005-06, prevalence of tobacco use (all forms) was 57% in men and 10.8% in women (24). One third of men (33.4%) and 1.4% of women were cigarette/ bidi smokers. The number of adult current daily smokers is reported to be higher in the rural areas (31.3%) as compared to urban areas

(21.5%) (25). In addition, daily consumption of all forms of tobacco use was higher among the lower income quintile (41.8%) compared to higher income quintile (15.5%) and in the elderly population (43.9% among 65+ age group) compared to younger age group (14.7% among 18-24 age group) (25). The relative risk of developing lung cancer is 2.64 for bidi smokers and 2.23 for cigarette smokers with 2.45 as the overall relative risk (23). Hukah smoking has also been associated with lung cancer with an odds ratio (OR) of 1.94, (95% confidence interval 0.85-4.44) (26).

Passive smoking

There is strong evidence of involuntary smoking and lung cancer risk in never-smokers, especially spouses of smokers (27). A meta-analysis of 41 studies in 2000, indicated that the relative risk of lung cancer for ever being exposed to environmental tobacco exposure at work was 1.16 (95% confidence intervals ((CI) 1.05–1.28)) in non smokers males and 1.2 (95% CI 1.12-1.29) in non smokers females exposed to their husband smoke (28). Risk increases with increase in exposure (28). An Indian study conducted in Chandigarh among non smokers, showed that environmental tobacco smoke exposure during childhood is strongly associated with the risk of later development of lung cancer OR of 3.9, (95% CI 1.9-8.2) the effect mostly arising from exposure to cigarettes smoke (29). The excess risk was observed with either a smoking father or mother. An increasing risk was found with increasing number of smokers and duration of exposure (29).

Occupational risk

Certain occupations have shown to increase exposure to lung cancer (30, 31). A study in Mumbai showed a significantly elevated risk (adjusted for smoking) for textile workers OR of 1.99, (95% CI; 1.3-3.6) and cooks OR of 4.48, (95% CI; 1.2-16.9). High risks were also observed among ship and dockyard workers OR of 2.87, (95% CI; 0.8-10) and hand wood workers OR of 2.88, (95% CI; 0.9-9.6) after adjusting for smoking (32).

A meta analysis of published case control studies which adjusted for smoking provided the following ORs of lung cancer and exposure to asbestos, cooking fuel, cooking fumes, motor and diesel exhaust: 1.6, 1.99, 2.52 and 1.42 ($p < 0.001$) respectively (33) Mostafa's study of lung cancer and arsenic exposure in contaminated drinking water in rural Bangladesh indicated that in non smokers, lung cancer increased steadily with

mean arsenic concentration at >100 µg/l OR of 1.45, (95% CI 1.16 to 1.80) (34). Exposure to fibres of biogenic amorphous silica (BAS) deposited in the leaves of the sugar cane crop may account for increased risk of lung cancer among sugar cane farmers (34). A case control study conducted among Indian farmers found an increased risk to lung cancer with an OR of 1.92, (CI; 1.08-3.40) after adjusting for confounders (smoking, exposure to asbestos, education, income, family history of lung cancer and farming other crops)(35).

Family history

Tokuhata and Lilienfeld provided the first epidemiological evidence of familial aggregation of lung cancer, suggesting the interaction of genes, shared environment and common lifestyle factors in the aetiology of the disease (36). Kumar M, 2009 studied the role of genetic polymorphism and lung cancer risk in North Indian population. The polymorphic genes explored were CYP1A1, GSTM1, GSTP1 and GSTT1 using techniques of polymerase chain reaction (PCR). The most significant risk for lung cancer was found in the association of the homozygous variant of CYP1A1 gene at A2455G base change at Exon 7 (Val/Val) genotype OR of 3.2, (95% CI: 0.7-3.8). There was a marginally significant association between lung cancer and GSTT1 null genotype OR of 1.3, (95% CI: 1.0-1.7) while no significant risk association was found between GSTP1 polymorphism and lung cancer (37).

