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Population Burden of Betel Quid Abuse and Its Relation to Oral Premalignant Disorders in South, Southeast, and East Asia: An Asian Betel-Quid Consortium Study

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Objectives. We investigated the population burden of betel quid abuse and its related impact on oral premalignant disorders (OPDs) in South, Southeast, and East Asia.

Methods. The Asian Betel-Quid Consortium conducted a multistage sampling of 8922 representative participants from Taiwan, Mainland China, Malaysia, Indonesia, Nepal, and Sri Lanka. Participants received an interviewer-administered survey and were examined for oral mucosal disorders.

Results. The prevalence of betel quid abuse was 0.8% to 46.3% across 6 Asian populations. The abuse frequency was over 40.5% for current chewers, with the highest proportion in Nepalese and Southeast Asian chewers (76.9%–99.6%). Tobacco-added betel quid conferred higher abuse rates (74.4%–99.6%) among Malaysian, Indonesian, and Sri Lankan men than did tobacco-free betel quid (21.8%–89.1%). Gender, lower education level, younger age at chewing initiation, and clustering of familial betel quid use significantly contributed to higher abuse rates. Indonesian betel quid abusers showed the highest prevalence of OPDs and had a greater risk of OPDs than did nonabusers.

Conclusions. Betel quid abuse is high in regions of Asia where it is customarily practiced, and such abuse correlates highly with OPDs. By recognizing abuse-associated factors, health policies and preventive frameworks can be effectively constructed to combat these oral preneoplasms. (*Am J Public Health.* 2012;102: e17–e24. doi:10.2105/AJPH.2011.300521)

The chewing of betel quid, a combination of areca nut, betel leaf, slaked lime, and region-dependent flavoring ingredients, is a uniquely Asian, culturally derived lifestyle habit. Bred from ancient tradition, its use is socially accepted in all groups, including women and young children, although other substance use such as tobacco smoking is deemed objectionable.[1,2] Chemical composition studies have showed that areca nut includes psychoactive alkaloids, of which arecoline contributes the most quantity.[3] By raising epinephrine and norepinephrine plus modulation of cholinergic and monoamine transmission, areca nut exerts neurobiological effects on the sympathetic and parasympathetic nervous systems.[3–5] In human studies, tolerance and withdrawal symptoms have been clearly detected in regular betel quid chewers.[6–8] Such a pharmacological profile is comparable with nicotine, a well-known substance that leads to abuse and dependence. In recent decades, successful marketing of commercially manufactured betel quid has dramatically increased its accessibility and widespread use throughout Asia.[9] An increased availability indicates that betel quid may be abused throughout different cultures, but the extent is unknown.

Studies on the natural history of oral cancer suggest that several oral premalignant disorders (OPDs), including oral lichen planus (OLP), oral submucous fibrosis (OSF), oral leukoplakia (OL) and oral erythroplasia, precede the development of this neoplasm.[10] In Asia, the prevalence of oral precancerous conditions and lesions was estimated to be 1.7% to 11.7% in western India,[11] 4.4% to 12.7% in southern Taiwan,[12,13] 0.1% to 4.7% in the Hunan province of Mainland China,[14] 1.4% in Malaysia,[15] and 6.7% in the central Sri Lanka.[16] Although there is evidence to support that chronic consumption of betel quid products, with or without added tobacco, is a central etiological agent for OPD and neoplasms of the oral cavity, pharynx, esophagus and larynx,[10,17–23] no data are available concerning the oral precancerous consequences among betel quid abusers.

To study the health effects of betel quid consumption in Asian populations and mobilize outreach activities in disease prevention, in 2008, the Center of Excellence for Environmental Medicine at Kaohsiung Medical University in Kaohsiung, Taiwan, in consultation with the World Health Organization (WHO) Collaborating Centre for Oral Cancer in the United Kingdom, launched an international collaborative project that constitutes the Asian Betel-quid Consortium (ABC) study. Six large research centers from East Asia (Kaohsiung Medical University, Taiwan, and Central South University, Changsha, Mainland China), Southeast Asia (Airlangga University, Surabaya, Indonesia and University of Malaya, Kuala Lumpur, Malaysia), and South Asia (University of Peradeniya, Peradeniya, Sri Lanka and Kathmandu University, Kavrepalanchwok, Nepal) participated in this investigation. Because of varying practices and particular marketing of betel quid products in those countries (detailed explanations shown in Table A, available as a supplement to the online version of this article at http://www/ajph.org), present study actions are promisingly warranted. The purposes of this report are twofold: (1) to present the current population burden of betel quid abuse and the factors associated with this behavior in the investigated Asian communities, and (2) to evaluate the impact of betel quid abuse on oral premalignant disorders.

