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# Transition in Incidence and Age at diagnosis of Tobacco Related Cancers in South India

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**Abstract**

**Objective:** To elucidate the impacts in incidence and shift in the age at diagnosis of tobacco related cancers (TRC) in south India after launching the national strategic action plan in India **Methods**: We analysed data of south Indian cancer registries, age-standardised rates (ASR)to estimate annual percentage changes (APC) and transition by gender and region using Join point regression. **Results**: Over the 25-year period, among men Trivandrum registry showed a significantly increasing trend by 0.9%, while among women, Chennai showed a decreasing trend by -1.3% annually. Lung cancer incidence trends changed significantly among women, increased by 2.3% per year from 1991-1998 and by 7.8% from 1998-2012 in Trivandrum. Rising trends for lung cancer was observed. Mouth cancer incidence declined significantly among men, APC shows a decreasing trend by 2.6% per year from 1991-2003 and by 1.8% from 2003-2012 in Trivandrum while rising trends showed in Kollam, Bengaluru and Chennai. **Conclusion**: Evidence showed decline in incidence rate of some TRCs. Gender and region disparities in incidence remain. Younger age shift in the age at incidence of TRC is alarming. The findings suggest that comprehensive cancer control efforts, evidence-based tobacco control interventions, are needed to reduce tobacco use and cancer burden in India.

**Key words:** age-specific cancer incidence rates; age-standardized cancer incidence rates; age at diagnosis; epidemiologic transition; tobacco-related cancers.

## Introduction

Tobacco related cancers (TRCs) account for major share of all cancers and updated of incidence data are helpful in policy changes. If the current trends in smoking and population growth continue, the number of current smokers is expected to reach 2 billion worldwide by 2030 [1]. Many countries launched a national strategic action plan, ending the tobacco epidemic, to co-ordinate tobacco control activities [2-4]. With the decline of tobacco use in many industrialized countries, the geography of smoking has shifted from the developed to the developing world, especially among men. About 50% men and 9% women are current smokers in developing countries, compared to 35% men and 22% women in high-resource countries [5].

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India is the second largest consumer and third largest producer of tobacco in the world [6]. Current prevalence of tobacco use among men is 48% and among women is 20% [7]. Tobacco use in the Indian subcontinent is centuries old, the two main forms of use are chewing and smoking [8]. Data show that, in India more than 35% of adults (274.5 million) use tobacco, of this 163.7 million use only smokeless tobacco; 68.9 million are only smokers while 42.3 million users of both smoking and smokeless tobacco [9].The proportion of TRCs in south India in relation to other cancers ranges from 34% (Bengaluru) to 43.2% (Kollam) among men [1]. Cancers related to tobacco use are preventable through primary prevention. Reporting the burden of TRCs from time to time in respect to geographical distribution of Indian population-based cancer registries (PBCRs) data would be helpful for action on preventive measures through policies related to control of disease.

The Government of India enacted the Cigarettes and Other Tobacco Products Act in 2003 to discourage the use of tobacco products, and the National Tobacco Control Programme was launched in 2007. A set of comprehensive rules has been notified, under which smoking will not be permitted in public places. The first ban on smoking in public places in an Indian state

was imposed in Kerala in July, 1999 and was a result of a court directive. In 2012, Kerala has declared the second state in India to ban all forms of chewing tobacco products.

Global Adult Tobacco Survey (GATS) [7]& National Family Health Survey (NFHS) -IV 2015–2016 [1])showed that there is significant rise in female smoking in India during the period 1993-2009.Contrary to this, NFHS-IV observed that the states such as Tamil Nadu, Kerala, and Karnataka recorded near zero female smoking prevalence [12]. The survey observed that tobacco use among men has fallen from 50% in 2005-06 to 47% in 2014 in Kerala. Understanding the geographical distribution of TRCs will be very useful to assess its association with tobacco prevalence. Also, age at incidence of TRCs varied in different regions. Early age at incidence may be due to early age at which the habit started and thus age at incidence of TRCs is an also important.