Air pollution

A case control study cases of 265 and control 535 conducted in Chandigarh, India reported that the cumulative exposure of > 45 years to indoor air pollution in women, among smokers from use of coal or wood for cooking or heating, was an increased risk of lung cancer with an estimated OR of 1.43 (95% CI=0.33-6.30)(26). Another Indian study showed that compared with never users, coal usage had an increased risk of lung cancer (adjusted for cumulative tobacco consumption) OR of 3.76 (CI 1.64-8.630) (40).

Joint hazards of risk factors

Danaei G, 2004(41) studied the comparative risk assessment of nine behavioral and environmental risk factors for cancers in the world. Individual and joint contributions

of risk factors to mortality from trachea, bronchus and lung cancers in different regions is shown in Table 3. It highlights that the Population Attributable Fraction (PAF) for low fruit and vegetable intake, and urban air pollution is relatively high in low and middle income countries compared to high income countries.

Table 3: Individual and joint contributions of risk factors to mortality from Trachea, Bronchus and lung cancers

Regions	Total deaths	PAF *(%) and number of attributable cancer deaths (thousands) for individual risk factors	PAF due to joint hazards of risk factors
Worldwide	1 226 574	Smoking (70%, 856), low fruit and vegetable intake (11%, 135), indoor smoke from household use of solid fuels (1%, 16),urban air pollution (5%, 64)	74%
Low and middle income countries	770 938	Smoking (60%, 466), low fruit and vegetable intake (13%, 98), indoor smoke from household use of solid fuels (2%, 16),urban air pollution (7%, 52)	66%
High income countries	455 636	Smoking (86%, 391), low fruit and vegetable intake (8%, 36), indoor smoke from household use of solid fuels (0%),urban air pollution (3%, 12)	87%

* PAF - Population Attributable fraction

Prevention, Management and Treatment of Lung Cancer

Prevention of risk factors

Tobacco Control Policy

The International Agency for Research on Cancer (IARC) in its monograph states that tobacco smoking is the major cause of lung cancer of all types globally (27). In response, the World Health Organisation adopted a Framework Convention on Tobacco Control (WHO FCTC) in May 2003: 168 out of 192 member countries signed the treaty and 152 countries ratified it (53). Approximately 70% of the member states who have ratified it, have to date, passed national legislation or made agreement with their respective national parliaments and/or cabinets to implement the FCTC. (53). India is an elected coordinator of the group of countries affiliated to the WHO South-East Asia Regional Office (SEARO) (54). Their broad objective is to set strategies to help low and middle countries to strengthen their tobacco control policies such as bans on tobacco advertising and sponsorship implementation, tax increases on tobacco products and smoking cessation programmes (54).

Ban on tobacco advertising

Ban on advertising has shown to reduce tobacco consumption in many countries (Table 4) (43, 55). In India, the Cigarettes and Other Tobacco Products Act 2003 banned direct and indirect advertising of all tobacco products (55). However surrogate advertisements are still prevalent. For example 502 pataka beedi which is consumed among the low socio-economic sections of the society in northern India is advertised in television as 502 pataka chai(tea leaves) (55). Evidence suggests that a complete ban on advertisements coupled with an intensive public information campaign on the ill effects of using tobacco products may lead to a reduction in tobacco consumption by 6% (67).

Price Increase on tobacco products through taxation

Increasing prices through taxation is also effective in reducing the demand for tobacco: for example, in high income countries, a 10% price rise will lead to a 4% reduction in demand (price elasticity of -0.4) and an 8% reduction in low and middle income countries(price elasticity of -0.8) (56). Young people, people belonging to low socio-economic groups and less educated people are the most price sensitive groups (56). A study in India found that price elasticity estimates of different tobacco products ranged between -0.4 to -0.9 , with bidis and leaf tobacco estimates close to unity. Cigarettes were least price elastic of all. The study also showed that tax on bidis can be increased

to Rs. 100 per 1000 sticks compared with the current Rs. 14 and the tax on an average cigarette can be increased to Rs. 3.5 per stick without any fear of losing revenue (57).

