

Betel Nuts, Health Policies, and Adolescent Health

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ABSTRACT

Areca nut and betel quid (AN/BQ) products are largely scrutinized by the scientific community because of their toxicological and carcinogenic properties. However, at the same time there exists an ever-growing user base in low- and medium-income countries, whose users are responding to innovative products preparation processes and are initiated to AN/BQ products by their parents and family at a young age. This report compiles current cessation policies, implemented interventions, and comments on their corresponding effectiveness and/or potential effectiveness. The report also highlights the need for further research from both an adolescent health and a Chinese perspective, as data regarding the region with the second largest user group after India are largely unknown or unavailable for scientific review. Ultimately, recent studies involving analytical methods to observe how different cultivation environments, and/or processing methods change the chemical composition of the AN/BQ product have also presented a potential insight in better understanding and eventually regulating AN/BQ across all population groups, including adolescents. The rise of digital solutions may also encourage development of applications to track consumption and usage and distribution of AN/BQ products for policy makers to design targeted campaigns.

Keywords: areca nut, betel quid, adolescent health, health policy, southeast Asia, China

INTRODUCTION

Consumption of areca nut and betel quid (AN/BQ) has been a long tradition in human history, and modern cohort studies have revealed its oncogenic properties. Since the establishment of the International Agency for Research on Cancer (IARC), many substances and/or products have been classified according to the nature of their carcinogenicity to humans.^[1] Alcoholic beverages were one such product that was reviewed, and its harmful properties recorded in a systematic scientific manner, analyzed, and reviewed.^[2] This work resulted in a global change of public health policies, including health warnings, advertisement bans, purchase age limits, sale licensing, and taxations specifically designed to reduce alcohol usage.^[3,4] Since then, other substances have also followed a similar classification pipeline. Notably, areca nuts and betel quid are both currently classified in the IARC Group 1 for their oral cancer-

causing potential and other mutagenic effects, specifically mentioning betel quid with tobacco, betel quid without tobacco, and areca nut on its own, all being carcinogenic to humans.^[5] Arecoline, an AN alkaloid, has been identified as a significant contributor toward cancer progression of oral cells as well as the addictiveness of the product.^[6] Moreover, the mechanistic action of chewing AN/BQ induces events of chronic mucosa lesions due to friction, contributing toward oral cancer progression.^[7]

Similar to the case of tobacco, public health policies aiming to control consumption would have to take any potential socioeconomic impact into account.^[8] Socioeconomic assessments for tobacco were relatively representative, given the following factors: established taxation systems and worldwide consumption, including both in developed and developing countries. In contrast, most of the AN/BQ consumers are located at the Pacific Islands, Southeast Asia, China, and India,^[9] and many were introduced to AN/BQ

during their adolescence.^[10] Most of these countries are developing economies, with weak public health and educational systems and public health frameworks, as well as limited connectivity to established scientific cohort infrastructures to fully assess the detailed impact AN/BQ products have on their populations.^[11] For example, despite China being one of the leading consumers of AN/BQ products, and indications that use is ubiquitous,^[12] the AN/BQ impact on adolescent health, and its socioeconomic studies and representations in global AN/BQ regulatory policies have been low, and associated research remains inconsistent and limited. Digital innovations could be developed for AN/BQ users and implemented for improved consumer data collection and aggregation, providing policy makers with sufficient and suitable quality data to make decisions on cessation policies. As there is likely an underestimate on AN/BQ usage in areas of limited resources, data collected through innovative digital practices could provide a more accurate representation of the user demographic and consumption practices. A transition into such digital platforms can ultimately lead to more precise and sustainable public health policies.

Therefore, in this narrative review, the aim was to identify the publications on AN/BQ and adolescent health, taking into consideration public health interventions (e.g., cessation policies) in relation to adolescent health and associated socioeconomic aspects. Particular insight is provided to the socioeconomic aspects in China, as a preamble for more systematic, future research attempts.

