PREVALENCE OF BETEL OR ARECA NUT (AN) USE AND ITS
ASSOCIATED FACTORS AMONG BHUTANESE POPULATION AGED
15-69 YEARS OLD: AN ANALYSIS OF NATIONAL HEALTH DATA OF
NON-COMMUNICABLE DISEASE (NCD) SURVEY IN 2019

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Public Health in Public Health
COLLEGE OF PUBLIC HEALTH SCIENCES
Chulalongkorn University
Academic Year 2022
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ความชุกของการเคี้ยวหมากพลูและปัจจัยที่เกี่ยวข้อง
ในกลุ่มประชากรประเทศภูฏาน อายุ 15-69 ปี: การวิเคราะห์ ข้อมูลการส
ารวจสุขภาพแห่งชาติของโรคไม่ติดต่อเรื้อรัง ปี 2562

นายทาชิ เป็นจอว์

Thesis Title   PREVALENCE OF BETEL OR ARECA NUT (AN)
                         USE AND ITS ASSOCIATED FACTORS AMONG
                         BHUTANESE POPULATION AGED 15-69 YEARS
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ทาชิ เป็นจอว์ : ความชุกของการเคี้ยวหมากพลูและปัจจัยที่เกี่ยวข้อง ในกลุ่มประชากรประเทศภูฏาน อายุ 15-69 ปี: การวิเคราะห์ข้อมูลการส รวจสุขภาพแห่งชาติของโรคไม่ติดต่อเรื้อรัง ปี 2562. (PREVALENCE OF BETEL OR ARECA NUT (AN) USE AND ITS ASSOCIATED FACTORS AMONG BHUTANESE POPULATION AGED 15-69 YEARS OLD: AN ANALYSIS OF NATIONAL HEALTH DATA OF NON-COMMUNICABLE DISEASE (NCD) SURVEY IN 2019) อ.ที่ปรึกษาหลัก : วัฒน์สิทธิ์ ศิริวงศ์, อ.ที่ปรึกษาร่วม : Mark G. Robson

มาของปัญหา: แม้ว่าการใช้หมาก (betel or areca nut) จะได้รับความตระหนักทางด้านสาธารณสุขจากทั่วโลกน้อยกว่าการใช้ยาสูบ แต่โดยเฉพาะอย่างยิ่ง การใช้หมาก (เคี้ยวหมาก) ยังคงแพร่หลายและเป็นปัญหาสาธารณสุขเชิงระบาดวิทยาที่ถูกละเลยในภูฏาน การใช้งานยังได้รับการผสมผสานโดยตรงกับประเพณี และโครงสร้างทางสังคมของชาวภูฏาน ปัจจุบันไม่มีนโยบายที่กำหนดเป้าหมายการควบคุมและการบริโภคการใช้และการค้าถั่วลันเตาในภูฏานโดยเฉพาะ ในขณะที่ถูกจัดเป็นสารก่อมะเร็งในมนุษย์โดยวิจัยการเกิดมะเร็งขององค์กรอนามัยโลก (WHO IARC) ในปี พ.ศ. 2547 ชุดข้อมูลการสำรวจสุขภาพระดับประเทศ แสดงให้เห็นความชุกของการใช้หมากนั้นสูงมากอย่างต่อเนื่องในภูฏาน และการสำรวจสุขภาพแห่งชาติ (NHS) ของภูฏาน ปีพ.ศ. 2564 พบว่า มีการใช้หมากร้อยละ 43.9 ของชาวภูฏาน อายุระหว่าง 15-75 ปี ในรูปหมากพลู และในปี 2016 การสำรวจสุขภาพนักเรียนตามโรงเรียนทั่วโลกประจำปี พ.ศ. 2559 (Global School-based Student Health Survey, GSHS) ได้ประเมินความชุกของการใช้หมากในหมู่นักเรียนอายุ 13-17 ปีที่ 65.8 เปอร์เซ็นต์ โดยพบว่า 48.9 เปอร์เซ็นต์โดยวิธีการเคี้ยวหมาก นอกจากนี้ผลสำรวจระดับโลกเรื่องการใช้ยาสูบในวัยรุ่น (Global Youth Tobacco Survey, GYTS) ของภูฏานในปี 2019 ระบุว่า 56.9 เปอร์เซ็นต์ของนักเรียนวัยรุ่นอายุ 13-15 ปี มีการบริโภคหมากหรือผลิตภัณฑ์ต่างๆ ที่มีหมากเป็นส่วนผสม ในทำนองที่คล้ายคลึงกันในรายงาน WHO STEPS 2019 แสดงให้เห็นความชุกของการใช้หมากในกลุ่มอายุ 15-69 ปี ร้อยละ 56.8 อย่างไรก็ตามการศึกษาเชิงวิเคราะห์เกี่ยวกับปัจจัยที่เกี่ยวข้องกับความชุกสูงนี้โดยใช้ข้อมูลที่ล่าสุดนั้นยังมีน้อยมากและไม่ได้รับการปรับปรุงให้เป็นปัจจุบัน ดังนั้นวัตถุประสงค์ของการศึกษาเพื่อการประเมินความชุกของการใช้หมากและสถานะทางสุขภาพของบุคคลและพฤติกรรมทางสังคมที่เกี่ยวข้องในปีล่าสุด

วิธีการศึกษา: งานวิจัยนี้เป็นการศึกษาภาคตัดขวางเชิงวิเคราะห์ข้อมูลทุติยภูมิที่รวบรวมจากรายงานการเฝ้าระวังปัจจัยเสี่ยงโรคไม่ติดต่อที่เป็นตัวแทนระดับประเทศของการสำรวจ WHO STEPS ปี 2019 ของภูฏาน ซึ่งดำเนินการในหมู่ชาวภูฏานอายุ 15-69 ปี โดยการสำรวจมีผู้เข้าร่วมทั้งหมด 5575 คนที่ผ่านการคัดเลือกแบบสุ่มตัวอย่างแบบแบ่งชั้นหลายขั้นตอน โดยวิเคราะห์ตัวแปรการความชุกของใช้หมากในปัจจุบัน การวัดพฤติกรรมส่วนบุคคลและสถานะสุขภาพส่วนบุคคล และ ใช้สมการวิเคราะห์ปัจจัยเดี่ยว และสมการถดถอยลอจิสติกแบบหลายตัวแปร เพื่อหาความสัมพันธ์ของปัจจัย

ผลการศึกษา: พบว่าความชุกของการใช้หมากในปัจจุบันคือ 56.82 % (95% CI: 54.27-59.33) ของประชากรภูฏานอายุ 15-69 ปี พบความชุกสูงขึ้นอย่างมีนัยสำคัญที่ 63.58 % (95 % CI: 60.58 - 66.48) ในกลุ่มอายุ 25-39 ผู้สูบบุหรี่ที่มีแนวโน้มที่จะใช้หมาก 17% เมื่อเทียบกับผู้ที่ไม่บริโภคยาสูบ (aOR 1.17 , p=.0001) ในทำนองเดียวกัน ผู้บริโภคเครื่องดื่มแอลกอฮอล์ในอดีต คือ 12% และผู้บริโภคเครื่องดื่มแอลกอฮอล์ในปัจจุบันมีแนวโน้มที่จะบริโภคหมากมากขึ้น 45% เมื่อเทียบกับผู้ที่เลิกบริโภคแล้ว โดยภาพรวมของการวิเคราะห์ปัจจัยแล้ว พบว่าอายุ การดื่มแอลกอฮอล์และการสูบบุหรี่สัมพันธ์กับการใช้หมากหรือหมาก

สรุปผลการศึกษา: จากผลการวิจัยชี้ให้เห็นว่าประชากรภูฏานมากกว่าครึ่งยังคงบริโภคหมากอยู่ในวัยเยาวชนและวัยกลางคนรวมถึงผู้ใช้แอลกอฮอล์และผู้ใช้ยาสูบนั้นควรเป็นกลุ่มเป้าหมายในการริเริ่มการแทรกแซงเชิงการเปลี่ยนพฤติกรรมสุขภาพ รวมถึงการจัดการแบบหลายภาคส่วนในการควบคุมการค้าของผลิตภัณฑ์ที่มีหมากเป็นส่วนผสมและกำหนดมาตรการเพื่อควบคุมการใช้หมากในประเทศ

สาขาวิชา	สาธารณสุขศาสตร์	ลายมือชื่อนิสิต ....
ปีการศึกษา	2565	ลายมือชื่อ อ.ที่ปรึกษาหลัก ....
		ลายมือชื่อ อ.ที่ปรึกษาร่วม ....

6574023853 : MAJOR PUBLIC HEALTH

KEYWORD: Areca nut, Betel, Prevalance, Bhutan

Tashi Penjor : PREVALENCE OF BETEL OR ARECA NUT (AN) USE AND ITS ASSOCIATED FACTORS AMONG BHUTANESE POPULATION AGED 15-69 YEARS OLD: AN ANALYSIS OF NATIONAL HEALTH DATA OF NON-COMMUNICABLE DISEASE (NCD) SURVEY IN 2019. Advisor: Assoc. Prof. Dr. WATTASIT SIRIWONG, Ph.D. Co-advisor: Prof Dr. Mark G. Robson, Ph.D.

Background: Although betel or areca nut use has less global attention and public health concern than smoked tobacco uses, but it is particularly one of a neglected public health problem in Bhutan in which the masticatory use of betel is rampant and epidemic. Its use is also directly infused in Bhutanese tradition and social fabric. There are currently no policies that specifically target the regulation and consumption of areca nut use and trade in Bhutan, while it is classified as carcinogenic to human by the WHO (International Agency for Research on Cancer, IARC) in 2004. Series of national surveys have consistently shown high prevalence of betel or areca nut use in Bhutan. The National Health Survey (NHS) of Bhutan 2021, found that 43.9 percent of Bhutanese aged 15-75 years old used areca nut in the form of betel quid. In 2016, the Global School–based Student Health Survey (GSHS) assessed the prevalence of areca nut use amongst students aged 13-17 years old at 65.8 percent with 48.9 percent chewing betel quid. Furthermore, the Global Youth Tobacco Survey (GYTS), Bhutan on 2019 indicated that 56.9 percent of adolescent students aged 13-15 years consumed betel nut or various product containing it. Likewise, the WHO STEPS 2019 reported prevalence of areca nut users at 56.8 percent amongst 15-69 years old. However, analytical studies pertaining to the factors associated with this high prevalence using the latest data were significantly rare and not updated. The objective of the study is to assess the prevalence of betel or areca nut use and its associated socio-demographic, personal behavioural and individual health status in recently year.

Methods: This is an analytical cross-sectional study. The secondary data collected in a nationally representative Non-communicable Disease Risk Factor Surveillance WHO STEPS Survey 2019 of Bhutan conducted among Bhutanese aged 15-69 years old. The survey included a total of 5575 participants; selected through a multistage stratified cluster sampling. The outcome variable of interest is current betel or areca nut use. Weighted analysis was done to calculate the prevalence of betel or areca nut use, personal behavioural measurements, and individual health status. Univariate and multiple logistic regression were performed to identify correlates for betel or areca nut use and to estimate the unadjusted and adjusted odd ratios.

Results: The prevalence (weighted) of current betel or areca nut use was 56.82 % (95% CI: 54.27-59.33) of Bhutanese aged 15-69 population. Significantly higher prevalence of 63.58 % (95 % CI: 60.58 - 66.48] were found in the age group 25-39 years. Tobacco users are 17% more likely to use betel nut as compared to those who don't consume tobacco (aOR 1.17, p=.0001) Similarly, former alcohol consumers were 12% and alcohol consumers were 45% more likely to consume betel nuts as compared to lifetime abstainers. Associated factors to betel or areca nut use i.e age, alcohol use and tobacco use were found.

Conclusion: The findings indicate that more than half of the Bhutanese population consume betel or areca nut. Young and middle-aged individuals, Alcohol users and tobacco users should be targeted with public health initiatives and behavioural interventions. Including, a multisectoral approach to regulating areca nut trade and commerce should be initiated while also forming measures to national control betel or areca nut use.

Field of Study:	Public Health	Student's Signature ....
Academic Year:	2022	Advisor's Signature ....
		Co-advisor's Signature ....

ACKNOWLEDGEMENTS

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CHAPTER ONE: INTRODUCTION

1.1   BACKGROUND

The consumption of areca Nut (AN) or commonly known betel nut1 is a social habit and cultural practice endemic in Bhutan, as it is in most countries of Asia and the Pacific Region, where the "use of areca nut is strongly interwoven in local art and craft, folklore, social customs, religious practices and cultural rituals" (Gupta & Warnakulasuriya, 2002).

Considering its addictive nature, it is the fourth most self-administered and universally abused psychoactive substance and widely accepted masticatory product after nicotine, ethanol and caffeine (Sharan et al., 2012). Current available studies estimate that up to 600 million individuals chew areca nut and that approximately 10-20 % of the global population use areca nut in some preparation and mostly the form of betel quid (Gupta & Warnakulasuriya, 2002). A study by Boucher & Mannan (2002) mentions that almost one-tenth of the global population chew areca nut regularly. Another study, however, estimates that the global areca nut users stand in between 200-400 million chewers and concentrated mainly to "IndoAsians and Chinese" (Warnakulasuriya et al., 2002). In tandem with the variations in the estimates of areca nut users, it should also be timely and significant to question the relevance of these estimates given the aggressive commercial marketing and diversification of products using areca nut as the primary ingredient.

The WHO Framework Convention on Tobacco Control (FCTC) defines a list of 34 smokeless tobacco (SLT) out of which 10 SLT contains areca nut as a primary

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1 The IARC (2004) does not recommend the use of the term 'betel nut' as a synonym for areca nut as it is not botanically correct and for the reason that it caused "considerable confusion in the scientific literature" and hence should be avoided. Therefore, during the rest of the document the term areca nut will only be used. Francoise Pommaret (2005) a notable researcher on Bhutan also argues the wrong impression of most westerners in considering betel as the areca nut.

composition or used with areca nut. SLT are used by more than 300 million individuals worldwide with the highest concentration and prevalence in South and South-east Asia which also has the greatest product diversity of SLT and areca nut. The South –east Asian region also bears the highest burden of disease from using SLT (Siddiqi et al., 2020). The study also highlights high consumption by males in Bhutan (26.5%) corroborating the high incidence of male oral and esophagus cancer in Bhutan (Ministry of Health, 2019) as shown in the figure 2.

Figure 1: Average annual incidence of top 10 cancer per 100,000 population in Bhutan (2014-2018)
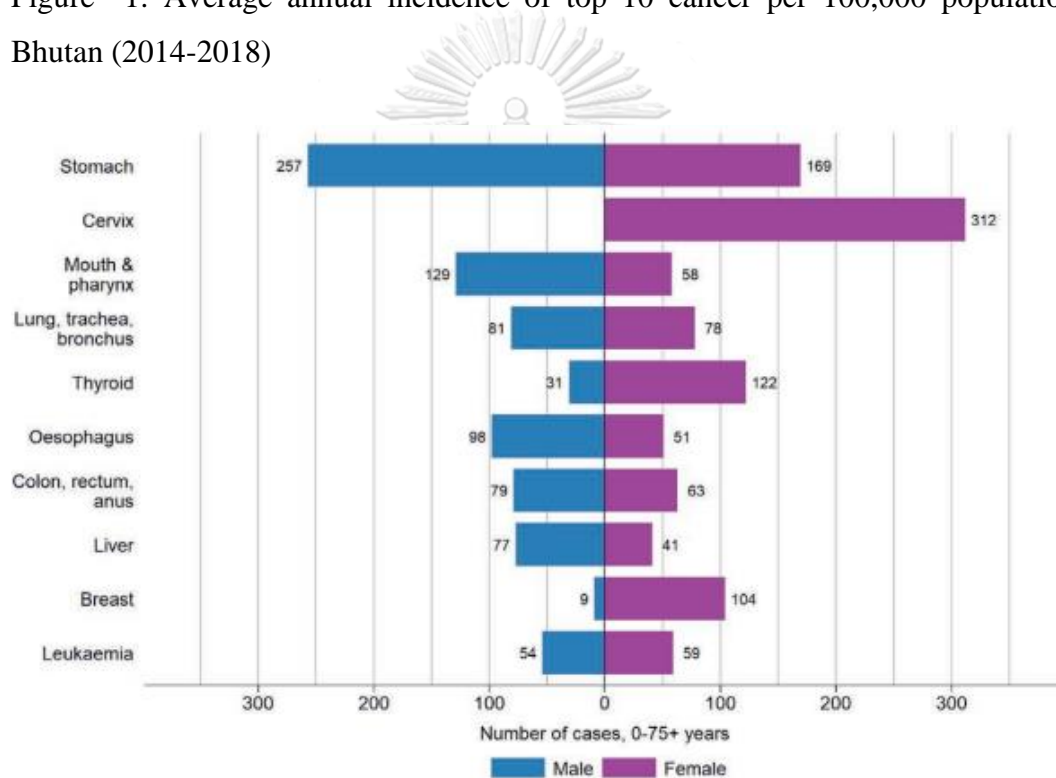
Source: Replicated from Bhutan Cancer Control Strategy

Globalization and international trade have made its access easy and affordable to the wider segment of the population. Several studies consistently show that Asian-migrant communities are hugely responsible for importing the practice and expanding its consumption in other parts of the world (Boucher & Mannan, 2002; Gupta & Ray, 2004; Warnakulasuriya & Peters, 2002). This is a worrying scenario given the flexibility and fluidness of international migration and the increasing evidence of high mortality and morbidity attributed to the use of areca nut in itself and other

forms/mixtures. Therefore, global use of areca nut use is expected to have increased over time given the access and affordability compounded by the age-old tradition and cultural significance in most endemic countries.

