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Smokeless tobacco and health in India and South Asia

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Abstract: South Asia is a major producer and net exporter of tobacco. Over one-third of tobacco consumed regionally is smokeless. Traditional forms like betel quid, tobacco with lime and tobacco tooth powder are commonly used and the use of new products is increasing, not only among men but also among children, teenagers, women of reproductive age, medical and dental students and in the South Asian diaspora. Smokeless tobacco users studied prospectively in India had age-adjusted relative risks for premature mortality of 1.2–1.96 (men) and 1.3 (women). Current male chewers of betel quid with tobacco in case-control studies in India had relative risks of oral cancer varying between 1.8–5.8 and relative risks for oesophageal cancer of 2.1–3.2. Oral submucous fibrosis is increasing due to the use of processed areca nut products, many containing tobacco. Pregnant women in India who used smokeless tobacco have a threefold increased risk of stillbirth and a two- to threefold increased risk of having a low birthweight infant. In recent years, several states in India have banned the sale, manufacture and storage of *gutka*, a smokeless tobacco product containing areca nut. In May 2003 in India, the Tobacco Products Bill 2001 was enacted to regulate the promotion and sale of all tobacco products. In two large-scale educational interventions in India, sizable proportions of tobacco users quit during 5–10 years of follow-up and incidence rates of oral leukoplakia measured in one study fell in the intervention cohort. Tobacco education must be imparted through schools, existing government health programmes and hospital outreach programmes.

Key words: areca, asthma, health policy, hypertension, intervention studies, morbidity, mortality, neoplasms, oral submucous fibrosis, pregnancy outcomes, smokeless tobacco, South Asia.

INTRODUCTION

The Europeans introduced tobacco into South Asia in the 1600s, for pipe smoking and probably also as snuff. The chewing of betel quid (a mixture of the leaf of the *Piper betle* vine, aqueous calcium hydroxide paste [slaked lime], pieces of areca nut [*supari*], and frequently some spices) was a popular habit that had already been integrated into social and cultural life in this region for over a millennium. Believed to have originated in prehistoric times, this practice extends eastwards as far as the South Pacific islands. After its introduction, tobacco soon became a new ingredient in betel quid (*pan*), which has become the most commonly used form of smokeless tobacco, although its use varies in different parts of the world.

An estimate of the number of betel quid users globally is 600 million.¹ Smokeless tobacco users in India and Pakistan together have been estimated to number 100 million.²

Habitual betel quid chewing is commonly practised by men and women in Bangladesh, India, Pakistan and Sri Lanka, while tobacco smoking is much more common among men in these countries compared to women, except for certain small geographic areas.

Countries in South Asia are major producers of tobacco and the region is a net exporter. Current production figures are shown in Table 1. Tobacco leaf production has been increasing steadily for many decades, and has doubled since the 1960s.³ The increasing demand for tobacco in Bangladesh is being met by imports, especially from India.⁴

About 35–40% of tobacco consumption in India is in smokeless forms, mostly of the species *Nicotiana rustica*, while most smoking tobacco is *N. tabacum*.^{6,7} Samples of *N. rustica* have been found to contain higher concentrations of tobacco-specific nitrosamines than *N. tabacum*.⁸

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Table 1 Current raw tobacco production in selected countries in the year 2002⁵

Major producing countries	Production (metric tonnes) of tobacco leaves
South Asian region	
Bangladesh	37 000*
India	575 000 [†]
Pakistan	85 100*
World	
Brazil	654 250
China	2 400 000*
USA	401 890

*FAO estimate; [†]unofficial figure.

SMOKELESS TOBACCO USE IN SOUTH ASIA

Smokeless tobacco use in South Asia raises various concerns. It is commonly used and increasingly so, especially as new forms of smokeless tobacco have been emerging over the last few decades, enticing new consumers.⁹ Increasing use has been reported not only among men, but also among such vulnerable groups as children, teenagers, women of reproductive age and by immigrants of South Asian origin wherever they have settled. In India, per capita smokeless tobacco consumption has increased among the poor between 1961 and 2000 in both rural and urban areas.¹⁰ Lately, a European company has begun marketing one of its smokeless tobacco products in India. This review attempts to highlight these issues and the concern for the health consequences.

Forms of smokeless tobacco

In South Asia, the use of smokeless tobacco is common. The various forms are chewed, sucked or applied to teeth and gums.^{11,12} Generally sun- or air-cured smokeless tobacco can be used by itself in unprocessed, processed or manufactured form. It can be used with lime, with areca nut or in a betel quid (*pan*) (Fig. 1). The use of unprocessed tobacco, the cheapest form, varies in different parts of India. It is sold as bundles of long strands in Kerala or as leaf tobacco (*hogesoppu*) in Karnataka. *Kaddipudi* are cheap 'powdered sticks' of raw tobacco stalks and petioles, used in Karnataka. Sometimes this powder is formed into bricks or blocks mixed with jaggery (solid molasses) and water. *Gundi*, also called *kadapan*, is a mixture of coarsely powdered tobacco with coriander seeds, other spices and aromatic, resinous oils, popular in Gujarat, Orissa and West Bengal. *Kiwam* or *qiwam*, used mainly in north India and Pakistan, is a thick paste of boiled tobacco mixed with powdered spices such as saffron, cardamom, aniseed and musk, and is also available as granules or pellets. A commercial mixture of tobacco, lime and spices is *zarda*. It is typically flavoured with cardamom and saffron and often



Figure 1 A *pan* seller outside a major railway station in Mumbai, India.

chewed in betel quid, and is popular in north India, Pakistan and Bangladesh.

Pattiwala is sun-dried, flaked tobacco with or without lime, used mainly in Maharashtra and several north Indian states. A similar preparation popular in northern areas is *khaini*, a mixture of tobacco and lime generally made by the user but now available ready made in sachets as well. *Khaini* is placed in the mandibular or labial groove and sucked slowly for 10–15 min, occasionally overnight.

In India there are several smokeless tobacco preparations incorporating areca nut and slaked lime. *Mainpuri* tobacco, taking its name from a district in the northern state of Uttar Pradesh, contains finely cut areca nut, camphor and cloves. *Mawa*, popular among teenagers especially in Gujarat, contains thin shavings of areca nut with some sun-dried tobacco and slaked lime. A similar product used in Maharashtra is called *kharra*.

Gutka, a dry preparation commercialized since 1975, containing areca nut, slaked lime, catechu, condiments and powdered tobacco, was originally available custom-mixed from *pan* vendors. For the last couple of decades, *gutka* has been available in several brands. A similarly packaged mixture without tobacco, often with an identical brand name, is called *pan masala*. These products have become very popular especially among teenagers and young adults in many states of India, as shown by a number of surveys, both published and unpublished, in Gujarat, Maharashtra, Bihar and Punjab (Fig. 2).



Figure 2 Smokeless tobacco seller on a busy road near a marketplace in Mumbai, India.

Products containing tobacco and areca nut together are highly addictive. Having begun to experience the public health impact of these products and having been warned by tobacco control experts about the high carcinogenicity of *pan masala* and *gutka*, three state governments (Tamil Nadu, Andhra Pradesh, Maharashtra) have taken the initiative to ban the sale of these products. The loopholes in the law however, are being well exploited. For example, substitutes such as ‘*supari mix*’ packets, containing areca nut, lime, spices and condiments are sold with a free packet of chewing tobacco, in the form of *zarda* or *khaini*. None of these products are individually banned, but a user can mix the two packets to create his own ‘*gutka*’.

Dry snuff (*tapkeer*) was once commonly used nasally, but is now used mainly orally. Other dry tobacco products are used to clean the teeth. For example, dried forms of smokeless tobacco, such as *mishri*, *bajjar* and *gul*, are mainly used in Goa, Maharashtra, Gujarat and eastern parts of India. These are frequently prepared at home by roasting coarsely cut tobacco on a griddle and then powdering it. Such products are widely used by the poorer classes, especially by women, and tend to be used many times a day, due to their addictive properties. *Gudakhu* is tobacco paste made with molasses and is sold in small bottles. Creamy snuff or tobacco toothpaste, an industrially manufactured product advertised as being an antibacterial, is popular in western parts of India (Fig. 3).

