INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND DENTAL HEALTH
(ISSN: 2454-4191)
www.ijmsdh.org (2026)

Check for updates

Received: 30 Sep 2026
Revised: 12 Oct 2026
Accepted: 20 Oct 2026
Published: 30 Oct 2026

2026: OCTOBER - IJMSDH
Page No – 102-107
DOI - 10.55640/ijmsdh-spc-16

Article Citation: Dr. Arief Wibowo. (2026). Systemic and Neuropsychiatric Implications of Betel Quid and Areca Nut Use: A Multidisciplinary Review of Carcinogenesis and Mental Health Outcomes. International Journal of Medical Science and Dental Health, 1(01), 102-107. https://doi.org/10.55640/ijmsdh-spc-16

Copyright: © 2026 The Authors. Published by IJMSDH under the Creative Commons CC BY License

Systemic and Neuropsychiatric Implications of Betel Quid and Areca Nut Use: A Multidisciplinary Review of Carcinogenesis and Mental Health Outcomes

Dr. Arief Wibowo

Universitas Indonesia, Indonesia

Abstract

Background: Betel quid (BQ) and areca nut (AN) chewing are ancient cultural practices prevalent across the Asia-Pacific region. While the carcinogenic potential of BQ is well-documented by the IARC, emerging research suggests a complex profile of systemic toxicity and profound neuropsychiatric effects. This review aims to synthesize current findings regarding the association between BQ use, systemic malignancies, and mental health disorders.

Methods: A multidisciplinary review was conducted analyzing epidemiological, genomic, and behavioral studies. The scope includes cancer risks beyond the oral cavity, genomic instability mechanisms, and psychiatric correlations ranging from dependence to psychosis.

Results: BQ use is strongly associated with Oral Potentially Malignant Disorders (OPMD) and Oral Squamous Cell Carcinoma (OSCC), alongside significant risks for esophageal, stomach, and breast cancers. Molecular studies indicate that AN induces chromosomal instability and alters mitotic checkpoint genes. Neuropsychiatrically, BQ use is linked to DSM-5 Use Disorders, schizophrenia, and common mental disorders. Mechanistic data reveals that arecoline affects Monoamine Oxidase A (MAO-A) activity and Brain-Derived Neurotrophic Factor (BDNF) signaling, creating a complex interplay of nociceptive and anxiodepressive responses.

Conclusion: The health impact of BQ extends far beyond oral hygiene. It represents a dual public health burden, driving systemic carcinogenesis and contributing to psychiatric morbidity. Effective health policy must address the neurobiological addiction mechanisms to mitigate cancer risks effectively.

Keywords: Betel quid, Areca nut, Oral cancer, Neuropsychiatry, MAO-A, Carcinogenesis, Public health.

Introduction

The consumption of betel quid (BQ) and areca nut (AN) constitutes one of the most widely practiced addictive behaviors globally, particularly entrenched within the socio-cultural fabric of the Asia-Pacific region. For centuries, the preparation—often comprising the areca nut, betel leaf, slaked lime, and occasionally tobacco or spices—has been utilized for its mild stimulant properties, social symbolism, and perceived medicinal benefits. However, the modern epidemiological landscape paints a starkly different picture, one characterized by a significant burden of chronic disease. While the International Agency for Research on Cancer (IARC) has definitively classified areca nut as a Group 1 carcinogen [8], the scope of pathology associated with its use is frequently underestimated when limited solely to oral hygiene perspectives.

The narrative surrounding BQ has historically focused on the oral cavity. This is a logical starting point, given the direct contact between the abrasive, chemically potent quid and the oral mucosa. Yet, recent investigations have begun to elucidate a far more systemic and insidious impact. The chemical constituents of the areca nut, primarily alkaloids such as arecoline, are absorbed into the systemic circulation, affecting distant organs and physiological systems. There is growing evidence connecting BQ usage not only to esophageal and gastric malignancies but also to genomic alterations in breast cancer patients, suggesting a mutagenic potential that transcends local tissue contact [5, 7].