Smoking ban in public places

In 2008, India passed national anti-tobacco legislation which banned smoking in public places (44). Effective policies for smoke-free public places are required to guide implementation at various levels and ensure strict enforcement of the existing laws (58). Evidence from developed countries (Ireland, United States, Scotland, Norway and New Zealand) which have in recent years passed similar legislation indicates that a total ban of indoor smoking in public places reduces the prevalence of smoking by 3.8% (68). There are only a few documented examples in India of success in achieving smoke-free environments (54). Bans have been introduced in certain areas (Indian airlines domestic and international flights (59), Indian railways (60), Lucknow University (61)) but as yet there is lack of data on its effectiveness.

Tobacco cessation programmes

Tobacco cessation provides the most immediate benefits of tobacco control and maximizes the advantages for a tobacco user who quits the habit (56). According to the projections by WHO, majority of the tobacco-related deaths could be prevented over the next 40 years if current smokers can be persuaded to quit (62). For example, it has been estimated that if all current adult smokers stopped smoking for next 20 years; 20-30 million tobacco related deaths would be avoided in first quarter (2000-2024) and 140 million deaths in the next quarter of the century (2025-2049) (62). A review conducted in 2004 suggests that 3-5% of self quitters achieve prolonged abstinence for 6-12 months after a given tobacco quit attempt (76). Recognising this need, the Ministry of Health and Family Welfare, Government of India supported by WHO initiated 13 Tobacco Cessation Clinics (TCC) on pilot basis in 2002(82). The centres, based in cancer treatment or psychiatric centres, medical colleges and in some NGOs are located in set up in Anand (Gujarat), Bhopal, Bangalore, Chandigarh, Chennai, Cuttack, Delhi, Goa, Jaipur, Lucknow, Mumbai and Patna. Pilot results show a tobacco quit rate of 18% and 26% at 6 weeks for behavioural change counselling and pharmacotherapy intervention respectively (54). A community based model for preventing tobacco use among disadvantaged adolescents in urban slums of India reported significantly lower fresh uptake 0.3% of tobacco use compared to control group 1.7% (63).

Table 4: Studies in different countries showing an effect on smoking prevalence before and after a ban on advertising

Country, year	Description of anti-tobacco measures	Effect
Norway, 1975	Complete ban on advertising and sponsoring coupled with health warnings, public information and age limits on sales	Long-term reduction in the prevalence of smoking by 9%.
Finland, 1977	Complete ban on advertising, no smoking in public buildings, age limit on sales, strong public information campaigns	Reduction of cigarette consumption by 6.7%
Canada, 1989	Complete ban on advertising and sponsoring, with higher tobacco prices	Corrected for price increases, a long-term reduction of 4% on the prevalence of smoking
New Zealand, 1990	Ban on advertising and sponsoring, higher tobacco prices	Reduction in tobacco sales by 7.5%, of which 5.5% can be attributed to the ban on advertisements
France, 1991	Complete ban on advertising, limiting smoking in public buildings, removal of tobacco from the consumer price index	Reduction of smoking prevalence by 7% in 1991-1993

Occupational hazards e.g Asbestos

WHO advises on the dangers of the association between the risk of lung cancer and working with asbestos in India (45). People most at risk of lung cancer death are workers producing asbestos-filled concrete and pipes, along with labourers using such products (64). Traditionally, Indian school roofs are made with asbestos, putting students and teachers at risk if asbestos cement sheets are damaged which may lead to release of asbestos fibres in the air (64). The WHO is currently planning to hold regular workshops across Asia on the risk of dangers of asbestos and recommending safer building materials that the building industry could use as an alternative (45).