Naswar or *Niswar*, used widely in Afghanistan and Pakistan, is a mixture of powdered tobacco, slaked lime, and indigo and can be home made or available commercially. In Pakistan, *naswar* is tobacco flavoured with cardamom and menthol. *Nass*, a mixture used in Pakistan, Iran and the Central Asian Republics contains local tobacco, sometimes only partially cured, ash, cotton or sesame oil and in some areas, lime. It is placed either under the tongue or in the lower labial groove.



Figure 3 Manufactured chewing tobacco products made in India.

With globalization, the moist Swedish *snus* is being marketed in large cities in India under the brand name ‘Click’, as a more convenient tobacco product to use than cigarettes. Many shops and billboards carry attractive advertisements for this product.

A newly described tobacco product for oral use is tobacco water (*tuibur* or *hidakphu*) i.e. water through which tobacco smoke has been passed, which is used for gargling in Manipur and Mizoram states in India.

Prevalence of smokeless tobacco habits

In some parts of India, such as the states of Bihar and Maharashtra, smokeless tobacco use is more common than smoking. Apart from regional preferences due to differing socio-cultural norms, the preference for smokeless tobacco is inversely related to education and income.¹³

Table 2 Distribution of basic types of tobacco habits in seven areas of India

Area	Male users (% total men)				Female users (% total women)			
	Chew or apply	Smoke	Mixed	Total users	Chew or apply	Smoke	Mixed	Total users
Mainpuri, Uttar Pradesh ¹⁵	21	41	20	82	9	11	1	21
Bhavnagar, Gujarat ¹⁶	9	56	6	71	15	*	*	15
Ernakulam, Kerala ¹⁶	14	45	22	81	38	1	1	39
Srikakulam, Andhra Pradesh ¹⁶	4	70	7	81	3	64	*	67
Singbhum, Bihar ¹⁶	17	50	14	81	26	5	2	33
Darbhanga, Bihar ¹⁶	28	24	26	78	7	41	4	51
Pune, Maharashtra ¹⁷	53	6	2	62	49	*	*	49
Goa ¹⁸	3	61	5	69	23	24	2	49
Mumbai (urban), Maharashtra ¹³	46	14	10	69	57	*	*	57.5
Trivandrum (urban), Kerala ¹⁹	27	56	nr	83	26	2	nr	28

*Prevalence < 0.5%; nr, not reported.

In countries of South Asia, particularly India, traditional values do not favour smoking by the young or by women, but there is no such taboo against using smokeless tobacco. Thus, most women who use tobacco use it in smokeless forms. Tobacco use, in whatever form, generally begins during adolescence.

Awareness of the hazards of smokeless tobacco use is very low in rural populations. On the other hand, many believe tobacco, smoked or smokeless, has medicinal value for curing or palliating common discomforts such as toothache, headache, and stomach ache. This leads to advice for initiating tobacco use from adults to other non-users, even children.

In India it has been estimated that roughly one-third of women and two-thirds of men use tobacco in one form or another.¹⁴ In prevalence surveys in eight rural areas of India, smokeless tobacco use was 3–53% among men and 3–49% among women (Table 2). Also, in these areas 2–26% of men and 0–4% of women practised both smoking and smokeless tobacco habits.^{15–18}

In a study from the large metropolitan city of Mumbai¹³ the prevalence of tobacco use was 57.5% among women (Table 2), almost solely in smokeless form (57.1%). Among men, 69.3% used tobacco, including 45.7% in smokeless form. The proportion of tobacco users who both smoked and used smokeless forms was nearly 10%.

In a surveyed population 35 years of age or older in a northern suburb of Trivandrum, Kerala, where residents were mostly of lower socio-economic status, chewing habits were practised by 26.8% of men ($n = 25\,453$) and 26.4% of women ($n = 34\,441$) (Table 2). These habits consisted mainly of chewing betel quid with tobacco.¹⁹

In Bangladesh, 20–30% of women in rural areas are estimated to use smokeless tobacco.²⁰ In Turkmenistan, 12% of the population has been reported to use *nass*.¹⁴

In a survey in Karachi, Pakistan, conducted in 1980, about 21% of men and 12% of women chewed tobacco in some form. Excluding those who chewed tobacco by itself and including those

who chewed *pan* without tobacco, about 30% of men and 30% of women chewed betel quid.²¹

Other countries where many habitual betel quid chewers add tobacco to their quid include Indonesia, Thailand, Cambodia, the Philippines and the US territory of Guam. The practice is also found wherever South Asians have emigrated, such as in South Africa, Malaysia, Singapore, Australia, New Zealand, the UK and the USA.¹¹ The easy availability of the areca nut and chewing tobacco in Australia and New Zealand suggests that there are significant groups in these countries at risk of developing oral cancer.^{22,23}

In several studies of immigrant communities of Bangladeshi origin in the UK, over 80% of the adults surveyed, both male and female, chewed betel quid regularly. The majority of the women incorporated tobacco (as leaf or zarda) in the quid, while under half of the men did. Burnt tobacco leaves were used as dentifrice by 20% of the women studied.^{24–27} In a study in which 42% of adults used betel quid, an interesting finding was that the traditional method of betel-quid chewing was being replaced with readily available processed areca nut and tobacco products.²⁸

Acquisition of smokeless tobacco habits and habit prevalence among youth

The acquisition of tobacco habits occurs mainly at young ages and according to patterns of product preference established among adults. In a small study, one-third to one-half of children under the age of 10 years in three rural areas of India (Gujarat, Tamil Nadu and Karnataka) had experimented with smokeless tobacco or smoking, imitating parents, grandparents, other elders in the family, or peers.²⁹ In a study encompassing the entire state of Goa,³⁰ 6271 school children aged 5–10 years from 73 village schools, about 13.4% of boys and 9.5% of girls used tobacco, mostly as smokeless tobacco (*mishri* or tobacco toothpaste, followed by chewing), and family members were most influential in this regard.

Acquisition of tobacco habits was studied in a 10-year follow-up of Indian villagers aged 15 years and over, conducted during 1966–1977, in three diverse rural areas (Ernakulam, Kerala; Srikakulam, Andhra Pradesh and Bhavnagar, Gujarat). About 3.5% of the non-users, mainly in the lower ages, acquired tobacco habits for the first time, reflecting the already established area-wide patterns of chewing or reverse smoking for women and smoking for men.³¹ Almost all males who acquired a habit were in the lowest age group studied (15–34 years), although some females in the middle age group (35–54 years) acquired a habit as well.

It is popularly perceived that the chewing of betel quid with tobacco is becoming a less common habit in India and that it is more confined to the elderly. Yet younger generations have readily taken up the use of mixtures of areca nut and tobacco. Some evidence for such a trend was gathered during a survey carried out in Bhavnagar, Gujarat. The prevalence of *mawa* use rose from 4.7% in 1969, mainly among older women, to 19% in 1993–1994 mainly among younger generations.^{32,33}

Still more evidence for a trend toward use of tobacco and areca nut products by youth has been gathered in several recent studies. In a survey of 95 boys and girls in the 8th and 9th grades of a small town private school in Gujarat, 16% of boys used *gutka*. In a village community in Gujarat, 72% of males under 26 years of age used tobacco, mainly bidis and *gutka*, and 50% of females used tobacco in the forms of *gutka* and tobacco toothpaste. Approximately one-eighth of 476 high school students in the 10th to 12th standards in Patna, Bihar, used *pan masala*.³⁴ Despite the tradition of low tobacco use in Punjab, in a recent survey of 100 rural school-going teenagers in five villages, two-thirds of respondents reported using *gutka* regularly.³⁵

The use of sweetened areca nut, betel quid or both, among 74.2% of 160 school children aged 4–16 years in a fishing community in Karachi,³⁶ could conceivably make them more likely to use smokeless tobacco products in future.