In many low income countries, the import and production is also encouraged for economic prospect. In 2021, Bhutan observed a huge parliamentary debate over areca nut trade and local commercial production involving the Prime Minister of Bhutan. The Royal Government of Bhutan (RGoB) initiated a mass fermentation and encouraged farmers to adapt the process to make the freshly picked areca nut useable and marketable.[2] Consequently, areca nut is considered one of the commodities, implicitly, identified for import substitution and employment generating commercial activity in Bhutan.

Bhutan produces about 15,000 tonnes of areca nut besides increasingly huge import annually, mostly from India, not only causing public health concerns but also draining foreign exchange reserve on such non-essential item. The table below shows two consecutive years import of areca nut and related products:

Figure 2: Areca nut imports to Bhutan in 2020 and 2021
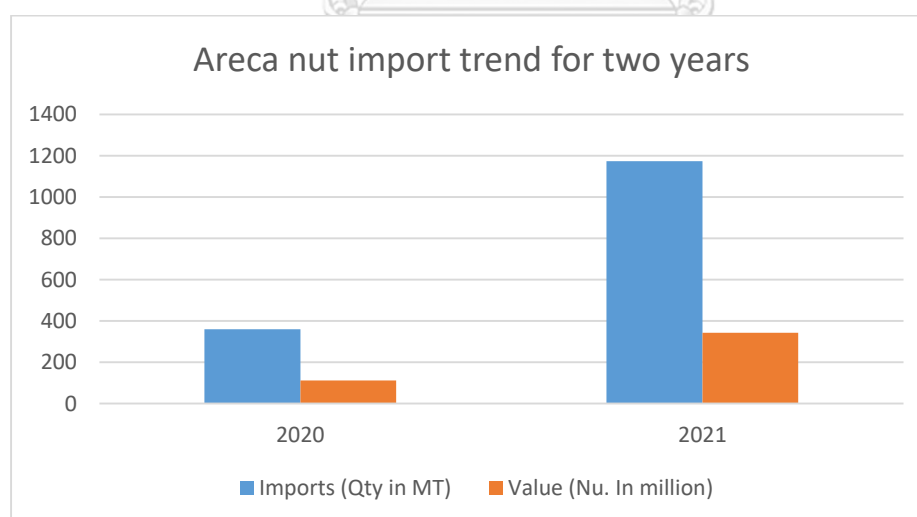
Source: Adapted from Bhutan Trade Statistics 2020 & 2021.

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[2] This was reported by the Prime Minister of Bhutan to a question raised by a Member of Parliament on what efforts the RGOB is initiating to increase the livelihood of farmers growing areca nut and widely broadcasted in the national print and broadcast media such as The Bhutanese, Kuensel and the Bhutan Broadcasting Service.

A simple analysis of the figure presents that areca nut consumption has increased by more than three times in one year with an equivalent loss of foreign exchange reserve for an unproductive economic trade. If Bhutan continues to experience this level of areca nut trade and its use, both of which are unregulated, the economic consequences and its impact on human health in the long term will be non-justifiable and significant for a small nation which is landlocked and resource constrained.

Recorded history clearly mentions the areca nut use as far back as 1673 and that it was imported from India and hence not indigenous to Bhutan (Pommaret, 2003). The consumption and access, then, were limited to influential and higher levels of society. Considering its rarity and hierarchical significance, areca nut and/or betel quid was usually granted as a gift from the aristocrats to the common people as a token of appreciation or goodwill. Such was the value and significance of betel quid in Bhutanese society.

It was only in the 1960s that the cultivation of areca nut cultivation started as favorable conditions prevailed when Bhutan initiated its first five year development plan around the same time period. Bilateral trade with neighbouring India also contributed to an increased access and affordability as shown in figure 2.

Betel or areca nut is commonly used by chewing areca nut along with slaked lime and various other additives, such as tobacco, betel leaf (Piper betel L.), and spices. The most common and traditional form of its use in Bhutan is a combination of the areca nut enclosed and rolled in betel leaf (Piper betel L.) on which slaked limed is smeared. The quid obtained from this simple combination is and lavishly available is called *doma/ doma khamtog*.

Francoise Pommaret (2003), a French anthropologist whose research focused on Bhutan, provides in detail the first written account on the origin and importance that areca nut and betel quid holds in the Bhutan. She highlights the almost mandatory offering of betel quid during social interactions and/or as a necessary item in ceremonial events, marriage or promotion, inclusive. Therefore, any attempt to

discriminate its consumption can be seen as an act of disregard to the Bhutanese culture. She further informs its use as an informal customary leitmotif each time when two individuals meet or after meals and as an item for leisure. The assumingly therapeutic properties from consumption of areca nut s are explained in its role in providing constipation relief, improve concentration and alertness and warmth during the harsh winters of Bhutan.

It is the widely accepted addictive substance in Bhutan while tobacco in general is strongly despised. Despite its tradition and cultural significance, the use of betel or areca nut poses significant health risks. Several studies have linked betel or areca nut consumption to a range of adverse health effects, including oral submucous fibrosis, oral cavity and pharyngeal cancers, periodontal diseases, cardiovascular diseases, and addiction, which is presented in chapter two.

The WHO working group of the International Agency on Research for Cancer (2004) provided their overall evaluation with sufficient evidence in humans as well as experimental animals proving the carcinogenicity of areca nut use and betel quid and classified areca nut as Group 1 human carcinogens.[3]

1.2   PROBLEM STATEMENT

The widespread use of areca nut is further exacerbated by the lack of regulation and policy, globally and in Bhutan. The WHO FCTC provides guidelines, policy options and recommendation to member states in their effort to reduce tobacco use including a specific protocol, concurred by the member states in 2012, to eliminate illicit trade in tobacco products. However, it does not target areca nut and betel use as a specific item for control and regulation. As such there is almost a complete absence of internationally agreed and negotiated instrument or global policy to control areca nut use and betel quid. Bhutan too, does not have any policy to control and regulate the

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[3] This means that areca nut consumption is carcinogenic to humans and that there is enough evidence to conclude that it can cause cancer in human.

use and trade of areca nut and products. The only regulation is the imposition of an indirect tax of 50 percent custom duty and 20 percent sales tax at the point of entries (Ministry of Finance, 2022). The Tobacco Control Act of Bhutan and the National Health Policy does not mention areca nut in their provisions for control and regulation. The health ministry lacks a strategy or an action plan to address the areca nut use concerns in Bhutanese. Quite interestingly there are also no cessation support interventions available in the existing health system. There is also little appreciation by policy makers and officals to consider this as a neglected public health problem, primarily, as they fail to find evidence of its impact on public health in Bhutan. Moreover, it is culturally engrained and widely used by respected segments of the population such as the monk body.

Existing policies and regulations in Bhutan especially those relating to health and tobacco control does not address the concern of smokeless tobacco including the wide use of areca nut and quid. Multidisciplinary research is of urgency to garner partnership and efforts to initiate regulatory mechanism and policy options. To seek the attention of the authorities in Bhutan, an initial study to associate areca nut users and build its profile with individual health status and health behaviors will provide the much required information to trickle interest in this neglected area of public health concern in Bhutan.

Several studies have scientifically established that, BQ with or without any additives such as tobacco, are clinically associated with increased risk for the development of cancer further supporting the evidence of the IARC's classification of areca nut in Group 1 carcinogen (IARC, 2004). The masticatory habit of areca nut consumption was found to have a "strong etiological correlation with human susceptibility to cancer, particularly oral and oropharyngeal cancers" (Sharan et al., 2012).

In Bhutan, oral and esophagus cancers fall within the top ten cancer incidence (Ministry of Health, 2019) and a possibility to study the association of areca nut users in Bhutan to cancer is an opportunity. Research, specific to Bhutan, is therefore, required to provide adequate evidence to provide association and causality of areca

nut use to cancer and its association with individual health status and personal behavioral such as alcohol and smoking status to bring together public health policies and clinical interventions to address this unregulated social habit.

All nationally representative surveys in Bhutan confirms statistical evidence of high consumption of areca nut and/or quid. As per the report of the Global School-based Student Health Survey (GSHS) 2016, 48.9 percent of the adolescent students aged 13-17 years in Bhutan currently chew quid and 65.9 percent use areca nut in the form of any other products. The GSHS findings aligns with a youth tobacco survey in 2019, where 48.9 percent students in grade 7-11 and within the age range 13-15 years currently chew quid while 56.9 percent use areca nut and various products containing it (World Health Organization, 2020).

Considering the similarity in the addictive nature of areca nut with nicotine addiction (N. Chatterjee & H. A. Gupte, 2023) and evidence that those who initiate tobacco use early in life tend to have lower odds of quitting during their life time (Lal et al., 2016), the high prevalence of areca nut users among adolescent students aged 13-17 years old in Bhutan is a cause of concern requiring immediate interventions at both the individual and schools.

A homegrown survey to measure happiness estimated an alarming number of 250,000 adult Bhutanese, which is one third of the entire population, consuming areca nut and chewing quid (Bhutan Broadcasting Service, 2012).

The WHO STEPwise approach to NCD risk factor surveillance (STEPS) in Bhutan 2014 indicated a prevalence of 6.1 percent of Bhutanese aged 18-69 years old chewing betel quid with tobacco (World Health Organization, 2015). A multi country analysis of data from 127 countries to estimate the global burden of diseases due to smokeless tobacco consumption estimated that atleast 26.5 % of Bhutanese men use smokeless tobacco in combination with betel or areca nut (Siddiqi et al., 2020). Consistent results revealing high prevalence of areca nut in use in Bhutan is a strong evidence to call for further exploration with demographic, physical and biochemical

variables to generate stronger intervention and solutions targeted to regulate access and reduce consumption.

Bhutan has a strong repository of nationally representative surveys relating to areca nut use and associated products. However, a nationally representative study was rarely undertaken using these data to generate evidence for public health intervention and policy making.

A thesis was completed in 2004 but was limited to students in grade 7-11 and concentrated in only one district,[4] which showed prevalence of chewing betel at 59.1 percent and that 60 percent generally chew at home with the indication that home environment and influences from older siblings and friend impacts betel nut use (Wangchuk, 2004). Another research limiting the study population to health care providers and taking sample from a particular hospital in Bhutan showed the prevalence of betel quid chewing at 26.6 percent drawing comparable conclusion that betel quid use is positively associated with family ecosystem, alcohol drinking and smoking (Dorji et al., 2012). A similar retrospective secondary data analysis using the National Health Survey (2012) reported that the prevalence of current betel quid use in Bhutan was 45.4 percent and that alcohol use and smoking was associated with chewing betel quid (Wangdi & Jamtsho, 2020). A recent study by Patel et al. (2023) reported that in Bhutan the use of areca nut is "associated with morbidity and mortality due to carcinogenic effects of its ingredients" and ease of access to areca nut.

As such there are no studies using the data available from the WHO STEPS, in general, and 2019 survey, in particular. Past few researches mentioned above did not study the associated factors including socio-demographic, individual health (status) and health behavioral factors related to areca nut use in Bhutan.

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[4] The study was done as a thesis for Master of Public Health at the College of Public Health sciences in 2004 by Mr. Norbu Wangchuk titled "The practice of betel nut chewing among the students grades 7 up to 11 from the secondary government schools in Thimphu, Bhutan".

There is significant research gap and hence the current study is timely and urgent to provide findings and quantitative evidence on the prevalence of areca nut use and set the context for further exploration to encourage prevention and cessation interventions and set agenda for national policy setting.

It will also be an attempt to analyze areca nut use from a health perspective on which there are only few scientific studies in Bhutan.

1.3   RESEARCH QUESTION

The study seeks to determine the following:

  a.   What is the prevalence of betel or areca nut use among Bhutanese aged 15-69 years?
  b.   What are the associated factors of the betel or areca nut use among Bhutanese aged 15-69 years?

1.4   RESEARCH OBJECTIVES

The study seeks to establish the following by analysis of data of the NCD STEP Survey (2019) of Bhutan:

1.4.1   GENERAL OBJECTIVE

The general purpose of the study is to determine the prevalence of betel or areca nut use in Bhutan and its associated factors.

1.4.2   SPECIFIC OBJECTIVE

The specific objectives are as follows:

  1.   To determine the prevalence of betel or areca nut use among individuals (15-69 years) in Bhutan
  2.   To identify the associated factors including the socio-demographic, individual health (status) and health behavioral factors related to betel or areca nut use among individuals (15-69 years) in Bhutan.

1.5 HYPOTHESIS

The hypotheses for the given specific objective is as follows:

1. H_O: There is no significant association between betel or areca nut use and socio-demographic, individual health (status), and health behavioral factors among individuals (15-69 years) in Bhutan.

   H_a: There is a significant association between betel or areca nut use and socio-demographic, individual health (status), and health behavioral factors among individuals (15-69 years) in Bhutan.

The study aims to analyze the WHO STEP survey (2019) of Bhutan and present statistical findings to either support or reject these hypotheses.

1.6 CONCEPTUAL FRAMEWORK

Figure 3: Conceptual framework of the study
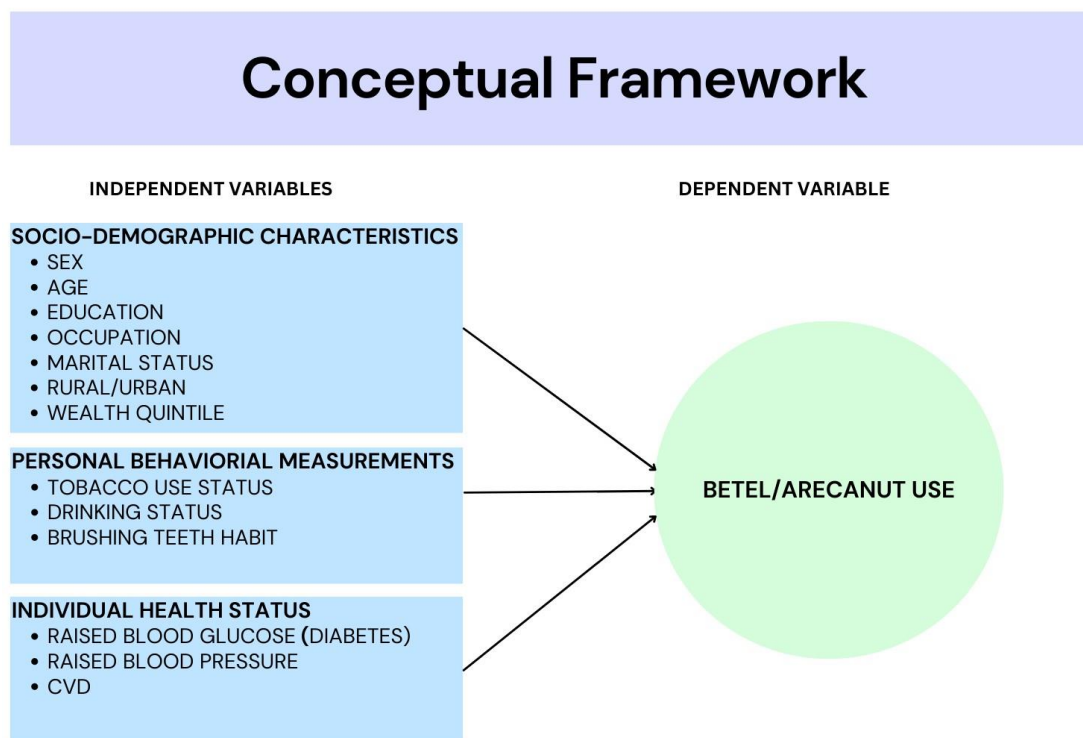
1.7   OPERATIONAL DEFINITIONS

The operational definition for the key variables analyzed, examined, and measured in this study are:

Age:

Age of the participant, calculated as interval of time between the date of birth and the date of the survey, expressed in completed solar years.

Betel or Areca nut use:

For the purpose of this study, betel or areca nut use means the consumption of areca nut in isolation, betel quid (*doma*, *paan*)[5] and products containing areca nut as the primary ingredient (*supari* and others).[6] |The current use of betel is taken as the dependent variable.

