

Cancer Research in ICMR

Achievements in Nineties

The process of carcinogenicity presents a major challenge to scientists and provides limited tools for its control. Indian health services are also not adequately equipped with facilities and expertise for management of cancers. Mortality and morbidity due to tobacco use is very high. In view of the national priorities, the focus of research in the field of cancer has been on the aetiology with identification of preventable risk factors, understand the mechanism of carcinogenesis and on operational research for control of tobacco use and common cancers through existing infrastructures. The multi-disciplinary research involved clinical, epidemiological as well as basic sciences including modern molecular techniques. The cancer registries helped in understanding the magnitude & trends in cancer occurrence and plan control activities. The above mentioned task force projects helped in addressing national priorities. However, high importance was also accorded to supporting projects submitted by individual scientists, which spanned practically all specialties concerned with cancer and different sites in the body.

National Cancer Registry Programme

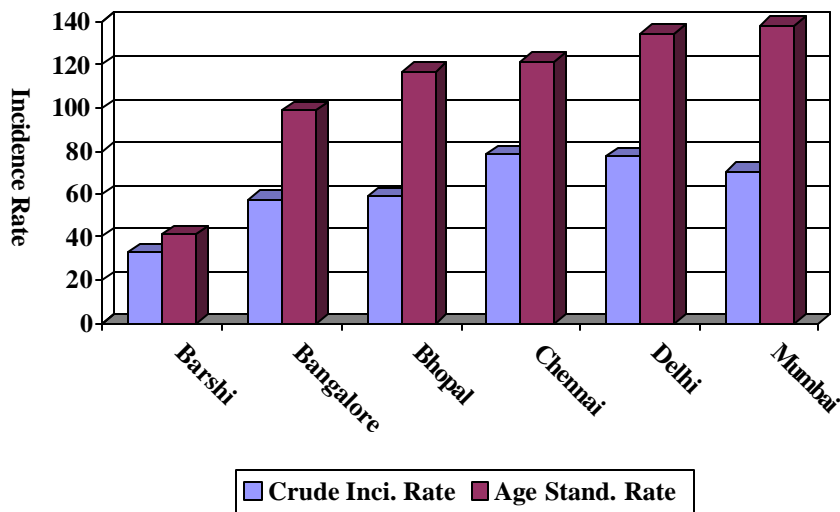
The National Cancer Registry Programme (NCRP) was initiated in 1982, with three population based (existing Mumbai registry and new registries at Bangalore and Chennai), and three hospital based registries (at Chandigarh, Dibrugarh & Thiruvananthapuram). Further expansion saw the initiation of urban population based cancer registries at Bhopal & Delhi; rural population based cancer registry at Barshi (Maharashtra); & hospital cancer registries at Mumbai, Bangalore & Chennai. Chandigarh registry functioned till 1992. At present the network has 6 population based and 5 hospital based cancer registries. Coordinating unit at Bangalore & Delhi, with the help of a steering committee, carries out the monitoring and coordination of activities. The data from cancer registries helped in highlighting the magnitude and common sites of cancer in India, and was useful in planning the National Cancer Control Programme.



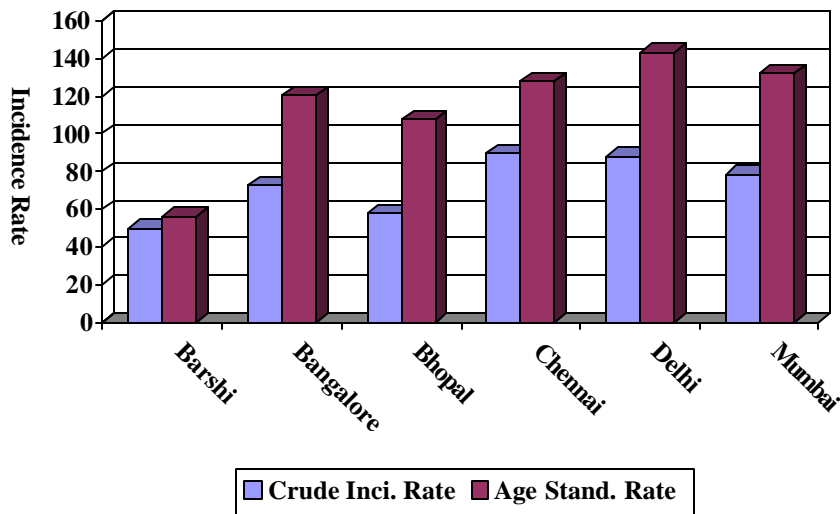
Network of National Cancer Registry Programme

In 1994, the crude incidence rates of cancer in India varied between 57.5 and 78.6 per 100,000 men; and between 57.7 and 89.7 per 10,000 women in urban registry areas. The age standardized incidence rates range from 98.7 to 138.3 per 100,000 men; and from 108.0 to 143.4 per 100,000 women in urban areas. The crude incidence rate for cancers at all sites in rural Barshi was reported to be 32.9 per 100,000 men and 49.7 per 100,000 women. The age standardized incidence rate in Barshi was 41.1 and 56.3 per 100,000 men & women, respectively.

Incidence Rate of Cancer in India, Men (1994)



Incidence Rate of Cancer in India, Women (1994)



Global comparison shows that India has high incidence rates of cancers of oral cavity, pharynx, & cervix. The age standardized cancer incidence in Indian registries as compared to incidence in certain developed countries is about half to one third in men and about half in women. Based on the data from population based cancer registries in Bangalore, Bombay & Madras, the estimated number of new cancer cases for the year 1992 was 644,600. Considering no change in age specific incidence, 806,000 cases are expected to occur during the year 2001.