METHODS

The ABC study was designed as a multicountry population-based cross-sectional study. To furnish a comparable framework, all centers used an identical research protocol. Recruitment was initiated in January 2009 and completed in February 2010. All participants provided written informed consent.

Study Participants

Figure A and Table B (available as supplements to the online version of this article at http://www/ajph.org) illustrate the study areas, which included Southern Taiwan; Hunan Province of Mainland China; Selangor, Sabah, and Sarawak States of Malaysia; North Sumatra, East Java, Bali, West Nusa Tenggara, South Sulawesi, and Papua Provinces of Indonesia; and Middle of Nepal and Central Province of Sri Lanka. We used a multistage sampling procedure to identify the noninstitutionalized and representative inhabitant samples from the general population aged 15 years or older, as previously described.[24] This was accomplished in multiple stages. For stage 1, a number of cities and counties were individually selected to represent the economic and geographic characteristics of each study population. For stage 2, a planned number of administrative districts or townships were randomly selected. For stage 3, the street districts (each has about 1000–2000 households) within each administrative district and township were enumerated, and 1 or 2 street districts were randomly selected according to the sample size projected. Random samples of their households were then chosen from each street district. Finally, study participants were drawn from a list of family members living in selected households and invited to participate in this survey. On average, 2.2 to 2.6 (±0.5–1.5) members were selected per household in Taiwan, Indonesia, Malaysia, and Sri Lanka. Because the One-Child policy was introduced in Mainland China to reduce China's burgeoning population, and owing to some administrative and performance problems in Nepal, only 1 family member was randomly chosen per household from Mainland China and Nepal.

Data Collection

Each ABC study center comprised a principle investigator; several dentists, dental hygienists or medical officers; and 4 to 5 staff members. Interviewers specifically trained for this project collected the data. Using modified materials from WHO surveys and nationwide prevalence investigations, we developed a standardized questionnaire for the ABC study. To check whether this questionnaire would function effectively, a pilot test was conducted in Taiwan. The betel quid abuse score was closely related to the amount of betel quid consumed, indicating good concurrent validity. The initial questionnaire was written in English and translated accordingly into the appropriate language for each study area. The questionnaire was also retranslated into English to confirm translation validity. Under a few circumstances in which the participants were unable to understand the questions, investigated items were translated into local dialects by researchers with the assistance of local, native people. Pictograms were used to elucidate betel quid ingredients reported by the respondents. The interview was conducted by door-to-door home visits. The aims and procedures involved were explained to all participants. As displayed in Table B, the number of samples obtained from each center ranged from 1002 to 2356. Because betel quid chewing is socially accepted in all groups and the study purposes have been well described and recognized, a high response rate was achieved (68%–100%).

Using the developed questionnaire, trained interviewers collected data on sociodemographic factors and habits of lifetime betel quid use, alcohol intake, and tobacco consumption (including smoking and smokeless tobacco use), as well as further information on age when starting use, daily consumption, years used, and the type and frequency of substance consumed. For betel quid chewers, additional information was obtained as to the ingredients added to the areca nut. Areca chewers were requested to answer whether they customarily swallowed the masticating fluid. Subsequently, dentists, dental hygienists, or medical officers inspected each participant for the diagnosis of OLP, OSF, and OL based on the clinical criteria. The medical staffs were unaware of the answer given to the interviewers about the chewing habits. Also, before the examination, they had to complete 1 month of standardized training with regard to performing oral cavity examination under the supervision of each team's principle investigator. Because the natural history of these 3 disorders has a similar potential to become cancer, they were grouped as OPD.

Screening for Current Betel Quid Abuse

We defined betel quid chewers as participants who had consumed at least 1 quid of any type of betel or areca nut product per day for a minimum of 6 months. Because there are no standardized protocols to identify betel quid abuse, a questionnaire-based screening was used to detect harmful chewing patterns. We used the Self-report Screening Test for Areca quid Abuser (SSTAA) to evaluate the level of the betel quid chewer's substance abuse. It was developed from a previous study and was based on the taxonomy of substance use disorder in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, the *Schedules for Clinical Assessment in Neuropsychiatry* system, and the *ICD-10 Classification of Mental and Behavioural Disorders*.[25] The initial screening test included 52 items; however, only 11 questions were appraisingly chosen by the validity evaluation based on the receiver operation characteristic curve (area under the curve= 0.915; Table C, available as a supplement to the online version of this article at http://www.ajph.org). This short-form screening test consists of 10 positive and 1 negative abuse-related statements, including 5 items of subjective craving and feeling, 3 items of oral symptoms, 1 item of psychological and abstinence-related problems, and 2 items of motivation and capacity to abstain. The answer to each question was recoded as "1" (yes) or "0" (no), but scoring was reversed for the negative statement (item 8). Chewers who regularly consumed betel quid in the past year prior to the interview and who reported an SSTAA score of 4 or greater were classified as current betel quid abusers (12-month betel quid abusers). The sensitivity and specificity for this screening test were previously evaluated to be 87.2% and 83.7%, respectively.[25] Alternatively, in appraisal of the internal consistency of test scores obtained from SSTAA, Cronbach's α coefficient (α) was calculated for each study sample. This index is extensively used to indirectly measure the extent to which a set of questions determines a particular unidimensional latent construct. Almost all the investigated samples showed an excellent degree of internal reliability (α=0.912