The current use of betel or areca nut is considered as per the STEPS survey questionnaire design. Although the NCD STEPS survey doesn't explicitly define the current user. The respondents are simply asked if they currently use betel nut or not, therefore, respondents would be categorized as current user irrespective of frequency and quantity of betel nut so long the respondents report that they currently use it. The NCD STEPS survey usually similar definition for tobacco use. Frequency of betel or areca nut use is defined as the number of areca nut or betel consumed in a day.

Brushing Teeth Habit:

The frequency of cleaning teeth (daily or more, less than daily, and never) is considered as brushing teeth using a tooth brush and paste. Those who did not brush

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[5] Most commonly in Bhutan, the quid obtained from the simple combination of areca nut rolled in betel piper L. on which slaked lime is applied is called *doma/ doma khamtog*. In some instances a small piece of dried coconut is also chewed together.
[6] Dried areca nut containing products flavoured with catechu, tobacco (in some products) and commercially marketed in Bhutan.

their teeth atleast once in the last one month are considered as having "Never" brushed their teeth.

Cardio-vascular disease (CVD):

Any incident of suffering from heart attack or chest pain from heart disease or stroke is considered as CVD.

Generally, CVDs are a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other condition (Department of Public Health, 2020).

Drinking Status:

Used as a personal behavioral measurement to check for episode of alcohol use. Alcohol consumption, whether commercial or home-brewed, in past 12 months is defined as "current" user; those who reported drinking in the past but didn't drink in the past 12 months are defined as "Former", and those who didn't drink alcohol currently or formerly is defined as "Life-time abstainer".

Household/Usual household members:

Household is defined as a person/group of persons, with a head of household and who live (or are likely to live) together in the same dwelling unit and share same living arrangements for atleast six months.

Raised Blood Glucose:

Sample collected after a 12 hour fasting with the following are considered raised blood glucose level:

1. Fasting blood glucose >=126 mg/dl during the study
2. Fasting blood glucose <126 mg/dl but currently taking medications to lower blood sugar based on previous diagnosis

Raised Blood Pressure:

History of blood pressure (systolic and diastolic) measurement and treatment during the past two weeks are asked. Three readings are done and mean of second and third readings are taken for analysis purpose with the following levels as raised blood pressure:

1. systolic blood pressure ≥140 mmHg and/or
2. diastolic blood pressure ≥90 mmHg)

Tobacco Use Status:

Tobacco use is defined as the use of any tobacco product (both smoked and smokeless tobacco). Smoking of any tobacco products such as cigarettes, *bidis*, pipes or cigars including the use of smokeless tobacco such as snuff, chewing tobacco, or betel, quid with tobacco), is considered as current user.

Wealth Quintile:

Household wealth, as a valid marker of economic status and not as a direct assessment of household income, assessed based on selected household characteristics such as possession of selected consumer goods, ownership of luxury cars (SUV), materials used for wall, floor and roof construction and number and type of domestic animals owned, amongst others.

The household scores were then derived using principal component analysis and dividing the distribution into five equal categories.

CHAPTER TWO: LITERATURE REVIEW

This chapter presents a summation of the available scientific evidence, scholarly findings and literature related to areca nut, its chemical composition and metabolic effects on the human body including health impacts from its use. These are aligned to the variables defined in the conceptual framework of the study.

2.1   ARECA NUT

Areca nut, known as *Doma* in Bhutanese, is the seed of the fruit of the *Areca catechu L.* palm tree. The areca palm is native to South Asia and is also found in several South-East Asian countries and Pacific islands. It is grown along the southern part of Bhutan bordering India, for its economic value. Areca nut is also commonly known as betel, although the use of the term should be avoided as it is botanically incorrect and is a concern for causing confusion in the scientific literature (IARC, 2004). Pommaret (2005) also supports that using the term synonymously causes confusion and incorrect impression of considering betel as areca nut. Hence, in this study, betel or areca nut use means the consumption of areca nut in isolation, betel quid and products containing areca nut as the primary ingredient.

Areca nut is generally orange-yellowish in colour when ripe and is usually consumed fresh after removing the fibrous pericarp or consumed after fermentation, in Bhutan. The fresh areca nut is called *Doma Kang*za and the fermented version is known as *Doma Muza*, the latter of which is very prominent in the market and palatable to the Bhutanese consumers.

As per the most recent data available on the Food and Agriculture Organization of the United Nations (FAO), in 2021 alone, the global production of areca nut alone stands at approximately 1.61 million tonnes using an area of over 2.53 million hectares of land (FAO, 2023,June). Compared to a decade ago, this is a 2.6 fold increase in the production, which is an indication of increased prevalence of areca nut use, while there was only a minute increase in area used as shown in the figure below:

Figure 4: Time series trend in areca nut production and area used: Global(2012-2022)
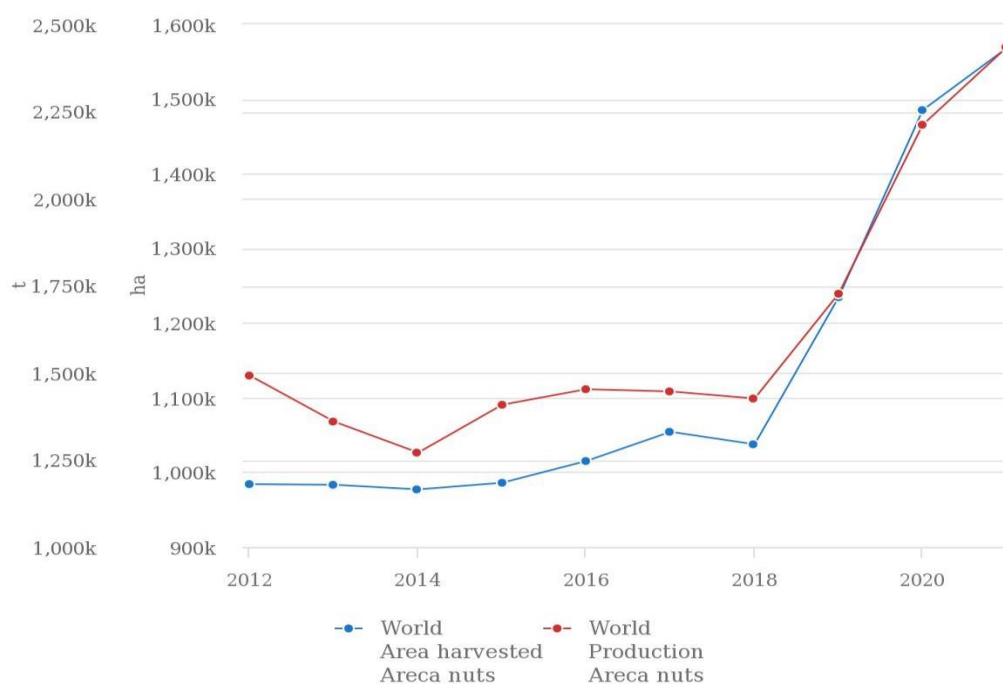
Over the same time period, similarly trend in production of areca nut was observed in Bhutan but with simultaneous increase in the area used.

Figure 5: Time series trend in areca nut production and area used: Bhutan (2012-22)
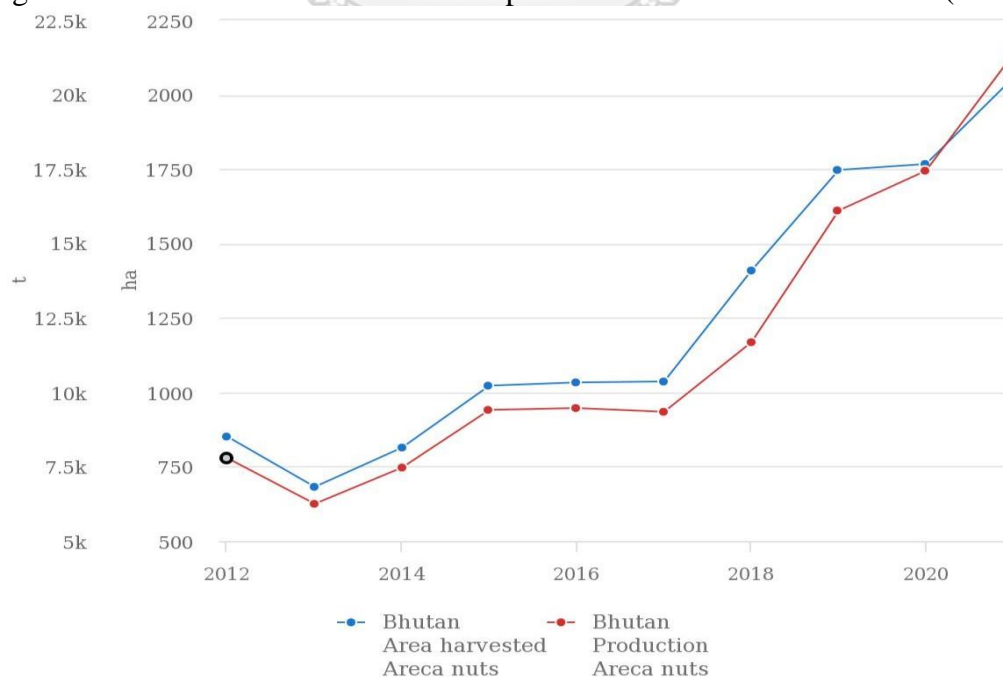
2.2   ARECA NUT USE IN BHUTAN

The use of betel or areca nut dates back to the 16th century, when it was introduced as an item of distribution in the order of service during *Zhugdrel*[7] ceremony to extend and express hospitality and friendship to, *Zhabdrung Ngawang Namgyel*, the founding father of Bhutan (The Centre for Bhutan Studies, 2009). This event, officially, marked the initiation of including areca nut use in Bhutanese tradition, culture and religion and became part of both religious and secular affairs. The widespread use of betel quid and areca nut in Bhutan is attributed to various cultural, social and economic factors, such as poverty, low levels of education, lack of awareness about its health risks, and social pressure (Dorji et al., 2012). A small scale study assessing the correlates of cessation of betel quid revealed a strong correlation between the family and health risk behaviors and quitting of betel quid (Dorji, 2017). The degree to which the society willingly accepts areca nut use in Bhutan is the greatest hindrance to reduce the consumption and to implement or design policies and interventions.

Despite its cultural significance, the use of areca nut has become a public health concern due to its attribution to the high incidence of "other commoner cancers of head and neck, such as the oral cavity, hypopharynx, larynx and oropharynx" (Tshering et al., 2020). Several studies also establish the association of areca nut use to cancers such as oral, oropharyngeal, esophagus and stomach including its association with diabetes and raised blood pressure (Arora & Squier, 2019; Asthana et al., 2019; Guha et al., 2014; R. Gupta et al., 2018; Yu et al., 2022).

Worldwide there are variations in the way areca nut is consumed. The IARC monographs (2012), building on their previous monographs where areca nut was considered, prepared the following composition of areca nut use, worldwide:

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[7] A traditional ceremony, significantly infused with Buddhist religious blessings, and performed during initiation of any important activities such as promotion, welcoming guests, house construction etc. Part of which entails offering different varieties of fruits and nuts, including areca nut and betel leaves.

Figure 6: Composition of chewing substances containing areca nut globally

	Areca nut[a]	Betel[b]			Catechu[d]	Tobacco[e]	Slaked lime
		Leaf	Inflorescence	Stem[c]			
Areca nut	X						
Betel quid without tobacco	X	X			(X)[f]		X
Betel quid with tobacco	X	X			(X)[f]	X	X
Gutka	X				X	X	X
Pan masala[g]	X				X		X
Mawa	X					X	X
Mainpuri tobacco	X					X	X
Lao-hwa (Taiwan, China)	X[g]		X				X
Betel quid (Taiwan, China)	X[g]	X					X
Stem quid (Taiwan, China)	X[g]			X			X

[a] May be used unripe, raw or processed by baking, roasting or baking with sweetening, flavouring and decorative agents (see Table 1.2)
[b] In place of the leaf, the inflorescence or its stem may also be used (see Table 1.2)
[c] Stem of inflorescence
[d] In powdered or paste form (see Table 1.2)
[e] In flaked, powdered or paste form, with or without processing, with or without sweetening (see Table 1.2)
[f] (X) means optional
[g] Used in unripe form
Adapted from IARC (2004)

Source: IARC 2012

Additionally, areca nut can be consumed in various forms, with or without tobacco, such as sweet *supari*, *chali*, *paan*, and *khara* (Gupta & Warnakulasuriya, 2002). Bhutanese commonly consume the quid from combining areca nut enclosed in a betel piper L. on which slaked lime is applied. Some common forms or compositions of areca nut chewed in Bhutan are shown below:

Figure 7: Composition of chewing substances containing areca nut in Bhutan
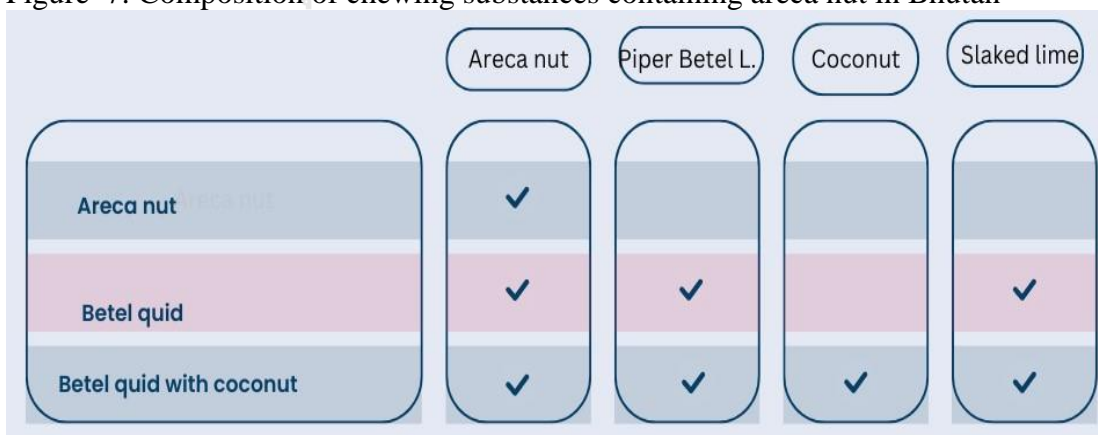
All national surveys have consistently shown that areca nut use in Bhutan is high with prevalence consistently ranging approximately from 45- 66 percent.

1. The National Health Survey (NHS) of Bhutan (2012) found that 43.9 percent of Bhutanese aged 15-75 years old used areca nut in the form of betel quid.

2. The 2016 Global School–based Student Health Survey(GSHS) (2017) assessed the prevalence of areca nut use amongst students aged 13-17 years old at 65.8 percent with 48.9 percent chewing betel quid.

3. The Global Youth Tobacco Survey (GYTS), Bhutan, 2019 indicated that 56.9 percent of adolescent students aged 13-15 years consumed "betel nut or various product containing it" (World Health Organization, 2020).

The survey results explicitly show that areca nut use and specifically betel quid chewing is epidemic and that all sections of the society ranging from 13-75 years old captured within the scope of the surveys significantly consume areca nut, betel quid and products containing areca nut.

Despite its classification as a Group1 carcinogen and its sustained epidemic use, areca nut use, trade and commerce in Bhutan is extremely unregulated and widely available in the market to all ages without restriction.

2.3   CONSTITUENTS OF ARECA NUT AND CARCINOGENICITY

The predominant chemical ingredients in areca nut are carbohydrates, fats, proteins, crude fiber, polyphenols such as tannins and flavonols, alkaloids such as arecoline and mineral matters such as copper, bromine, magnesium. These are well documented in an authoritative study undertaken in an IARC monograph dedicated to assessing the evidence of carcinogenicity of areca nut constituents to human (IARC, 1985).

The main constituents found in areca nut and betel quid, which often include the areca nut as one of its main components are as follows:

2.4.1   ALKALOIDS:

The alkaloids in areca nut; arecoline, arecaidine, guvacoline and guvacine, are strongly linked to the areca nut induced carcinogenetic and addictiveness

(Senevirathna et al., 2023). Arecoline, which is the most abundant and predominant alkaloid in areca nut, and is "believed to have systematic effects including cancer" (Dorji, 2017) and was recently classified into Group 2B "possibly carcinogenic to humans (IARC, 2021) on the basis of "sufficient" evidence of carcinogenicity in experimental animals and "strong" mechanistic evidence" (Marques et al., 2021). Arecoline in areca nut was also determined to cause major psychoactive effects, parasympathetic and muscarinic effects, mainly stimulating the nicotinic receptors. It is also linked to causing increased heart rate and blood pressure irrespective of the frequency of usage (Garg et al., 2014). Studies show that it is the primary chemical component contributing to the carcinogenic nature of areca nut (Liu & Chang, 2023).