METHODS

The literature search was performed in April 2023 using the databases of PubMed and the UBC Library collection, with keywords used in combination, including “areca,” “areca nut,” “betel,” “betel quid,” “income,” “low income,” “middle income,” “guidelines,” “health policies,” “public health,” “programs,” “government,” “interventions,” and “regulations.” Country and region names were also added to locate specific articles, including “South Asia,” “East Asia,” “South East Asia,” “China,” “India,” “Nepal,” “Indonesia,” “Pakistan,” “Sri Lanka,” “Myanmar,” “Papua-New Guinea,” and “Pacific Islands.” The search focusing on China was performed also in Chinese through Baidu Xueshu, using the direct translation of the search terms in Chinese of “betel nuts,” “China,” “country,” “intervention,” “cessation,” “government,” and “regulations.”

The study selection flow chart is shown in Figure 1. All studies published in English since 2000 and relevant to AN/BQ consumption (alone or in conjunction with smokeless tobacco) were included. Posters and conference reports were excluded, as well as studies before 2000, as for the latter the evidence on carcinogenicity was not fully revealed. In addition, the publications used were biased toward being published within the past 10 years (2013–2023) to obtain relevant information since the IARC announcement regarding AN/BQ. For example, if a research group had two similar publications before

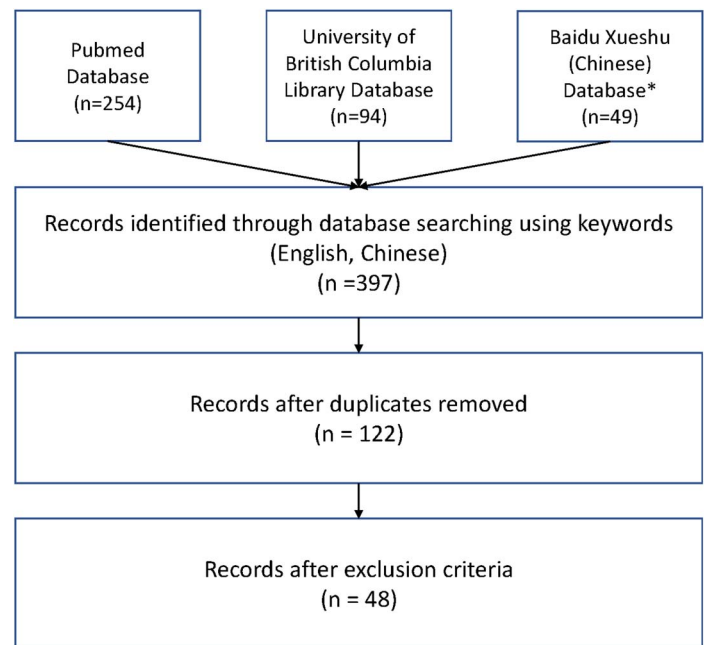


Figure 1. Flow diagram of literature review results. Searches hits (*n*) were recorded and identified using a combination of different key search terms through the following databases: PubMed, UBC Library Database, and Baidu Xueshu (*used specifically for sources in Chinese regarding the Chinese regions). Duplicate sources across the databases and keyword combinations. Records (see supplemental material available online) were filtered based on the abstract, and excluded articles related to adults, demographically located in the European Union and United States/Canada, isolated case studies, and cases with majority focus on tobacco.

and after 2013, only the latter would be included, as it was able to incorporate and respond to the IARC guidelines. To focus on the main user groups in southeast Asia, published use cases from the United States and Europe were excluded because of the smaller scope of AN/BQ use, as well as AN/BQ not being as readily available. Studies focusing on southeast Asian populations in the United Kingdom and United States were excluded.

The identified studies were reviewed independently by two reviewers: J.H.C.L. and I.H.C. The selection was verified by a third reviewer, Z.K., and differences of opinion were settled by a fourth reviewer, H.W.

RESULTS

In total, 122 manuscripts were identified as containing the search terms described in the methodology section. Studies concerning adults, located within the European Union and United States/Canada, isolated case studies, and cases that placed majority focus on tobacco were removed, and following a review of the abstracts, a final list of 48 publications was identified (available in the Supplemental Table 1). They have been grouped thematically, and are presented in the following sections.