About half of the cases among men and one fifth of cases among women, pertain to sites mainly attributable to tobacco use. Overall, about one-third of cancers in India pertain to tobacco related sites. The most common cancer among men is lung & bronchus in Mumbai, Delhi & Bhopal; stomach cancer in Bangalore & Chennai & hypopharygeal cancer in Barshi. However, all these cancers occupy important ranks in all the registries. The other important cancers sites among men are that of oral cavity, pharynx, larynx & rectum. Cancer of cervix followed by breast cancer are the commonest cancers among women in Barshi, Bangalore, Bhopal & Chennai. Breast cancer is the commonest cancer followed by cervix, in Delhi & Mumbai. Other common forms of cancer among women are mouth, oesophagus, ovary, & stomach. Incidence of cancer of gall bladder is very high in Delhi.

Common Cancers in among Men in India

Rank	Bangalore	Bhopal	Chennai	Delhi	Mumbai	Barshi
1	Stomach 10.9	Lung 14.5	Stomach 15.4	Lung 13.2	Lung 14.3	Hypopharynx 6.1
2	Oesophagus 9.4	Tongue 10.6	Lung 10.9	Larynx 9.7	Oesophagus 11.0	Oesophagus 4.9
3	Lung 9.2	Hypopharynx 8.5	Oesophagus 9.2	Prostate 7.1	Larynx 8.5	Penis 3.4

4	Hypopharynx 6.4	Oesophagus 8.3	Mouth 7.3	Oesophagus 6.6	Hypopharynx 8.2	Mouth 3.1
5	Prostate 5.1	Mouth 7.5	Hypopharynx 5.7	Uri Bladder 6.3	Prostate 7.5	Larynx 2.7

Common Cancers in among Women in India

Rank	Bangalore	Bhopal	Chennai	Delhi	Mumbai	Barshi
1	Cervix 30.8	Cervix 24.9	Cervix 41.9	Breast 29.0	Breast 27.1	Cervix 27.7
2	Breast 21.4	Breast 22.2	Breast 22.4	Cervix 29.0	Cervix 19.5	Breast 8.0
3	Mouth 9.9	Ovary 6.1	Mouth 8.0	Gall Bladder 8.4	Oesophagus 8.2	Oesophagus 2.1
4	Oesophagus 9.0	Mouth 5.8	Stomach 7.0	Ovary 8.4	Ovary 7.2	
5	Stomach 5.8	Oesophagus 5.8	Oesophagus 6.4	Lymphoma 4.9	Mouth 4.6	

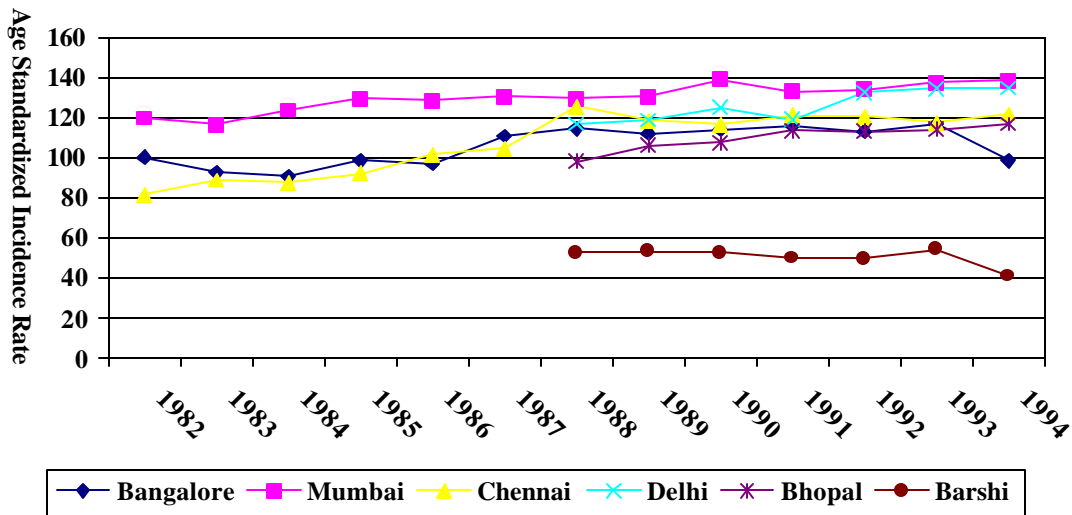
Figures are age-standardized rates for the specific cancer sites.

Figures for Bangalore, Chennai & Mumbai are for the years 1982-94. For other registries the figures are for the years 1988-94.