Arecoline is also an activator of the nicotine addiction causing brain receptors and hence can also be considered the cause of areca nut addiction. Studies has shown that it has led to severe physical dependence and withdrawal symptoms similar to those of nicotine addiction and that it encourages users to add tobacco to existing areca nut use (Nilesh Chatterjee & Himanshu A Gupte, 2023).

2.4.2 POLYPHENOLS:

Areca nut and betel quid both contains multiple polyphenol compounds, including flavonoids, catechins, and phenolic acids. The majority of these compounds are proven to have potential health benefits.

2.3.2.1 *Flavonoids*:

Of the 11 flavonoids separated from areca nut, nine are found to have positive health benefits with pharmacological activities during its metabolism. However, there are evidence that two flavonoids from areca nut (calquiquelignan N and calquiquelignan M) provide cytotoxicity to human cancer HepG2 cell line (Liu & Chang, 2023; Yuan et al., 2019)

2.3.2.2 Tannins:

Another major polyphenol compounds found in areca nut and betel quid are tannins. An assessment by Maugeri,A. et. al (2022) found that tannins have pharmacological

use and health benefits through its "anti-inflammatory, anti-bacterial, antioxidant and anticancer effects and prevents CVD, neuroprotective and general metabolic diseases" and potential treatments including for diabetes and oral diseases from all the 12 tannins separated from areca nut (Liu & Chang, 2023). Tannins are also attributed to the unique taste of areca nut and play a key role in the development of the characteristic red stain from chewing betel quid.

2.4.3   NITROSAMINES:

Nitrosamines are exhibited in the saliva of both areca nut users and betel quid chewers, with prominent exposure by the later. The nitrosated derivatives of alkaloids, such as guvacine, was found to cause oxidative stress as well as DNA breaks ultimately leading to oral carcinogenicity (Zhang et al., 2022).

The detailed study of areca nut derived nitrosamines in saliva of user and the probable origin of their formation during betel quid chewing in the monograph 85 of the IARC. Saliva of betel quid chewers were found to contain N-Nitrosoguvacoline, N-nitrosoguvacine and 3-methylnitrosopropionitrile. On overall evaluation, 3-methylnitrosopropionitrile was classified into Group 2B "possibly carcinogenic to humans" with sufficient evidence from experimental animals for its carcinogenicity (IARC, 2004)

2.4.4   TRACE ELEMENTS:

Areca nut and betel quid are found to contain trace elements such as sodium, magnesium, chlorine, calcium, manganese, vanadium, bromine and copper. In an Indian Food Report mentioned in a review study by Sharan et al. (2012) focusing on the consequences of areca nut use from a clinical perspective, copper constituent of processed areca nut was found to be 2.5 times higher than that of fresh areca nut signaling the strong possibility of processing ingredients with copper content being used. The same study also reported higher content of copper in raw areca nuts compared to other nuts consumed by humans.

The figure below shows how areca nut use eventually lead to carcinogenesis, summarizing all claims by different studies that areca nu use leads to adverse health impacts, over the long run.

Figure 8: Main events of areca nut use induced carcinogenesis
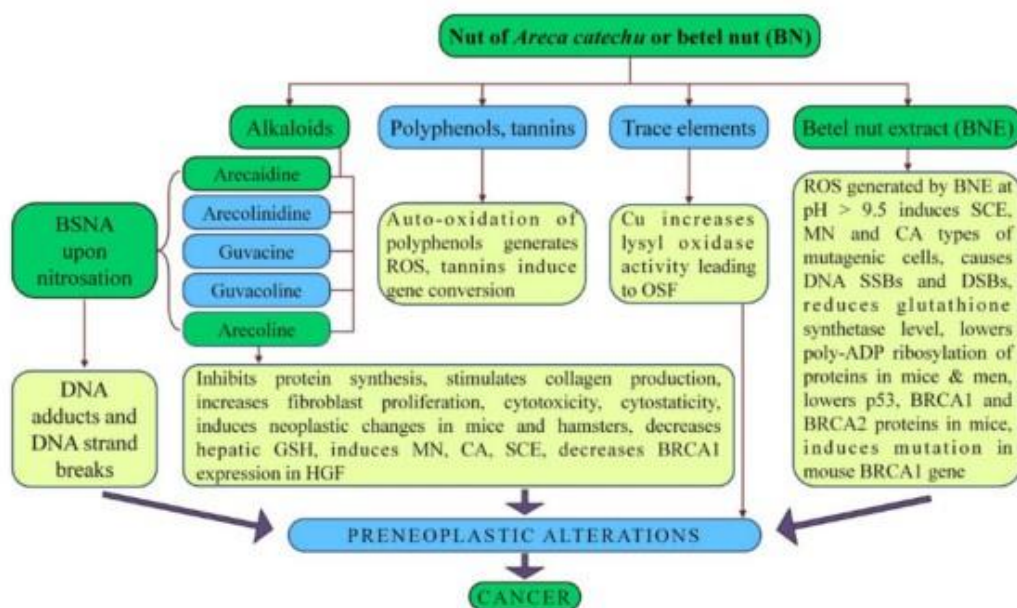
Note: The image shows the flow chart how areca nut and its constituents and their metabolic effects lead to carcinogenic transformation. Reprinted from Sharan et al (2012). Association of Betel Nut with Carcinogenesis: Revisit with a Clinical Perspective.

However, it is important to consider that the composition as well as the concentration of the constituents will have regional variation considering the manner in which it is consumed, process of fermentation or curing and chemicals used, additional ingredients used in betel quid such as with tobacco and most importantly the pesticides used during plantation. In Bhutan, no such assessment of the chemical constituents of areca nut grown and imported, has ever been conducted. This may be an area for future assessment to provide more concentrated and sharper findings to improve appropriate policies, programmes and interventions.

2.4   HEALTH IMPACTS OF ARECA NUT USE

Use of areca nut and betel quid with or without tobacco or other combinations was classified as carcinogenic to humans (Group 1) in 2004. The conclusion has been arrived after scientific evaluation of carcinogenic risks with several evidences from both in-vivo studies done on animals and in-vitro studies in relation to the chemical elements found in areca nut (IARC, 2004).

There are substantial evidence to associate the health effects of areca nut use on the "cardiovascular, gastrointestinal, metabolic, respiratory and reproductive system" (Mehrtash et al., 2017) including the aggravation of preexisting conditions such as "cardiac arrhythmias, asthma, central obesity, type II diabetes, metabolic syndrome…" (Javed et al., 2010). A cohort study conducted in Bangladesh found that betel quid chewing association were significant for all causes of death (HR: 1.26; 95% CI: 1.09–1.44) and for cancer (HR: 1.55; 95% CI: 1.09–2.22) (Wu et al., 2015). The findings indicated high mortality for betel users with 56.5 percent of deaths attributed to CVD (439 deaths) and cancers (167 deaths) over the 10 year follow-up period.

Considering this, it is now a fact that habitual use of areca nut alone and betel quid can lead to negative health consequences including oral cancer, CVD, diabetes mellitus, addiction and toxic effects.

The immediate physiological effects of areca nut use due to direct absorption into bloodstream of the constituents through the oral mucosa are dizziness, heart palpation, alertness, sweating, epigastric discomfort, relaxation, euphoric feeling and reduced hunger/thirst (World Health Organization, 2012).

The IARC in their regular monographs presented the epidemiology of areca nut, its pharmacology, impacts on health through both in-vivo and in-vitro studies to draw a positive conclusion of the carcinogenicity of areca nut on humans (IARC, 1985, 2004, 2012, 2021).

A scientifically proven effects of areca nut use are well summarized in a study by Winstock (2013), including both short term and long term effects, which is replicated below:

Figure 9: Short term and long term adverse effects of areca chewing

Short term effects	Long term effects	
Tachycardia/palpitations hypotension and bradycardia	Oral	Discoloration of teeth and gums Mouth ulcers, mucositis, gingival disease, gum recession, periodontitis, molar wearing and cavitation Leukoplakia Eyrthoplakia Submucous fibrosis 10-fold increase in risk of oral squamous cell carcinoma
Tremor		
Sweating		
Dizziness		
Diarrheas, nausea and vomiting	CVS	Inconsistent data supports increased risk of cardiovascular disease and cerebrovascular accidents
Shortness of breath, worsening of asthma		
	Metabolic	Hyperglycaemia and increased risk of type 2 diabetes and central obesity
	Gastrointestinal	Peptic ulceration Liver cirrhosis and hepatocellular carcinoma
	Pregnancy outcomes	Low birth weight
	Psychiatric	Dependence

Note: Replicated from Winstock (2013). Chapter 87 - Areca Nut, Betel Quids, and Associated Products

2.4.1 ORAL HEALTH

Areca nut, mainly through oral malignancy, remains the most significant cause of mortality as well as morbidity worldwide (Winstock, 2013). Poor oral hygiene associated with areca nut use and betel quid chewing are the leading factor in periodontal disease with evidence of arecoline cytotoxicity linked to exacerbating periodontal diseases (World Health Organization, 2012).

There are sufficient evidence that areca nut use induces oral precancerous lesions (World Health Organization, 2012). A clinical study showed evidence of oral submucous fibrosis (OSF), leukoplaki and erythroplakia, precancerous conditions, among betel or areca nut uses, with or without tobacco, that have "malignant potential, with conversion rate of 5%-10% over a 10-year period" (Kondaiah et al., 2019). Majority of betel chewers experience these precancerous clinical conditions including betel chewers mucosa and are more prone to develop OSF and cancer over a short duration and die earlier compared to smokers. (Sharan et al., 2012). A cross-sectional study involving 150 participants with clinical examination and incisional

biopsy and histopathological confirmation presented strong positive association of betel to Oral submucous fibrosis (OSF) (Avinash Tejasvi et al., 2019).

A meta-analysis of studies conducted in Asia found that betel quid chewers (with or without tobacco) are at increased risk of oral cancer. The meta-relative risk (mRR) for oral/oropharyngeal cancer in the Indian subcontinent was 2.56 (95%CI, 2.00-3.28; 15 studies) for betel quid without tobacco and 7.74 (95%CI, 5.38-11.13; 31 studies) for betel quid with tobacco, showing that exposure to tobacco in combination with areca nut significantly increases the risk of oral/oropharyngeal cancer (Guha et al., 2014). In a case-control studies done in multiple countries where betel quid is a common habit, there were strong evidence of a higher risk of oral cancer in BQ chewers compared to non-chewers (Warnakulasuriya & Chen, 2022). A similar case-control study engaging 150 case and 150 control subjects at a military hospital in Pakistan showed that those who consumed betel were 2.28 times more likely to develop head and neck cancer as compared to people who did not consume betel and other products including tobacco ((Nouman et al., 2022). A recent study confirmed high incidence of OSF in areas where habitual use of AN is prevalent (Senevirathna et al., 2023). Zhang et al. (2022) examined the putative role of betel constituents in oral carcinogenesis and concluded that the components of betel possibly enhances tumor progression in oral submucous fibrosis and oral squamous cell carcinoma.

The IARC assessed that the percentage of oral cancers diagnosed in hospitals is always higher in Asia compared to the western countries (IARC, 2004). Gunjal et al. (2020) estimated using data from GLOBOCAN 2018 the age-standardized rate (ASR) incidence of lip and oral cavity cancer in Bhutan at 3.1 percent with 2.6 percent ASR mortality rate and overall prevalence of 5.51 percent while it is reported as 9.1 percent, 5.6 percent and 19.6 percent respectively for India and 9.5 percent, 6.2 percent and 16.61 percent respectively for Bangladesh, which are the largest consumers of areca nut in the world.

The detrimental effect of areca nut and betel quid on human health is well documented (IARC, 1985).

2.4.2   CARDIOVASCULAR SYSTEM

Areca nut contains various alkaloids, including arecoline, which can stimulate the release of adrenaline. This can lead to an increase in heart rate and blood pressure, which may strain the cardiovascular system. Arecoline in areca nut can cause vasoconstriction, narrowing the blood vessels. This can reduce blood flow and oxygen supply to the tissues and organs, including the heart. Prolonged vasoconstriction can potentially increase the risk of cardiovascular problems.

Several studies have suggested a link between areca nut chewing and an increased risk of cardiovascular diseases, such as coronary artery disease, heart attacks, and strokes.

In a prospective cohort study it was found that betel quid chewing was associated with an increased risk of hypertension, coronary artery disease, and stroke. After adjusting for confounders, the following findings were presented leading to the independent association of areca nut use to increased "risk of CVD and all-cause mortality in Taiwanese men" (Lin et al., 2008) :

> the RRs (95% CI) of CVD and all-cause mortality among the former betel nut chewers were 1.56 (1.02, 2.38) and 1.40 (1.17, 1.68), respectively, and those among current chewers were 2.02 (1.31, 3.13) and 1.40 (1.16, 1.70), respectively, compared with persons who had never chewed betel quid. Current and former betel nut chewers had a higher risk of CVD mortality (RR: 2.10; $P < 0.05$) than did current and former smokers. Greater frequency of betel nut chewing was associated with greater CVD and all-cause mortality.

Amongst current chewers, majority were young adults, who also had higher waist circumference, BMI and triAglycerol compared to those who never use betel nut.

The findings of a cross-sectional study by Lin et al. (2014) suggested that BQ chewing is associated with obesity and a higher CVD risk as estimated by hs-CRP.

BQ chewing was an independent risk factor for general obesity (odds ratio [OR] 1.43, 95% confidence interval [CI] 1.07-1.91, p= 0.017) and an elevated hs-CRP level (OR 1.38, 95% CI 1.03-1.85, p= 0.029). Subjects who chewed more frequently had a higher systolic blood pressure (p= 0.025) and baPWV (p= 0.006) with the waist circumference (p= 0.015) and waist-to-height ratio (p= 0.022) of current chewers greater compared to former chewers.

Current surveys in Bhutan show high prevalence of areca nut use of close to 50 percent of school going youths aged 13-17 years old and studying in grade 7-11 (World Health Organization et al., 2017; World Health Organization, 2020).

2.4.3 DIABETES MELLITUS (DM)

The IARC (2004) explains a study by Benjamin (2001) where chewing betel quid without tobacco was found to be a predominant independent risk factor for diabetes. The OR for diabetes in betel chewers were 3.4; 95 % CI, 2.0-5.9. Areca nut chewing was found to impair glucose regulation in the body. It can lead to elevated blood sugar levels and reduced insulin sensitivity, both of which are key factors in the development of diabetes. It also mentions an experimental study on mice fed with areca nut for 2-6 days. The study of the progeny of the mice suggested that areca nut use may be "diabetogenic and induce heritable abnormality" (IARC, 2004).

Positive correlation was observed between duration of areca nut use habit and DM in a study involving diabetic patients who were habitual betel chewers in India, which has approximately 73 million cases of diabetes in the adult population above 50 years (Dangore-Khasbage et al., 2021). The age of onset of DM was earlier in habitual users $(36.50 \pm 7.67$ years) compared to non-habitual users $(47.56 \pm 4.89$ years).

Similar results were observed in a risk analysis study in Bangladesh on evaluation of the random blood sugar (RBS) of 961 diabetic patients in a hospital (Hasan et al., 2020). Raw areca nut use compared to its fresh counterpart was found to contribute to a more raised hyperglycemic effect amongst the diabetic patients, as shown below:

Higher RBS was found in BQ chewer patients than non-chewer (mean ± SEM, 263.3 ± 4.768 vs. 251.0 ± 5.915mg/dl). Interestingly, it is significantly higher in raw areca nut user than dry nut (mean ± SEM, 278.0 ± 8.790 vs. 252.1 ± 6.835 mg/dl) only from BQ chewer group, suggesting that the habit of chewing raw nut may contribute to more hyperglycemic effect among diabetic patients. (p.6)

Tung et al. (2004) reported similar findings in their exploration to validate whether the diabetogenicity of areca nut demonstrated experimentally in mice contributes to hyperglycemia/DM in a Taiwanese men. Using data from a cross sectional survey, the study results showed that areca nut users have higher age-adjusted prevalence rates for hyperglycemia and DM with the areca nut chewing independently increasing the risk of hyperglycemia (adjusted odds ratio [OR] 1.19, 95% CI 0.97–1.45) and Type 2 diabetes (adjusted OR 1.29, 95% CI 1.04–1.60).

The prevalence of raised blood sugar remained consistent at around 2 percent in both the WHO Step survey of 2014 and 2019 with a slight increase observed in women (1.9 to 2.1 percent) and an equal decree in man (2.2 to 1.8 percent).

2.4.4   BLOOD PRESSURE (BP)

Growing body of evidence has linked areca nut use to increased risk of developing hypertension primarily characterized by elevated blood pressure. The stimulating effects of areca nut, particularly its primary alkaloid arecoline, can lead to vasoconstriction and increased heart rate, resulting in elevated blood pressure.