In a survey of 1200 students from junior and degree colleges in Maharashtra, 9.9% took *pan masala*, and 9.6% chewed *gutka*.³⁷

Surveys conducted among medical and dental students in Patna, Bihar, India have revealed high levels of tobacco use, especially smokeless forms, such as *khaini* and *gutka*. Chewing of *pan masala* is also common. Current use was higher among senior students, even though their awareness was much higher; this is believed by the researchers to be due to the students being already addicted before learning of the associated diseases. Assessment of the use of tobacco and areca nut products among medical and dental students is important because of the impact of the example they will set for their patients as future caregivers and the unlikely prospect that they would counsel their patients against using tobacco, a major determinant of oral health status.^{38,39}

A disturbing parallel to the use of tobacco in betel quid and the increasing popularity among teenagers of areca nut and tobacco mixtures in South Asia

comes from some of the Pacific islands, such as Palau. There, betel-quid chewing has been nearly universal for some time. Throughout Palau, single chews, which are sold in many retail stores, consist of half a tender green areca nut, some lime, a piece of pepper leaf and half a cigarette, all wrapped in aluminium foil. A study conducted in Palau in 1995 on a purposive sample of 1110 residents aged 5–74 years in Koror and Airai states, with an age structure similar to that of the whole population, found that 55% of children aged 5–14 years chewed a quid containing areca nut, and that 77% of 15–24-year-olds and over 80% of most other age groups chewed it. Tobacco was added to the quid by 65–96% of the respondents in the different age groups (83% in the total sample), and by 87% of chewers in the youngest age group (5–14 years). The two youngest age groups (5–14 and 15–24 years) rarely used betel leaf in the quid.⁴⁰

RISKS OF MORTALITY AND MORBIDITY DUE TO SMOKELESS TOBACCO

Mortality

Smokeless tobacco use in South Asia is believed to be a significant contributor to excess mortality. The evidence is available from three cohort studies.

A large cohort study in Mumbai showed elevated relative risks of death for both male and female users of smokeless tobacco (mainly in the forms of *mishri* and betel quid). Interim results were based on 5–6 years of follow-up of 52 000 persons, with 114 980 person years for female and 57 890 for male smokeless tobacco users. The age-adjusted relative risk for smokeless tobacco users compared with non-tobacco users among men was 1.22, and for women it was 1.35, with a suggestion of a dose–response relationship for daily frequency of use. Risks for smokers were somewhat higher, with the relative risk of death for male smokers being 1.63 (1.39 for cigarettes and 1.78 for bidi), with a clear dose–response relationship for daily smoking frequency. There were too few women smokers to be able to estimate their risks.⁴¹

In an earlier cohort study in Ernakulam, Kerala on a cohort of 10 287 individuals aged 15 years and over, who were followed for 10 years, the relative risk of death for men who were chewers (mainly *pan* with tobacco) was 1.2 (not significant), and among women chewers it was 1.3 ($P < 0.05$), while for men who smoked (mainly bidi) the relative risk was 1.5, with $P < 0.05$.⁴²

In another cohort study in Srikakulam district, Andhra Pradesh, 10 169 persons were followed for 10 years. The predominant habit was reverse chutta smoking but there were some tobacco chewers among the men with 41 deaths recorded during 1460 person-years of observation, giving an age-adjusted relative risk of 1.96.⁴³

It can be concluded from the above studies that the age-adjusted relative risk of mortality for users of smokeless tobacco, like that of smokers, is elevated compared to that of non-tobacco users.

Morbidity

The major health consequences associated with smokeless tobacco use in South Asia include cancers of several sites (e.g. the upper respiratory and digestive tracts), and poor reproductive outcomes. There are some research results on the impact of smokeless tobacco on blood pressure and cardiac disease. In addition, use of areca nut, often chewed with tobacco, can predispose to diabetes mellitus and aggravate asthma. Epidemiological evidence from selected studies on the relationship of smokeless tobacco use with various diseases is summarized below.

Cancers

In India, the number of newly diagnosed tobacco-related cancers has been estimated at approximately 250 000 out of a total of 700 000–900 000 new cancers diagnosed each year.⁴⁴ Tobacco-related cancers account for about one-third of all cancers in Bangladesh, India, Pakistan and Sri Lanka.¹⁴

In men in India, lung cancer is the commonest cancer among all registered cancers in the six population-based registries (Bangalore, Barshi, Bhopal, Chennai, Delhi and Mumbai), but when cancers at all oral sites are combined—oral cavity, tongue and lip—oral cancer vies for first place with lung cancer in four registries.

Oral cancers: Oral and pharyngeal cancers have a high incidence in South Asia, even among women.⁴⁵ In this area, the oral use of smokeless tobacco is considered the predominant risk factor for these cancers, especially oral cancer.

In an evaluation of epidemiological studies on the carcinogenic risk to humans of tobacco habits other than smoking, the IARC Working Group concluded that there was sufficient evidence that the habits of chewing betel quid containing tobacco and tobacco mixed with lime were carcinogenic to humans.¹¹ Since then, nine case-control studies from India and one from Pakistan on cancers of the oral cavity have provided fresh evidence of the oral cancer risk to chewers of betel quid with tobacco. In six of the studies from India, relative risks of oral cancer for men who were current chewers of *pan* with tobacco compared to non-chewers varied from 1.8 (95% CI: 1.2–2.7) to 5.8 (95% CI: 3.6–9.5). In contrast, for men who were current bidi smokers the relative risks varied from non-significant to around 2.^{46–51} Relative risks of oral cancer for women who currently chewed *pan* with tobacco varied from 30.4 (95% CI: 12.6–73.4) to 45.9 (95% CI: 25.0–84.1).^{48,49} The odds ratio for men who currently chewed areca nut without tobacco compared to non-chewers was 1.7 in one study.⁵¹

Relative risks of oral cancer in men, stratified by habit as 'ever' chewers and 'never' chewers or smokers, were reported in three studies conducted in Trivandrum, as 6.1 for tongue and floor of the mouth (95% CI: 3.3–11.4), 8.75 for gingiva (among non-drinkers only; 95% CI: 3.6–21.5) and 14.3 for buccal and labial mucosa (95% CI: 8.2–24.8).^{52–54} In a study from Pakistan, the likelihood of people who had ever

been chewers of *pan* with tobacco developing oral cancer was 8.4 times (95% CI: 2.3–30.6) and without tobacco 9.9 times (95% CI: 1.8–55.6) greater than that of never-chewers, after adjustment for oral submucous fibrosis, ever cigarette smoking, alcohol drinking and other chewing habits.⁵⁵

Significant dose–response trends were observed for frequency of chewing per day in all 10 studies, and for duration of habit in seven of them. Retention of the quid overnight, analysed in another study, showed a 36-fold increased risk.⁵⁶

In a case series study from Bangladesh, the site of origin of the majority of the lesions corresponded with the site maximally exposed to betel quid, usually in the buccal mucosa.⁵⁷ A case series study from Myanmar indicated a clear association of oral cancer with betel-quid chewing.⁵⁸

Use of tobacco with lime was identified as a definite risk factor for oral cancer. Two large hospital-based case-control studies from India and Pakistan, reported two- and 14-fold increases in the risk of oral cancer. The study from Pakistan and another case-control study from the Kazakh Soviet Socialist Republic showed highly elevated risks of oral cancer in users of *nass* as well as *naswar*. However, all these studies lacked adjustment for smoking and betel-quid habits.¹¹ In a recent study from Pakistan, the odds ratio for ever chewers of *naswar* developing oral cancer was 9.5 (95% CI: 1.7–52.3) after adjustment for ever cigarette smoking, alcohol drinking and other chewing habits.⁵⁵

In one study of oral cancer from India, current users of nasal snuff had a relative risk of 3.9 ($P < 0.05$) for cancer of the gingiva.⁵²

Due to a lack of reported studies, the IARC Working Group had stated that there was inadequate evidence that oral use of *mishri*, and *gudakhu* are carcinogenic in humans. Not much further published evidence has emerged since then.¹¹

Oropharyngeal cancers: Three case-control studies of oropharyngeal cancers (ICD-9 code 146) reported only non-significant relative risks for tobacco chewers (mainly betel quid), but highly elevated and significant relative risks for smokers (5.6–18.4) after adjustment for chewing.^{47,51,59} A significant relative risk of 1.74 (95% CI: 1.25–2.43) was found for oropharyngeal cancer in men who chewed betel quid with tobacco, after adjusting for smoking and alcohol consumption, in one study.⁵⁰ A significant dose–response for the frequency and duration of chewing was reported in another study.⁵¹

Laryngeal cancers: One case-control study from India showed a highly significant relative risk of laryngeal cancer for occasional pan-tobacco chewing, but not for having 'ever' had the habit of chewing.⁵⁹ Smoking posed a much greater risk for cancer of the larynx.^{59,60}

Oesophageal cancers: Five case-control studies from India were available for analysis. In three case-control studies of oesophageal cancer, significant odds ratios for tobacco chewers (generally betel quid) varied from 2.1 to 3.2 in multivariate models.^{50,61,62} In two other studies of oesophageal cancer, only insignificant odds ratios for tobacco chewing (mostly betel

quid) were found.^{63,64} In one of these studies, the adjusted odds ratio for the lower third of the oesophagus for chewers was 6.6 ($P < 0.001$).⁶¹ Two case-control studies found a dose-response relationship for oesophageal cancers with chewing of areca nut/betel quid with or without tobacco.^{50,64} The study from Assam⁶⁵ found highly elevated risks for the use of fermented areca nut, *tamol*, with any form of tobacco (7.1 for men and 3.6 for women). Smoking was also found to pose elevated risks for oesophageal cancers in the available studies.