Diet

A case control study in Kerela, South India showed that green vegetables and bananas may have a protective effect on the development of lung cancer (38): the odds associated with the highest quartile of vegetable consumption compared with the lowest was 0.32 (95% CI 0.13-0.78). Behera et al (39) reported that B-carotene and

vitamin A levels and vitamin C levels in patients with lung cancer compared to healthy controls were not significantly different.

Management and treatment of lung cancer

Early detection

If cancers are detected early, treatment may be curative (65). One means to that end is educating people regarding symptoms of lung cancer. A second approach to early cancer detection is through population screening; namely the identification of people with asymptomatic disease by applying simple tests (65). Currently, there is evidence that low-dose CAT scans, chest X-rays and sputum cytology can detect lung cancers earlier than they would be found without screening, but there is little evidence that these screening tests actually prevent people from dying from lung cancer (47). Lung cancer is not amenable for early detection as symptoms are similar to pulmonary tuberculosis and cases are often presented at later stage hence primary and secondary prevention by reducing the prevalence of tobacco consumption is the most effective way of reducing lung cancer mortality (67). The most prevalent clinical features are presented in table 5 (14).

Table 5: Presenting the features of Indian lung cancer patients (%)

Symptoms	Jindal and Behera(1990)	Other –Indian studies(range)
Cough with expectoration	88	40-94.3
Chest pain	52.2	16-66.7
Loss of weight	90	11.4-77
Breathlessness	Not Reported	24-59
Weakness	90	4-60
Heamoptysis	69.2	8-60
Fever	19.6	22-68.6
Anorexia	90	20.5-70
Hoarseness of voice	29.9	9-33
Nausea and vomiting	6	25
Puffiness of face	19.8	2.9-8.3
Dysphagia	20.8	2.9-6
Others	30.5	-

Management and Treatment

Lung cancer has usually fatal consequences (70) and unfortunately, management guidelines for lung cancers are produced in the developed world and not in India (52). In India, lung cancer is rarely detected at its early stages and it is often diagnosed at an advanced stage (15). Diagnosis at early stages where surgery could be offered is possible only in less than 5% of the cases in India whereas it is possible in 80% of all lung cancer cases in the western world (72). It is argued that delayed diagnosis of lung cancer is because symptoms are similar to pulmonary tuberculosis (which is common in India) and most patients receive anti-tubercular therapy for a varying time periods before a definite diagnosis of lung cancer can be made (72). O'Rourke and Edwards have shown that 21% of potentially curable lung cancer patients became incurable whilst waiting for treatment in UK. The median delay between the diagnostic and planning CT scans was 54 days, between the first hospital visit and starting treatment was 94 days and the delay between the date of radiotherapy request and starting the treatment was 44 days (71).

Moreover, should lung cancer be presumed, diagnostic facilities like fiberoptic bronchoscopy and fine needle aspiration cytology /biopsy are not available uniformly throughout India (72). For example: diagnostic facilities for cytology are available in less than ten rural areas in India (52).

Surgery, radiotherapy and chemotherapy are the three treatment options available for the management of lung cancer. In the early stages of Non-Small Cell Lung Carcinoma (Stage I to IIIA), surgery if feasible is the treatment of choice. The five-year survival rate after surgery is as follows: Stage I: 60%-70%, Stage IA: 80%, Stage II: 35-40%, Stage IIIA: 10-15% (14).

Most cases of lung cancer present in an advanced and inoperable stage, and radiotherapy offers the only local form of therapy, chemotherapy has an important role in the management of lung cancer (14). Radiotherapy facilities are not available at all the medical colleges in India (72). In 2006 there were 347 tele-therapy units in the country as against the requirement of 1059 (73). The existing treatment facilities for cancer control in terms of radiotherapy and financial allocation are inadequate to take care of the present need (73). Chemotherapeutic drugs are costly, toxic and need expertise to deliver them(72). In government settings the cost of the best combinations of chemotherapeutic drugs vary between 15,000 INR to 20,000 INR per cycle (72). The average minimum daily wage earner employed in agriculture varies between 150 INR - 170 INR (78) which would make it extremely difficult for an Indian farmer to afford such treatment.