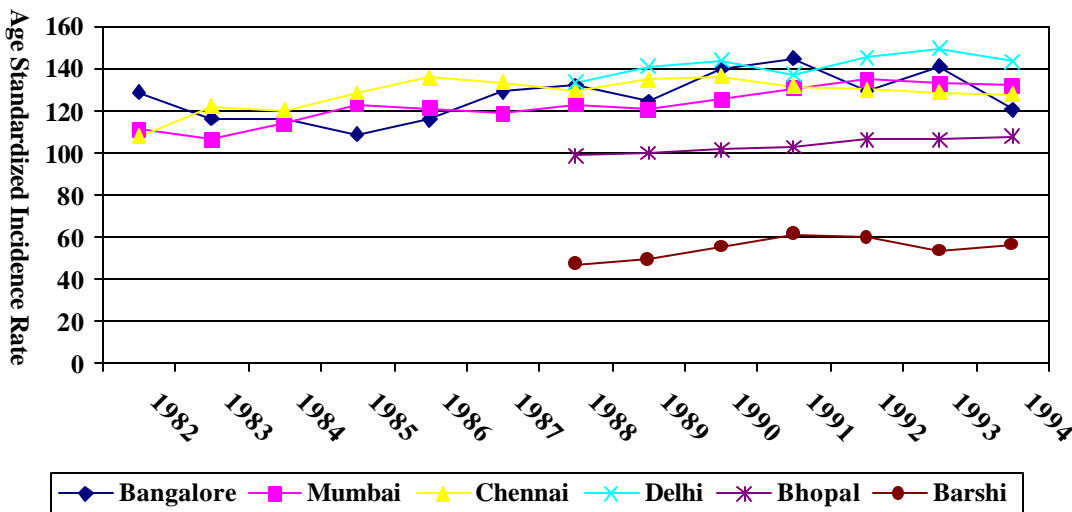
Time trend analysis of the data from population based cancer registries over the last decade shows a small but significant increase in the overall incidence of cancer in all the urban cancer registries, both among men & women. Though there are large year-to-year variations, data suggests that among men incidence increased for oesophagus in Bangalore & Chennai; leukaemia in Bangalore, Chennai & Barshi; gall bladder, colon & brain in Mumbai & Delhi; prostate in Mumbai, Chennai & Delhi; urinary bladder & lymphomas in Mumbai & Chennai; lungs, stomach & rectum in Chennai & Delhi; tongue, oropharynx & larynx in Chennai; mouth in Delhi; and kidney in Mumbai. Among women increased incidence has been observed for cancer of breast in Bangalore, Mumbai, Chennai, Delhi & Bhopal ; gall bladder in Mumbai, Chennai & Delhi; leukaemia in Bangalore, Mumbai & Chennai; colon in Bangalore & Mumbai; lymphoma in Bangalore & Chennai; uterus & urinary bladder in Mumbai & Chennai; brain in Mumbai & Delhi; rectum in Chennai & Delhi; mouth in Mumbai; and oesophagus, stomach, lungs & ovary in Chennai.

A decreased incidence over last decade has been observed for cancer of mouth among men in Bangalore; and pharynx among men in Mumbai. Among women decrease incidence has been observed for cervix in Bangalore & Chennai; mouth in Bangalore; and stomach in Mumbai. The work at rural registry at Barshi has contributed in bringing down the proportion of patients with late stages. The proportion of women with early stage (stage I & II) cervical cancer has increased from 32.6% in 1987-88 to 48% in 1991.

Trends in Age standardized Cancer Incidence Rates among Men in India (1982 to 1994)



Trends in Age standardized Cancer Incidence Rates among Women in India (1982 to 1994)

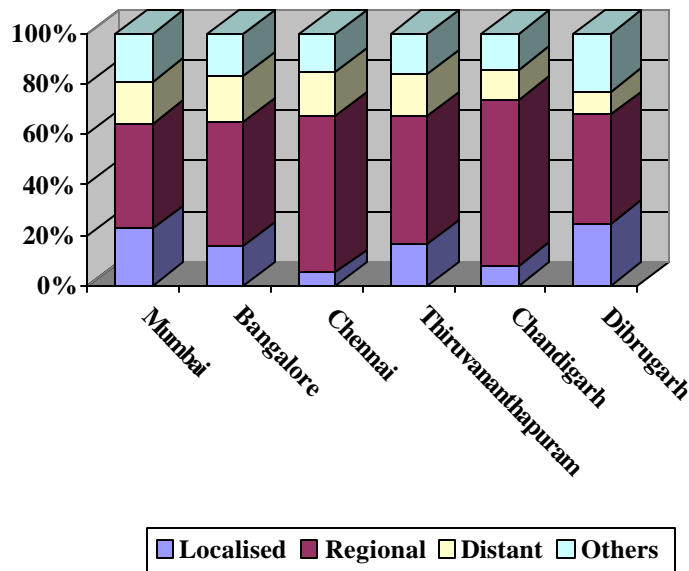


The age specific incidence rates of cancer gradually increase with age. There is a decline in incidence rate in old age in all registries, except Bombay. There are small variations in age specific incidence rates in different registries, except Barshi where the rates are consistently lower after 40 years of age. The incidence rates in the rural registry of Barshi are of special interest, as these are likely to throw light on rural-urban differentials in cancer occurrence. Incidence rate of cancer of penis as recorded by this

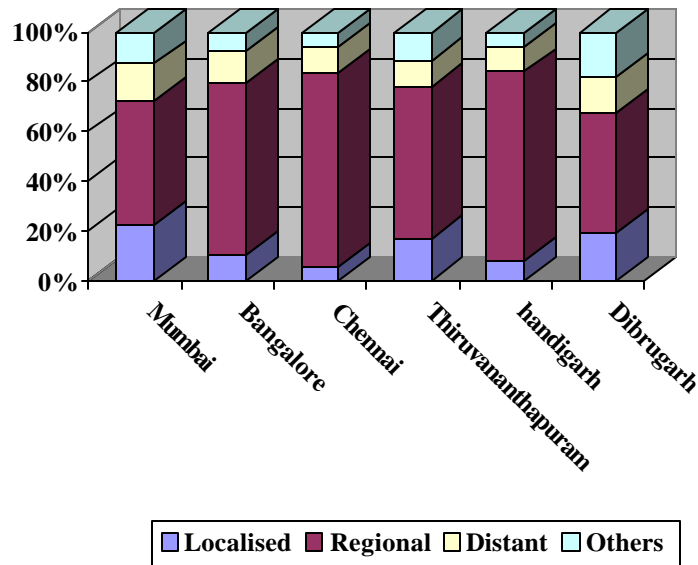
registry is the highest in the country. The incidence rates of mouth, hypopharynx, oesophagus, rectum & larynx are comparable to some urban registries. The incidence rates of smoking related cancers in men, all tobacco related cancers in women, and cancers of not easily accessible sites in both sexes are lower than urban registries.

A comprehensive ten years (1984 to 1993) report of the hospital cancer registries under NCRP shows that microscopic verification of the diagnosis of cancers ranged from 70% to 95% among men and from 72% to 96% among women. The cases diagnosed on clinical examination alone varied from 1% to 23% among men and 2% to 26% among women. At the time of initial reporting, the disease had spread to regional tissues or metastasis had occurred in most of the cases. The proportion of patients who did not receive any treatment varied from 16% to 46% among men, and from 15% to 40% among women. Detection at the stage of localized disease varied from 5% to 24% among men and from 6% to 23% in women. Radiotherapy was the commonest modality of treatment at all stages; surgery was used for localized cancers and chemotherapy for patients having distant spread.