The present paper assessed the transition in incidence rates and age at incidence of TRCs(all sites together and separately) by gender in the four PBCRs (Trivandrum, Kollam, Chennai, & Bangalore) in south India, during the past three decades. All these above registries are under the network of National Cancer Registry Programme (NCRP) of Indian Council of Medical Research (ICMR), Government of India.

## Materials & Methods

Data is available for 25 years period (1990-2014) from all the four registries. The data used for trend analysis from these four registries has been coded in one format i.e. for topography ICD-10 [13] has been used. The data on TRC sites (along with International Classification of Diseases code) collected from each cancer registry were lip (C00), tongue (C01–C02), mouth (C03–C06), oropharynx (C09-C10), hypopharynx (C12–C13), pharynx (C14), oesophagus (C15), larynx (C32), lung (C33–C34) and urinary bladder (C67).Age standardization in all the analyses was performed by the direct method based on the 2000 world standard population [14]. Join point analysis with Join point Regression Program (Version 4.2.0.2) [15] from the Surveillance Research Program of the US National Cancer Institute (http://surveillance. cancer.gov/join point) was performed to model the rates and annual percentage change (APC) was used to quantify changes in rates from 1990-2014 and was calculated using least squares regression. Join point regression identifies points of significant change in the log linear slope of the trend. The optimal number of join points was selected with permutation test. For each line segment separated by join points, the APC was presented with 95% confidence intervals (CI)and the figure performed using Graph Pad Prism version 6.04 [16]. All analyses were done separately by gender. Mean age at diagnosis along with standard deviation (SD) for TRCs was calculated. Statistical significance between the mean values was assessed using ANOVA (p-value of 0.05 considered significant).