Furthermore, a critical and often overlooked dimension of BQ usage is its neuropsychiatric profile. The psychoactive properties of arecoline, which acts as a partial agonist at muscarinic acetylcholine receptors, create a complex web of dependence and neurological alteration. Recent studies have highlighted associations between BQ use and a spectrum of psychiatric conditions, including schizophrenia, brief psychotic disorders, and common mental disorders (CMDs) [10, 11, 12]. The introduction of specific diagnostic criteria for Betel-Quid Use Disorder in the DSM-5 underscores the recognition of this substance as a genuine agent of addiction, rather than merely a habit [1].

This review aims to bridge the gap between these two distinct but related fields of study: the oncological and the neuropsychiatric. By synthesizing data from molecular studies, animal models, and human epidemiological cohorts, we seek to provide a comprehensive overview of the systemic risks posed by BQ. This analysis is crucial for developing integrated public health strategies that address not only the physical consequences of chewing but also the underlying neurobiological drivers of addiction that perpetuate the behavior.

Methods

This article employs a narrative review methodology to synthesize interdisciplinary findings regarding the physiological and psychological impacts of BQ/AN use. The review prioritizes high-impact literature that addresses the "dual burden" of carcinogenesis and psychiatric morbidity.

Selection Criteria and Scope

The analysis is anchored in a selection of sixteen pivotal studies that represent a cross-section of current knowledge. These references were selected based on their relevance to three core thematic areas:

1. Systemic Carcinogenesis: Studies investigating the incidence of Oral Squamous Cell Carcinoma (OSCC), esophageal cancer, and distant malignancies such as stomach and breast cancer in BQ endemic populations.
2. Genomic Stability: Basic science research focusing on chromosomal instability, mitotic checkpoint gene expression, and genomic alterations associated with BQ exposure.
3. Neuropsychiatry and Addiction: Clinical reports, population-based studies, and animal models exploring the relationship between BQ use, DSM-5 dependence criteria, psychosis, depression, and neurochemical pathways (e.g., MAO-A, BDNF).

Data Synthesis

The review integrates epidemiological data from high-prevalence regions, specifically Taiwan, India, and Micronesia (Palau). It juxtaposes human observational data with mechanistic insights derived from murine and rat models to construct a cohesive understanding of how areca nut alkaloids function at cellular and systemic levels. The discussion extends to public policy evaluation, examining the effectiveness of taxation and regulatory measures in these specific cultural contexts.

Results

The analysis of the selected literature reveals a pervasive impact of BQ/AN on human health, categorized distinctively into carcinogenic pathways, genomic instability, and neuropsychiatric outcomes.

The Carcinogenic Spectrum: From Oral to Systemic

The most immediate and well-characterized consequence of BQ use is the development of Oral Potentially Malignant Disorders (OPMD) and subsequent malignancy. Lee

et al. (2018) demonstrated a robust association between DSM-5 defined Betel-Quid Use Disorder and OPMD in endemic Asian populations, suggesting that the severity of dependence correlates directly with pathological risk [1]. This dose-response relationship is further complicated by the concurrent use of tobacco. However, even in the absence of tobacco, the IARC confirms that the areca nut itself contains carcinogenic nitrosamines [8].

The risk extends significantly beyond the oral cavity. Wu et al. (2001) identified a clear risk correlation between betel chewing and esophageal cancer in Taiwan, highlighting that the swallowing of quids or areca-infused saliva exposes the upper aerodigestive tract to prolonged carcinogenic contact [4]. More alarmingly, systemic absorption appears to facilitate distant malignancies. Adel et al. (2016) noted poor outcomes in patients with oral cavity squamous cell carcinoma who developed fourth primary tumors, emphasizing the aggressive and multifocal nature of cancers in BQ chewers [3]. Furthermore, Kurkalang et al. (2013) provided experimental evidence in mice showing that exposure to areca nut extracts induced stomach cancer, a finding that challenges the notion of local toxicity only [7].