**Proportion of Patients according to Clinical Extent of Disease
Hospital Cancer Registries under NCRP, Men**



**Proportion of Patients according to Clinical Extent of Disease
Hospital Cancer Registries under NCRP, Women**



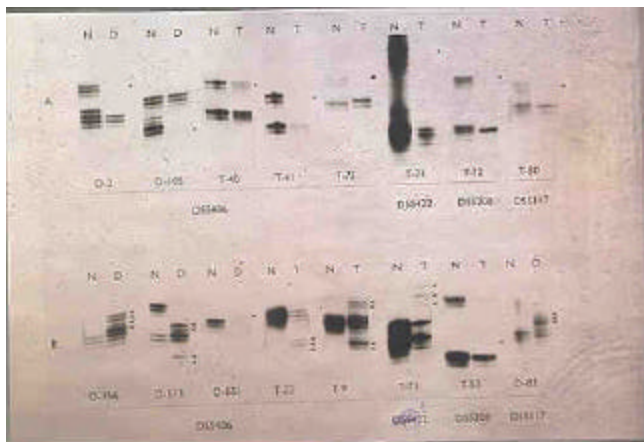
Institute of Cytology and Preventive Oncology, New Delhi

The Institute of Cytology and Preventive Oncology (ICPO) carried out two long term prospective studies on uterine cervical dysplasia (UCD I and UCD II), to understand the natural history of cervical cancer, for the first time on a sizeable cohort. Various risk factors, both biologic and behavioural, were identified and the role of different microbial aetiologies such as Herpes simplex virus (HSV), Human papilloma virus (HPV) and reproductive tract infections (RTIs) was examined. The role of genetic factors and micronutrients in the process of cervical carcinogenesis was also probed. The Institute gave for the first time alternative strategies/modalities for early detection of cervical cancer both unaided and aided visual inspection. The Institute proposes to organise a national workshop for early detection of cervical cancer. The studies demonstrated strong association of HPV high risk type for cervical precancerous and cancerous lesions and demonstrated the role of certain transcriptional factors in the regulation of E6 and E7 oncogene expression. Further it was also informed that Her-2/neu oncogene was found to be frequently amplified and in cervical cancer and a novel tumour suppressor gene on 5p at D5S406 has also been identified which could act as a genetic marker for the identification of high risk dysplasias. Over years ICPO developed the required infrastructures to carry out in depth studies for cervical cancer such as accredited cytology laboratory for teaching, training and diagnostic purposes, centralised colposcope facilities, day care clinic for management of precancerous lesions and molecular oncology and genetic infrastructure. The Institute has initiated a multi disciplinary study on breast cancer with the main emphasis for studying risk factors involved in breast

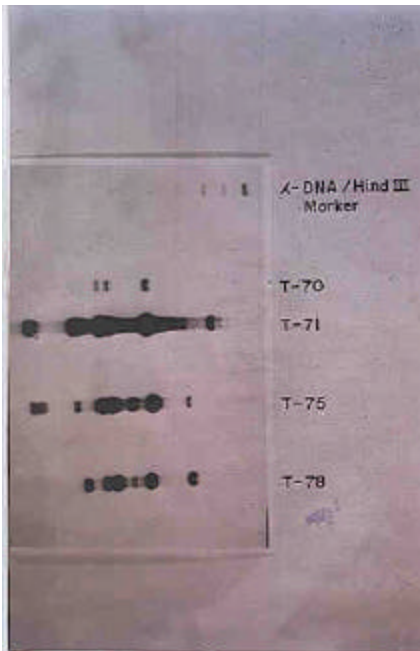
carcinogenesis and a pilot study for identifying susceptible genes in the families of breast cancer cases.

Cumulative Rates of Progression to Severe Dysplasia/ CIS

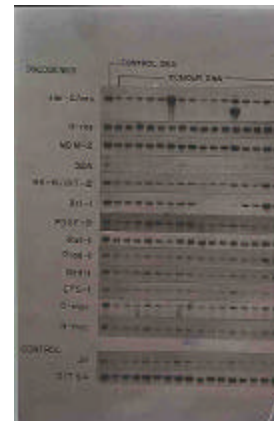
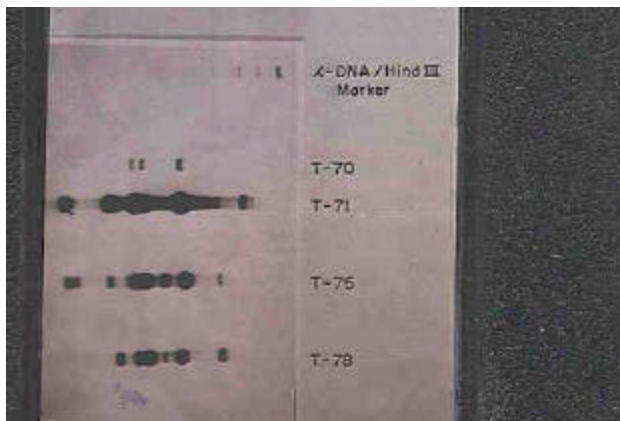
Period of Follow Up	Mild		Moderate		Mild+Moderate	
	No. of Women at Risk	Cumulative Progression Rate	No. of Women at Risk	Cumulative Progression Rate	No. of Women at Risk	Cumulative Progression Rate
6	51	0.03	29	0.09	80	0.08
12	44	0.06	24	0.22	68	0.12
18	40	0.08	20	0.22	60	0.13
24	36	0.08	15	0.26	51	0.14
30	30	0.10	13	0.26	43	0.16
36	24	0.14	11	0.26	35	0.18
42	21	0.14	8	0.32	29	0.21
48	15	0.14	8	0.32	23	0.21
54	13	0.14	5	0.32	18	0.21



**A novel tumour suppressor gene site at D55406 at 5p15
Has been identified by ICPO and may be specific to cervical
cancer. This genetic alteration is independent of HPV infection.**



More than 80% cervical cancer tissues have been observed to be associated with HPV. HPV DNA 16 has been found to be most common, in integrated or in episomal form.