Targeted Demographics

There was a good alignment from several publications indicating that the major user groups, and thus also

groups at risk, are adolescents, as the age of initiating most addictive behaviors, and those inhabiting low- and medium-income countries, such as India, China, Sri Lanka, Myanmar, Nepal, Indonesia, Papua New Guinea, and Pakistan.^[9,11,13–19] However, identifying the at-risk groups was not always aligned with the targeted demographics of intervention policies/cessation campaigns. In addition, these studies also suggested that the AN/BQ user demographics in different countries and regions also have different trends based on socioeconomic, cultural, and governance parameters, implicating the need to provide customized epidemiological analyses, and then interventions for different regions and tightly targeted demographic populations.^[20] For example, important demographic segments that require customized intervention policies are the school children and adolescents,^[18,21–23] as well as their parents, as several studies indicate that most long-term AN/BQ users were introduced either by older family members or school friends (including peer pressure), because of the lack of awareness of its harmful properties or did not think that it could ever become an addiction.^[24,25] Within a total of 2846 subjects interviewed from rural schools in Western Rajasthan, India, 34.5% of children aged 4–10 years and 72.8% aged 11–18 years had habits of AN chewing.^[26] At the time of writing, there is no publication available presenting comparable research in mainland China. As such, the lack of information, in particular for adolescent AN/BQ exposure and use, presents a challenge in being able to design targeted public health interventions in this population group.

Culturally, selling betel nuts is part of a family business for many consumers in rural areas of China, and up to 15,618 official businesses have been recorded as selling the product in Hunan alone since 2021.^[27] Thus, the economic dependency of these families on the AN/BQ business is considerable, as it helps provide basic income for their daily essentials. However, there is little information in terms of quantifying such socioeconomic dependency within China, and there is little information if any such information was available (i.e., regarding small, family-based retail activities) when existing policies were considered. In total, of the 48 publications identified, only seven were considering socioeconomic factors at any depth,^[19,28–33] and only one focused on mainland China. The degree of overlap between the chronic AN/BQ user base and these small, family-based businesses is also unknown for any of the included countries. Therefore, three major information gaps were evident through this literature search:

- (1) detailed information regarding adolescent exposure to AN/BQ use
- (2) information regarding user-base stratification within China
- (3) estimate of the AN/BQ socioeconomic impact, and by extension the impact of any potential public health policies both on users and on the economic livelihoods of those who are dependent on its trade.

Studies available to assess such user demographics by geography and age groups within China are severely lacking, in both Chinese and English. Therefore, the lack of such information makes it difficult to assess and suggest health interventions/policies for adolescents and reveals the acute need for more studies on Chinese AN/BQ consumption, with priority in younger populations and the socioeconomic landscape.

Public Health Interventions/Policies

Public health interventions and policies have been initiated in most countries of this narrative review, despite the lack of published information regarding the knowledge gaps identified previously. However, selection withdrawal symptoms and peer pressure have been implicated as the leading reasons for inability to quit AN/BQ chewing.^[34] BQ addiction also becomes a conditioned reflex and not dependent on the nicotine components, due to the action becoming almost habitual when chewing and performing daily tasks.^[35] Furthermore, the addiction and AN/BQ dependence induces withdrawal effects such as anxiety, irritability, mood swings, reduced energy, and concentration lapses, making it extremely difficult for users to follow through cessation programs,^[36] especially as AN/BQ is readily available and affordable in most regions.

Many of the published cessation programs followed protocols superimposed from tobacco cessation models,^[21,22] justified by the frequent contemporaneous use of AN/BQ and tobacco leaves. However, when applied to AN/BQ users, the social attachment of these products within different demographics was not initially fully evident. High relapse rates of the adult patients partaking in their cessation program trial was also observed, due to the unpleasant taste of the nicotine chewing gums, suggesting that the subjects would have preferred an AN/BQ-flavored gum, which could satisfy the subject's oral actions as well as lowering the relapse rates.^[34] Consumers in these countries can indeed refuse to support complete cessation policies; they feel attached to AN/BQ use as an integral part of their culture with historical and social connections.^[37] Therefore, tobacco cessation models, although representing a tested approach, are only partially adequate for AN/BQ-specific interventions, especially for adolescents, and might require further research and customization for these different population groups.