Oral submucous fibrosis

Oral submucous fibrosis (OSF) is a debilitating, potentially cancerous oral condition, caused primarily by chewing areca nut and its mixtures, as demonstrated by numerous epidemiological studies and other corroborative evidence.⁶⁶ The condition may sometimes extend beyond the mouth to the oesophagus.⁶⁷ The intense marketing of industrially manufactured products containing areca nut and tobacco has considerably increased the occurrence of OSF in the Indian population. In three recent case-control studies (in Bhavnagar, Gujarat; Nagpur, Maharashtra; and New Delhi) over 70% of the cases were under 35 years of age.⁶⁸⁻⁷⁰ In two studies from India, in which frequency and duration of chewing were analysed, frequency of chewing rather than the total duration of the habit was directly related to OSF^{69,70} but in one study from Pakistan duration of the habit was also significant.⁷¹ *Pan masala* chewers developed the condition in about half the time compared to quid users (betel quid, areca quid), with 75% of the *pan masala* chewers developing the disease within 4.5 years and quid chewers in about 9.5 years. The absence of betel leaf in *pan masala* and the proportionately higher dry weight of areca nuts may be responsible for the earlier development of OSF in *pan masala* chewers.⁷⁰ Tobacco as an ingredient in some areca nut mixtures is not a causative factor for OSF, but is responsible for a higher occurrence of OSF due to increased addiction and concurrent use of areca nut.

OSF is well established as a condition with high malignant potential and is considered irreversible. In a cohort study of 12 212 tobacco users in Ernakulam, Kerala, patients with OSF followed up for an average of 6.0 years showed a relative risk of developing oral cancer of 397.3 compared to those with no oral lesions but with tobacco habits.⁷² The suspicion that increased occurrence of OSF in the younger age groups would lead to an earlier development of oral cancer from OSF was confirmed by the demonstration of a significant increase in the incidence of oral cancer in the Ahmedabad population-based cancer registry data. A comparison of the age-specific incidence rates of mouth cancer (ICD 143-5) during 1983-1987 and 1995 shows that the incidence had significantly increased in the younger population (< 50 years). Since tongue cancer (ICD 141) did not show a similar increase, and OSF typically involves the mouth (inner cheek) more than the tongue, it was concluded that the increase in mouth cancer inci-

dence was real. Urgent public health measures are required to curb this new but avoidable epidemic.⁷³

Hypertension and blood lipid profile

There is some evidence that smokeless tobacco is a risk factor for hypertension and adverse blood lipid profile, although perhaps to a lesser extent than smoking. A study of Assam tea garden workers found that consumption of locally prepared alcohol, intake of extra salt and the habit of using *khaini* increased the risk of hypertension.⁷⁴ Another study found statistically significant increments in heart rate and blood pressure following the chewing of betel quid with tobacco for 15-30 min, while no significant differences were found after chewing betel quid without tobacco.⁷⁵

A study comparing serum lipid profile in 30 smokers, 30 tobacco chewers and 30 controls without any tobacco habit found that high-density lipoprotein-cholesterol was lower in both smokers ($P < 0.01$) and tobacco chewers ($P < 0.001$) than in the controls; it also found that both smokers and tobacco chewers had higher values for total cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein-cholesterol and triglycerides, as compared to the no habit group. Thus smoking and tobacco chewing both demonstrated comparable adverse effects on lipid profile and could increase cardiovascular risk.⁷⁶

Adverse effects on pregnancy

Adverse reproductive outcomes from smoking during pregnancy have been well documented. There is some evidence that the same relationship may hold for smokeless tobacco use as well. Studies from India have shown a nearly threefold increase in stillbirths⁷⁷ and a 100-400 g decrease in birthweight, in offspring of women who applied or chewed tobacco during pregnancy.^{77,78} Odds ratios varying from 2 to 3 have been found for low birthweight in infants born to mothers using smokeless tobacco.⁷⁹⁻⁸¹ Other associations included an average increase in placental weight of 66 g in tobacco chewers (mostly tobacco with lime)⁸² and increased male foetus wastage, compared to non-users.^{77,79}

Asthma

Asthma patients who chew betel quid with or without tobacco may find their condition aggravated by the arecoline from areca nut, which induces the contraction of bronchiolar smooth muscle by means of its acetylcholine-like (parasympathetic) actions.⁸³

EXISTING REGULATORY STRUCTURES

In the South Asian region, like everywhere else, existing tobacco control legislation focuses more on cigarettes.³⁴ Legislation in India began with the

promulgation of the Cigarette Act 1975 (Regulation of Production, Supply and Distribution), requiring manufacturers to add statutory health warnings in English ('Cigarette smoking is injurious to health') to cigarette packages and advertisements, and prohibiting tobacco advertising through government-controlled electronic media and publications. In 1990, the Government of India issued an Executive Order prohibiting smoking in all healthcare establishments, government offices, educational institutions, air-conditioned railway cars, buses, suburban trains, etc. In June 1999, Indian Railways, operating under the Government of India, banned the sale of tobacco on railway platforms. In September 2000, the Government amended the Cable Network Rules and banned television advertisements for tobacco.

In order to curb the use of tobacco in India, there was a long-standing demand for comprehensive legislation on the advertisement, sale and use of tobacco in the country. The Cigarettes and Other Tobacco Products Bill 2001,⁸⁴ which has incorporated several strategies for tobacco control, addressing all types of tobacco products, became an Act after passage through both houses of Parliament in April 2003 and assent by the President in May 2003. The new Cigarettes and Other Tobacco Products Act, 2003 prohibits direct advertising in all media and sports sponsorship by tobacco companies. It also prohibits smoking in public places to protect non-smokers, especially children, from environmental smoke. It disallows the sale of tobacco in any form to persons under 18 years and within 100 yards of educational institutions. Clear health warnings in local languages and in English have been made mandatory on all packages, with a pictorial warning of a skull and cross-bones. Also, the tar and nicotine content of cigarettes have to be specified on the packages. Issues of enforcement will have to be tackled next, and this will require the strong voice of prominent and knowledgeable citizens, including health professionals.

Since 1987 in India, beginning with the state of Maharashtra, a few other states (Goa, Delhi) have taken their own initiatives to prevent smoking and spitting in government premises and on railway platforms and have conducted educational campaigns against tobacco use. Prohibition of the sale of tobacco products within 100 metres of educational institutions and on railway platforms has been passed by some states.

Recently, beginning with Tamil Nadu in 2001, banning orders have been issued in several more states against the sale, manufacture and storage of *gutka*, and in some states other forms of chewing tobacco and *pan masala* as well. Similar initiatives have been taken by several other state governments but industry opposition through the courts has forced these states to modify the ban or postpone its implementation until the Supreme Court reaches a decision.

The intent of legislation can be reinforced by health education of the public and communities on the dangers of tobacco use. The potential for this is discussed in the next section.

THE POTENTIAL FOR EFFECTIVE HEALTH EDUCATION

The public have little knowledge about the dangers of chewing betel quid or any form of smokeless tobacco. Researchers in India have demonstrated the feasibility and efficacy of anti-tobacco education for the community in high tobacco-chewing areas through controlled intervention studies.^{85,86}

Intervention studies

Tobacco habits are widely prevalent in Kerala in the form of bidi smoking and betel-quid (*pan*) chewing. Overall, tooth-related problems (48%) and peer-group influence (38%) were reported to be common initiating factors for tobacco use in Ernakulam district. There was an inverse relationship between the levels of education and the use of tobacco.⁸⁷

A large controlled prospective intervention trial for primary prevention of oral cancer was conducted in three areas in India. These included the district of Ernakulam (Kerala), and two other areas. Results are presented here for Ernakulam district, which had the highest proportion of tobacco chewers who predominantly chewed betel quid with tobacco.