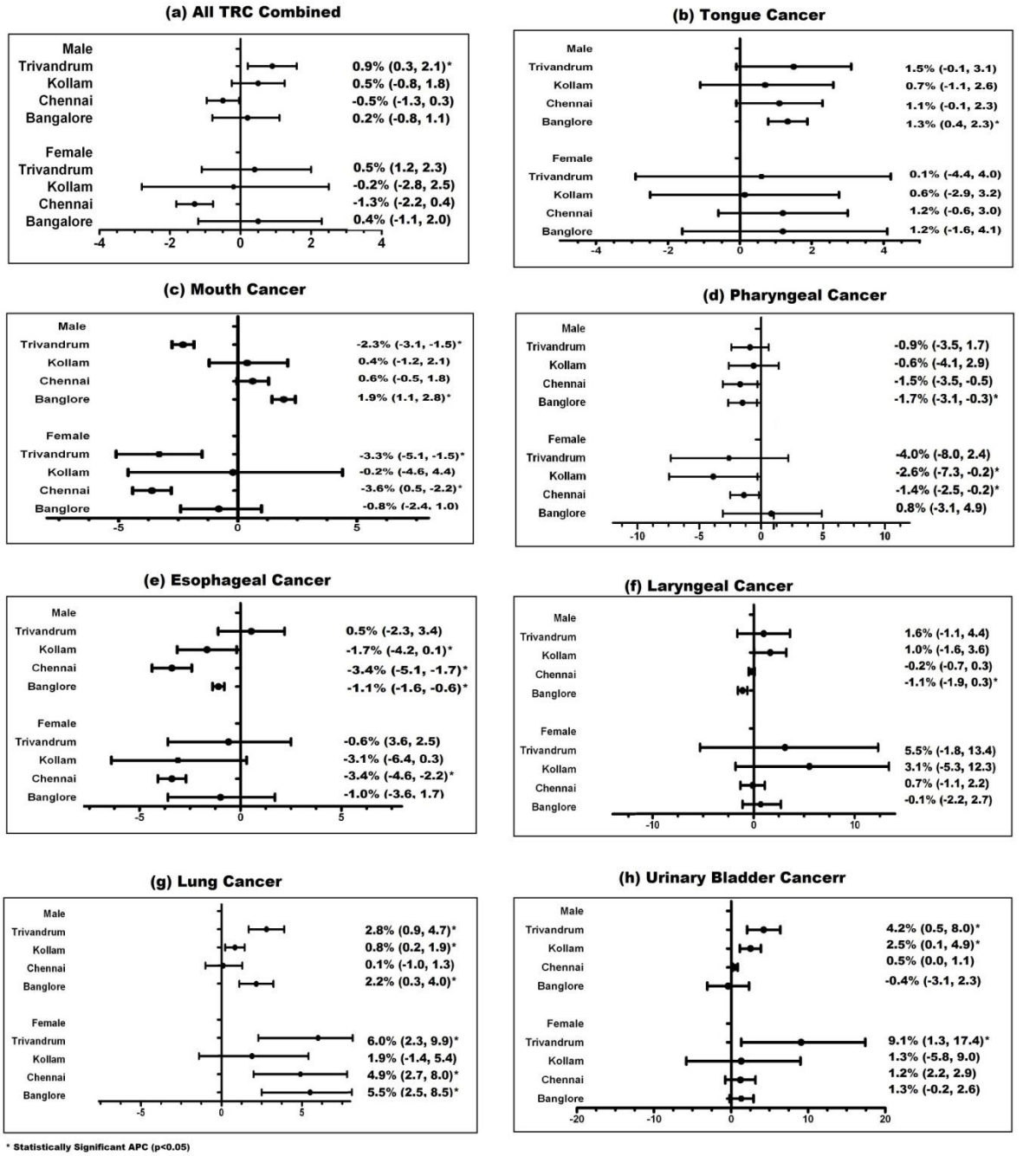
## Results

We observed substantial variation in TRC incidence in south Indian region. The TRCs accounted for 37.1%, 43.2%, 40.7% and 34.0% in men whereas 10.9%, 12.9%, 13.8%, and14.3% in women respectively in Trivandrum, Kollam, Chennai and Bangalore. Among men, overall TRC incidence increased significantly [APC:0.9% (95%CI:0.3,2.1)]in Trivandrum while among women, Chennai showed declining trend [APC:-1.3% (95%CI:-2.2,-0.4)](Figure 1.a) and none of the other registries show significant change. All south Indian registries showed an increasing tongue cancer incidence in men and women. Among men in Bangalore showed a significant increase and APC is 1.3% (95 %CI:0.4, 2.3) (Figure 1.b). Mouth cancer incidence decreased significantly among men ($p<0.05$) (APC is -2.6% in 1991-2003 and -1.8% in 2003-2012) in Trivandrum, while rising trends observed in Kollam, Bengaluru and Chennai. Among women, mouth cancer incidence decreased significantly, APC is -3.3%, -3.8% in Trivandrum and Chennai respectively (Figure 1.c).Decreasing trend in pharyngeal cancer incidence in both genders in all registries except women in Bengaluru and among men and women in Chennai registry showed a significant decrease and APC is -1.7% and -1.4% (Figure 1.d). Decrease in oesophageal incidence was more pronounced in menin almost all registries except Trivandrum (Figure 1.e) and among women, Chennai showed declining trend[APC: -3.4% (95% CI: -4.6, -2.2)].Laryngeal cancer incidence showed a significant decreasing trend in Bengaluru among men[APC: -1.1% (95% CI: -1.9, -0.3)](Figure 1.f). Lung cancer incidence trends increased significantly among women ($p<0.05$), (APC:2.3% in 1991-1998 and 7.8% in 1998-2012) in Trivandrum. Similarly, rising trends for lung cancer among women were observed in Bengaluru and Chennai also (Figure 1.g). Among men, urinary bladder incidence trend changed significantly increasing and APC is 4.2% (95 %CI:0.5,8.0) in Trivandrum and by 2.5% (95%CI:0.1,4.9) per year in Kollam (Figure 1.h).

The range of mean age at the time of diagnosis of TRC combined among men was 57-67 years and a significant variation observed in South Indian registries ( p value0.004) and among women the same was 56-

69 years and not showed a variation between registries. A significant variation in age at diagnosis of mouth cancer among men observed in South Indian registries ( p value0.038) and all the registries showed a downward shift.Mean age at incidence of mouth, larynx, lung and urinary bladder cancers among women was almost similar in all registries through the decades.