Most recently in 2019 in China, the Hunan Betel Food Industry Administration banned BQ advertisements for TV shows, movies, etc., and as of September 2021, the National Radio and Television Administration also decided against AN promotion by radio, television, and online platforms.^[7,38] However, this had little effect on

Table 1. A summary of cessation policies/public health interventions identified for AN/BQ per country

Country/Region	Cessation Policy/Public Health Intervention
China and Taiwan (China)	Cessation program ^[34,64] Advertising ban ^[7,38] Tax increase ^[47] Educational program ^[45]
India	Cessation program ^[21,22,35,44]
Guam	Cessation program ^[37,63]
Pacific islands	Cessation program ^[66]
Sri Lanka	None
Myanmar	Ban of sales (tobacco and AN/BQ) to adolescents ^[42]
Nepal	None
Indonesia	Cessation counseling ^[67]
Papua-New Guinea	Education program ^[18]
Pakistan	Cessation program ^[19,44,65]

AN/BQ, areca nut and betel quid; n/a, none identified through this approach.

the sales of the product in Hunan, at least in the short-term, as the production load of AN/BQ products increased by 8.3% between 2019 and 2020.^[26] This effect is exacerbated by the lack of media reporting of the carcinogenic effects of AN/BQ, while at the same time AN/BQ use is portrayed as a fashionable lifestyle choice in social media such as TikTok,^[39,40] used by most adolescents. Studies of Chinese AN/BQ users reported only knowing that the product had negative health effects, but not what they were specifically.^[41] This result indicates that an isolated approach of media ban for advertisements without any complementary activities (for example, through high-school educational activities) is not effective among users and is unlikely to be adhered to by those financially dependent on AN/BQ.

It should be noted here, that within southeast Asia there are specific regions with outright smokeless tobacco product bans through legislation—either through forbidding sales or public use—and these regions include Bhutan, Thailand, India, Myanmar, and the Democratic People's Republic of Korea.^[42] However, the capacity to oversee and enforce these rules is not always seen as a priority, for example in India, the largest user of AN/BQ through products such as pan masala and supari, where loopholes are used by vendors to continue the sale of said products.^[43] A summary of the cessation programs per country, as identified through the current narrative review, is shown in Table 1.

Effectiveness of Current Interventions

A study by Das et al.^[43] provided a commentary on their finds of AN/BQ intervention attempts between 1990 and 2018, with intervention methods such as product bans, mass media campaigns, cessation programs, increased taxations, and education programs. However, despite the wide search scope for policies and interventions spanning a 28-year period, only 21 published interventions were found by the group. Most of

the strategies used were in the form of individual-level interventions, such as cessation program studies, and/or education programs to provide awareness of the dangers. It was also reported that for some educational programs, even though many subjects understand the unfavorable effects of AN/BQ, they remain unwilling to quit, demonstrating that long-term programs, support, and incentivization are needed to try to help this demographic.^[44] Programs such as LifeFirst in India, which targets students to provide knowledge of the health risks of tobacco and AN/BQ, as well as teaching students how to say no and resist peer pressure, were evaluated to be successful in reducing both tobacco and AN/BQ usage among its students.^[21] However, they were not integrated as part of ongoing educational curricula or connected to other public health initiatives by the regional healthcare services.