In addition, there are not enough medical oncologists in medical colleges of India who can administer these drugs (72). The worst affected are cancer patients from the rural areas where they have to depend on other forms alternative medicine or on rural private practitioners(74). Studies have shown that there is marked reluctance to use free government health facilities even among the poorest section of the Indian society (74).

Behera D 2004 reviewed several regimens of chemotherapeutic agents for lung cancer in India (14). Table 6 and 7 show that without chemotherapy the median survival of unresectable Non Small Cell Lung Carcinoma (NSCLC) is five weeks, with a single agent it is 7.5, with less effective chemotherapy it is 9.5 weeks and with modern chemotherapy it is 23 weeks to more than 40 weeks (14).

Table 6: Chemotherapy with median survival in weeks in lung cancer at a tertiary care centre (Post Graduate Institute of Medical Education and Research - Chandigarh)

Regimen	No	SCLC	NSCLC	Total Survival	1-year survival
SFRT	28	-	-	5	-
CTX	24	-	-	7.5	-
Combination	38	26	9.5	16	8.3-12%
V+C+B	26	-	18	-	26.5%
V+C+M	20	23.5	31	-	33%
V+C+A	27	23.5	23	-	25-36%
VB+MIT+C	27	-	16-28	24	12%
E+V+C+CC	22	22.5-39	-	24	12.5%
IFO+V	16	35.5	-	-	26.5%

SFRT: Single fraction radiotherapy of 1000rads; CTX Cyclophosphamide; V: vincristine; Cisplatin;B:bleomycin;M:methotrexate;A:adriamycin;VB:vinblastin;MIT;mitomycin;CC: CCNU;IFO:Ifosamide,E:etoposide.

Table 7: Median survival (in weeks) of lung cancer with newer chemotherapeutic agents.

Regimen	NSCLC	SCLC	6M	1 year
MIC(n=299)	22(24-36)	-	30%	15.5%
VIE(n=98)	-	31	44.4%	12.7%
DOC+CISP(n=50)	38+	(30-32)	93.3%	23.3%
GCB+CISP(n=16)	36	-	69%	

MIC:Mitomycin,Ifosamide,Cisplatin;VIE:VP-16, Isosfamide,Etoposide; DOC:Docetaxel; CISP:Cisplatin, GCB: Gemcitabine

Palliative care

Pain relief and palliative care are important and integral parts of all cancer care. (52) Relatively simple and inexpensive treatment to control pain are available and include morphine treatment. (52) NCCP has identified that cancer patients with advanced stage require good palliative treatment, yet establishment of palliative care clinics has not moved ahead in India. (76). Oral morphine is the mainstay for cancer pain relief and it is not widely available to more than 99% of patients due to geographic and economic disparities (52,75). For example, oral morphine cannot be prescribed for pain among cancer patients in 21/28 states in India (52). Guidelines although not India specific for cancer pain relief have been produced and are available from the World Health Organisation (WHO) (48).

Ongoing Lung Cancer Research Programs in India

Currently the National Cancer Registry Programme (NCRP) is the programme which provides data on magnitude and patterns of all cancer types in India (49). The Indian Council of Medical Research initiated a network of cancer registries across the country in December 1981. This programme is one of the many activities of the division of Non-communicable Diseases of ICMR. Data collection under the NCRP is done both at Population Based Cancer Registries (PBCR) and Hospital Based Cancer Registries (HBCR) (11). Under the NCRP, Population Based Cancer Registries (PBCRs) have been established at 19 locations across India (Mizoram, Sikkim, Imphal, Kamrup, Silchar, Dibrugarh, Bangalore, Chennai, Mumbai, Delhi, Bhopal, Ahmedabad, Nagpur, Kolkata, Aurangabad, Pune, Kollam, Thiruvananthapuram and Barshi) and Hospital Based Cancer Registries (HBCRs) have been initiated at Dibrugarh, Chandigarh, Thiruvananthapuram, Bangalore and Mumbai (50). Where The PBCRs collect data on cancer incidence and mortality (49), the HBCRs collect data on cancer patterns, on patient care through information collected on details of clinical stage, data on different aspects of types of treatment and recording of follow-up information (50).