for Taiwan, 0.838 for Mainland China, 0.859 for Malaysia, 0.764 for Indonesia, 0.990 for Nepal, and 0.802 for Sri Lanka).

Statistical Analysis

We derived point estimates for prevalences, means, percentages, and odds ratios (ORs), as well as regression modeling for each study region adjusted for sample weight to account for diverse sampling fractions. We used linear and logistic regressions, respectively, to model effects of investigated factors on continuous and binary outcomes. To search for factors associated with betel quid abuse among current chewers, we utilized the SSTAA criterion count (range=0–11 with a higher score reflecting a higher level of abuse) to measure abuse propensity and defined a score of 4 or greater as abuse. Adjusted mean differences (measured in regression coefficients) and adjusted ORs derived from multiple linear and logistic regression modeling with backward elimination and forward selection procedures were used to appraise the effect of explored variables on continuous SSTAA count and dichotomous status of abuse. Factors considered included gender, education, age when starting betel quid use, consumption frequency, betel quid type and habit, family history of betel quid use, alcohol drinking, and tobacco smoking. Age was treated as a confounder and was adjusted for in each regression model. All analyses were performed using survey-data modules of Stata version 11 (StataCorp LP, College Station, TX) to accommodate the complex sampling design of the ABC study.

RESULTS

The socioeconomic factors, such as age, gender, and education are presented in Table B. Patterns for age and gender were diverse across the study areas. Participants from Malaysia, Indonesia, and Nepal had a higher proportion of low educational years.

The prevalences of betel quid use and abuse and chewing characteristics of abuse are presented by gender in Table 1. Current chewing prevalence rates were diverse in both genders across study countries ($P<.005$). The 12-month betel quid abuse prevalence rates in men (4.9%–13.0%) were higher than those in women (0.8%–1.7%) in Taiwan and Hunan of Mainland China, but this observation was reversed in Malaysia and Indonesia, in which the rates for women (22.7%–46.3%) were higher than those for men (8.9%–11.6%). In several populations, the prevalence of betel quid abuse varied by age. Among current chewers, more than 40.5% were abusers, and overwhelmingly high abuse rates occurred in Nepal and Southeast Asia (76.9%–99.6%, Figure A). Betel quid abusers generally consumed greater quantities (4.7–23.7 quid/day) and at higher frequencies (5.7–7.0 days/week) than did nonabusers (1.2–14.7 quid/day and 2.8–5.7 days/week). Except for abusers in Hunan, all betel quid abusers had a use history of more than 14 years (14.7–43.1 years).

Table 2 shows the abuse rate among current chewers by different betel quid product, preferred chewing habit, and whether they concomitantly consumed tobacco or alcohol. All Nepalese chewers consumed tobacco-added betel quid, in contrast to Taiwan and Mainland Chinese chewers who used tobacco-free betel quid, whereas in other countries chewers used both. Significant differences in the abuse rates among tobacco-free betel quid and tobacco-added betel quid users emerged for men in Malaysian and Indonesian and for both genders in Sri Lanka. Compared with betel quid–only users, Indonesian male chewers who jointly consumed tobacco or tobacco and alcohol tended to have a lower betel quid abuse rate.

Table 3 displays the influence of demographic and substance use factors on the continuous screening score and binary status of betel quid abuse. Results for Nepal were not shown owing to almost all chewers being betel quid abusers. The mean SSTAA scores for male chewers from Mainland China, Malaysia, Indonesia, and Sri Lanka were higher than those for their female counterparts (mean difference=0.80–1.51), whereas female chewers in Taiwan had a higher abuse score than did male chewers (mean difference=1.76). There was a 2.5 to 5.4-fold increased risk of betel quid abuse among Malaysian, Indonesian, and Sri Lankan chewers with less schooling. One year of younger age at starting chewing was associated with a 5% to 7% increase in the likelihood of developing betel quid abuse among Taiwanese and Malaysian participants. In Sri Lanka, betel quid consumers who habitually chewed tobacco-added betel quid or swallowed the chewing juice both had increased abuse risks (OR=14.9 and 3.7, respectively). Family history of betel quid use in study regions sampled from Mainland China, Indonesia and Sri Lanka was a significant predictor for abuse. Further, a lower inclination of betel quid abuse was noted among Malaysian and Indonesian smokers.