As such, educating the general population on the negative effects at a young age helped limit adolescents from transitioning into heavy users, at least in two national contexts, and can also help educate indirectly the parents of these students.^[45,46] However, such educational campaigns would need to be complemented by other policies as well. For example, increased targeted taxation on specific products, as a simulated comparative analysis of implementing an “areca nut tax” to evaluate future tax implementation in parallel to cigarette smoking, concluded that such a tax implementation would decrease overall AN/BQ consumption.^[47] In contrast to India and other southeast Asian regions, China implemented their outright media ban for promoting AN/BQ only recently, due to the “Healthy China 2030” policy and the “Oral Health Action Plan 2019–2025.” These are horizontal bans, and the effectiveness of these policies in lowering AN/BQ usage in China at the regional and local levels remains to be seen.^[7]

Perceptions and Behavioral Changes

Finally, nine of the identified publications focused on perceptions, knowledge, and attitudes as the foundations driving AN/BQ consumption behaviors in adolescents.^[10,13,32,39,48–52] Once more, knowledge adapted from similar successful studies on tobacco was applied in studying AN/BQ. Although they represent diverse geographies, study approaches, and population groups, there exist underlying commonalities. For example, in the same context as AN/BQ use would be found feelings such as euphoria, pleasure, alertness, and good taste. The presence and widespread appeal from social media have accelerated misconceptions regarding AN/BQ use, in particular within those who frequently consume social media, and the real outcome of the influence of social media can only be assessed at an individual level through systematic KAP (knowledge, attitude, and practice) analyses. In addition, there were no studies identified regarding the perceptions relating to primary health practitioners or public health physicians and allied staff, as

they are the ones likely to implement public health interventions in the longer-term. As such, the current gaps include the following:

- (1) Detailed information on KAP for adolescents, and healthcare practitioners
- (2) Understanding of the behavioral changes possible through the use of social media
- (3) Estimating the socioeconomically driven resistance toward behavioral changes.

DISCUSSION

This brief report has identified several socioeconomic knowledge gaps, especially in China, where due to its diverse cultural groups and geographical locations, the plurality of user and financially dependent population groups has been insufficiently explored.^[53] As such, it may be beneficial for regulatory bodies to communicate with the betel product industry so that at least some of these gaps can be addressed. Furthermore, more detailed knowledge in the differing chemical compositions of AN/BQ products post-processing would be required,^[54] including findings such as formulations with carcinogenic components or dosage (as AN/BQ use is likely to be maintained as part of traditional medicine applications). Scientific research advancements such as liquid chromatography tandem mass spectroscopy could also lead to new findings for specific formulations of AN/BQ processing that can limit the alkaloid components, as recent studies showed that using combinations of cooking, soaking, and marinating with specific brines can lower polyphenol and alkaloid content by more than 50%.^[55] Also, different AN/BQ mixtures may potentially reduce the risk of oral submucous fibrosis.^[56] However, these remain isolated studies and can be considered indications, as further systematic research is required.

Moreover, Chinese researchers in Hunan have been developing self-rating dashboards on AN/BQ abuse for AN/BQ users, testing the reliability to self-diagnose substance abuse, such as the Self-report Screening Test for Areca-quid Abusers, Betel Quid Dependence Instrument, Betel Quid Dependence Scale for fresh areca use areas, and others, for processed BQ users.^[57] Although not entirely novel for self-assessing addictive behaviors, such population-level, self-help applications can become vehicles for the provision of relevant, accurate information as well as form the launchpads for self-assisted cessation initiatives. Furthermore, digital based initiatives aids and solutions could be developed for BQ users and implemented for greater statistical aggregation or encouragement for cessation, providing policy makers with sufficient and suitable data to make decisions. Alternatively, the rise of wellness applications available directly to the general public, often with the attachment of wearable devices, may provide an additional opportunity to collect AN/BQ usage data as an additional customized

component of personal information. This may provide the basis for a more accurate data collection at a personal level, and provide the opportunity to aggregate such data at the population level.

Novel approaches are researching the effects that AN/BQ products have on the human body. For example, the People's Hospital of Hainan Province of China compared the neuronal activity between 33 BQ-dependent users and 32 control individuals through resting state functional magnetic resonance imaging between 2013 and 2014.^[58] It was observed that BQ-dependent users who are not tobacco users or alcoholics displayed significant decreases in neuronal intensities and neural coherence of the right rostral anterior cingulate cortex, in an area of the brain theorized to be associated with its role in addiction-related impulse control.^[59] It should be noted that the sample size of both studies is relatively small, thus, the investigation of AN/BQ impact on the brain remains to be defined further, inclusive of adolescent populations.