Genomic and Molecular Instability

The mechanism by which BQ drives carcinogenesis appears to be deeply rooted in genomic instability. Kurkalang et al. (2013) observed that areca nut exposure altered the expression pattern of mitotic checkpoint genes, leading to chromosomal instability—a hallmark of cancer progression [7]. This instability is not confined to gastric or oral tissues. Kaushal et al. (2012) reported distinct genomic alterations in breast cancer patients who were BQ chewers compared to non-chewers, suggesting that the mutagenic compounds in AN may influence tumor biology and genetic susceptibility in tissues entirely remote from the site of consumption [5].

Neuropsychiatric Comorbidities and Neurobiological Mechanisms

Perhaps the most complex findings relate to the impact of BQ on the central nervous system. The transition of BQ use from a cultural habit to a diagnosable disorder is significant. Lee et al. (2018) highlighted the validity of DSM-5 criteria for Betel-Quid Use Disorder, linking the intensity of addiction to adverse health outcomes [1].

The psychiatric implications are profound. Sullivan et al. (2000) investigated the effects of chewing betel nut on schizophrenia symptoms in Palau, Micronesia. While some patients reported subjective symptom relief, the study pointed toward complex interactions where high-consumption users might experience distinct symptomatic profiles [11]. This aligns with case reports by Li et al. (2024), documenting brief psychotic disorders directly precipitated by areca nut use, suggesting an "areca psychosis" distinct from primary schizophrenia [10].

Population-based studies reinforce these clinical observations. Lin et al. (2018) found that areca nut chewing is associated with common mental disorders, challenging the user perception of the nut as a harmless anxiolytic [12]. Similarly, Chandra et al. (2003) noted a high prevalence of areca nut use among psychiatric patients in India, raising questions about self-medication versus causative contribution [13].

Neurobiologically, these behavioral phenotypes are supported by molecular evidence. Chen et al. (2012) identified that Monoamine Oxidase A (MAO-A) variants are associated with heavy betel quid use, implicating the monoaminergic system—which regulates mood and anxiety—in the etiology of BQ dependence [15]. Additionally, Yao et al. (2023) demonstrated in rat models that Areca catechu extracts could ameliorate stress-induced depression behavior via the BDNF signaling pathway, providing a biological basis for why users might initiate chewing for stress relief, despite the long-term negative consequences [16]. Conversely, Chen et al. (2024) found that arecoline inhibited cortical synaptic transmission and modulated nociceptive and anxiodepressive responses in mice, further illustrating the potent and often contradictory neuromodulatory effects of the nut [14].

Discussion

The synthesis of these findings presents a paradox of BQ usage: it is a substance that induces profound genomic instability and carcinogenesis while simultaneously hijacking neurobiological reward and stress-relief pathways to reinforce use.

The Mechanism of Addiction and "Self-Medication"

The intersection of the genomic and psychiatric data suggests that BQ dependence is not merely a failure of willpower but a complex neurochemical event. The findings regarding the BDNF signaling pathway [16] are particularly illuminating. Brain-Derived Neurotrophic Factor is crucial for neural plasticity and mood regulation. If areca nut components temporarily enhance BDNF signaling or mimic antidepressant effects in animal models, it explains the deep-seated cultural reliance on the substance for stress management. Users are, in effect, self-medicating. However, this comes at a steep physiological cost. The inhibition of cortical synaptic transmission described by Chen et al. (2024) suggests that chronic use may lead to cognitive or sensory processing deficits over time, potentially exacerbating the very psychiatric conditions users attempt to alleviate [14].

This "relief" mechanism is complicated by the findings of Sullivan et al. (2000) and Li et al. (2024) regarding psychosis [10, 11]. While low doses may provide anxiolysis, the data suggests that higher concentrations or chronic accumulation of alkaloids can precipitate acute psychosis or worsen schizophrenia. This biphasic effect—anxiolytic at one level, psychotogenic at another—mirrors the pharmacological profiles of other potent stimulants and complicates clinical management. A clinician treating a patient for schizophrenia in a BQ-endemic area must determine if symptoms are primary or substance-induced, a distinction made difficult by the social acceptability of the habit.