The association between betel quid abuse and population prevalence of OPDs is presented in Table 4. A higher prevalence of OPDs was observed among abusers than nonabusers in communities of Mainland China, Indonesia, Nepal, and Sri Lanka. Indonesian areca nut abusers showed a significantly increased prevalence risk of OLP, OSF, and OL than did nonabusers (OR=4.5–13.5 vs 2.1–5.8). A similar risk pattern was detected for OSF in Taiwan betel quid chewers.

DISCUSSION

Using a validated betel quid abuser screening tool and scoring approach, the ABC study revealed a heterogeneous prevalence pattern for betel quid abuse among 6 Asian communities. The results also revealed region-dependent factors for abuse and its health consequences on 3 types of OPD.

Neurochemical studies have exhibited that arecoline, the central areca alkaloid, has agonist activity at the muscarinic acetylcholine receptors,[3,4] which is consistent with subjective claims of betel quid users that chewing can improve alertness, cause euphoria, and increase heart rate.[3–5] Another psychoactive alkaloid of areca nut (i.e., arecaidine) has the property of reducing the reuptake of γ-amino butyric acid to create anxiolytic effects.[3,5] In human investigations, areca nut chewers were observed to remain persistently exposed to a biologically relevant concentration of salivary arecoline (≥0.1 μg/mL) long after betel quid consumption.[26] Furthermore, the developments of dependence and withdrawal syndromes among habitual betel quid chewers have been confirmed in previous studies.[7,8]

Betel quid use deriving from cultural traditions in Asian and South Pacific populations is typically integrated into significant ceremonies and gatherings and becomes a part of daily life.[7,9] Owing to its pharmacological properties, some Asian ethnic groups use this substance as

TABLE 1—Prevalences of Betel Quid Use and Chewing Characteristics Associated With Abuse, by Gender: Self-Report Screening Test for Areca-Quid Abuser, Asia, 2009–2010

	Men							Women						
	Taiwan (n = 736)	Mainland China (n = 1225)	Malaysia (n = 383)	Indonesia (n = 965)	Nepal (n = 664)	Sri Lanka (n = 385)	*P*[a]	Taiwan (n = 812)	Mainland China (n = 1131)	Malaysia (n = 620)	Indonesia (n = 976)	Nepal (n = 338)	Sri Lanka (n = 687)	*P*[a]
Chewing category														
Nonchewer, %	84.4	71.0	89.7	87.6	56.4	78.8		97.0	97.7	67.9	32.1	63.3	83.1	
Ex-chewer, %	4.8	5.1	0.5	0.4	0.0	3.2		0.5	0.5	2.6	1.0	0.0	0.9	
Current chewer, %	10.7	23.9	9.8	12.0	43.6	18.0	<.005	2.5	1.8	29.5	46.8	34.9	13.5	<.005
Nonabuser	5.8	10.9	0.9	0.4	0.2	10.7		0.8	1.0	6.8	0.5	0.4	7.3	
Abuser	4.9	13.0	8.9	11.6	43.5	7.3	<.005	1.7	0.8	22.7	46.3	34.5	6.3	<.005
Abuser age, y														
≤34, %	3.4	17.7	0.7	1.7	45.0	2.2		0.0	0.9	3.5	22.4	28.5	0.0	
35–54, %	6.5	12.7	15.0	18.5	38.0	12.1		1.0	0.8	36.8	51.7	44.2	6.7	
≥55, %	5.0	2.8	24.5	20.5	49.8	10.0		5.8	0.9	56.6	91.2	51.1	16.7	
P for trend	.41	<.001	<.001	<.001	.994	.004		.002	.964	<.001	<.001	.051	<.001	
Betel quid abuse rate in current chewers, %	46.0	54.3	90.6	97.0	99.6	40.5	<.005	68.8	46.2	76.9	98.9	98.9	46.2	<.005
Chewing characteristic														
Amount														
Nonabuser, quid/d, mean ±SE	14.7 ±2.3	8.5 ±0.6	1.2 ±0.2	1.3 ±0.2	10.0 ±0.0	2.0 ±0.2	<.005	7.9 ±2.8	4.3 ±1.1	2.9 ±0.4	2.9 ±0.5	10.4 ±4.1	1.4 ±0.1	<.005
Abuser, quid/d, mean ±SE	23.7 ±4.0	12.7 ±0.9	5.3 ±0.6	6.5 ±0.4	9.0 ±0.3	6.3 ±0.9	<.005	18.9 ±2.3	7.3 ±1.3	6.2 ±0.4	5.3 ±0.2	9.0 ±0.9	4.7 ±0.6	<.005
P[b]	.054	<.001	.001	<.001	.003	<.001		.006	.1	<.001	<.001	.77	<.001	
Frequency														
Nonabuser, d/wk, mean ±SE	5.4 ±0.3	5.7 ±0.2	2.8 ±0.7	3.6 ±0.9	5.0 ±0.0	5.2 ±0.3	<.005	4.8 ±1.0	4.9 ±0.6	4.7 ±0.5	4.8 ±1.0	5.4 ±0.3	4.0 ±0.4	NS
Abuser, d/wk, mean ±SE	6.4 ±0.3	6.3 ±0.1	5.9 ±0.5	6.5 ±0.1	6.0 ±0.1	6.9 ±0.1	NS	6.4 ±0.6	7.0 ±0.0	6.6 ±0.1	5.7 ±0.2	5.8 ±0.1	6.5 ±0.2	<.005
P[b]	.027	.001	.02	.002	<.001	<.001		.196	.002	<.001	.358	.197	<.001	
Years of chewing														
Nonabuser, mean ±SE	17.4 ±1.7	7.8 ±0.5	12.6 ±6.3	14.8 ±3.2	16.3 ±3.3	16.5 ±2.1	<.005	19.8 ±4.5	9.1 ±1.7	12.8 ±1.5	19.2 ±6.1	12.4 ±3.0	18.8 ±2.2	NS
Abuser, mean ±SE	23.1 ±3.1	9.8 ±0.5	31.5 ±1.8	14.7 ±1.3	15.5 ±1.9	29.0 ±2.8	<.005	43.1 ±4.9	10.8 ±2.4	28.8 ±1.5	23.8 ±1.6	16.0 ±2.0	29.9 ±3.1	<.005
P[b]	.015	<.001	.036	.716	<.001	<.001		<.001	.58	<.001	.157	.709	.098	