The NCRP has a system of data quality and consistency checks which after analysis; disseminate information in the form of periodical reports, which are available, publicly (51). The indices for measuring reliability and the completeness of data in a cancer registry are; proportion of cancer cases microscopically verified (MV%), proportion of cases categorised as death certificates only (DCO%) and mortality incidence ratio (M/I%). Unfortunately, the data is not always complete. For example the MV% in males ranged from 79.1% in Ahmedabad to 88.3% in Kolkatta but was better for females 80.4%

in Ahmedabad to 91.6% in Kolkatta. For men, the highest M/I% was found in Barshi (68.6%), the lowest was in Delhi (11.3%), and for females; the highest was Barshi (74.0%) and the lowest in Delhi (8.8%) (75).

Other organisations which conduct research on Lung cancer include:

Post Graduate Institute of Medical Education and Research (PGIMER) in Chandigarh is currently conducting research on assessment of health related quality of life in patients with lung cancer using generic and disease specific questionnaires. Regional Cancer Institute in Chennai is doing Randomized phase II trial comparing Paclitaxel + Carboplatin versus Paclitaxel + Carboplatin + Lactoferrin in unresectable advanced non small cell lung cancer. Dharamshila Hospital and Research centre in Delhi is conducting a Gene Therapy trial in lung cancer comparing conventional chemotherapy and gene therapy.

The Advocacy Forum for Tobacco Control (AFTC) is ongoing coalition of organisations and individuals working in the areas of advocacy, awareness and research related to tobacco control in India. Few of these NGO's include Rajasthan Cancer Society (Rajasthan), Salaam Bombay Foundation (Mumbai), and School of Preventive Oncology (Bihar) Healis Sekhsaria Institute of Public Health (Mumbai). Healis Sekhsaria Institute of Public health is a part Global tobacco surveillance which is currently collecting data through three surveys; the global youth tobacco survey, the global school personnel survey, the global health professional for adults. Salaam Bombay Foundation is carrying out research to study the actions individuals (18-45 years) would take if they found someone smoking around them.

Ongoing research is also undertaken by non-profit voluntary organisations. For example, Health Related Information Dissemination Amongst Youth - Student Health Action Network (HRIDAY-SHAN) is conducting research on tobacco control. One such project: "Advancing Cessation of Tobacco in Vulnerable Indian Tobacco Consuming Youth (ACTIVITY)" is a group-randomised intervention trial designed to test the efficacy of a community-based, comprehensive tobacco control for youth (10-19 years) living in 14 low income communities in Delhi, India. This trial is funded by the Fogarty International Center and National Institutes of Health (NIH). Currently the baseline survey in all the selected communities is in process. The objective of the survey is to obtain information on prevalence, patterns of tobacco use and to explore determinants that promote tobacco use and tobacco cessation (79).

Another youth campaign was led by HRIDAY to monitor the implementation of ban on smoking in public places to make Delhi Smoke Free. As an awareness and advocacy

campaign “Smoke Free Restaurant” it attempts to sensitise restaurant and hotel owners in Delhi about the rules notified by Government of India related to prohibition of smoking in public places (79). The results of the programme are yet to be published.

The Cancer Foundation of India (CFI) is another example of a non voluntary organisation. CFI is recognised as a Scientific & Industrial Research Organisation (SIRO) by Department of Scientific & Industrial Research (DSIR), Ministry of Science and Technology, Government of India in recognition of its research work in Cancer (66).CFI has engaged in conducting epidemiological surveys since 2004 which includes tobacco prevalence among school children in West Bengal, tobacco prevalence in corporate sector blue collar employees in India (66).The results of these epidemiological surveys are yet to be published .