The intervention cohort, at baseline, in Ernakulam District consisted of 12 212 tobacco users 15 years of age and older in the intervention group and there were 6075 subjects in a non-concurrent control cohort.⁸⁵ Both cohorts were interviewed about their tobacco use by trained investigators, and subjects were examined for the presence of oral lesions by dentists and subjected to 10 annual follow up examinations.

In the intervention cohort at baseline, 66% of men were bidi smokers, 6% were cigarette smokers, 16% were chewers (mostly betel quid with tobacco) and 12% had multiple habits. Among women tobacco users, 92% were chewers. The percentages were somewhat similar in the control cohort. At baseline, the prevalence of leukoplakia was 2.9% in the intervention cohort and 2.7% in the control cohort.⁸⁸

In the intervention villages, social scientists provided personal communication on tobacco habits using photographs and pictorial booklets and addressed the factors that can influence continuation of tobacco use. Two documentary films were made with the involvement of the local people to reinforce the messages imparted during home visits. The first film imparted information on the relationship between tobacco use and oral cancer and the second one addressed the reasons for initiation and tips on tobacco cessation. Cinema slides, posters, folk dramas, radio programs and newspaper articles were also used, with content based on feedback received from the field. At the request of the population, cessation camps were conducted, with group discussions on problems faced in cessation and possible solutions, as well as a few days of regular daily counselling of individuals. Ten annual follow-up surveys were conducted after the baseline survey, covering a 10-year period for the intervention cohort during

Table 3 Stoppage of tobacco chewing habits in intervention and control cohorts in Ernakulam District during 10 years of follow up

Interval	Intervention %	Control† %
1 year ⁸⁸	2.7	nr
5 years ⁸⁹	10.2 (men)	nr
	14.9 (women)	nr
8 years ⁹⁰	13.9 (all) ⁹¹	4.2 (all) ⁹¹
	13.0 (men)	1.0 (men)
10 years ⁸⁵	18.0 (women)	6.0 (women)
	15.1 (men)	2.3 (men)
	18.4 (women)	7.8 (women)

nr, not reported.

†Minimal intervention.

1977–1988. In the control cohort (1966–1977), no active programme of health education was undertaken, but during the surveys, the dentists routinely explained the association of tobacco use with oral cancer and advised against tobacco use, more forcefully so if the individual had a precancerous lesion.

Results for 1 year, 5 years, 8 years and 10 years of follow-up were reported (Table 3). After 1 year of follow up, 2.7% of the intervention cohort had stopped and 6.5% had reduced their chewing habits. The rate of regression of leukoplakia among those who had stopped or reduced their tobacco use was 5.3%, which was significantly higher than the rate (1.1%) in those who did not change or increased their tobacco use.⁸⁸

After 5 years of follow up, the percentage stopping their tobacco use (of every type) was higher in the intervention cohort compared to the control cohort: 3% in the control group versus 9% in the intervention cohort, but for chewers in particular, 10.2% of men and 14.9% of women chewers in the intervention cohort had stopped. Furthermore, the reduction in tobacco use by continuing users was much higher in the intervention cohort than in the control group.

For chewers after 5 years, the age-adjusted incidence rate of leukoplakia per 1000 men was 44.6 in the control cohort versus 22.6 in the intervention cohort, and 33.5 versus 6.2 among women (Table 4). The rate ratio for the protective effect of the intervention against leukoplakia ranged from 0.19 to 0.51 in women and men chewers, respectively.⁸⁹

Intervention was helpful to all categories of tobacco users but was more helpful to men and chewers (mainly betel quid with tobacco), especially those with habits of long duration. In a multiple logistic regression analysis of the first 5 years of intervention data, the odds ratio calculated for quitting tobacco use by men who had chewed tobacco for 11 or more years was 240.1 for the intervention relative to the control cohort.⁹¹

By the end of 10 years, 15.1% of men and 18.4% of women tobacco chewers in the intervention cohort had discontinued their tobacco use, as compared to 2.3% and 7.8% in the control cohort. The reduction in the daily frequency of overall tobacco use was higher

Table 4 Annual age adjusted incidence rates per 1000 of leukoplakia in tobacco (betel quid) chewers in intervention and control cohorts in Ernakulam District over 10 years of follow-up

Interval	Intervention	Control†	Odds ratio
5 years ⁸⁹	22.6 (men)	44.6 (men)	nr
	6.2 (women)	33.5 (women)	
8 years ⁹⁰	3.5 (men)	7.4 (men)	nr
	4.8 (women)	6.2 (women)	
10 years ⁸⁵	3.3 (men)	5.2 (men)	0.63*
	2.0 (women)	4.6 (women)	0.45*

* $P < 0.05$.

nr, not reported.

†Minimal intervention.

in the intervention than in the control cohort. The relapse rates were much lower in the intervention cohort than in the control cohort. The overall incidence of leukoplakia in the control group was 40% higher (Table 4) than in the intervention cohort and the differences in observed and expected incidence rates of leukoplakia among tobacco users of all types were statistically significant ($P < 0.05$).^{85,92}

In a detailed analysis of the effect of cessation of tobacco use, it was shown that it led to a substantial fall in the incidence of leukoplakia. The incidence ratios between those who stopped their habits and all others ranged from 0.15 to 0.81 in different gender and tobacco use groups. For female chewers this was 0.31 and for male chewers it was 0.81. The fact that all ratios were below unity implied a reduced risk of oral cancer after cessation of tobacco use, since oral leukoplakia demonstrated a high premalignant potential.^{72,92}

The educational intervention was helpful in reducing the use of tobacco, in increasing quit rates and decreasing relapse rates. Spontaneous regression rates of oral precancerous lesions were higher among individuals who reported stopping or reducing their tobacco use compared to those who did not. The incidence rates of oral precancer were lower in the intervention cohort than in the control cohort. This study was felt to have demonstrated the feasibility and practicality of primary efforts in preventing oral cancer in rural India.

Another educational intervention, in the Kolar District of Karnataka, India, was carried out by specially trained primary health centre (PHC) workers in the government system, in one experimental and two control areas with similar populations. The PHC workers performed the baseline habit prevalence survey in the three areas and provided anti-tobacco education of the community in the experimental area. They performed a repeat survey after 2 years and a final survey after another 3 years. Health education methods included screening of films, exhibits, and personal contact with a display of photographs of the harmful effects of tobacco. Results after the final survey showed that in the experimental area, the decline

in the prevalence of tobacco use (compared with the baseline) was 10.2% in males and 16.3% in females. The quit rates in men and women in the intervention cohort were 26.5% and 36.7%, respectively, compared to 1.1% and 1.5% in a control cohort.⁸⁶

In the state of Goa, 4th and 5th grade students in 46 villages in the northern and central zones were taught how to communicate anti-tobacco information to their parents and to the community. Quit rates of 8.9% among men and 11% among women were observed after about 1.5 years from baseline.³⁰

Mass media intervention

As a special project during 1990, educational information about the use of tobacco was broadcast on All India Radio (the only radio medium at that time), through 30 Sunday morning episodes in 16 languages from 84 stations. Community surveys (without comparison groups) conducted in Karnataka and Goa to evaluate the broadcasts showed that about 30% of the potential audience listened to the programmes in both states. In Karnataka, nearly 6% of tobacco users reported quitting the habit, as did 4.3% in Goa. In addition, about one-third of tobacco users intended to quit and another third had reduced their consumption.⁹³

Educational messages, materials, and related issues

Methods of communication used in the Ernakulam intervention study included personal communication, films, posters, newspaper articles, folk dramas, radio programmes, exhibits, group meetings and cessation camps. The study experience showed that the health messages should be personally relevant to the consumer, and tailored to his/her beliefs and lifestyle, including the prevalent tobacco habits in the area.⁹⁴ Some of the main messages were as follows: (i) tobacco cannot cure toothache, but can cause oral cancer; (ii) tobacco can harm the heart and make you die earlier; (iii) tobacco use during pregnancy may harm your child; (iv) chewing tobacco can cause cancer of the food pipe; (v) betel quid can aggravate asthma; (vi) those who have given up tobacco have said that the discomforts do not last long; (vii) children are more likely to use tobacco if their parents do; (viii) tobacco use is harmful to health and is expensive (part of the expense is in treating the diseases it causes. Money saved—health gained); and (ix) parents who die prematurely due to tobacco use deprive their children of social support.