Note. NS = nonsignificant.
[a]*P* for proportion difference in chewing behaviors across study areas was obtained adjusted for age.
[b]*P* for mean difference between betel quid abusers and nonabusers was obtained adjusted for age.

TABLE 2—Betel Quid Abuse Rates Among Current Chewers, According to Type, Habit, and Joint Substance Use, by Gender: Self-Report Screening Test for Areca-Quid Abuser, Asia, 2009–2010

	Men							Women						
Betel Quid Abuse Rate	Taiwan (n = 61)	Mainland China (n = 272)	Malaysia (n = 42)	Indonesia (n = 187)	Nepal (n = 254)	Sri Lanka (n = 88)	*P*[a]	Taiwan (n = 13)	Mainland China (n = 20)	Malaysia (n = 254)	Indonesia (n = 671)	Nepal (n = 124)	Sri Lanka (n = 106)	*P*[a]
Type-specific chewers, %														
Tobacco-free betel quid	46.0	54.3	78.1	89.1	–	21.8	<.005	68.8	46.2	78.1	99.5	–	32.4	<.005
Tobacco-added betel quid	–	–	97.8	99.2	99.6	74.4	<.05	–	–	75.0	98.7	98.9	91.7	<.005
P[b]	–	–	.046	.012	–	<.001		–	–	.506	.360	–	<.001	
Habit-specific chewers, %														
Nonswallowing juices	66.0	44.8	89.6	98.8	–	36.3	<.005	79.3	36.6	75.6	99.6	–	46.6	<.005
Swallowing juices	32.0	56.1	95.6	96.3	99.6	52.0	<.005	50.0	48.1	86.2	97.3	98.9	45.6	<.005
P[b]	.144	.161	.532	.25	–	.193		.428	.759	.369	.115	–	0.904	
Joint substance users, %[c]														
Betel quid only	59.0	62.0	100.0	99.9	100.0	25.9	<.005	67.2	47.6	76.4	99.0	98.1	45.5	<.005
Betel quid and tobacco	42.4	54.5	0.0	85.5*	100.0	42.3	<.05	–	0.0	65.8	100.0	100.0	–	<.005
Betel quid and alcohol	0.0	54.1	100.0	100.0	98.5	36.2	<.005	–	0.0	89.7	–	100.0	100.0	<.005
Betel quid, tobacco, and alcohol	51.2	51.9	81.6	75.5*	100.0	48.3	<.05	100.0	100.0	100.0	80.9	98.0	–	NS