Genomic Instability as a Systemic Threat

The traditional view of BQ causing cancer via direct irritation (the "sandpaper effect") is insufficient to explain the molecular data. The alteration of mitotic checkpoint genes [7] indicates that areca nut components act as genomic destabilizers. If these compounds circulate systematically, as evidenced by their impact on breast cancer genomics [5] and the induction of stomach cancer in mice [7], then BQ must be viewed as a systemic toxin. This redefines the risk profile for long-term users. Screening programs that focus solely on the oral cavity may be missing early signs of esophageal, gastric, or other systemic malignancies. The association with fourth primary tumors in OSCC patients [3] further suggests a "field cancerization" effect that is not localized but organism-wide.

Societal Implications and Policy Failure

The deep cultural roots of BQ use described by Burton-Bradley (1966) in Papua and New Guinea [9] illustrate why eradication is difficult. It is not just a drug; it is a social currency. This cultural entrenchment often blunts the impact of regulatory measures. Chen et al. (2011) analyzed the cross-effects of cigarette and betel nut consumption in Taiwan following tax increases. While taxation is a proven strategy for tobacco control, the substitution effect—where users switch between cigarettes and BQ based on price—can undermine public health goals [2]. If BQ remains cheaper or less regulated than tobacco, it becomes a refuge for nicotine-seeking behavior (when tobacco is added) or habit maintenance.

Furthermore, the "Systemic Adverse Effects" reviewed by Garg et al. (2014) indicate that the public health burden includes cardiovascular, metabolic, and reproductive health issues not fully covered in this cancer-focused review [6]. The economic cost of treating these chronic conditions, alongside the psychiatric burden identified in the results, likely dwarfs the revenue generated by the BQ industry.

Integrated Expansion: The Neurobiological-Oncological Interface

To fully appreciate the public health crisis posed by Betel Quid, one must delve deeper into the intricate relationship between its neurobiological drivers and its oncological outcomes. This is not merely a case of concurrent comorbidities; rather, it represents a mechanistic feedback loop where the psychiatric effects of the nut directly facilitate the conditions necessary for carcinogenesis.

The role of Monoamine Oxidase A (MAO-A) serves as a critical bridge in this discussion. Chen et al. (2012) established the association between MAO-A variants and heavy BQ use [15]. MAO-A is responsible for the degradation of amine neurotransmitters, including dopamine, norepinephrine, and serotonin. Variations in the gene encoding this enzyme can lead to altered levels of these neurotransmitters, influencing impulsivity, aggression, and susceptibility to addiction. In the context of BQ, individuals with specific MAO-A polymorphisms may be genetically predisposed to heavier consumption to achieve the same neurochemical equilibrium or "high." This genetic predisposition leads to higher frequency and duration of exposure to the carcinogenic alkaloids in the nut. Therefore, the psychiatric genotype drives the oncological phenotype. The inability to quit, reinforced by these monoaminergic pathways, ensures that the oral and systemic tissues are bathed in carcinogens for decades.

This relationship is further compounded by the cognitive impact of chronic use. As noted, BQ use is associated with common mental disorders [12] and cognitive impairments via the inhibition of cortical synaptic transmission [14]. Individuals suffering from depression, anxiety, or cognitive decline are statistically less likely to engage in proactive health behaviors, such as attending cancer screenings or adhering to oral hygiene protocols. They are also less likely to successfully navigate cessation programs that rely heavily on cognitive-behavioral strategies. Thus, the neurotoxic effects of areca nut actively erode the user's capacity to mitigate the carcinogenic risks.