Comorbidity is established with diabetic patients also experiencing raised blood pressure. Analysis of a cross sectional telephone survey in Taiwan reported significant association of betel nut chewing with hypertension in Taiwanesen population with type2 DM (Tseng, 2008). The conclusive findings are presented below:

The multivariate-adjusted odds ratios for hypertension in chewers vs. non-chewers were 1.067 (1.007–1.131) and 1.897 (1.534–2.346) for men and women, respectively.

In multiple linear regression, although no adjustment was made for the use of antihypertensive agents, betel nut chewing was significantly associated with blood pressure, with regression coefficients of 0.958±0.163 (SEM) for systolic and 0.441±0.108 for diastolic blood pressure in men; and the respective values for women were 1.805±0.618 and 1.198±0.393.

There are multiple literature establishing the causal relationship of smoking to blood pressure, while evidence is rarely established from smokeless tobacco especially areca nut and betel. In a prospective cohort study in Bangladesh, general hypertension and systolic hypertension was associated with betel quid use and in general, chewing betel quid use was associated with hypertension [odds ratio (OR) 1.48, 95% CI; 1.04–2.10] and systolic hypertension (OR 1.55, 95% CI 1.01–2.37). (Heck et al., 2011)

The prevalence of raised blood pressure declined in 2019 compared to 2014 from 35.7 percent to 28.2 percent respectively in the WHO Step survey of 2014 and 2019 for Bhutan.

2.5   POLICIES RELATING TO ARECA NUT USE IN BHUTAN

There are rarely any policies globally that regulate the use of areca nut and its products including in the form of betel quid combination. The WHO FCTC does not target areca nut use and betel quid but mentions its impact when being used with tobacco products. While noting its epidemic use and adverse health impacts, thre are no global movement to set policies that impact both its use and trade. Its clinical studies, carcinogenicity and relationship with human health has been considered in several monographs of the IARC (IARC, 1985, 2004, 2012, 2021). However, no recommendations has, yet, been recommended to protect human health. The WHO Western Pacific Region undertook a comprehensive review of areca nut and betel use in the pacific regions, which led to the development of the only regional strategy to reduce and regulate its consumption. The Regional Action Plan (20120-2014) has not been updated. Such meager effort from the global health community is a clear indication of the failure to acknowledge and act on this epidemic habit.

With heavy social acceptance compounded by its ceremonial importance in socio-cultural convening both in secular and temporal environments, the use of areca nut in Bhutan, mostly in the form of betel quid, it is a highly unregulated habit with possible adverse health impacts. Currently there are only two minor interventions that target its control viz. the application of an indirect tax of 50 percent custom duty and 20 percent sales tax at the point of entries (Ministry of Finance, 2022) and rare advocacies by Bhutan's Ministry of Health (MoH) on health issues relating to areca nut use and betel chewing on national television programmes. In the MoH, there are no recorded advocacy messages pertaining to health impacts from areca nut use and betel chewing. The advocacies happened in the mainstream media when clinical doctors and dental surgeons were interviewed on issues pertaining to oral health and caners (personal interview with Tandin Dhendup, media spokesperson, MoH).

However, such gaps are opportunities to design prevention strategies including national polices to address and regulate the trade and use of areca nut and betel quid.

CHAPTER THREE: RESEARCH METHODOLOGY

This chapter outlines the research methodology adopted and used for the study. This study adopted a cross-sectional quantitative design using the WHO STEP survey 2019 data. The area of study, population targeted, sampling techniques used, and research instrument are discussed in this chapter.

3.1 STUDY DESIGN

This study was a retrospective cross-sectional analysis of secondary data collected in a nationally representative Non-communicable Disease Risk Factor Surveillance WHO STEPS Survey 2019 of Bhutan.[8] The National STEPs survey is a population based cross sectional survey conducted to determine the prevalence of the key behavioral and physiological risk factors for NCDs in the population aged 15 to 69 years, using the WHO STEPwise approach to non-communicable diseases surveillance.

3.2 STUDY SETTING

The study was conducted in Bhutan, a South Asian nation in the Himalayas located in between the Republic of India and People's Republic of China. The country has total land area of 38,394 km². The country is divided into 20 districts known as *Dzongkhags*. Each district comprises of several administrative blocks (*Gewogs)* and urban centers (*Thromdes*). Each block comprises of several villages (*Chiwogs*). The country has a total of 205 blocks with 1044 villages and 65 urban centers. Bhutan has an estimated population of 763,249 with 69.86% of the population between 15-69 years old in 2022 (National Statistics Bureau, 2022).

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[8] The WHO STEPwise approach to surveillance (STEPS) is an internationally comparable, standardized and integrated surveillance tool through which countries can collect, analyze and disseminate core information on NCDs. Available at https://www.who.int/europe/tools-and-toolkits/who-stepwise-approach-to-surveillance#:~:text=The%20WHO%20STEPwise%20approach%20to,on%20noncommunicable%20diseases%20(NCDs).

Health is a matter of right and predominantly state funded. Article 9 of the Constitution of the Kingdom of Bhutan (2008) mandates free access to basic health service in both traditional and modern medicine and financial protection to individuals in the event of illness.

Towards that end, health service in Bhutan is provided through a network of health facilities established in a three-tier structure with the outreach clinics, sub-posts, and Primary healthcare centres at the lowest level and then the district hospital and 10-bedded hospitals considered as the secondary level and then referral hospitals (at regional and national level) as the tertiary level. The hierarchy is depicted as below:

Figure 10: Structure of health care system in Bhutan
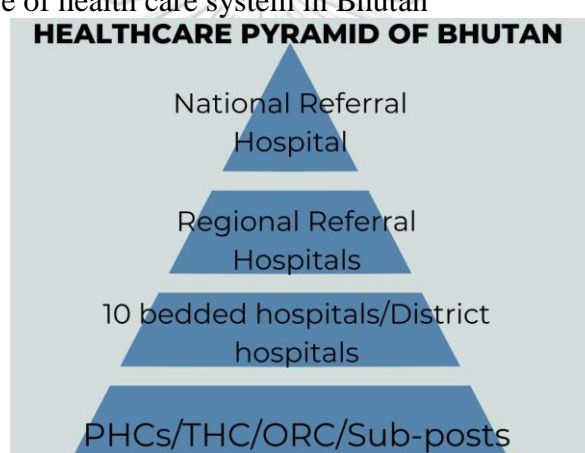
Note: PHC: Primary Health Centres, THC: Thromde Health Centres, ORC: Out-reach Centres

There is one national referral hospital, two regional referral hospitals and a network of 24 district hospitals, 27 10-bedded hospitals, three urban health centers and 184 PHC with 54 sub-posts (Ministry of Health, 2022).

3.3   STUDY POPULATION

The target population of the Bhutan STEPS survey 2019 included all household members falling within the age range of 15-69 years old during the survey period conducted between April 2019 and June 2019.

3.4   SAMPLING FRAME

The sampling frame for the Bhutan STEPS 2019 was used from the National Population and Housing Census conducted in 2017.

3.5   SAMPLE DESIGN

The Bhutan STEPS survey (2019) adopted a stratified three-stage sampling design to select the enumeration areas, households, and eligible participants at each of the selected households. Two mutually exclusive sampling frame, as the main sampling strata, rural and urban areas within each district, were used. These are to ensure a nationally representative sample. The Noncommunicable Disease Risk Factors: Bhutan STEPS Survey Report, 2019 details the steps involved as follows:

Stage 1: involved selection of Primary Sampling Units (PSUs), which are *Gewogs*/Blocks in rural areas and towns in urban areas. The PSU from each strata (rural and urban) of each region was selected using Probability Proportionate to Size (PPS). A total of 88 PSUs comprising of 33 urban PSUs and 55 from rural areas.

Stage 2: involved selection of Secondary Sampling Units (SSUs), which are *Chiwogs*/Village(s) in rural areas and Enumeration Areas (EAs) in urban areas. The SSUs were selected using PPS where number of household is used a measure of size (MOS) variable. For every PSU, four SSUs were selected leading to the selection of 352 SSUs comprising of 220 SSU from the rural area and 132 SSUs from the urban.

Stage 3: involved selection of households within each SSU using circular systematic sampling (CCS). The list of household with a unique identification number was developed by the enumerators which functions as the sample frame for the household selection. From each SSU, 16 households were selected.

Stage 4: The final step involved selection of one eligible member from the selected household. All eligible members of the households are listed in order of decreasing

age starting with males and then females, and then one eligible respondent was randomly selected using the automated program for Kish selection method.[9]

3.6   SAMPLE SIZE AND SAMPLING TECHNIQUE

The required sample size (n=5632), as per the WHO STEPS 2019, was calculated using the following sample size estimation formulae (Department of Public Health, 2020)

$$n = \frac{Z^2 P(1-P)}{d^2} = \frac{1.96*1.96((0.488(1-0.488))}{0.5*0.5} = 383.9387238$$

Where, Z = level of confidence measure, 1.96, for 95% confidence

P (Baseline level of indicators) = percentage not engaging in vigorous activity[10] (48.8%) from the 2014 NCD STEPS survey (closest value to 50%) was considered.

d = Margin of error (taken as 0.05 for the study)

Further, to ensure sufficient representation, 8 domains were considered; 1. Gender (male and female), 2. Rural and urban resident, 3. Age groups (15-39 and 40-69) and 4. Three regions for the sample size calculation. Too address the issue of cluster sampling, a design effect of 1.5 was applied. The estimated sample size was

$$n = \frac{Z^2 P(1-P)}{d^2} = \frac{1.96*1.96((0.488(1-0.488))}{0.5*0.5} = 383.9387238*1.5*8 = 4607.264686$$

Finally, after adjusting for the 15 percent non-response rate of previous NCD STEP survey conducted in 2014, the estimated sample size required was 5421 (rounded off)

$$n = \frac{1.96*1.96((0.488(1-0.488))}{0.5*0.5} = 383.9387238*1.5*8 = (4607.264686/.85)= 5420.311395$$

Considering 16 households were selected from the 352 SSU, the final sample was arrived at 5632 as follows.

$$n = 16 * 352 \text{ SSU} = 5632$$

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[9] After ranking the eligible household members stratified and listed as male and female, in decreasing age order, a member is randomly selected using automated program in a handheld tablet.

[10] One of the indicators related to the risk factors currently being measured.

A non-response rate of 0.99 was detected with the final sample size at 5575, which fulfilled all the criteria for inclusion and was taken for the analysis in this study.

3.6.1   INCLUSION CRITERIA:

All usual household members aged 15-69 years of age.

3.6.2   EXCLUSION CRITERIA:

The following were excluded from the study:

1. Usual household members who are severely sick/disabled to participate in the national survey in 2019

2. Incountry boarding students who are away from home during the time of survey for six months or more

3. All students living outside Bhutan

3. Armed forces personnel who live in barracks and

4. Monks, who live in institutions, whether in Bhutan or outside

3.7   MEASUREMENT TOOL

The study analyzed data from the survey conducted using the WHO NCD STEPS instrument. The structured questionnaires relevant to this study are presented in four sections (Annex 1):

1. Socio-demographic characteristics
2. Personal behavioral measurements
3. Individual health status
4. Areca nut use

The socio-demographic questionnaires pertains to demographic information such as gender, age, and education level and employment status. A wealth quintile is derived from household economic status questionnaire which includes property ownership

(moveable and immoveable) such as land and luxury cars, poultry/livestock and construct of residence.

Personal behavioral measurements included the use of tobacco and alcohol drinking status. For tobacco the frequency is measured with questions pertaining to daily, weekly or monthly use and ever used while for alcohol frequency of use in the past 12 months, 30 days, weekly and daily was measured. For both, the amount of use is also measured. In addition, the frequency of brushing teeth is also considered.

Individual health status is measured with indicators pertaining to raised blood pressure and raised blood glucose along with history of CVD and issues related to oral health from 5 year backwards.

The use of areca nut was measured in its frequency of usage per day/week or ever used and the status of areca nut use. The variables are classified as follows with appropriate description of scales for measuring them and the type of data collected classified under dependent and independent category.

Table 1: Overview of primary variables, scales and type of measurement

Variable		Scale	Type
Independent Variables			
Demographic characteristics	Sex	Male and Female	Dichotomous
	Age	In number of years	Interval
	Education	Highest level of education completed	Ordinal
	Marital status	Married or not (divorce, cohabitating, separated, widowed, never married)	Nominal
	occupation	Level of employment	Nominal
	Rural/urban	Rural or urban	Dichotomous
	Wealth Quintile	Household score derived using PCA	Ordinal
Personal Behavioral measurements	currently use tobacco	Yes and No	Dichotomous
	smokeless tobacco user	Yes and No	Dichotomous
	Currently drink	Life-time abstainer, former user and current user	Nominal
	frequency of	Never, less then daily	Ordinal

	brushing teeth	(once a week, once a month) once a day or more	
	History of Raised Blood Glucose	Yes and No	Dichotomous
	History of Raised Blood Pressure	Yes and No	Dichotomous
Individual Health status	History of Cardiovascular diseases	Yes, No	Dichotomous
Dependent variables			
Betel or areca nut usage	current user	Yes and No	Dichotomous
	ever used	Yes and No	Dichotomous

3.8   DATA COLLECTION

The STEPS data of 2019 in Bhutan was conducted using the standard WHO NCD STEPS instrument, which is an internally accepted statistical practice. The structured questionnaire consisted of three steps. Bhutan also included a specific set of questionnaire relating to areca nut use in addition to all the core modules being included in the survey (refer Annex 2).

The NCD STEPs survey involves three stages of data collection as follows:

STEP 1 is an interview of participants to assess behavioral risk factors and health history related to NCDs through a structured questionnaire which includes socio-demographic information, aspects of individuals' medical history related to the main NCDs, and risk behaviors including tobacco use, alcohol consumption, unhealthy diet and physical inactivity

STEP 2 involves physical measurements (height and weight and waist and hip circumference, systolic/diastolic blood pressure) to assess overweight, obesity, increased blood pressure

STEP 3 includes blood chemistry rapid diagnostic tests to assess raised blood glucose, total cholesterol, high density lipids, and urinary sodium and creatine levels.

Steps 1 and 2 were conducted at the respondent's house and were asked to perform an overnight fasting after 10 PM until morning of the next day. They were asked to collect a urine sample before their fast and to approach a testing centre, along with the urine sample, where blood samples were taken for biochemical analysis.

3.9   DATA ANALYSIS

The data was extracted from the Bhutan STEPS Survey 2019 using unique identification number used during the actual data collection.

The socio-demographic characteristics of the participants were summarized as unweighted percentages. A weighted analysis were carried out for calculating the prevalence and in estimating the unadjusted and adjusted odds ratios as the NCD STEPS survey have used multistage cluster sampling. The overall weight was derived through the multiplication of the sample weight (inverse of the probability of selection within the population), and population weight (distribution of the target population by age and sex) as per the recommendation given in the WHO STEPS Surveillance Manual.

The non-response weight was not taken into account in this study as the response rate was very high so the weight would be close to one even if it is taken into consideration. Moreover, the same methodology used in the main report was adopted in this study to maintain the consistency in the findings. The prevalence of use of current betel/areca nut users disaggregated by demographic characteristics, behavioral measurements, and health status were calculated with 95% confidence interval.

A binary logistic regressions were performed to assess the association between the Demographic characteristics, Behavioral measurements, and Health status, Clinical characteristics, and use of betel/areca nut. The variables significant at $p \leq 0.1$ were included in the multiple logistic regression. The odds ratios were calculated with 95% confidence interval. The p –value of <0.05 were considered as a strong evidence

against the null hypothesis of no association for data interpretation in this thesis report.

Adjusted Wald tests instead of likelihood-ratio tests were used to test the association between the primary outcome variable and the putative factors. According to the questions and answers section on the STATA website, the adjusted Wald tests are useful when the total number of clusters is less than or approximately equal to 100. There were only 88 primary sampling units in this survey. Therefore, these adjusted Wald tests may be appropriate in this study.

As the samples in the survey were selected based on a multistage clustered sampling, therefore, the 95% confidence interval (95% CI) in this study were calculated with robust standard errors, viz., Taylor linearized variance estimation, to take account of correlations in data.

The statistical analysis was conducted using STATA software (version 17.0 MP, Statistics and Data Science, Copyright 1996-2023 StataCorp LLC, 4905 Lakeway Drive, College Station, Texas 77845-4512 USA).

3.10   CONTROLS TO ENSURE VALIDITY

While drawing the questions for the research instrument, Bhutan included questions that were relevant for analysis in Bhutan such betel or areca nut use. For the study appropriate questions and variables are chosen to ensure that it matched with the associations being investigated with reference to the conceptual framework and objectives.

The sample selection process ensured that the criteria established in identifying and selecting the sample from the target population will ensure generalizability of the findings to the target population.