Note. NS = nonsignificant. A dash indicates nonappreciable rate owing to no participants in the group studied.
[a]*P* for difference in betel quid abuse rate across study areas was obtained from logistic regression model adjusted for age.
[b]*P* for difference in betel quid abuse rate between diverse betel quid type or chewing habit chewers was obtained adjusted for age.
[c]Compared with betel quid–only users, Indonesian male chewers who jointly used tobacco or tobacco and alcohol had a significantly lower betel quid abuse rate.

a therapeutic agent.[1,27] Unlike tobacco smoking and heavy alcohol drinking, people are indifferent to linking betel quid use to any health risk.[28,29] These conditions form a complex social-environmental network of prolonged betel quid use and abuse. In this consortium survey, we outlined that more than 40% of current chewers abused areca nut, and chewers from Malaysia, Indonesia, and Nepal had a high abuse rate (76.9%–99.6%). Because some cultural groups consider betel quid not as an addictive substance but rather as a coffee or tea-like "drug food,"[8] health education is important for those users.

As with other findings on areca nut abuse and dependence,[7,8,25] our results showed that the amount consumed, frequency practiced, or years of use were generally higher among abusers than

TABLE 3—Mean Differences and Risks Associated With Demographics and Substance Use Among Current Chewers From Continuous Screening Score and Binary Status of Abuse: Self-Report Screening Test for Areca-Quid Abuser Survey, Asia, 2009–2010

	Taiwan		Mainland China		Malaysia		Indonesia		Sri Lanka	
	b	OR (95% CI)	b	OR (95% CI)	b	OR (95% CI)	b	OR (95% CI)	b	OR (95% CI)
Demographic factors										
Age, y										
35–54 vs <35	0.24	1.0 (0.2, 5.0)	0.28	1.1 (0.7, 1.8)	1.76	3.7 (0.9, 14.0)	-0.06	4.5 (0.7, 29.2)	0.50	1.9 (0.3, 11.1)
≥55 vs <35	0.66	2.2 (0.4, 13.1)	-0.23	0.8 (0.3, 2.1)	3.01**	8.2 (1.9, 35.0)	0.08	0.8 (0.2, 3.7)	0.98	3.3 (0.6, 19.0)
Gender: male vs female	-1.76*		1.25*		1.51**	9.5 (2.9, 30.9)	1.35**		0.80*	
Education: ≤6 vs >6 y					1.24*	2.7 (1.1, 6.9)		5.4 (1.4, 20.9)		2.5 (1.0, 5.9)
Substance use factors										
Age starting chewing, y	-0.10*	0.93 (0.9, 0.99)			-0.09**	0.95 (0.9, 0.99)				
Betel quid type: tobacco-added vs tobacco-free									3.04**	14.9 (5.2, 42.5)
Betel quid juice swallowing: yes vs no										3.7 (1.5, 9.3)
Family history of betel quid use: yes vs no			1.32**	2.4 (1.5, 3.9)				6.7 (1.3, 34.0)	0.93*	3.2 (1.2, 8.9)
Smoking: yes vs no					-1.97**	0.15 (0.04, 0.6)	-2.00**	0.04 (0.01, 0.2)		

Note. CI = confidence interval; OR = odds ratio.
*$P < .05$; **$P < .005$.

TABLE 4—Prevalence Rates of Oral Premalignant Disorders Among Betel Quid Nonchewers, Nonabuse Chewers, and Abuse Chewers: Self-Report Screening Test for Areca-Quid Abuser, Asia, 2009–2010