We must also scrutinize the molecular mimicry involved in "Areca Psychosis." The case report by Li et al. (2024) serves as a sentinel warning [10]. The pharmacological action of arecoline involves muscarinic and nicotinic acetylcholine receptors. Overstimulation of the cholinergic system can lead to a delirium-like state or acute psychosis. In endemic areas like Papua New Guinea or rural Taiwan, such presentations might be culturally interpreted through spiritual lenses or misdiagnosed as primary psychiatric breaks [9]. If medical professionals fail to recognize the toxicological origin of the psychosis, the patient may be treated with antipsychotics while continuing the BQ habit. This is problematic because certain antipsychotics can alter

metabolic profiles and seizure thresholds, potentially interacting adversely with the stimulant properties of the nut. Moreover, the chronic inflammation caused by systemic BQ usage—a precursor to cancer—may also contribute to neuroinflammation, a pathway increasingly implicated in the pathophysiology of schizophrenia and severe depression.

The study by Kurkalang et al. (2013) on mice provides a terrifying insight into the "silent" progression of disease [7]. The induction of chromosomal instability through the alteration of mitotic checkpoint genes implies that cells are being forced into division despite having damaged DNA. In a healthy organism, checkpoints arrest the cell cycle to allow for repair or apoptosis. Areca nut components appear to override these safety brakes. When this molecular mechanism is viewed alongside the findings of Kaushal et al. (2012) regarding breast cancer [5], a hypothesis emerges: Areca nut alkaloids may act as systemic mutagens that create a "fertile soil" for cancer anywhere in the body, not just where the juice touches. The breast tissue, highly responsive to hormonal and chemical signals, becomes a collateral victim of this systemic instability. This necessitates a paradigm shift in oncology. A history of BQ use should trigger a higher index of suspicion for non-head-and-neck cancers.

Furthermore, the interaction between BQ and stress responses described by Yao et al. (2023) creates a vicious cycle [16]. If BQ use mimics the BDNF-promoting effects of antidepressants in the short term, the cessation of use would logically precipitate a crash—a rapid drop in neurotrophic support leading to severe rebound depression or anxiety. This withdrawal syndrome is a powerful barrier to cessation. Public health campaigns often focus on the "fear" of cancer (OSCC images on packaging), but they fail to address the "fear" of the psychological crash. If a user relies on BQ to maintain their mood homeostasis via the BDNF pathway, showing them a picture of a tumor is insufficient motivation to quit. They are chemically trapped. Cessation programs, therefore, must include pharmacological support that addresses this neurotrophic deficit, perhaps utilizing antidepressants or other neuroprotective agents during the withdrawal phase.

Finally, the transcultural psychiatry perspective brought by Burton-Bradley (1966) and updated by modern epidemiological data requires a nuanced policy approach [9]. In many endemic regions, BQ is the poor man's luxury and the working man's stimulant. It suppresses hunger and increases alertness. Economic instability often drives increased consumption. Chen et al. (2011) showed that tax increases on cigarettes might drive users toward BQ if it remains the cheaper alternative [2]. This suggests that "sin taxes" must be synchronized. If tobacco is taxed but BQ is not, policy inadvertently promotes the substitution of one carcinogen for another. Moreover, given the systemic risks (stomach, breast, esophagus), the economic cost calculation used by governments to justify BQ regulation often underestimates the true burden. It accounts for oral surgeries but rarely attributes the cost of a mastectomy or gastric resection to the areca nut. Correctly attributing these systemic diseases to BQ use would likely reveal a massive economic drain, providing the political capital necessary for stricter regulation.

In summary, the BQ user is fighting a war on two fronts: a genomic war where their cells are losing the ability to regulate division, and a neurochemical war where their brain is rewired to demand the very agent causing the damage. Addressing one without the other is destined to fail.

Conclusion

The consumption of betel quid and areca nut represents a multifaceted public health challenge that transcends the boundaries of dentistry and oral surgery. The evidence synthesized in this review demonstrates that BQ is a systemic toxin capable of inducing genomic instability and malignancy in organs as distant as the stomach and breast. Concurrently, it acts as a potent psychoactive substance, capable of inducing dependence, psychosis, and mood disorders through specific molecular pathways involving MAO-A and BDNF.

The correlation between DSM-5 defined BQ use disorder and the incidence of potentially malignant disorders suggests that the intensity of the addiction drives the severity of the disease. Therefore, clinical interventions must be dual-purpose. Oncologists treating BQ-associated cancers must screen for psychiatric dependence and comorbidities, while psychiatrists in endemic areas must remain vigilant for the signs of oral and systemic malignancy in their patients.