Oncogene Her-2/neu amplification is commonly observed in cervical cancer.

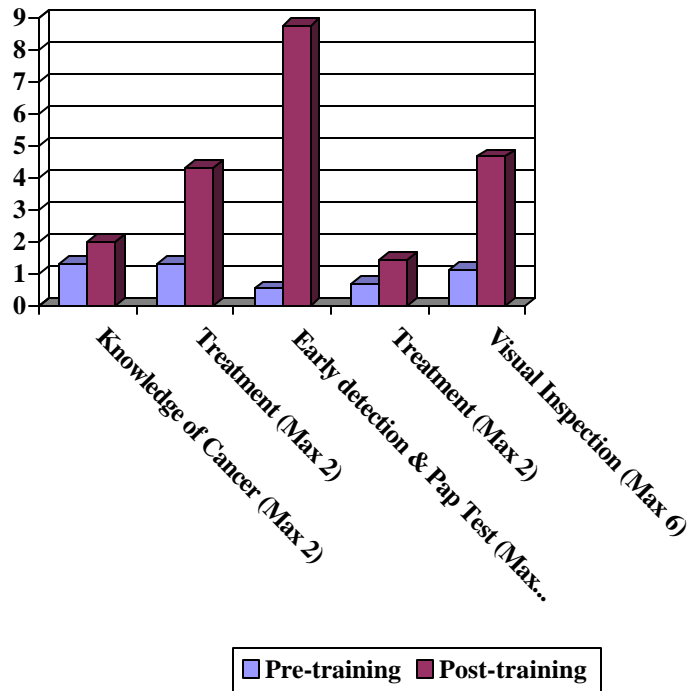


A simple instrument, Magnavisualizer, costing about Rs. 1,000 has been developed at ICPO. The instrument is expected to be helpful in visual examination of cervix.

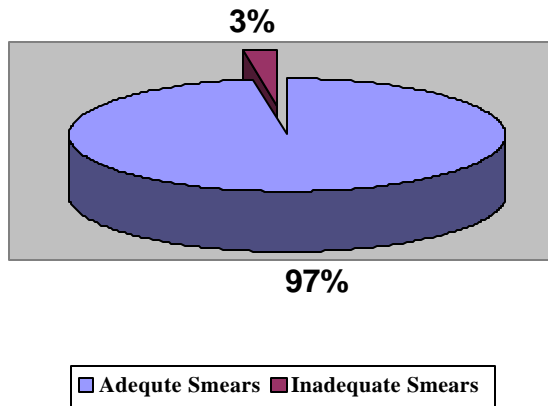
Operational Research Projects for Control of Cervical Cancer

The twin center project (in Gujarat and Karnataka) aimed at assessing the efficacy of clinical downstaging with selective cytology for control of cervical cancer. The project was carried out in three PHC areas, with intervention in one PHC area being provided at the subcentre level; while in the second PHC area, the strategy of imparting health education to the women, and advising the eligible women to attend the PHC for a clinical examination was adopted. The project is proposed to be carried out at a district level. After an 18 months intervention, the proportion of women covered for health education at Karnataka was 8.3% in the area with clinical examination in the field, and 22.0% in the area with only health education in the field. The coverage for health education at Gujarat was near total. The coverage for clinical examination of cervix was more in Gujarat, if the examination was carried out in the field (28.3% vs 0.8%). The coverage for clinical examination in Karnataka was 8.3% when the examination was done in the field, and 9.3% in the PHC approach. The compliance of referral to cancer institute was poor, the major reasons being, monetary difficulties, feeling of no obvious problem, and domestic responsibilities. A total of 147 dysplasia cases were detected out of total of 2,044 women screened in the area with clinical examination in the field, in Gujarat.

Pre- & Post-training Knowledge Score of Paramedical Workers, Kheda Centre



Adequacy of Pap Smears at Karnataka Centre

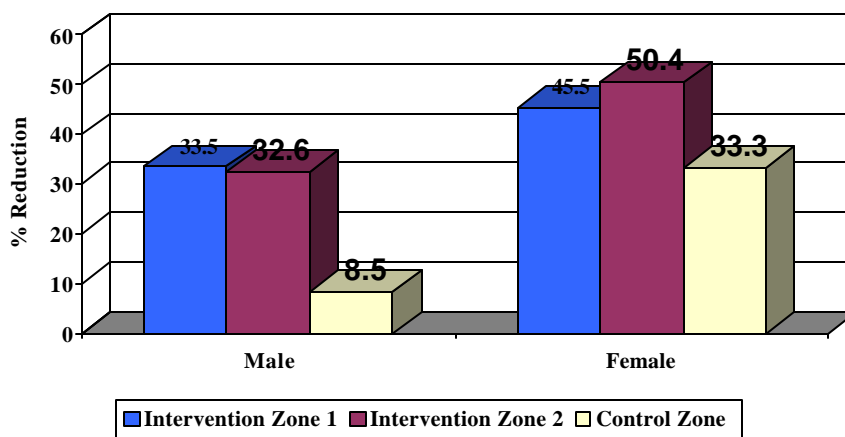


The feasibility of involving health infrastructure for early detection of cervical cancer, through scheme on Reorientation of Medical Education, was studied during late 80s and early 90s in Delhi. The project adopted the strategy of screening of community with Pap smear collected by ANMs. Medical interns, medical officers of the PHC and angawadi workers were also involved. Coverage in the age group above 35, during the