	Taiwan	Mainland China	Malaysia	Indonesia	Nepal	Sri Lanka
Study sample, no.						
Nonchewers	1300	1991	682	995	624	854
Nonabuse chewers	31	137	49	13	4	107
Abuse chewers	36	160	247	811	374	82
Oral lichen planus						
Nonchewers, %	0.1	0.1	0.0	4.3	0.0	0.0
Nonabuse chewers, %	7.7	0.0	0.0	16.5	0.0	0.0
Abuse chewers, %	5.4	0.6	0.0	15.7	0.0	0.0
Nonabuse chewers vs nonchewers, OR[a] (95% CI)	66.9* (4.1, 1091.1)	–	–	5.8 (0.7, 50.0)	–	–
Abuse chewers vs nonchewers, OR[a] (95% CI)	60.8* (10.5, 352.7)	12.8* (3.0, 54.0)	–	13.0* (5.8, 29.0)	–	–
Oral submucous fibrosis						
Nonchewers, %	0.0	0.05	0.0	3.4	0.1	0.03
Nonabuse chewers, %	7.7	5.0	0.0	10.0	0.0	0.0
Abuse chewers, %	9.6	4.9	0.0	8.8	0.0	0.0
Nonabuse chewers vs nonchewers, OR[a] (95% CI)	9.2[b] (0.2, ∝)	157.7* (19.4, 1280.1)	–	2.6 (0.4, 19.4)	–	–
Abuse chewers vs nonchewers, OR[a] (95% CI)	37.5*,[b] (4.0, ∝)	148.8* (17.6, 1256.3)	–	4.5* (1.9, 10.9)	–	–
Oral leukoplasia						
Nonchewers, %	0.03	0.1	0.0	6.0	0.1	0.0
Nonabuse chewers, %	4.5	1.5	0.0	7.0	0.0	0.0
Abuse chewers, %	3.8	0.0	0.0	17.2	0.9	1.0
Nonabuse chewers vs nonchewers, OR[a] (95% CI)	27.4* (3.3, 230.1)	25.5* (1.5, 427.7)	–	2.1 (0.6, 8.1)	–	–
Abuse chewers vs nonchewers, OR[a] (95% CI)	19.9* (1.4, 280.1)	–	–	13.5* (4.4, 41.4)	4.7 (0.5, 41.6)	1.8[b] (0.1, ∝)
All oral premalignant disorders						
Nonchewers, %	0.1	0.2	0.0	10.4	0.3	0.03
Nonabuse chewers, %	12.2	5.0	0.0	29.5	0.9	1.0
Abuse chewers, %	9.6	5.6	0.0	29.5	0.9	1.0
Nonabuse chewers vs nonchewers, OR[a] (95% CI)	46.3* (5.4, 393.5)	34.5* (9.2, 129.1)	–	3.4 (0.5, 21.0)	–	–
Abuse chewers vs nonchewers, OR[a] (95% CI)	41.8* (7.8, 222.4)	36.6* (9.3, 143.8)	–	14.4* (6.3, 32.9)	2.5 (0.4, 14.4)	17.2 (0.3, 984.8)

Note. CI = confidence interval; OR = odds ratio. A dash indicates nonappreciable value.
[a]OR of oral mucosal lesions was adjusted for age, gender, drinking, and smoking. (In Indonesian sample, smoking conveys a negative confounding effect for betel quid abuse on all of the 3 oral disorders.)
[b]OR was calculated using the median unbiased estimates with the aid of exact logistic regression.
*$P < .05$.

among nonabusers in all study regions (Nepal is the exception because nearly all chewers were abusers). These data corroborate the discrimination of betel quid abuse by the use of SSTAA. Alternatively, the validity study for this screening tool showed similar false-negative (12.8%) and false-positive rates (16.3%), implying that abuse misclassification was limited.[25] The prevalence of betel quid abuse among chewers was relatively high. This often results in an underestimate of the actual abuse rate. Because an identical screening instrument was used throughout communities, the difference in intercountry betel quid abuse rates has been conservative.

In communities where tobacco-added betel quid products were regularly consumed, a great proportion of chewers were abusers (>74%). The abuse rate among male tobacco-added betel quid chewers was appreciably higher than it was among those who used tobacco-free betel quid in Southeast Asian communities. This difference was repeatedly observed for both genders in Sri Lanka and was analogous to results from an earlier study exploring areca nut–related dependence syndromes.[7] This behavior may be accentuated by the addictive consequences of nicotine, although it is ingested in combination with areca nut. In India, industrially manufactured tobacco-containing pan masala (*gutka*) has been consumed by school children, and its use has been observed to act as a gateway to future tobacco use and oral cancer among youths.[29]

Contrary to regions in which male chewers had a higher abuse propensity than did female chewers, Taiwanese women reported a greater abuse inclination than did men. In Taiwan, indigenous people form the major female population of betel quid users.[30] Our data showed that all Taiwanese female chewers were aborigines, but the overwhelming majority of male chewers were Han (95.6%). In aboriginal

communities, betel quid chewing is a behavior closely connected to their cultural heritage, such as for inviting guests and making acquaintances. Because Taiwanese female chewers were observed to have a long duration of betel quid use (43.1 years), this distinguishing social norm might be associated with their abuse of this type of substance.

In previous investigations, a lower level of education has been linked to increased betel quid use.[30,31] In our study, lower education level was further associated with a 2.5 to 5.4-fold likelihood of abusing betel quid in Malaysian, Indonesian and Sri Lankan chewers. A Sri Lankan community-based study reported that 76% of participants were not aware of any ill-effects for areca nut chewing, particularly in the lower socioeconomic groups.[32] Inhabitants of Indian communities were aware of the relationship between cancer risk and *gutka* or tobacco use; however, this awareness did not extend to other betel quid ingredients or areca nut alone.[33] Given the limited health warning listed for betel quid chewing, health promotion should be administered in low-educated chewers in these Southeast and South Asian countries.