ACTION NEEDED NOW

There is a paucity of educational materials on smokeless tobacco. Keeping in mind the high quality of tobacco advertising that commands the attention of the public, skilled commercial artists should be moti-

vated to work with health professionals and health authorities in preparing such materials which must be attractive, with simple language and unequivocal meaning, incorporating messages about all forms of smokeless tobacco and smoking.⁹⁵ Anti-tobacco education must be imparted through schools, hospital outreach programmes, existing government health programmes such as maternal and child health programmes and routine home visits, using suitable materials.

In view of the available knowledge about the damaging effects on health caused by tobacco, it should follow that medical and health-related conferences be made tobacco free, including all venues attached to the conference, and this should apply to all participants, staff, advertisers and volunteers.⁹⁶ If these conferences and meetings clearly enunciate and adhere to specific tobacco control policies, this would help to raise awareness about tobacco control issues and the seriousness of tobacco control among participants and non-participants connected with the event. The International Union Against Cancer (UICC) has already adopted these guidelines for all conferences, meetings or workshops that it sponsors or that are held under UICC auspices. Specific guidelines for such a policy are outlined in the UICC Tobacco Control Fact Sheet No. 20.⁹⁷

There is a lot of indirect advertising still tolerated in healthcare settings in the form of advertisements in magazines left in patient areas. One suggestion for tackling this problem comes from an organization in the USA called, Doctors Ought to Care. Each tobacco advertisement should be crossed out with a black marker and a notice displayed on the cover debunking the claims of glamour and machismo associated with tobacco use and declaring that tobacco destroys health, makes one poorer and leads to premature death.⁹⁸

When doctors examine patients of South Asian origin, it is not enough to ask them about smoking habits, but they should also be asked about whether they use smokeless tobacco. Health professionals in areas with South Asian immigrants should become aware of the effects of betel-quid chewing. The tell-tale staining of gums and teeth can alert an observant practitioner.

Outreach programmes from hospitals can educate the community about the dangers of tobacco and the signs of tobacco-related cancer. Such a programme, conducted through a large cancer hospital over the last several years, approximately doubled the outpatient attendance for oral examination and the number of oral precancers seen.³⁴ As the programme develops, it has been attracting tobacco users (smokers and smokeless) to its cessation programme.

Children are a potentially powerful motivating force for health and against tobacco use. Because personal communication is very effective for tobacco cessation and children communicate personally with their parents, they can be very effective in changing tobacco use behaviour. Hence school and community programmes to raise tobacco awareness among children are recommended.

REFERENCES

- 1 Gupta PC, Warnakulasuriya S. Global epidemiology of areca nut usage. *Addict. Biol.* 2002; **7**: 77–83.
- 2 International Union Against Cancer. *Tobacco Control Fact Sheet 8*, December. International Union Against Cancer, Tobacco and Cancer Programme, Geneva, 1996.
- 3 World Bank Economics of Tobacco for the South Asia Region, 2003. <http://www.worldbank.org/tobacco/pdf/country%20briefs/South%20Asia%20Region.doc> Accessed 6 July, 2003.
- 4 Deb U. Agricultural Situation in Bangladesh, India and Pakistan: Part I. Agrinet Bangladesh, 3, August: 1997. <http://www.members.tripod.com/~UTTAMDEB/policy2.html>. Accessed 2 July 2003.
- 5 Food and Agriculture Organization. Major Food and Agricultural Commodities and Producers. Data extracted from the FAOSTAT database. Rome. <http://www.fao.org/es/ess/top/commodity.jsp?commodity=27&lang=EN>. Accessed 2 July 2003.
- 6 Chari MS, Rao BVK. Role of tobacco in the national economy: past and present. In: Gupta PC, Hamner JE III, Murti PR (eds). *Control of Tobacco-Related Cancers and Other Diseases*. Proceedings of an International Symposium, TIFR. Bombay, January 15–19, 1990. Oxford University Press, Bombay, 1992; 57–64.
- 7 Indian Council for Medical Research. *Report of the Expert Committee on the Economics of Tobacco Use*. Department of Health, Ministry of Health and Family Welfare, Government of India, New Delhi, 2001.
- 8 Bhide SV, Kulkarni JR, Padma PR *et al.* Studies on tobacco specific nitrosamines and other carcinogenic agents in smokeless tobacco products. In: Sanghvi LD, Notani PP (eds). *Tobacco and Health: The Indian Scene*. Proceedings of the UICC Workshop, 'Tobacco or Health', 15–16 April 1987. Tata Memorial Centre, Bombay, 1989; 121–31.
- 9 Gupta PC. Smokeless tobacco use in India. In: *Smokeless Tobacco or Health—an International Perspective*. USA Smoking and Tobacco Control Monograph 2. NIH Publication no. 92–3461, September 1992; 19–25.
- 10 National Sample Survey Organization. NSS Report Nos. 184 & 461 (55/1.0/4). Reports covering 1961–62 and 1999–2000.
- 11 International Agency for Research on Cancer. Tobacco habits other than smoking; betel-quid and areca-nut chewing; and some related nitrosamines. In: *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol 37. IARC, Lyon, 1985.
- 12 Bhonsle RB, Murti PR, Gupta PC. Tobacco habits in India. In: Gupta PC, Hamner JE III, Murti PR (eds). *Control of Tobacco-Related Cancers and Other Diseases*. Proceedings of an International Symposium, TIFR. Bombay, January 15–19, 1990. Oxford University Press, Bombay, 1992; 25–46.
- 13 Gupta PC. Survey of sociodemographic characteristics of tobacco use among 99,598 individuals in Bombay, India using handheld computers. *Tob. Control* 1996; **5**: 114–20.
- 14 World Health Organization. *Tobacco or Health, a Global Status Report*. WHO, Geneva, 1997.
- 15 Wahi PN. The epidemiology of oral and oropharyngeal cancer. A report of the study in Mainpuri district, Uttar Pradesh, India. *Bull. World Health Organ.* 1968; **38**: 495–521.
- 16 Mehta FS, Pindborg JJ, Gupta PC, Daftary DK. Epidemiologic and histologic study of oral cancer and leukoplakia among 50,915 villagers in India. *Cancer* 1969; **24**: 832–49.
- 17 Mehta FS, Gupta PC, Daftary DK, Pindborg JJ, Choksi SK. An epidemiologic study of oral cancer and precancerous conditions among 101,761 villagers in Maharashtra, India. *Int. J. Cancer* 1972; **10**: 134–41.
- 18 Bhonsle RB, Murti PR, Gupta PC, Mehta FS. Reverse dhumi smoking in Goa. An epidemiologic study of 5449 villagers for oral precancerous lesions. *Indian J. Cancer* 1976; **13**: 301–5.
- 19 Sankaranarayanan R, Mathew B, Jacob BJ *et al.* Early findings from a community-based, cluster-randomized, controlled oral cancer screening trial in Kerala, India. The Trivandrum Oral Cancer Screening Study Group. *Cancer* 2000; **88**: 664–73.
- 20 Islam N. Challenges and opportunities for tobacco control in Islamic countries. In: Slama K (ed.) *Tobacco and Health*. Proceedings of the Ninth World Conference on Tobacco and Health, 10–14 October 1994, Paris. Plenum Press, New York, 1995; 178.
- 21 Mahmood Z. Smoking and chewing habits of people of Karachi—1981. *J. Pak. Med. Assoc.* 1982; **32**: 34–7.
- 22 Cox S. Oral cancer in Australia—risk factors and disease distribution. *Ann. R. Australas. Coll. Dent. Surg.* 2000; **15**: 261–3.
- 23 Yoganathan P. Betel chewing creeps into the New World. *NZ. Dent. J.* 2002; **98**: 40–5.
- 24 Ahmed S, Rahman A, Hull S. Use of betel quid and cigarettes among Bangladeshi patients in an inner-city practice. Prevalence and knowledge of health effects. *Br. J. Gen. Pract.* 1997; **47**: 431–4.
- 25 Bedi R, Gilthorpe MS. The prevalence of betel-quid and tobacco chewing among the Bangladeshi community resident in a United Kingdom area of multiple deprivation. *Prim. Dent. Care* 1995; **2**: 39–42.
- 26 Pearson N, Croucher R, Marcenes W, O'Farrell M. Dental service use and the implications for oral cancer screening in a sample of Bangladeshi adult medical care users living in Tower Hamlets, UK. *Br. Dent. J.* 1999; **186**: 517–21.
- 27 Summers RM, Williams SA, Curzon ME. The use of tobacco and betel quid ('pan') among Bangladeshi women in West Yorkshire. *Community Dent. Health* 1994; **11**: 12–16.
- 28 Shetty KV, Johnson NW. Knowledge, attitudes and beliefs of adult South Asians living in London regarding risk factors and signs for oral cancer. *Community Dent. Health* 1999; **16**: 227–31.
- 29 Krishnamurthy S, Ramaswamy R, Trivedi U, Zachariah V. Tobacco use in rural Indian children. *Indian Pediatr.* 1997; **34**: 923–7.
- 30 Vaidya SG, Vaidya NS, Naik UD. Epidemiology of tobacco habits in Goa, India. In: Gupta PC, Hamner JE III, Murti PR (eds). *Control of Tobacco-Related Cancers and Other Diseases*. Proceedings of an International Symposium, TIFR. Bombay, January 15–19, 1990. Oxford University Press, Bombay, 1992; 315–22.
- 31 Gupta PC, Mehta FS, Daftary DK *et al.* Incidence rates of oral cancer and natural history of oral precancerous lesions in a 10-year follow-up study of Indian villagers. *Community Dent. Oral Epidemiol.* 1980; **8**: 283–333.
- 32 Sinor PN, Murti PR, Bhonsle RB, Gupta PC. Mawa chewing and oral submucous fibrosis in Bhavnagar, Gujarat,