3.11   ETHICAL CONSIDERATION

Administrative clearance has been sought from the Ministry of Health, Royal Government of Bhutan authorizing the use of data and conduct of the study (Refer Annex 3). A data use agreement was signed with the Health Management Information System and Research Unit, MoH for the use of data (Annex 4). Ethical review was submitted to the Research Ethics Board of Health (REBH), Bhutan, and the REBH provided exemption letter (Annex 5).

The primary data were obtained with informed consent from the study participants after obtaining ethical clearance from REBH and survey methodology clearance from the National Statistics Bureau (NSB) of Bhutan.
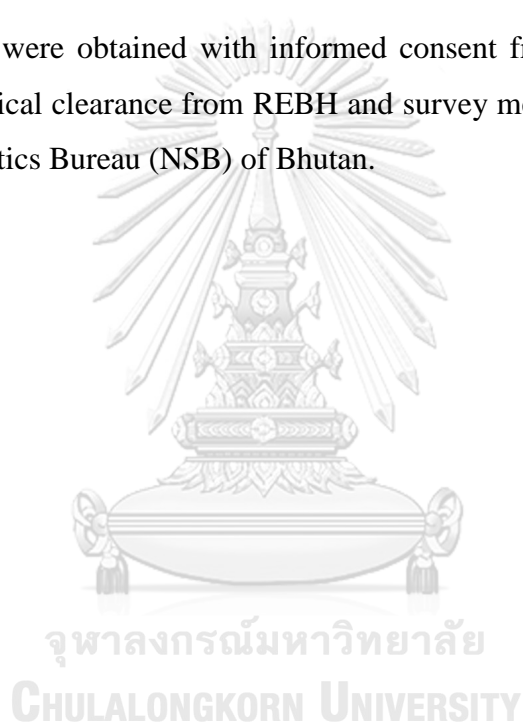
CHAPTER FOUR: RESEARCH FINDINGS/RESULTS

This chapter presents the findings of the study using the data from the WHO STEPS 2019 in Bhutan. It describes and presents socio-demographic characteristics of the study participants. It also describes personal behavioral measurements and individual health status of the target population. It presents the prevalence of betel use by the characteristics of the target population. It also presents the bivariate analysis to establish association between the outcome variable of interest and the independent variable and finally any factors significant in the bivariate model were included as candidate in the multivariable model.

5.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION

A total of 5575 individuals, with a mean age of 39.82 years and age range 15-69 years were included in the study, of which 3416 (61.3%) were females. The socio-demographic characteristics of the study participants are presented in Table 1.

A significant portion of the study population were in the age group 25-39 years comprising of 2317 (41.6%) adults. Approximately half of the study population, which is 2826 (50.7%), had no formal education and one-third (1700) had alteast a primary education and a minority of 73 (1.3%) had monastic education. The lower the formal education status, excluding monastic education, the higher the frequency. Three missing values were observed.

A little over a third of the study population comprising 1955 (35.1%) are subsistence farmers and followed almost equally by salaried employees and homemakers at 1361 (24.2%) and 1367(24.5%), respectively. Others, which included students, unemployed and retired individuals and business/self-employed persons showed similar composition with 464 (8.3%) and 428 (7.7%), respectively.

Further, of the 5575 participants, significant percentage of 77.6 % (4325) are those who are married/co-habiting and 13.1 % (728) were never married while 9.3 % (521) were either separated, widowed or divorced, combined. One missing value has been observed.

A total of 3495 (62.7 %) were residents of rural area while the remaining 2080 (37.3 %) are from the urban area. Almost half (2773) of the participants are from the western region of the country while the central and eastern regions showed almost equal representation with 1407 (25.2 %) and 1395 (25 %), respectively.

The distribution of individuals across the wealth quintile are almost equally spread with each quintile showing approximately 20%. Figure 10 presents the comparable frequency of participants distributed across the wealth quintile indicating equal representation by wealth category.

Figure 11: A dot plot showing participants frequency across wealth quintile
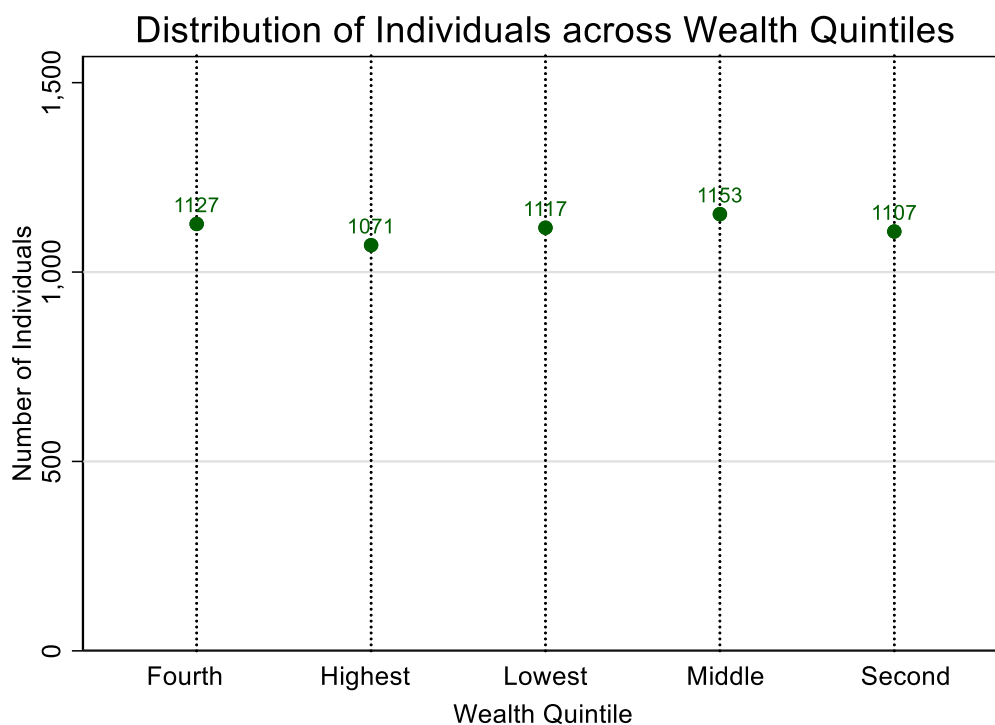
Table 2: Socio-demographic characteristics of the participants (n=5575)

Characteristics	Survey Participants	
	Number	Percentage
Total	5575	100.0
Sex		
Female	3416	61.3
Male	2159	38.7
Age		
15-24	680	12.2
25-39	2317	41.6
40-54	1641	29.4
55-69	937	16.8
Education*		
None or <Primary	2826	50.7
Primary-Secondary (6-10)	1700	30.5
Higher Secondary Plus	973	17.5
Monastic	73	1.3
Occupation		
Subsistence Farmer	1955	35.1
Salaried employee	1361	24.4
Business/Self-employed	428	7.7
Homemakers	1367	24.5
Others[1]	464	8.3
Marital status**		
Never Married	728	13.1
Married/Co-habiting	4325	77.6
Separated/widowed/divorced	521	9.3
Area of Residence		
Rural	3495	62.7
Urban	2080	37.3
Region of Country		
Central	1407	25.2
East	1395	25.0
West	2773	49.7
Wealth quintile		
Lowest	1117	20.0
Second	1107	19.9
Middle	1153	20.7
Fourth	1127	20.2
Highest	1071	19.2

[1]Others includes students, unemployed, and retired individuals.

* missing = 3

** missing = 1

5.2   PREVALANCE OF PERSONAL BEHAVIORAL MEASUREMENTS

The prevalence (weighted) of current tobacco use (either smoked or smokeless form) was 22.9 % of Bhutanese aged 15-69 population. Table 3, below provides the weighted percentage of the target population by personal behavioral measurements.

Table 3: Percentage of Bhutanese people aged 15-69 years by personal behavioural measurements (n=5575)

Characteristics	Number of participants	Percentage[1]
Tobacco use (any)		
No	4469	77.1
Yes	1106	22.9
Alcohol use		
Life-time abstainer	2208	40.7
Former	953	16.4
Current	2414	42.9
Frequency of brushing teeth[2]		
Daily or more	2539	90.9
Less than daily	187	5.8
Never (last one month)	114	3.3

[1]Weighted percentage
[2]Missing=2735

Of the total population, 42.9 % consumed alcohol in the past 12 months (current drinkers) followed by 40.7% who are life-time abstainers while the remaining 16.4% were former drinkers.

Almost 91 % of individuals brushed their teeth atleast once or more a day, 3.3 % never brushed their teeth, and 5.8 % brushed less than a day (brushed once a month or 2-3 times a month or once a week or 2-6 times a week). However, it must be noted that there was a significant missing response to this particular question (close to 50 % are observed as missing).

5.3   PREVALANCE OF INDIVIDUAL HEALTH STATUS

The variable pertaining to oral health status has been dropped from the analysis since there were insufficiency of data for analysis. This was due to an error found in the questionnaire design which led to significant skipping of self-reported questions pertaining to state of mouth, teeth or gums.

The table below shows the weighted percentage of the target population by individual health status.

Table 4: Percentage of Bhutanese people aged 15-69 years by their individual health status (n=5575)

Characteristics	Number of participants	Percentage[1]
Raised Blood Glucose (Diabetes)[2]		
No	5277	98.1
Yes	122	1.9
Raised Blood Pressure[3]		
No	3764	72.0
Yes	1752	28.0
History of Cardiovascular Diseases		
No	183	96.6
Yes	5392	3.4

[1]Weighted percentage
[2]Missing=176
[3]Missing=59

The prevalence (weighted) of raised blood sugar based on prior diagnosis, medication history and measured from a sample collected after a 12 hour fasting with fasting blood glucose level >= 126mg/dl, was 1.9 %.

Overall, 28.0 % of the respondents have raised blood pressure based on actual measurement and medication history. Thre readings of systolic and diastolic blood pressure were measured with three minutes rest between each reading. The average of second and third reading was considered. However, if the third reading was invalid

then the first and second reading average was considered. There were 176 missing values were observed for this question in the dataset.

Among respondents aged 15-69 years, those who reported ever having a heart attack or chest pain from heart disease or stroke was 3.4 %. A total of 59 missing values were observed.

5.4   PREVALANCE AND CHARACTERISTICS OF BETEL OR ARECA NUT USE BY SOCIO-DEMOGRAPHIC PROFILE

These findings provide an overview of the percentage of Bhutanese individuals aged 15-69 years who currently use betel or areca nut, disaggregated by various background characteristics.

As shown in Table 5, the prevalence (weighted) of current betel or areca nut use among Bhutanese aged 15-69 population was 56.82 % (95% CI: 54.27-59.33). There was no much difference in the prevalence of betel or areca nut use between women and men (55.94 % versus 57.61 %).

The highest prevalence was found in the age group 25-39 years with 63.58 % (95 % CI: 60.58 - 66.48] of them using betel or areca nut which was followed by the age group 40-54 years old with the prevalence of 57.35 % (95 % CI; 53.76-60.87). The two other age groups of 15-24 years old and 55-69 years old had the prevalence of 50.62 % and 47.21 % respectively.

The prevalence of betel or areca nut use did not differ across the level of education. The prevalence was only slightly higher for those with monastic education (59.98 %) compared to the rest while the prevalence was lowest for those without education or education level below primary education (55.25 %).

Amongst occupational strata only incremental difference in prevalence of betel or areca nut use was observed except for others (42.41 %). Subsistence farmer had the

highest prevalence (63.96 %) followed by those doing business/self-employed (61.14%). There was not much significant difference in prevalence between salaried employees and home makers (56.31 % versus 58.07 %)

Table 5: Percentage of Bhutanese aged 15-69 years who currently use betel by background characteristics (n=5575)

Background characteristic	Total	Currently use betel or areca nut % [95%CI]	
		Yes	No
Total	**5575**	**56.82 [54.27,59.33]**	**43.18 [40.67,45.73]**
Sex			
Women	3416	55.94 [52.85,58.99]	44.06 [41.01,47.15]
Men	2159	57.61 [54.29,60.85]	42.39 [39.15,45.71]
Age			
15-24	680	50.62 [45.63,55.59]	49.38 [44.41,54.37]
25-39	2317	63.58 [60.58,66.48]	36.42 [33.52,39.42]
40-54	1641	57.35 [53.76,60.87]	42.65 [39.13,46.24]
55-69	937	47.21 [42.00,52.48]	52.79 [47.52,58.00]
Education[1]			
None or <Primary	2699	55.25 [51.62,58.83]	44.75 [41.17,48.38]
Primary-Secondary (6-10)	1634	57.12 [53.81,60.37]	42.88 [39.63,46.19]
Higher Secondary Plus	923	59.03 [54.44,63.47]	40.97 [36.53,45.56]
Monastic	70	59.98 [44.35,73.81]	40.02 [26.19,55.65]
Occupation			
Subsistence Farmer	1877	63.96 [60.71,67.08]	36.04 [32.92,39.29]
Salaried employee	1288	56.31 [51.29,61.2]	43.69 [38.8,48.71]
Business/Self-employed	413	61.14 [54.34,67.53]	38.86 [32.47,45.66]
Homemakers	1300	58.07 [54.45,61.6]	41.93 [38.4,45.55]
Others	450	42.41 [36.3,48.76]	57.59 [51.24,63.7]
Marital status[2]			
Never Married	710	48.04 [42.87,53.26]	51.96 [46.74,57.13]
Married/Co-habiting	4119	59.6 [56.9,62.25]	40.4 [37.75,43.1]
Separated/widowed/divorced	498	57.73 [51,64.18]	42.27 [35.82,49]
Residence			
Rural	3495	56.37 [52.66,60.01]	43.63 [39.99,47.34]

Urban	2080	57.46 [54.25,60.61]	42.54 [39.39,45.75]
Region			
Central	1407	56.73 [52.12,61.23]	43.27 [38.77,47.88]
East	1395	53.54 [46.5,60.45]	46.46 [39.55,53.5]
West	2773	58.19 [54.98,61.34]	41.81 [38.66,45.02]
Wealth quintile			
Lowest	1117	51.64 [45.55,57.67]	48.36 [42.33,54.45]
Second	1107	57.03 [51.84,62.08]	42.97 [37.92,48.16]
Middle	1153	60.73 [55.81,65.45]	39.27 [34.55,44.19]
Fourth	1127	55.5 [51.63,59.3]	44.5 [40.7,48.37]
Highest	1071	58.01 [53.16,62.7]	41.99 [37.3,46.84]

[1] missing = 3

[2] missing = 1

The prevalence of betel or areca nut use was highest for those who are married/co-habiting (59.6 %). Never married individuals reported the lowest prevalence of betel or areca nut use at 48.04 % (95 % CI; 42.87-53.26).

Between urban and rural strata, there was only a minor difference in the prevalence of betel or areca nut use (57.46 % versus 56.37 %). Similarly no major variation in the prevalence was found between the three regions and across wealth quintile (Table 5).

5.5   PREVALANCE AND CHARACTERISTICS OF BETEL OR ARECA NUT USE BY PERSONAL BEHAVIOUR AND INDIVIDUAL HEALTH STATUS

Table 6 provide insights into the percentage (weighted) of Bhutanese individuals aged 15-69 years who currently use betel, stratified by personal behavior and individual health status.

The prevalence of betel use was higher among individuals who currently use tobacco (69.21%, 95% CI: 64.77-73.31) compared to non-users (53.14 % 95% CI: 50.25,56). Individuals who reported current alcohol use had a higher prevalence of current betel or areca nut use (69.81%, 95% CI: 66.83-72.63) compared to lifetime abstainers (45.26 %, 95% CI: 41.17,49.42).

Among those with raised blood pressure, betel use prevalence was 55.48% (95% CI: 51.81-59.09), while individuals with a history of cardiovascular diseases reported a prevalence of 56.71% (95% CI: 54.03-59.35).

Higher prevalence of betel or areca nut use was observed for those who brush their teeth atleast once a day or more (61.2 %, 95% CI: 57.82-64.48). The prevalence for those individuals who chew betel or use areca nut but never brush their teeth (55.36%, 95% CI: 32.79-50) and do not brush their teeth daily (58.88%, 95% CI: 50-67.21) are worryingly high.