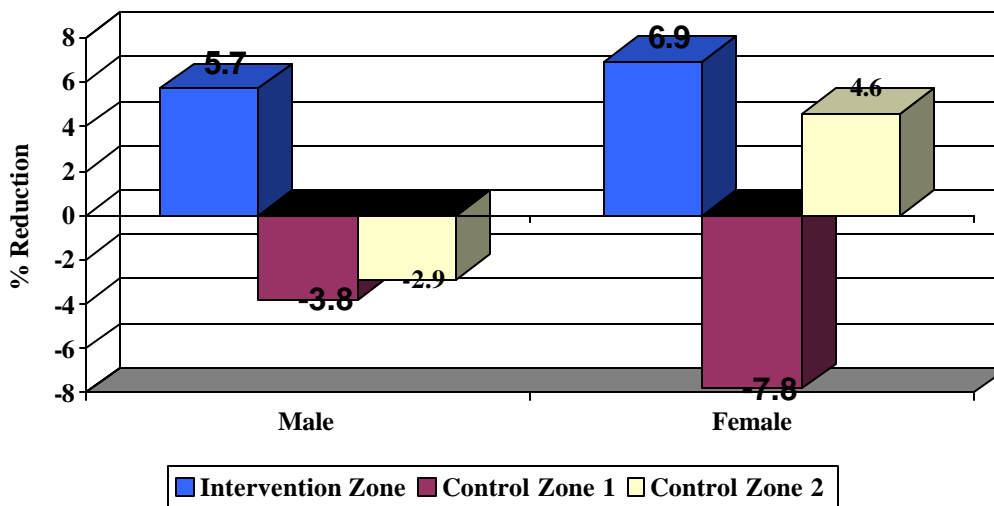
classify lesions. Pre-tested health education material was prepared by the project staff and used by the existing infrastructure personnel. Pre-intervention and post-intervention surveys on knowledge, attitude and practice of tobacco use, measured the effect of intervention. The overall reduction in the prevalence of tobacco usage in Goa was 11.8% among men and 9.1% among women in intervention zone 1; 13.4% among men and 13.3% among women in intervention zone 2; and 2.0% for men and 10.2% for women in control zone. The proportional reduction in the rate of tobacco habit was 33.5% in men and 45.5% in women of intervention zone 1; 32.6% in men and 50.4% in women of intervention zone 2; and 8.5% in men and 33.3% in women of control zone. Based on the experience of this project, Ministry of Education, state of Goa, included an 8 hour course on tobacco as a part of co-curricular activities for standard five and above.

The intervention through community volunteers at Agra centre showed that 26.3% males and 10.5% females left tobacco and another 10.1% males and 4.3% females as likely quitters (6 months have not passed after leaving tobacco), after an intervention of about one year. The project at Trivandrum centre could not achieve optimum participation of health care workers. The nine workers who worked on the project, referred 408 patients out of which 258 reported, giving a compliance of 63.2%. About 59% of these were found to have cancers (10) or pre-cancers. Of the 10 cancer cases five were in stage I & II. 29 old cases were also examined, out of which four recurrences were detected. Intervention at Bangalore centre achieved a reduction of tobacco habit in experimental area, amounting to 5.7% in the males and 6.9% in the females. The control area I showed an increase of 3.8% among male and 7.8% among female, while in control area II, among men there was a 2.9% increase in habit and 4.6% decrease among females.

Proportionate Reduction in Tobacco Use in Goa



Proportionate Reduction in Tobacco Use in Goa



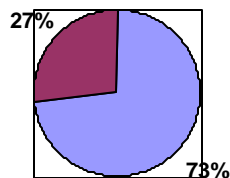
Radio DATE (Drug, Alcohol & Tobacco Education)

The project Radio DATE was a collaborative effort of Indian Council of Medical Research and All India Radio. The acronym DATE stood for Drugs, Alcohol, and Tobacco Education. The radio programme was in the form of 30 weekly episodes of 20 minutes each. Ten episodes focussed on tobacco, eight each on alcohol and drugs, and two episodes on legal aspects. The introductory and concluding episodes touched all the three themes. The episodes were broadcast from 84 stations of All India Radio (out of 104 existing at that time) at prime time, simultaneously in sixteen languages. The prototype was developed in Hindi and was sent to selected radio stations of All India Radio for translation in regional language, as per the specified guidelines. The broadcast was during a specified time (between 8.00 A.M. and 9.00 A.M. on Sundays, with a repeat broadcast during the week, generally in the evening). While the name Radio DATE was used all over the country, different radio stations also coined and used names in local languages.

Evaluation of the reach and effect of the tobacco component of the programme was carried out through two community based surveys, carried out after the broadcast of tobacco episodes (which was the first topic to be covered). These surveys were among persons above 15 years of age in selected rural Goa and Karnataka, where no organized anti-tobacco programmes were being conducted. The surveys showed that the potential listeners of radio comprised 80.4% of the population in Goa and 59.1% of the population in Karnataka. In Karnataka 31.6% of the potential listeners and in Goa 26.7% of the potential listeners, heard at least one of the first eleven episodes (on tobacco). Education was determinant of reach in Goa; while education and occupation influenced the reach in Karnataka. The mean number of episodes heard by the listeners was 2.6 ± 1.46 in Goa and 2.57 ± 1.13 in Karnataka. The factors associated with listening higher number of episodes

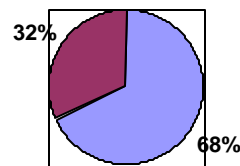
included higher education, male sex, non-usage of tobacco and radio ownership in Goa; and, higher education, radio ownership and caste in Karnataka. Most of the listeners considered the programme to be very good or good, and felt that it would have effect on the tobacco users to quit their habit as well as on children to prevent the initiation of habit. About 4% tobacco users in Goa and about 6% users in Karnataka quit their habit after hearing the programme. About 98% to 99% of the listeners expressed that such programmes should continue.