**Figure 1: Annual Percentage Change & Confidence Interval of Tobacco Related Cancer in South Indian Registries by Gender**



**Discussion**

We have utilized data from four cancer registries operational in south India to study the time trend in TRC rates for more than 25 years.The existing registry data give a reflection of the cancer burden in their respective areas. Epidemiological studies from around the world have provided sufficient evidence that the smoking of tobacco as cigarettes and bidis causes cancer of the respiratory tract and the upper digestive tract and tobacco smoking is associated with stomach, liver, pancreas, kidney, cervix-uteri and acute myeloid leukaemia (AML) [17].

In terms of gender distribution, male TRCs were more common as compared to female TRCs. The gender ratio of TRC incidence gradually increased from the year 1991 to 2012 (3.4 to3.7 in Trivandrum, 2.9 to 4.3 in Kollam, 2.5 to 2.6 in Chennai)and the same is decreased in Bangalore (2.4in 1991 to 1.9 in 2012).In this study, the TRCs among male proportion was 3times higher than women in all the registries in southern India. The lower proportion of TRCsamong women was mostly explained by the fact that, tobacco use, especially smoking, was more common among men than among women [18].Among men significant increases were observed in Trivandrum. Among women, Chennai showed a decreasing trend for all TRC sites combined. However on comparing the cancer incidence across the various regions of the countries, it is evident that the south India has a less incidence of cancer as compared to the other areas [19]. The results indicated that there is a declining trend in some tobacco-related cancer incidence rates in both gender in south India. Declining trend was observed for cancer sites such as mouth and pharynx in men and mouth and oesophageal cancers in women. Increase in lung cancer rates among men and women in all registries suggest that tobacco control remains priority for cancer control in India. It has been conclusively established that prolonged exposure to environmental tobacco smoke (ETS) causes lung cancer [20,21].The observations of current study are similar to those observed by previous studies [22,23].

Some registries showed a downward shift in the age at diagnosis of tobacco-related cancers.Age at diagnosis of TRC was observed in middle age among both genders, however, a significant difference in age at diagnosis was observed in all South Indian registries. An epidemiologic transition in cancer pattern is taking place and is changing to more similar to “western” jurisdictions [24]. Younger age shift in the age at diagnosis of tobacco related cancers is alarming and the effect was greater in women. This is consistent with reports that women are more susceptible to the carcinogenic effect of smoking in other malignancies. Subjects who smoked more than 40 pack-years, the risk of developing lung adenocarcinoma, bladder cancer, and oral cancer in men were 13.8, 2.5, and 2.1, respectively, whereas for women they were markedly higher, 32.7, 4.5, and 5.4, respectively [25].The estimates of the GATS conducted among persons 15 years of age or older during 2009-2010 indicate that 34.6% of the adults (47.9% men and 20.3% women) are current tobacco users. Fourteen percent of the adults smoke (24.3% men and 2.9% women) and 25.9% use smokeless tobacco (32.9% menand 18.4% women)which indirectly indicated that the productive life-years lost, will be higher than the earlier decades.

Although many factors might contribute to tobacco-related cancer disparities, they generally align with disparities in cigarette smoking prevalence by sex, geography, and socio-economic status [26]. TRC defined in this text might underestimate the true burden, because evidence is still accumulating that tobacco use might cause additional cancers [27]. Many tobacco-related cancers could be prevented by reducing tobacco use through sustained, comprehensive, evidence-based tobacco prevention and control interventions [28]. These interventions include increased tobacco product prices, implementation and enforcement of comprehensive smoke-free laws, aggressive mass media campaigns, and promotion of smoking cessation resources proven to help users quit tobacco use [29].Following implementation of the National Tobacco Control Programme in 2007, historical data (7,11) revealed that the smoking rates for adults aged 18 years are decreasing among men. Further studies are required to identify effects of birth cohort and calendar period on trends in cancer in India so as to undertake informed and evidence-based policy decision on steps for cancer prevention and cancer control [30].

Our findings suggest that continued efforts in tobacco prevention and control are needed to further reduce tobacco-related cancer burden. The Indian government has enacted and implemented various tobacco control policies at national and sub-national level. The study showed an overall improvement in tobacco control over last few years. This can help motivate the government agencies to further strengthen up tobacco control efforts including evidence-based tobacco control interventions, can reduce tobacco use and the burden of cancer in India.

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