- India. In: Gupta PC, Hamner JE III, Murti PR (eds). *Control of Tobacco-Related Cancers and Other Diseases*. Proceedings of an International Symposium, TIFR. Bombay, January 15–19, 1990. Oxford University Press, Bombay, 1992; 107–12.
- 33 Gupta PC. Oral cancer and tobacco use in India: A new epidemic. Tobacco the growing epidemic. Proceedings of the 10th World Conference on Tobacco or Health, 24–28 August 1997, Beijing, China. 2000.
 - 34 Gupta PC, Ray CS. Tobacco and youth in the South East Asian region. *Indian J. Cancer* 2002; **39**: 5–35.
 - 35 Kaur S, Singh S. Cause for concern in Punjab villages. High levels of Gutka intake among students. *Lifeline* 2002; **7**: 3–4.
 - 36 Shah SM, Merchant AT, Luby SP, Chotani RA. Addicted schoolchildren: prevalence and characteristics of areca nut chewers among primary school children in Karachi, Pakistan. *J. Paediatr Child Health* 2002; **38**: 507–10.
 - 37 Hans G. *Prevention of Cancer in Youth with Particular Reference to Intake of Paan Masala and Gutkha*. NSS Unit, TISS, Mumbai, India, 1998.
 - 38 Sinha DN, Gupta PC. Tobacco and areca nut use in male medical students of Patna. *Natl Med. J. India* 2001; **14**: 176–8.
 - 39 Sinha DN, Gupta PC, Pednekar MS, Singh JP. Tobacco use among students of Patna Dental College—Bihar. *Lifeline* 2001; **6**: 11–12.
 - 40 Ysaol J, Chilton JJ, Callaghan P. A survey of betle nut chewing in Palau. *Isla. J. Micronesian Studies* 1996; **4**: 244–55.
 - 41 Gupta PC, Mehta HC. Cohort study of all-cause mortality among tobacco users in Mumbai, India. *Bull. World Health Organ.* 2000; **78**: 877–83.
 - 42 Gupta PC, Bhonsle RB, Mehta FS, Pindborg JJ. Mortality experience in relation to tobacco chewing and smoking habits from a 10-year follow-up study in Ernakulam District, Kerala. *Int. J. Epidemiol.* 1984; **13**: 184–7.
 - 43 Gupta PC, Mehta FS, Pindborg JJ. Mortality among reverse chutta smokers in south India. *BMJ* 1984; **289**: 865–6.
 - 44 National Cancer Registry Programme (NCRP). 2001 Population Based Cancer Registries, Consolidated Report. <http://icmr.nic.in/ncrp/bcfuture.pdf>.
 - 45 Moore SR, Johnson NW, Pierce AM, Wilson DF. The epidemiology of mouth cancer: a review of global incidence. *Oral Dis.* 2000; **6**: 65–74.
 - 46 Rao DN, Desai PB. Risk assessment of tobacco, alcohol and diet in cancers of base tongue and oral tongue—a case control study. *Indian J. Cancer* 1998; **35**: 65–72.
 - 47 Rao DN, Ganesh B, Rao RS, Desai PB. Risk assessment of tobacco, alcohol and diet in oral cancer—a case-control study. *Int. J. Cancer* 1994; **58**: 469–73.
 - 48 Nandakumar A, Thimmasetty KT, Sreeramareddy NM *et al.* A population-based case-control investigation on cancers of the oral cavity in Bangalore, India. *Br. J. Cancer* 1990; **62**: 847–51.
 - 49 Balaram P, Sridhar H, Rajkumar T *et al.* Oral cancer in southern India: the influence of smoking, drinking, paan-chewing and oral hygiene. *Int. J. Cancer* 2002; **98**: 440–5.
 - 50 Znaor A, Brennan P, Gajalakshmi V *et al.* Independent and combined effects of tobacco smoking, chewing and alcohol drinking on the risk of oral, pharyngeal and esophageal cancers in Indian men. *Int. J. Cancer* 2003; **105**: 681–6.
 - 51 Dikshit RP, Kanhere S. Tobacco habits and risk of lung, oropharyngeal and oral cavity cancer: a population-based case-control study in Bhopal, India. *Int. J. Epidemiol.* 2000; **29**: 609–14.
 - 52 Sankaranarayanan R, Duffy SW, Day NE, Nair MK, Padmakumary G. A case-control investigation of cancer of the oral tongue and the floor of the mouth in southern India. *Int. J. Cancer* 1989; **44**: 617–21.
 - 53 Sankaranarayanan R, Duffy SW, Padmakumary G, Day NE, Padmanabhan TK. Tobacco chewing, alcohol and nasal snuff in cancer of the gingiva in Kerala, India. *Br. J. Cancer* 1989; **60**: 638–43.
 - 54 Sankaranarayanan R, Duffy SW, Padmakumary G, Day NE, Krishan-Nair M. Risk factors for cancer of the buccal and labial mucosa in Kerala, southern India. *J. Epidemiol. Community Health* 1990; **44**: 286–92.
 - 55 Merchant A, Husain SS, Hosain M *et al.* Paan without tobacco: an independent risk factor for oral cancer. *Int. J. Cancer* 2000; **86**: 128–31.
 - 56 Ghosh S, Shukla HS, Mohapatra SC, Shukla PK. Keeping chewing tobacco in the cheek pouch overnight (night quid) increases risk of cheek carcinoma. *Eur. J. Surg. Oncol.*, 1996; **22**: 359–60.
 - 57 Ahmed F, Islam KM. Site predilection of oral cancer and its correlation with chewing and smoking habit—a study of 103 cases. *Bangladesh Med. Res. Council. Bull.* 1990; **16**: 17–25.
 - 58 Sein K, Maung KK, Aung TH. An epidemiologic study of 70 oral cancer cases at the Institute of Dental Medicine, Yangon, Myanmar, 1985–1988. *Odontostomatol. Trop.* 1992; **15**: 5–8.
 - 59 Rao DN, Desai PB, Ganesh B. Alcohol as an additional risk factor in laryngopharyngeal cancer in Mumbai—a case-control study. *Cancer Detect. Prev.* 1999; **23**: 37–44.
 - 60 Sankaranarayanan R, Duffy SW, Nair MK, Padmakumary G, Day NE. Tobacco and alcohol as risk factors in cancer of the larynx in Kerala, India. *Int. J. Cancer* 1990; **45**: 879–82.
 - 61 Nandakumar A, Anantha N, Pattabhiraman V *et al.* Importance of anatomical subsite in correlating risk factors in cancer of the oesophagus—report of a case—control study. *Br. J. Cancer* 1996; **73**: 1306–11.
 - 62 Nayar D, Kapil U, Joshi YK *et al.* Nutritional risk factors in esophageal cancer. *J. Assoc. Physicians India* 2000; **48**: 781–7.
 - 63 Rao DN, Sanghvi LD, Desai PB. Epidemiology of esophageal cancer. *Semin. Surg. Oncol.* 1989; **5**: 351–4.
 - 64 Sankaranarayanan R, Duffy SW, Padmakumary G, Nair SM, Day NE, Padmanabhan TK. Risk factors for cancer of the oesophagus in Kerala, India. *Int. J. Cancer* 1991; **49**: 485–9.
 - 65 Phukan RK, Ali MS, Chetia CK, Mahanta J. Betel nut and tobacco chewing; potential risk factors of cancer of oesophagus in Assam, India. *Br. J. Cancer* 2001; **85**: 661–7.
 - 66 Murti PR, Bhonsle RB, Gupta PC, Daftary DK, Pindborg JJ, Mehta FS. Etiology of oral submucous fibrosis with special reference to the role of areca nut chewing. *J. Oral Pathol. Med.* 1995; **24**: 145–52.
 - 67 Misra SP, Misra V, Dwivedi M, Gupta SC. Oesophageal subepithelial fibrosis: an extension of oral submucosal fibrosis. *Postgrad. Med. J.* 1998; **74**: 733–6.
 - 68 Gupta PC, Sinor PN, Bhonsle RB, Pawar VS, Mehta HC. Oral submucous fibrosis in India: a new epidemic? *Natl Med. J. India* 1998; **11**: 113–16.