Proportion of Persons Hearing the Programme in Rural Goa



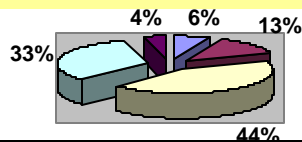
■ Heard Programme ■ Did not Hear

Proportion of Persons Hearing the Programme in Rural Karnataka



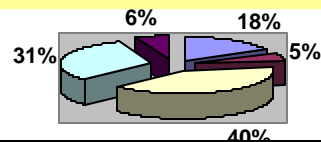
■ Heard Programme ■ Did not Hear

Effect of Radio DATE in Rural Goa



■ None ■ No Comments
 ■ Planning to Quit ■ Reduced Frequency
 ■ Quit Habit

Effect of Radio DATE in Rural Karnataka



■ None ■ No Comments
 ■ Planning to Quit ■ Reduced Frequency
 ■ Quit Habit

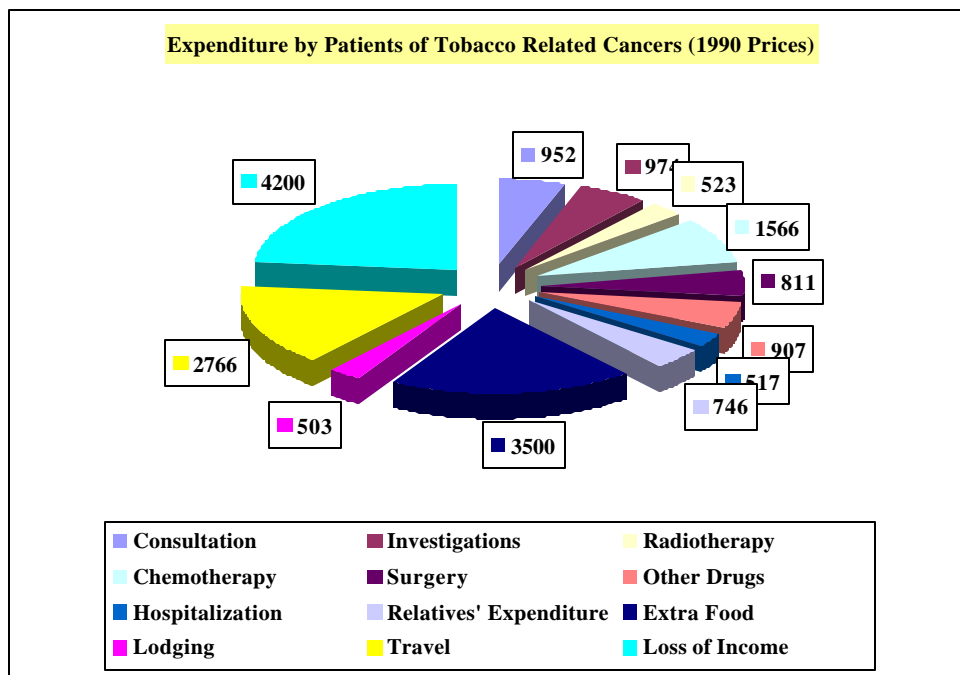
Support for Tobacco Control

The rich experience in research related to tobacco was utilized in helping and guiding decision makers in matters related to tobacco control. Some of the specific areas where major inputs were provided, included, economics of tobacco in India (through an expert committee constituted by the Ministry of Health & Family Welfare), health hazards of pan masala containing tobacco (through expert committee constituted by the Director General of Health Services), preparation of health education messages to be broadcast through television (at request of Ministry of Health & Family Welfare), provision of facts and information to the Parliament's Committee on Sub-ordinate Legislation on the Cigarette Act, organization of International conference on Global Tobacco Law: Towards a WHO Framework Convention on Tobacco Control, and

organization of an inter-ministerial committee meeting to discuss issue related to frame work convention on tobacco control. ICMR was also represented in the meeting of the WHO's Working Group on Framework Convention on Tobacco Control.

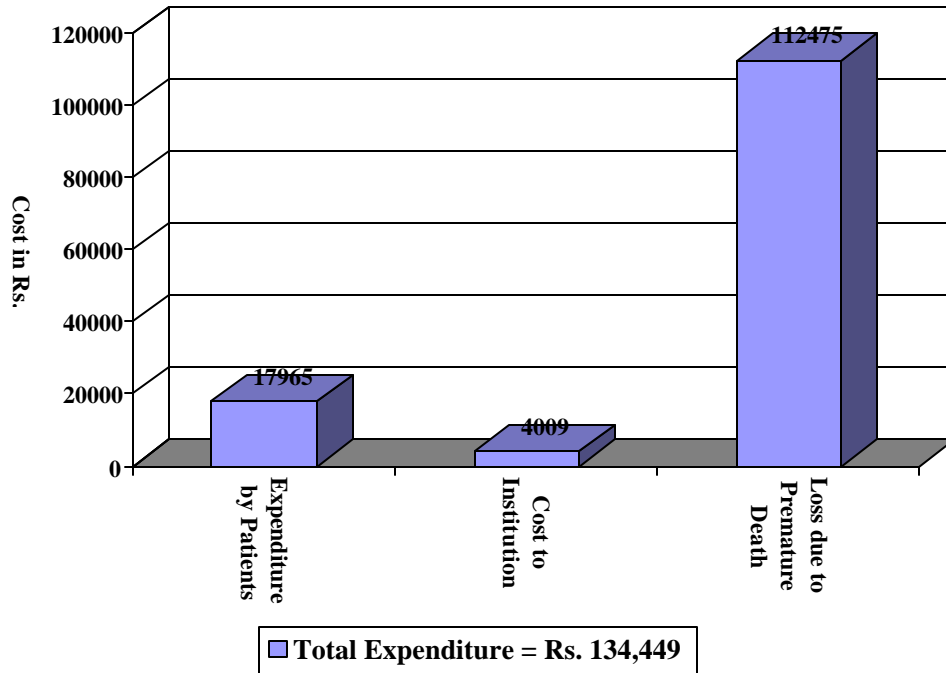
Cost of Management of Tobacco Related Diseases