Lung Cancer Policy in India

Programme for cancer control in India

The National Cancer Control Program set up under the Ministry of Health and Family Welfare, Government of India 1975-76 and revised in the year 1984-85 with the emphasis on primary prevention and early detection of cancer (46). The focus is on covering the geographical gaps for providing comprehensive cancer care in the country (46). Twenty four Regional Cancer Centres (RCCs) have been established under this programme and with 210 institutions possessing radiotherapy installations (46).

There are 5 schemes under the Revised Programme:

- 1) Recognition of new Regional Cancer Centres (RCCs);
- 2) Strengthening of existing RCCs;
- 3) Development of Oncology Wing by providing enhanced grant-in-aid to the Government institutions (Medical Colleges as well as government hospitals);
- 4) District Cancer Control Programme by providing the grant-in-aid;
- 5) Decentralised NGO Scheme by providing support to NGOs for information education and communication activities (46).

Despite this however, there is a substantial shortage of cancer treatment facilities in the country, which is further magnified by regional disparities Table 8 (52).

Table 8: Radiation oncology structure in India (gaps between demand and supply)

<i>Parameter</i>	<i>Current Existing</i>	<i>Ideal Scenario* (international norms)</i>	<i>XIth Plan- Practical Recommendation</i>	<i>Shortfall</i>
Equipment				
Tele-density	0.33 per million population	2 per million population	0.5 per million population	0.17 per million
Tele-units	337 (includes 76 units >20 years old)	2000	500	163 + 76 (old units for replacements)
Brachytherapy	186 (0.19 per million)	330 (0.33 per million population)	250 (0.25 per million population)	64
Simulator	41	1 per RT centre	1 per sec/tertiary centre	59
3-D TPS	48	1 per RT centre	1 per sec/tertiary centre	52
Personnel				
Radiation Oncologist	700 (1 per 715 patients annually)	2000 (1 per 250 patients annually)	1000 (1 per 500 patients annually)	300
Medical Physicist	500 (1 per 1000 patients annually)	1250 (1 per 400 patients annually)	1000 (1 per 500 patients annually)	500
Dosimetrist	Nil	500 (1 per 1000 patients annually)	1 per RT centre	250
RT Technologist	700 (2 per MV unit)	8000 (4 per MV units)	1500 (3 per MV unit)	800

***Ideal scenario (ACR guidelines)**

Source: NCCP Task Force Reports for XIth Plan, 2008

Gaps in Lung cancer research in India

Gaps in surveillance

Currently, in India, there is limited data on the incidence and mortality of cancer in the population. Significant progress has been made by the NCRP since its inception, however, it presently covers approximately only 5% of the Indian population (67) and most are placed in urban settings. Therefore valid estimates of the burden of cancer, when over 70% of the population of India resides in rural areas are difficult to ascertain (51). A population based surveyed revealed that except in Chennai where the coverage of cancer cases within the PBCRs is 100%, coverage in Mumbai was 72% and in Bangalore and 78% in Mumbai (15). Minimal data is available with gross underreporting on cancer mortality from population based registries except Chennai (67).

Gaps in research in health promotion and prevention activities

The Cigarettes and Other Tobacco Products Act, 2003 has banned direct and indirect advertising of all tobacco products. However, advertising has been permitted at the point of sale of tobacco products. It is, therefore, ideal if the act is amended to extend the ban to such point of sale advertising as well. Studies need to be conducted to evaluate the impact of tobacco advertising ban and the incidence of lung cancer.

Research on tobacco cessations programme needs to test the efficacy/success rates of the tobacco quit programmes. Research needs to be carried out over longer periods in middle aged and older generation.

Gaps in access to health care.

Access to health care is difficult for the under privileged. Most Cancer patients in India do not have health insurance. Hospital admission and chemotherapeutic drugs consume a sizeable share of a poor household's resources (76). Private for-profit insurers in India target the better off section of the society but have little to offer the poor in India (81).