Table 6: Percentage of Bhutanese aged 15-69 years who currently use betel by personal behaviour and individual health status (n=5575)

Personal behaviour or individual health status		Total	Currently use betel % [95%CI]	
			Yes	No
	Total	5575	56.82 [54.27,59.33]	43.18 [40.67,45.73]
	Tobacco use (any)			
	No	4469.00	53.14 [50.25,56]	46.86 [44,49.75]
	Yes	1106.00	69.21 [64.77,73.31]	30.79 [26.69,35.23]
	Alcohol use			
Personal behaviour	Life-time abstainer	2208.00	45.26 [41.17,49.42]	54.74 [50.58,58.83]
	Former	953.00	51.49 [47.07,55.89]	48.51 [44.11,52.93]
	Current	2414.00	69.81 [66.83,72.63]	30.19 [27.37,33.17]
	Frequency of brushing teeth[1]			
	Daily or more	2539.00	61.2 [57.82,64.48]	38.8 [35.52,42.18]
	Less than daily	187.00	58.88 [50,67.21]	41.12 [32.79,50]
	Never	114.00	55.36 [43.72,66.45]	44.64 [33.55,56.28]
	Raised Blood Glucose (Diabetes)[2]			
	No	5277.00	56.84 [54.32,59.32]	43.16 [40.68,45.68]
	Yes	122.00	58.72 [45.95,70.41]	41.28 [29.59,54.05]
Individual health status	**Raised Blood Pressure[3]**			
	No	3764.00	57.19 [54.41,59.93]	42.81 [40.07,45.59]
	Yes	1752.00	55.48 [51.81,59.09]	44.52 [40.91,48.19]
	History of Cardiovascular Diseases			
	No	183.00	60.04 [50.01,69.29]	39.96 [30.71,49.99]
	Yes	5392.00	56.71 [54.03,59.35]	43.29 [40.65,45.97]

5.6 FACTORS ASSOCIATED WITH CURRENT BETEL OR ARECA NUT USE

The unadjusted odds ratios with 95% confidence interval were calculated to assess possible association of factors with betel or areca nut use. The analysis is presented in Table 7 with putative associated factors of betel or areca nut use.

There was no statistically significant difference in betel or areca nut use between urban and rural areas (56.37% versus 57.46%, p-value 0.6567).

In the binary logistics regression analysis, age groups, occupation, marital status, tobacco user, and alcohol use were found to be significantly associated with current betel or areca nut use (Table 7). These variables are considered as candidate variables for the multivariable analysis. In addition, sex was also considered as a variable as it has a bearing on the analysis and considering that age and sex are normal contributors to outcome variable of interest, generally.

Table 7: Prevalence of current betel use and its associated factors: crude Odds Ratio (weighted analysis) n=5328

Characteristics	Total	Current Betel Use %[95% CI]	Crude OR (95% CI)	P-value[1]
Sex				
Female	3283	55.94 [52.85,58.99]	Ref	0.3938
Male	2045	57.61 [54.29,60.85]	1.03 [0.96,1.10]	
Age				
15-24	658	50.62 [45.63,55.59]	Ref	
25-39	2214	63.58 [60.58,66.48]	1.26 [1.14,1.39]	<0.0001
40-54	1563	57.35 [53.76,60.87]	1.13 [1.02,1.26]	
55-69	893	47.21 [42.00,52.48]	0.93 [0.81,1.08]	
Education				
None or <Primary	2699	55.25 [51.62,58.83]	Ref	
Primary-Secondary (6-10)	1634	57.12 [53.81,60.37]	1.03 [0.96,1.12]	0.5549
Higher Secondary Plus	923	59.03 [54.44,63.47]	1.07 [0.97,1.18]	
Monastic	70	59.98 [44.35,73.81]	1.09 [0.85,1.39]	
Occupation				
Subsistence Farmer	1877	63.96 [60.71,67.08]	Ref	
Salaried employee	1288	56.31 [51.29,61.2]	1.14 [1.03,1.26]	<0.0001
Business/Self-employed	413	61.14 [54.34,67.53]	1.09 [0.95,1.25]	
Homemakers	1300	58.07 [54.45,61.6]	1.03 [0.94,1.13]	
Others	450	42.41 [36.3,48.76]	0.75 [0.64,0.88]	
Marital status				0.0009

Never Married	710	48.04 [42.87,53.26]	Ref	
Married/Co-habiting	4119	59.6 [56.9,62.25]	1.24 [1.11,1.39]	
Separated/widowed/divorced	498	57.73 [51,64.18]	1.20 [1.03,1.40]	
Area of **Residence**				
Rural	3340	56.37 [52.66,60.01]	Ref	0.6567
Urban	1988	57.46 [54.25,60.61]	1.02 [0.94,1.11]	
Region of Country				
Central	1330	56.73 [52.12,61.23]	Ref	0.494
Eastern	1358	53.54 [46.5,60.45]	0.94 [0.81,1.10]	
Western	2640	58.19 [54.98,61.34]	1.03 [0.93,1.13]	
Wealth quintile				
Lowest	1057	51.64 [45.55,57.67]	Ref	
Second	1055	57.03 [51.84,62.08]	1.10 [0.98,1.24]	0.1693
Middle	1114	60.73 [55.81,65.45]	1.18 [1.02,1.36]	
Fourth	1078	55.5 [51.63,59.3]	1.07 [0.94,1.23]	
Highest	1024	58.01 [53.16,62.7]	1.12 [0.98,1.29]	
Tobacco use (any)				
No	4469	53.14 [50.25,56]	Ref	<0.0001
Yes	1106	69.21 [64.77,73.31]	1.30 [1.21,1.41]	
Alcohol use				
Life-time abstainer	2208	45.26 [41.17,49.42]	Ref	<0.0001
Former	953	51.49 [47.07,55.89]	1.14 [1.00,1.29]	
Current	2414	69.81 [66.83,72.63]	1.54 [1.41,1.69]	
Frequency of brushing teeth[2]				
Daily or more	2539	61.2 [57.82,64.48]	Ref	0.5848
Less than daily	187	58.88 [50,67.21]	0.96 [0.83,1.12]	
Never	114	55.36 [43.72,66.45]	0.90 [0.74,1.11]	
Raised Blood Glucose (Diabetes)[3]				
No	5277	56.84 [54.32,59.32]	Ref	0.7646
Yes	122	58.72 [45.95,70.41]	1.03 [0.83,1.28]	
Raised Blood Pressure[4]				
No	3764	57.19 [54.41,59.93]	Ref	0.3675
Yes	1752	55.48 [51.81,59.09]	0.97 [0.91,1.04]	
History of Cardiovascular Diseases				
No	183	60.04 [50.01,69.29]	Ref	0.5234
Yes	5392	56.71 [54.03,59.35]	0.94 [0.79,1.13]	

[1]Adjusted Wald test

[2] missing = 2735
[3] missing = 176
[4] missing = 59

The multivariable analysis found that adjusted odds ratio (OR) for males, using females as the reference category, is 0.95. The p-value (adjusted Wald test) for this association is 0.183. The adjusted odds ratio (OR) of 0.95 suggests that there is no statistically significant association between sex and current betel use after adjusting for other factors. The p-value of 0.183 further supports this finding, indicating that the observed association is not statistically significant at the predetermined significance level (0.05) (Table 8).

The association of age groups up to 69 years old with current betel or areca nut use were compared taking 15-24 age category as the reference group. Compared to all other age group, the prevalence of current betel or areca nut use is higher for the age group 25-39 (63.58%, 95% CI: 6058-66.48). The adjusted odds ratio (OR) for this age group, using the reference category of age 15-24, is 1.01. The p-value (adjusted Wald test) for the overall age category was 0.0003 showing a statistically significant relationship.

Age category, therefore, seems to be a significant factor associated with current betel or areca nut use, with the different age category demonstrating varying levels of prevalence and odds. Individuals in the age groups of 40-54, aOR=0.94 and 55-69, a OR=0.78, seems to have lower odds of current betel use compared to those in the age group of 15-24 years. On the other hand, individuals in the age group of 25-39 have a slightly higher odds of current betel use, aOR=1.01, although the effect size is relatively small.

Overall, with the p-value at 0.2784, there is no statistically significant association between occupation and current betel or areca nut use.

Similar observation was made for association between marital status and current betel or areca nut use suggesting that no statistically significant association was established with p-value at 0.2513.

Table 8: Prevalence of current betel use and its associated factors: adjusted Odds Ratio (weighted analysis) n=5328

Characteristics	Total	Current Betel Use %[95% CI]	Adjusted OR (95%CI)	P-value (Adjusted Wald test)
Sex				
Female	3283	55.94 [52.85,58.99]	Ref	0.183
Male	2045	57.61 [54.29,60.85]	0.95 [0.88,1.03]	
Age				
15-24	658	50.62 [45.63,55.59]	Ref	
25-39	2214	63.58 [60.58,66.48]	1.01 [0.90,1.14]	0.0003
40-54	1563	57.35 [53.76,60.87]	0.94 [0.83,1.08]	
55-69	893	47.21 [42.00,52.48]	0.78 [0.65,0.94]	
Occupation				
Subsistence Farmer	1877	63.96 [60.71,67.08]	Ref	
Salaried employee	1288	56.31 [51.29,61.2]	1.04 [0.94,1.16]	
Business/Self-employed	413	61.14 [54.34,67.53]	1.05 [0.93,1.19]	0.2784
Homemakers	1300	58.07 [54.45,61.6]	1.04 [0.94,1.15]	
Others	210	42.41 [36.3,48.76]	0.87 [0.73,1.04]	
Marital status				
Never Married	710	48.04 [42.87,53.26]	Ref	
Married/Co-habiting	4119	59.6 [56.9,62.25]	1.11 [0.98,1.25]	0.2513
Separated/widowed/divorced	498	57.73 [51,64.18]	1.12 [0.95,1.32]	
Tobacco use				
No	4301	53.14 [50.25,56]	Ref	0.0001
Yes	1027	69.21 [64.77,73.31]	1.17 [1.08,1.26]	
Alcohol Use				
Life-time abstainer	2208	45.26 [41.17,49.42]	Ref	
Former	953	51.49 [47.07,55.89]	1.12 [0.99,1.27]	<0.0001
Current	2414	69.81 [66.83,72.63]	1.45 [1.32,1.59]	

Betel or areca nut consumption was founded to be associated with age, tobacco use and alcohol use when controlled for other variables included in the model. There was a strong evidence against the null hypothesis of no association between betel nut use and age (adjusted Wald test p-value 0.0003) when controlled for sex, occupation, marital status, tobacco use, and alcohol use.

There was a strong evidence against the null hypothesis of no association between betel nut use and tobacco (p-value 0.0001). Tobacco users were 17 % more likely to use betel nut as compared to those who don't use tobacco (aOR1.17, 95% CI: 1.08 to 1.26).

The former alcohol consumers were 12 % (aOR1.12, 95% CI: 0.99 to 1.27) and current alcohol consumers were 45 % (aOR1.45, 95% CI: 1.32 to 1.59) more likely to consume betel nuts as compared to lifetime abstainers. The adjusted Wald Test indicated strong evidence against the null hypothesis of no association between alcohol consumption and betel nut use (adjusted Wald Test P-value <0.0001).

The univariate multivariable logistic regression model indicated that sex, occupation, and marital status were not associated with betel nut use when controlled for confounding variables included in the model (Table 8).

CHAPTER FIVE: DISCUSSION, RECOMMENDATIONS AND CONLUSION

This findings of the study using the data from the WHO STEPS 2019 in Bhutan is presented in comparison with similar other studies. A summary of the main findings is also presented, highlighting the key results that addresses the research question and the subsequent hypothesis. The practical, theoretical or policy implication of the findings will also be discussed along with limitations.

5.1   DISCUSSION

There were four independent variables described in the conceptual framework under the individual health status, initially. However, the variable pertaining to oral health status has been dropped from the overall analysis and report since there were insufficiency of data for analysis. This was due to an error found in the questionnaire design which led to significant skipping of self-reported questions pertaining to state of mouth, teeth or gums.

This study using the nationally representative data set of the STEPS survey 2019 of Bhutan found that the national prevalence of betel or areca nut use in Bhutan was more than half of the target population. Meaning more than one out of every two adults use areca nut or betel in Bhutan, making it a significant neglected public health concern. This study confirms the national prevalence reported in the WHO STEPS survey 2019 (Department of Public Health, 2020).

The National Health Survey (NHS) of Bhutan 2012, found that 43.9 percent of Bhutanese aged 15-75 years old used areca nut in the form of betel quid. There seems to be an increase in the consumption of betel or areca nut use. However on closer examination the noticeable increase could be attributed to the variation/scope of the definition of outcome variable of interest. In this study, betel or areca nut included consuming areca nut in isolation, betel quid and any products containing areca nut as the primary ingredient. In the NHS 2012, only betel quid was considered in the

questionnaire and subsequent analysis (Ministry of Health, 2012). The WHO STEPS survey 2014 revealed the prevalence of "betel quid with tobacco" chewers at only 6.1% of the Bhutanese population (World Health Organization, 2015). This huge difference is because the WHO STEPS survey 2014 didn't include betel quid without tobacco. Therefore, the findings of this study and WHO STEPS survey 2014 are not comparable.

In absence of effective control measures, another plausible reason for the higher prevalence of areca nut use is due to easy access to betel and areca nut and associated products in the Bhutanese market. There are no regulations to control its sale, commercialization or use neither interventions to encourage cessation and quit. Any individual including minors can avail it from the market and at affordable rate. In addition, as mentioned in Chapter two, besides the increased local production of up to approximately 21,000 tonnes of areca nut, Bhutan imported around 1,100 tonnes of betel or areca nut alone in 2021. These are strong indication of the availability of areca nut in Bhutan and it's a neglected public health issue.

The prevalence of overall areca nut use in India is about 23.9% (95% CI; 23.1-24.8) of the adult population, which is approximately 223.79 million individuals (Singh et al., 2021). Another study reported that the prevalence of chewing betel quid with tobacco has been estimated on average at 5.8% with variation from zero to 39.5 % for different states in India (P. C. Gupta et al., 2018). Bangladesh's 2009 GATS, which is one of the few recent surveys encompassing areca nut use the overall prevalence of past and current user of betel nut estimated to be around 35% (Singh et al., 2020). Compared to these neighboring countries, the prevalence of betel or areca nut use in Bhutan is significantly high. Several countries reduced prevalence of areca nut use in their respective countries through policy shift, stricter regulations and educational advocacy such as in Thailand (IARC, 2012). Such effective solutions may be referred for replication and adoption in Bhutan to reduce this epidemic national habit.

Amongst occupation, the likelihood of subsistence farmers using betel or areca nut is lesser compared to other occupational groups (unadjusted), is perhaps, due to lesser

access of betel or areca nut to the farmers. The assumption is that subsistence farmers have lesser affordability including accessibility to betel or products containing areca nut in remote settings. A plausible reason could also be the less-likely decision of opportunity cost of spending on betel or areca nut over necessity household goods.

The study found that the correlates for current use of betel or areca nut were: age tobacco user and current alcohol use. Similar correlates were reported in an earlier systematic study using Bhutan's NHS 2012 data (Wangdi & Jamtsho, 2020) that those in the eastern region of Bhutan and participants in age group 55-69 years are less likely to be current betel or areca nut consumers.

In 2016, Bhutan's Global School–based Student Health Survey (GSHS) assessed the prevalence of areca nut use amongst students aged 13-17 years old at 65.8 percent. The 2019 Global Youth Tobacco Survey (GYTS), which studied the age group 13-15 years, revealed prevalence of 56.9 percent of adolescent students consuming betel or area nut. Although the difference in the age groups studied does not favor comparison between the three surveys, the higher prevalence of betel consumption amongst the young population remains same.

In this study, similar significantly high prevalence was found for the middle age group (25-29 and 40-54 years old) which is comparable to the prevalence reported in Nepal where the prevalence of areca nut use habit was found high among the students (30.4%) (Gunjal et al., 2020). In a study in Pakistan reported in Singh et al (2020), the consumption of areca nut users increased by grade among school children 4-16 years. Studies confirmed that the addictive nature of areca nut is similar to that of nicotine with reports stating an estimated 44% of areca nut users continuing the habit despite detrimental on mouth and uncontrollably indulging in the use in public places (Farooq & Abbas, 2016; Ko et al., 2020). Addiction and young population are a hazard for the development of the society and country. The public health burden from such a situation should be considered as a priority concern to be addressed especially when studies have revealed that "substantial and stable revenue streams accrue to the

industry over the lifetime of tobacco users who begin as minors" and tobacco and areca nut are consumed together in most instances (Lal et al., 2016).

Both genders in Bhutan consume areca nut either in the form of quid or other products/combinations, a practice, specifically, similar to other countries in the south East Asian region (Gupta & Warnakulasuriya, 2002; P. C. Gupta et al., 2018; IARC, 2004). In this study no significant difference are found in the prevalence of betel or areca nut use between male and female although being female is identified as a correlate in the univariate analysis (cOR 1.03). Similar finding was reported by an earlier study done using the NHS 2012 data, which also identified being female as a correlate for areca nut use with unadjusted OR 1.02 (Wangdi & Jamtsho, 2020). In the south and East Asian region, comparable differences are reported in several other countries. Bangladesh 2009 GATS revealed that the prevalence of betel quid chewing was 23.5% and 25.2 % for male and female respectively (Gunjal et al., 2020) while in India the prevalence was reported as 8.3% for men and 7.7% for women who use any form of betel or areca nut (Singh et al., 2021). However, the overall prevalence for both male (57.61%, 95% CI: 54.29-60.85) and female (55.94%, 95% CI: 52.85-58.99) are significantly high in Bhutan when compared to the neighbouring countries in the region. Such socially accepted habit, almost equally distributed among gender, requires a national effort to reduce the use as an immediate action, including clinically proven and effective quit program and cessation therapies, presented in systematic reviews of such interventions (Das et al., 2020; Ko et al., 2020).