The completed project on cost of management of tobacco related diseases (tobacco-related cancers, coronary heart disease (CHD) and chronic obstructive pulmonary disease - COPD) helped in assessing the burden posed by these diseases on the society. The study collected data from patients of these diseases and their relatives/ friends on the expenditure on diagnosis & treatment of their disease; travel for treatment/ diagnosis; additional expenses for lodging & food during the treatment period; and loss of wages because of the disease. The expenditure incurred by the treating institution on management of these patients was also collected. In case of premature death, the cost imposed upon the society (due to premature death) was also calculated. The average cost due to a case of tobacco related cancer was observed to be Rupees 134,449 (discounted to 1990 level). The patients in the cohort, spent an average of Rupees 17,965 (including loss of income due to absenteeism), with another Rupees 4,009 being contributed by the institution in the form of various services. The loss due to premature deaths of patients of tobacco related cancers amounted to Rupees 112,475. Annual per capita direct expenditure by patients of CHD and COPD was Rs. 8,520.3 and Rs. 2,257.6, respectively. The annual indirect losses by the patients & state/ employer for patients of CHD and COPD amounted to Rs. 6,388.4 & Rs. 9,694.1, respectively. Thus the total average annual expenditure for a patient of coronary artery disease was Rs. 14,909 and for a patient of chronic obstructive lung disease was Rs. 11, 952.

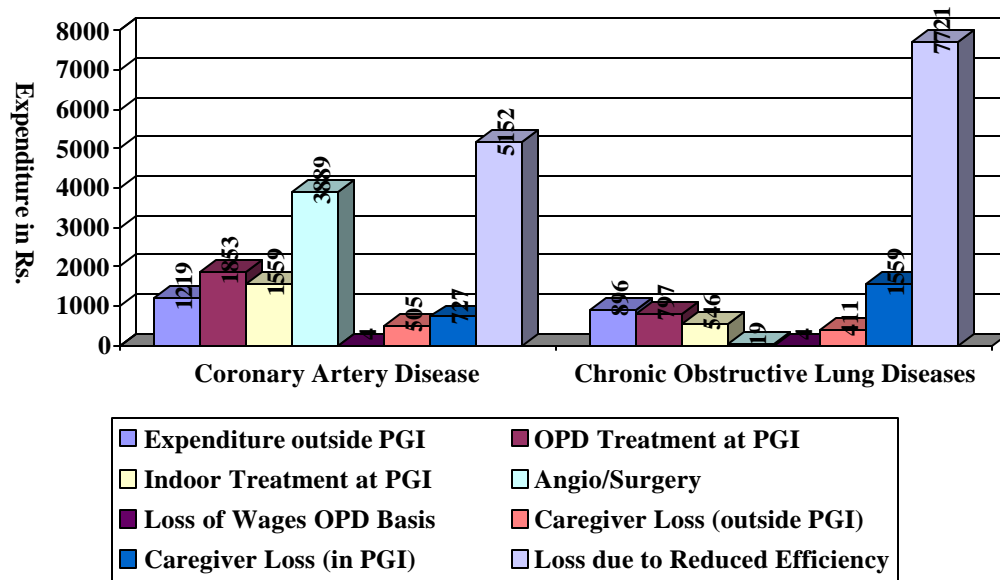


Total Average Expenditure by a Patient of Tobacco Related Cancer = Rs. 17,965

Average per Patient Cost of Tobacco Related Cancers (1990 Prices)



Average Expenditure by Patients of Coronary Artery Disease and Chronic Obstructive Lung Diseases (1992 Prices)



Total Average Expenditure by Patients of Coronary Artery Disease = Rs. 14,909
 Total Average Expenditure by Patients of Chronic Obstructive Lung Disease = Rs. 11,952

Economics of Tobacco Use in India:

The Ministry of Health & Family Welfare constituted an Expert Committee on Economics of Tobacco in India, to examining the tax revenue and foreign exchange earnings, employment and consumer expenditure due to tobacco on the one hand and the cost of tertiary level medical care facilities for treatment of tobacco related diseases, losses due to fire hazards, ecological damage due to deforestation and disposal of tobacco related wastes on the other hand. The ICMR is acting as the secretariat for this Committee and the Member Secretary is also from ICMR. The report of the Committee would help in providing the much needed information for the country.

Indo-German Collaboration in Cancer

Collaborative cancer research projects between India and Germany are coordinated by ICMR in India and German Science Foundation in Germany. To facilitate the development of newer projects and to review the progress of ongoing projects, the ICMR hosted the 4th Workshop from 21st to 25th February 1999 at Lonavala (Maharashtra). The workshop was organized by Tata Memorial Centre, Mumbai, with the help of a National Advisory Committee. Twenty two scientists from Germany and thirty eight scientists from India participated in the workshop. The programme of the workshop covered major cancers in India, namely, cancer of the cervix, head & neck and breast. Sessions were also organized on lung cancer and hepatocellular carcinoma. One of the major subjects was the role of HPV in cervix and head & neck cancers. The discussions were also held on mechanism of neoplastic development and the potential of vaccines in prevention and therapy of these cancers. The participants identified 29 collaborative research projects between India and Germany to be submitted by the scientists for review & funding. Out of the 13 projects received, 5 have been cleared by Health Ministry's Screening Committee, and the remaining are under consideration.