Studies need to be conducted to evaluate the impact of subsidised chemotherapeutic drugs on economic burden in Indian healthcare system and also to see if subsidy would be acceptable to the population, government and healthcare providers.

Money allocation needs to be distributed for social health insurance for all sections of the society and evaluated to see the impact of on economic burden.

Newer, indigenous chemotherapeutic drugs need to be developed and manufactured. Further evaluating their impact in reducing the economic burden of disease also needs to be considered.

Pain relief and palliative care are important and integral parts of all cancer care. (52) Qualitative study needs to be done at the various barriers of distribution of oral morphine in states where it is regulated by the Government of India.

Lack of uniform protocols for management of common cancers

There are no separate Indian guidelines for management of common cancers. Guidelines for lung cancer have been set up by different international bodies like www.nice.org.uk (80) but Indian scientists believe that these may not be suitable for Indian patients due to inherent differences or tolerability to certain drugs (52). Separate guidelines to distinguish between the diagnosis of TB and lung cancer are needed. ICMR are currently planning to review the existing management guidelines for oral cancer and have proposed to expand to include most cancer sites (52).

Gaps in Policy

Gaps in preventative measures

India does not have a specific national policy on Lung cancer control and prevention, and the NCCP doesn't have a specific lung cancer component within it. Nevertheless the National Task Force constituted for developing a "Strategy for Cancer Control in the 11th five year plan (2007-2011)" specified tobacco control/cessation for reduction in the incidence of tobacco related cancers as primary prevention measure (52).

Half of the Indian health budget is spent on secondary and tertiary care services which, if spent on preventive measures like tobacco control, may achieve better health outcomes (73).

Need of health awareness programmes for cancer prevention: Awareness programmes on risk factors, early warning signs and their management should be implemented uniformly throughout India (46). To improve the cancer care scenario in India extensive persuasive health education directed towards control/reduction tobacco is needed (76).

Need for strengthening existing laws on tobacco advertising: The Cigarettes and Other Tobacco Products Act, 2003 has banned direct and indirect advertising of all tobacco products. However, advertising has been permitted at the point of sale of tobacco products. It is, therefore, ideal if the act were to be amended to include the ban to point of sale of advertising (55).

Need for testing efficacy of ban on smoking in public places: Smoking is still prevalent in many public places despite bans imposed by Government of India. Effective policies for smoke-free public places are required to guide implementation at various levels and ensure strict enforcement of the existing laws (55).

For secondary and tertiary care the following policy gaps include:

Limited diagnostic and treatment facilities. The diagnostic infrastructure in India is limited. For example: diagnostic facilities like cytology are available only in less than ten rural areas in India (52). Treatment, namely surgery, radiotherapy and chemotherapy are also grossly inadequate in terms of personnel and equipment especially in the semi urban and rural areas of India (52). Uniform distribution of diagnostic and treatment facilities should be made available throughout India.

Limited trained manpower and Pain relieving drugs. There is a serious limitation of lack of manpower for providing palliative care. Actions to ensure the availability of oral morphine through amendment of regulations that might inhibit the use of oral morphine for cancer pain relief, and training of health professionals in palliative care are thus critical (45).

Conclusion

Globally, lung, trachea, bronchial cancers are the most common cancers found in men and lung cancer is the leading cancer among men, in terms of incidence rates in 6 out of the 12 Population Based Cancer Registries (PBCRs) in India. At a rate of 85 age-adjusted DALYs per 100,000 population, lung cancer accounts for 7% of total cancer DALYs in India. The International Agency for Research on Cancer states that tobacco smoking is the major risk factor of lung cancer. Furthermore, since Lung cancer is presented at an advanced stage, management and treatment becomes difficult and expensive in India. While India is attempting to treat the disease, efforts should be concentrated on the prevention of lung cancer, particularly with more aggressive and anti-smoking campaigns. The Cancer Patients Aid Association is following a combined approach of awareness and anti smoking campaign in India. Also attempts should be made to diagnose patients at an early stage, which can come with awareness and use of various diagnostic modalities.

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