- 69 Hazare VK, Goel RR, Gupta PC. Oral submucous fibrosis, areca nut and pan masala use: a case-control study. *Natl Med. J. India* 1998; **11**: 299.
- 70 Shah N, Sharma PP. Role of chewing and smoking habits in the etiology of oral submucous fibrosis (OSF): a case-control study. *J. Oral Pathol. Med.* 1998; **27**: 475–9.
- 71 Maher R, Lee AJ, Warnakulasuriya KA, Lewis JA, Johnson NW. Role of areca-nut in the causation of oral submucous fibrosis: a case-control study in Pakistan. *J. Oral Pathol. Med.* 1994; **23**: 65–9.
- 72 Gupta PC, Bhonsle RB, Murti PR, Daftary DK, Mehta FS, Pindborg JJ. An epidemiologic assessment of cancer risk in oral precancerous lesions in India with special reference to nodular leukoplakia. *Cancer* 1989; **63**: 2247–52.
- 73 Gupta PC. Mouth cancer in India—a new epidemic? *J. Indian Med. Assoc.* 1999; **97**: 370–3.
- 74 Hazarika NC, Biswas D, Narain K, Kalita HC, Mahanta J. Hypertension and its risk factors in tea garden workers of Assam. *Natl Med. J. India* 2002; **15**: 63–8.
- 75 Nanda PK, Sharma MM. Immediate effect of tobacco chewing in the form of 'paan' on certain cardio-respiratory parameters. *Indian J. Physiol. Pharmacol.* 1988; **32**: 105–13.
- 76 Khurana M, Sharma D, Khandelwal PD. Lipid profile in smokers and tobacco chewers—a comparative study. *J. Assoc Physicians India* 2000; **48**: 895–7.
- 77 Krishna K. Tobacco chewing in pregnancy. *Br. J. Obstet. Gynaecol.* 1978; **85**: 726–8.
- 78 Verma RC, Chansoriya M, Kaul KK. Effect of tobacco chewing by mothers on fetal outcome. *Indian Pediatr.* 1983; **20**: 105–11.
- 79 Mehta AC, Shukla S. Tobacco and pregnancy. *J. Obstet. Gynaecol. India* 1990; **40**: 156–60.
- 80 Krishnamurthy S, Joshi S. Gender differences and low birth weight with maternal smokeless tobacco use in pregnancy. *J. Trop. Pediatr.* 1993; **39**: 253–4.
- 81 Deshmukh JS, Motghare DD, Zodpey SP, Wadhwa SK. Low birth weight and associated maternal factors in an urban area. *Indian Pediatr.* 1998; **35**: 33–6.
- 82 Agrawal P, Chansoriya M, Kaul KK. Effect of tobacco chewing by mothers on placental morphology. *Indian Pediatr.* 1983; **20**: 561–5.
- 83 Nelson BS, Heischober B. Betel nut. A common drug used by naturalized citizens from India, Far East Asia, and the South Pacific Islands. *Ann. Emerg. Med.* 1999; **34**: 238–43.
- 84 Gupta PC. Tobacco Products Bill 2001: an aid to public health. *Natl Med. J. India* 2001; **14**: 131–4.
- 85 Gupta PC, Mehta FS, Pindborg JJ *et al.* Primary prevention trial of oral cancer in India: a 10-year follow-up study. *J. Oral Pathol. Med.* 1992; **21**: 433–9.
- 86 Anantha N, Nandakumar A, Vishwanath N *et al.* Efficacy of an anti-tobacco community education program in India. *Cancer Causes Control* 1995; **6**: 119–29.
- 87 Murti PR, Bhonsle RB, Gupta PC. Tobacco control activities in Kerala, India. *Tobacco Control SAARC Edition* 1994; **1**: 37.
- 88 Mehta FS, Gupta MB, Pindborg JJ, Bhonsle RB, Jalnawalla PN, Sinor PN. An intervention study of oral cancer and precancer in rural Indian populations: a preliminary report. *Bull. World Health Organ.* 1982; **60**: 441–6.
- 89 Gupta PC, Mehta FS, Pindborg JJ *et al.* Intervention study for primary prevention of oral cancer among 36 000 Indian tobacco users. *Lancet* 1986; **i**: 1235–9.
- 90 Gupta PC, Mehta FS, Pindborg JJ *et al.* Primary prevention study of oral cancer among Indian villagers. Eight-year follow-up results. In: Hakama M, Beral V, Culln JW, Parkin DM (eds). *Evaluating Effectiveness of Primary Prevention of Cancer*. IARC Scientific Publication Series No. 103. International Agency for Research on Cancer, Lyon 1990; 149–56.
- 91 Gupta PC, Aghi MB, Bhonsle RB *et al.* Intervention study of chewing and smoking habits for primary prevention of oral cancer among 12212 Indian villagers. In: Zaridze DG, Peto R. *Tobacco: A Major International Health Hazard*. IARC Scientific Publications No. 74. International Agency for Research on Cancer, Lyon, 1986.
- 92 Gupta PC, Murti PR, Bhonsle RB, Mehta FS, Pindborg JJ. Effect of cessation of tobacco use on the incidence of oral mucosal lesions in a 10 year follow-up study of 12,212 users. *Oral Dis.* 1995; **1**: 54–8.
- 93 Chaudhry K. Control or Promotion—the Paradox. *Tobacco Control, SAARC Edition*, 1994; **1**: 4.
- 94 Aghi MB. Strategies to motivate people against the use of tobacco. Presented at the WHO Regional Workshop on Control of Tobacco Related Diseases, New Delhi, 22–26 July 1985.
- 95 Narayanan RS. A comparison of cancer educational resources to prevent smokeless tobacco usage in India and the United States. *J. Cancer Educ.* 1988; **3**: 257–8.
- 96 Gupta PC. Ethical issues raised by smoking. *Proceedings of the Symposium on International Health and Medical Ethics—Harvard SPH Takemi Symposium*. Medical Association and Harvard School of Public Health, Tokyo, 1–2 December 2000.
- 97 Gupta PC. *No Smoking Policy at Scientific and Other Events Related to Health*. UICC Tobacco Control Fact Sheet No. 20, 1996. http://www.globalink.org/tobacco/fact_sheets/20fact.htm.