Ultimately, breaking the cycle of BQ use requires a recognition of its function as a "self-medication" tool for stress and anxiety in many cultures. Effective cessation strategies cannot rely solely on education regarding cancer risks; they must offer viable alternatives for stress management and addiction support. Only by addressing the neuropsychiatric roots of the habit can we hope to stem the tide of its carcinogenic consequences.

References

1. Adel M, Liao CT, Lee LY, et al. Incidence and Outcomes of Patients With Oral Cavity Squamous Cell Carcinoma and Fourth Primary Tumors: A Long-term Follow-up Study in a Betel Quid Chewing Endemic Area. Medicine. 2016 Mar;95(12):e2950.
2. Burton-Bradley BG. Papua and New Guinea transcultural psychiatry: some implications of betel chewing. The Medical journal of Australia. 1966 Oct 15;2(16):744-6.

3. Chandra PS, Carey MP, Carey KB, Jairam KR. Prevalence and correlates of areca nut use among psychiatric patients in India. Drug and alcohol dependence. 2003 2003/04/01/;69(3):311-6.
4. Chen PH, Tu HP, Wang SJ, et al. Monoamine oxidase A variants are associated with heavy betel quid use. Addiction biology. 2012 Jul;17(4):786-97.
5. Chen QY, Zhang Y, Ma Y, Zhuo M. Inhibition of cortical synaptic transmission, behavioral nociceptive, and anxiodepressive-like responses by arecoline in adult mice. Molecular brain. 2024 Jun 17;17(1):39.
6. Chen SH, Lee JM, Liu HH, Wang HC, Ye CY. The cross-effects of cigarette and betel nut consumption in Taiwan: have tax increases made a difference? Health policy and planning. 2011 May;26(3):266-73.
7. Garg A, Chaturvedi P, Gupta PC. A review of the systemic adverse effects of areca nut or betel nut. Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology. 2014 Jan;35(1):3-9.
8. IARC. Betel-quid and areca-nut chewing and some areca-nut derived nitrosamines. IARC monographs on the evaluation of carcinogenic risks to humans. 2004;85:1-334.
9. Kaushal M, Mishra AK, Sharma J, et al. Genomic alterations in breast cancer patients in betel quid and non betel quid chewers. PloS one. 2012;7(8):e43789.
10. Kurkalang S, Banerjee A, Ghoshal N, Dkhar H, Chatterjee A. Induction of chromosome instability and stomach cancer by altering the expression pattern of mitotic checkpoint genes in mice exposed to areca-nut. BMC cancer. 2013 Jun 28;13:315.
11. Lee C-H, Ko AM-S, Yang FM, et al. Association of DSM-5 Betel-Quid Use Disorder With Oral Potentially Malignant Disorder in 6 Betel-Quid Endemic Asian Populations. JAMA Psychiatry. 2018;75(3):261-9.
12. Li S, Li Z, Chen J, et al. Brief psychotic disorder related to areca nut use: a case report. Frontiers in psychiatry. 2024;15:1360493.
13. Lin TY, Chang HC, Hsu KH. Areca nut chewing is associated with common mental disorders: a population-based study. Social psychiatry and psychiatric epidemiology. 2018 Apr;53(4):393-401.
14. Sullivan RJ, Allen JS, Otto C, Tiobech J, Nero K. Effects of chewing betel nut (Areca catechu) on the symptoms of people with schizophrenia in Palau, Micronesia. The British journal of psychiatry : the journal of mental science. 2000 Aug;177:174-8.
15. Wu MT, Lee YC, Chen CJ, et al. Risk of betel chewing for oesophageal cancer in Taiwan. British journal of cancer. 2001 Sep 1;85(5):658-60.
16. Yao C, Zhang Y, Sun X, et al. Areca catechu L. ameliorates chronic unpredictable mild stress-induced depression behavior in rats by the promotion of the BDNF signaling pathway. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2023 Aug;164:114459.