Early exposure to a substance has been related to the acquisition of this substance use disorder, particularly in adolescents.[34] Taiwan and Malaysian chewers who started chewing at a younger age had an increased SSTAA score and a higher risk of abuse. The length of chewing identified from abusers in these 2 populations supported such findings (23.1–43.1 and 28.8–31.5 years in Taiwan and Malaysia, respectively). Because the duration of betel quid consumption is an imperative predictor for the development of oral premalignant and neoplastic lesions,[10,17–20] the age at chewing onset is a key characteristic for betel quid abuse.

Epidemiological studies conducted in Taiwan have found that among adolescent chewers, 54% of students first tried betel quid chewing with their family members, frequently the father or grandfather.[35] In our study, betel quid users with family members who habitually chewed areca nut had a 2.4 to 6.7-fold likelihood to be an abuser in Mainland China, Indonesia, and Sri Lanka. Chewing is often regarded as an innocuous behavior owing to cultural derivations, but the significant risk of abuse resulting from the clustering of familial betel quid use reflects a need for family-level intervention in health promotion. Alternatively, a decreased liability and a lower risk of betel quid abuse were detected among Malaysian and Indonesian smokers than among nonsmokers. This finding reflected the observations that chewing was negatively correlated with tobacco smoking ($r=-0.26$ and -0.54 for Malaysia and Indonesia, respectively, both $P<.001$). In these 2 chewer populations, tobacco-added betel quid was prevalently used (41.6%–69.0%); this type of combination product might competitively reduce tobacco smoking among betel quid chewers.

The International Agency for Research on Cancer has reported the prevalence of OLP, OSF, and OL in areca nut chewers to be 0% to 3.7%, 0% to 3.0%, and 0% to 40.1%, respectively, among selected Asian communities;[10] however, no population-based information has been widely available concerning the oral precancerous consequences among betel quid abusers. The present study revealed a high prevalence of OSF abusers from Taiwan followed by Indonesia. Overall, however, Indonesian areca nut abusers had higher risks of OLP, OL, and OPD. Because there are no credible markers at present to predict malignant transformation for these precancerous lesions,[36] these abusers and behaviors should be categorized as being at high risk for oral cancer.

Because the use of betel quid is socially accepted in all groups in our study communities, chewers who provided information in regard to betel quid abuse were comfortable participating in the study; this explains the high response rates achieved in this study. This social acceptance might also reduce underreporting of the degree of betel quid abuse among chewers. Allowing any household member to participate in this study in the investigated communities of Taiwan, Malaysia, Indonesia, and Sri Lanka might create a bias if more than 1 person in a household chews betel quid. Because a similar number of family members were randomly selected from each study household (2–3 persons were drawn in 80%–99% of the households of the study communities; total average=2.2–2.6 persons per household), this might reduce the influence from such bias. Alternatively, owing to the nature of cross-sectional study, this survey only offered a snapshot of betel quid abuse for the study populations. Also, because chewing habits and materials vary by area, the data obtained in this study may not be generalizable to neighboring areas within the respective countries. Because there are many neighboring countries in which betel quid chewing is prevalent (e.g., Vietnam, Laos, Cambodia), the study methodology and research network might be extended further to these countries.

In summary, given the lack of understanding about the extent to which betel quid is abused in regions where this substance is customarily practiced, our study uncovered a high frequency of betel quid abuse (>40%) among current chewers in 6 Asian populations. We also found that gender, lower education level, younger age at chewing initiation, tobacco-added betel quid use, and clustering of familial betel quid use significantly contributed to higher abuse in some specific communities. In this consortium study, betel quid abuse was highly correlated to OPDs, implying that betel quid abusers are the more significant targets than are nonabusers for disease prevention. Furthermore, by recognizing abuse-associated factors, health policies and preventive frameworks can be effectively constructed to combat these oral preneoplasms. ■

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Contributors

Y.C. Ko designed this study and directed its implementation, including quality assurance and control. C.H. Lee contributed to the development of the models, the data analysis, and the writing of the article. A.M. Ko contributed to the interpretation of study research findings. S. Warnakulasuriya provided guidance on the analytic plan and the final article. T.Y. Ling, Sunarjo, P.S. Rajapakse, R.B. Zain, S.O. Ibrahim, S.S. Zhang, H.J. Wu, L. Liu, Kuntoro, B. Utomo, S.A. Warusavithana, I.A. Razak, N. Abdullah, P. Shrestha helped supervise the field activities. T.Y. Shieh and C.F. Yen helped conduct the literature review.

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Human Participant Protection

Written informed consent was obtained from all participants upon entry into the study. Research protocol was reviewed and approved independently by the research and ethical review committees at each study center.

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