Finally, some studies argue that placing the many formulations and various substances under the same umbrella of classification and public health regulation—despite having a difference in the constituents with variable degree of carcinogenic potential—is likely to lead to more ambiguity and further fuel the misinformation on social media.^[39] Indeed, drinking coffee, originally classified as possibly carcinogenic to the human urinary bladder (Group 2B), was further qualified and reclassified with higher accuracy in 2016 (Group 3).^[60] As such, it is likely that existing AN/BQ classifications may be further qualified as additional scientific data emerge on processing methods and formulations. The more specific information is also likely to have an impact on the effectiveness of current regulatory approaches, as well as be beneficial to the cultural significance in different demographics, informing traditional medicine approaches and limiting any usage dangers.

As the largest producers and users of AN/BQ, it is important for India and China to initiate high-quality research of different health-related, industrial, and socioeconomic concerns. This would require a multidisciplinary approach, and should not be shouldered solely by the state, the industry, or academia. Such a multiple stakeholder approach is more likely to acknowledge the impact and effectiveness of public health measures to different targeted demographics, especially to adolescents. For example, up to 59% of the Hainan province population in China works within the agricultural sector where a major crop is areca and betel plants. Sudden complete restrictions and/or regulations without appropriate information and support initiatives can lead to spike of unemployment rates in regions that are heavily dependent on the AN/BQ industry to generate employment.^[61] Thus, public health measures should be considered alongside a nexus of supportive actions and multi-stakeholder engagement, as has happened previously for tobacco-free measures implementation.^[62]

Limitations and Weaknesses

As a limitation of this brief report, it is important to note that there exist records and documentation in local Asian languages relating to the application and use of AN/BQ, as well as potential local public health interventions, not readily accessible for analysis. However, these have not been investigated as part of this study, despite regular indications in the published English scientific literature that they do indeed exist. For example, the applications in traditional Chinese medicine contain detailed records about betel nut application as part of prescribed herbal interventions. Thus, there exist non-English sources that are potentially insightful and require further translated and systematic research.

In addition, as this narrative review includes publications that present aggregate data on India and China, it is important to note that these are vast geographies incorporating many different communities and cultural beliefs. As such, it is possible that the same public health intervention may be successfully implemented in one area, and not at all in another owing to these deep-rooted regional differences, which have not yet been characterized in any detail. Further studies will be required to provide a broad and applicable agenda against AN/BQ products, specifically targeted to adolescents, as supporting guidance for constructing a successful and inclusive public health intervention framework. Overall, this narrative review brings awareness to the pitfalls of the current policy implementations, but also underscores the need for higher-quality research to support a wider agenda against the ongoing public health crisis.

CONCLUSIONS

The continuous observed AN/BQ usage in southeast Asia is of concern, as it has not reduced significantly despite the classification of AN/BQ as a class 1 carcinogen by the IARC. Most users start addictive behaviors during their adolescence, and originate from resource-restricted socioeconomic contexts, where health interventions tend to be unavailable, or if available come at a considerable financial burden, as AN/BQ retail supports a considerable number of small, family-owned businesses. Therefore, it is important to identify the demographic segments in which any potential public health interventions would have the highest impact, and design appropriate policies targeted to those segments.

This review has highlighted the highly fragmented nature of available published information. In addition, as a product with significant historical, cultural, and social purpose, the best likely approach for reducing the product's harm is to use more local insights to inform public health policies, as part of a multi-stakeholder engagement strategy. In this approach, socioeconomic factors become even more relevant, as for example regions, like Hunan in China, are largely dependent on AN/BQ production and

sale. Overall, the direct implementation of health policies (such as bans, taxation, and cessation programs) like those implemented in the past decades for alcohol and tobacco for adolescents could be used as an initial basis for reducing AN/BQ usage, if adapted appropriately.

Supplemental Material

Supplemental materials are available online with the article.

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