In contrast to initial assumption, this study did not find association between betel or areca nut use and raised blood glucose (diabetes). Individuals with raised blood glucose have a slightly higher odds (cOR1.03) of current betel or areca nut use compared to those without raised blood glucose. However, studies have confirmed positive correlation between duration of diabetes and duration of areca nut use establishing association between its use and diabetes and the effect of arecoline leading to raised blood glucose (Dangore-Khasbage et al., 2021; Garg et al., 2014). An experimental study in Bangladesh among diabetic patient and betel use suggested that the "habit of chewing raw nut may contribute to more hyperglycemic effect

among diabetic patients" and it enhances higher raised blood glucose level, in general and highly raises blood sugar in patients with family history with diabetes (Hasan et al., 2020). In Papua New Guinea, in a systematic review, it was found that betel nut chewers had a high fasting capillary blood glucose which ultimately leads to hypoglycemia which causes diabetes over time (Joo et al., 2020). Therefore, such evidence should influence that association may exist between areca nut user and diabetes in Bhutanese, as well. Hence appropriate caution must be taken to ensure that individual with raised blood sugar must be provided with relevant advice from such scientific review.

Similarly, diverging from the initial assumption, this study did not find association between areca nut use and raised blood pressure. A cross sectional study by Tseng (2008) revealed that betel chewing is associated with hypertension in Taiwanese diabetic patient. An experimental study further showed evidence that arecoline, which is a principle component in areca nut, induces changes in blood pressure(Wu et al., 2020). The studies are not comparable due to different context and confounders. However, it is common knowledge that consuming areca nut or betel cause palpation, sweating and temporary increase in body heat (IARC, 2004). Bhutanese use areca nut and betel in cold seasons, welcoming such habits given the cold and harsh Himalayan climatic condition and are oriented to expecting these temporary changes/effects.

In the multivariable model analysis, betel or areca nut use is strongly associated with tobacco use and alcohol consumption. Betel consumption, alcohol drinking and tobacco use are three high risk factors for salivary gland, oral and throat cancers, interalia, and root causes of non-communicable diseases (Li et al., 2017; T.-H. Wang et al., 2017; T. H. Wang et al., 2017). These are however, modifiable lifestyle risk factors and with adequate and appropriate health education, behavioral interventions and control policies, the risk could be averted and reduced. Since there are no data on cancers especially oral cancer, in this study to statistically determine the association of oral cancer with betel or areca nut use, it could be an opportunity for a potential research in future.

A WHO monograph strongly suggested that tobacco smoking and betel use are associated with the use of each leading to the use of the other (IARC, 2004). Our study analysis also supported these evidences.

Since betel or areca nut consumption is significantly associated with tobacco consumption and alcohol drinking, public health interventions especially advocacy and awareness messages, against tobacco use and harmful use of alcohol should also include betel nut consumption and its health impact. More attention should be given to protect the younger population who are vulnerable to indulge in addictive behaviors including alcohol use, betel or areca nut use, and tobacco consumption.

5.2   STRENGTH AND LIMITATIONS OF THIS STUDY

5.2.1   STRENGHTS OF THE STUDY

The strength of this study are as follows:

1. It is the first nationwide study using the WHO STEPS 2019 data set exploring the factors associated with current use of betel or areca nut among population aged 15-69 years in Bhutan.

5.2.2   LIMITATION

However, there are certain limitations of this study as follows:

1. As this is a cross sectional study using secondary from WHO STEPS focused on NCD risk factor assessment, the study will not be able to make causal inference (no temporal sequence) for areca nut consumption and associated factors. Longitudinal studies in the future could provide solution to this limitation.

2. Also it does not include other groups such as military persons, monks and students staying in boarding facilities/institutions. There are betel users in age range of under 15 and above 69 which are also not included in the study.

3. There would be social desirability bias as the enumerators were healthcare providers so the actual prevalence may be higher than the report in the study. In order to mitigate the limitation, enumerators were advised not to introduce

themselves as health workers and secondly trained to make nonjudgmental and comfortable environment.

4. Generally, self-reported surveys such as the STEPS survey are subject to recall bias.

5.3   RECOMENDATIONS AND APPLICATION

The study generated statistical evidence to provide impetus and attention on betel quid or areca nut consumption which is a neglected public health issue in Bhutan. Consequently, this study will initiate production of public health interventions and appropriate polices in the near future such as in the National Health Policy and tax measures.

In order to get a comprehensive picture of the betel use, a qualitative study should be conducted in addition to longitudinal studies to draw conclusions about causal relationship between betel or areca nut use and its associated factors. As the current study found that a significant portion of the eligible population are excluded, an institutional based survey and analysis should be conducted in the future to get a realistic national prevalence and associated factors.

This study also found that amongst age category those in the age range 15-24 years and 25-39 years old had higher odds of areca nut use compared to other age categories. Considering the similarity in the addictive nature of areca nut with nicotine addiction (N. Chatterjee & H. A. Gupte, 2023) and evidence that those who initiate tobacco use early in life tend to have lower odds of quitting during their life time (Lal et al., 2016), future studies and surveys should include questions and analysis pertaining to age of initiation to probe and validate whether those who use areca nut at young age consume more areca nut stretched over long period of time or whether they tend to be lifelong users. Moreover, given the evidence, aggressive advocacy and education must be provided in the educational institutions so that it contributes to long term reduction of the epidemic use.

Considering the strong role of religious personalities in Bhutan, the Ministry of Health can collaborate with the *Dratsang Lhentsog* Secretariat to provide appropriate health guidance to the general public intermittently.[11]

Immediate measure should include health promotion and behavior change communication materials by different strata from analyzing in this study followed by cessation support programs. Customized education should be provided to those in age range 15-39 years as betel use amongst the young and middle aged are a concern.

Particularly, this study will intentionally spark evidence-based discussion and researches in this most neglected area of study, an area of concern in Bhutan where there is sustained epidemic use of areca nut and betel quid chewing. The highest governing body of the health sector in Bhutan known as the high-level committee will be sensitized on the alarming prevalence of areca nut use and what are the best practices in other countries to reduce consumption.

Regulations in advertisement ban, restricting sale to and by minors, ban on commercial licensing for industries producing betel products and raising taxation on import and income from betel trade are possible medium term measures to reduce consumption.

As this study revealed strong association between betel or areca nut use and, alcohol use and tobacco use, any existing intervention that are used to manage alcohol and tobacco must include and target reduction/regulation of betel or areca nut use.

In the longer term, an epidemic which concerns the south East Asian region should be tabled for regional cooperation in the WHO convening to jointly tackle this masticatory use.

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[11] This is the office that manages the affairs of the monk body in Bhutan and organizes frequent public gatherings for religious sermons, during which time the health ministry can take advantage to get health message across to the public and community through the monks/priests.

Most importantly, the Ministry of Health must also initiate provision of cessation support and quit programs through the numerous health facilities as an effective intervention to reduce this epidemic use.

5.4 CONCLUSION

This study revealed that, overall, there is significant association between betel or areca nut use and age, tobacco use and alcohol use.

There was also alarmingly high prevalence of betel or areca nut use Bhutan along with high alcohol and tobacco use. Current alcohol reduction strategies and policies must include betel or areca nut together in their implementation and interventions, ideally.

Considering higher prevalence in young adults, aggressive behavioral interventions should be implemented in institutions for reducing the epidemic use along with restrictive measures in the institutions.

Areca nut use is strongly linked to social customs and tradition in Bhutan. Therefore, a multisectoral approach is required to adopt prevention strategies by including local leaders, monastic community, in particular, and politicians.

Annex 1: QUESTIONNAIRE: INDEPENDENT VARIABLES

Questionnaire: Socio-demographic characteristics

Demographic Information		
Question	**Response**	**Code**
Sex (*Record Male / Female as observed*)	Male 1 Female 2	C1
What is your date of birth? *Don't Know 77 77 7777*	⌴⌴ ⌴⌴ ⌴⌴⌴⌴ *If Known, Go to C4* dd mm year	C2
How old are you?	Years ⌴⌴	C3
In total, how many years have you spent at school and in full-time study (excluding pre-school)? (Range 0 – 25 years)	Years ⌴⌴	C4
What is the **highest level of education** you have completed?	No formal schooling 1 Non-formal education 2 Less than primary 3 Primary (class 6) completed 4 Lower secondary (class 8) completed 5 Middle secondary (class 10) completed 6 Higher secondary (class 12) completed 7 Certificate/Diploma 8 Bachelor's degree and above 9 Monastic 10 Don't know 77 Refused 88	C5
What is your **marital status**?	Never married 1 Currently married 2 Separated 3 Divorced 4 Widowed 5 Cohabitating 6 Refused 88	C7
Which of the following best describes your **main work** status over the past 12 months? *(USE SHOWCARD)*	Government/DHI/SOE 1 NGO/CSO/IO employee 2 Private employee 3 Subsistence Farmer 4 Self-employed other than subsistence farmer 5 Student 6 Homemaker 7 Retired 8 Unemployed (able to work) 9 Unemployed (unable to work) 10 Non-paid 11 Other 12 Refused 88	C8
In total, how many persons live in this household (including infants)? (Range 1 – 30) 77, if not known; 88, if refused	Number of people ⌴⌴	C9x

Questionnaire: Socio-demographic characteristics (contd)

Household socio-economic status

Does your household own any land? (Record for all family member and irrespective anywhere in the country)			Yes	1		C10x
			No	0 Go to C12x		

How much land does your household own in decimal? Calculation chart e.g. 1 acre = 100 decimal	Type	Urban Area	Rural Area			
	Wet land	C11ax	C11dx			
	Dry land	C11bx	C11ex			
	Orchard	C11cx	C11fx			

Please ask /observe - whether this household or any person who lives in the household has the following items:	Items	Yes	No	
	Sofa set	1	2	C12ax
	Computer or laptop or tab	1	2	C12bx
	Fixed Telephone	1	2	C12cx
	Mobile phone (smart phone)	1	2	C12dx
	Mobile phone (simple phone)	1	2	C12ex
	Electric/coal iron	1	2	C12fx
	Rice cooker/curry cooker	1	2	C12gx
	Refrigerator/Fridge	1	2	C12hx
	Water boiler	1	2	C12ix
	Micro-wave oven	1	2	C12jx
	Jewelry	1	2	C12kx
	Family car	1	2	C12lx
	Other Vehicle (commercial)	1	2	C12mx
	Motor bike, scooter, gear bicycle	1	2	C12nx
	Machinery	1	2	C12ox
	Washing machine	1	2	C12px
	Vacuum cleaner	1	2	C12qx
	Television	1	2	C12rx
	DTH or cable line	1	2	C12sx
	VCR/ VCD/ DVD	1	2	C12tx
	Kitchen grinder machine	1	2	C12ux
	House/Building	1	2	C12vx
	Wrist watch	1	2	C12wx

What types of family car does your household own? (if C12lx=yes) [Multiple response]	SUV	1	C12lx1
	Non-SUV	2	

What main material used to build the **wall** of your main living house?	Cane/ palm/ trunks/bamboo	1	C13x / C13xOthers
	Bamboo with mud	2	
	Stone with mud	3	
	Plywood	4	
	Cardboard	5	
	Cement RCC wall	6	
	Stone with lime/cement	7	
	Bricks	8	
	Cement blocks	9	
	Wood planks	10	
	Rammed earth	11	
	Mud blocks	12	
	Others (specify)	13	

What main materials used to build the **roof** of your main living house?	Metal sheet	1	C14x / C14xOthers
	Concrete/Cement	2	
	Tiles/slate	3	
	Thatch	4	
	Planks/Shingles	5	
	Tarpaulin	6	

Questionnaire: Socio-demographic characteristics (contd)

	Bamboo	7	
	Cardboard	8	
	Others(specify)	9	
What main materials used to build the **floor** of your main living house?	Tiles/marbles	1	C15x / C15xOthers
	Concrete/Cement/Terrazzo	2	
	Clay/Earthen	3	
	Planks/Shingles	4	
	Bamboo	5	
	Polished wood	6	
	Others(specify)	7	
How many rooms does your household occupy, including bedrooms, living rooms and rooms used for family enterprise, but NOT counting toilets, kitchens and balconies?			C16x
Does your household have livestock/poultry?	Yes	1 go to C18x	C17x
	No	0	
If yes, how many? *(If the number is greater than 999 type 999)*	Cattle		C18ax
	Pigs		C18bx
	Buffalo		C18cx
	Horses		C18dx
	Goats		C18ex
	Sheep		C18fx
	Poultry		C18gx
	Yaks		C18hx
	Others (specify)		C18xOther

Questionnaire: Personal Behavioral Measurements (Smoking status)

Step 1 Behavioural Measurements			
Tobacco Use			
Now I am going to ask you some questions about tobacco use.			
Do you **currently** smoke any **tobacco** products, such as cigarettes, bidi, cigars or pipes? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to T8*		T1
Do you currently smoke tobacco products **daily**?	Yes 1 No 2		T2
How old were you when you **first started** smoking?	Age (years) Don't know 77 └┴┘ *If Known, go to T5a/T5aw*		T3
Do you remember how long ago was it? *(RECORD ONLY 1, NOT ALL 3)* Don't know 77	In Years └┴┘ *If Known, go to T5a/T5aw* OR in Months └┴┘ *If Known, go to T5a/T5aw* OR in Weeks └┴┘		T4 / T4type
		DAILY↓ WEEKLY↓	
On average, **how many** of the following products do you smoke **each day/week**? *(IF LESS THAN DAILY, RECORD WEEKLY)* *(RECORD FOR EACH TYPE, USE SHOWCARD)* Don't Know 7777	Manufactured cigarettes	└┴┴┴┘└┴┴┴┘	T5a/T5aw
	Hand-rolled cigarettes	└┴┴┴┘└┴┴┴┘	T5b/T5bw
	Bidis	└┴┴┴┘└┴┴┴┘	T5c/T5cw
	Cigars, cheroots, cigarillos	└┴┴┴┘└┴┴┴┘	T5d/T5dw
	Other	└┴┴┴┘└┴┴┴┘ *If Other, go to T5other, else go to T6*	T5f/T5fw
	Other (please specify):	└┴┴┴┴┘	T5other/ T5otherw

Questionnaire: Personal Behavioral Measurements (Smoking status) contd…

Question	Response			Code
During the past 12 months, have you tried to **stop smoking**?	Yes	1		T6
	No	2		
During any visit to a doctor or other health worker in the past 12 months, were you advised to quit smoking tobacco?	Yes	1	If T2=Yes, go to T12; if T2=No, go to T9	T7
	No	2	If T2=Yes, go to T12; if T2=No, go to T9	
	No visit during the past 12 months	3	If T2=Yes, go to T12; if T2=No, go to T9	
In the past, did you **ever smoke** any tobacco products? *(USE SHOWCARD)*	Yes	1		T8
	No	2	If No, go to T12	
In the past, did you **ever** smoke **daily**?	Yes	1	If T1=Yes, go to T12, else go to T10	T9
	No	2	If T1=Yes, go to T12, else go to	
How old were you when you **stopped** smoking?	Age (years)			T10
	Don't Know 77	└─┴─┘ If Known, go to T12		
How **long ago** did you stop smoking? *(RECORD ONLY 1, NOT ALL 3)* *Don't Know 77*	Years ago	└─┴─┘ If Known, go to T12		T11a
	OR Months ago	└─┴─┘ If Known, go to T12		T11b
	OR Weeks ago	└─┴─┘		T11c
Do you **currently use** any **smokeless tobacco** products such as *[snuff, chewing tobacco, betel with tobacco]?(USE SHOWCARD)*	Yes	1		T12
	No	2	If No, go to T15	
Do you **currently use smokeless tobacco** products **daily**?	Yes	1		T13
	No	2	If No, go to T14aw	

		DAILY↓	WEEKLY↓	Code
On average, how many **times a day/week** do you use …. *(IF LESS THAN DAILY, RECORD WEEKLY)* *(RECORD FOR EACH TYPE, USE SHOWCARD)* *Don't Know 7777*	Snuff, by mouth	└─┴─┴─┴─┘	└─┴─┴─┴─┘	T14a/ T14aw
	Snuff, by nose	└─┴─┴─┴─┘	└─┴─┴─┴─┘	T14b/ T14bw
	Chewing tobacco	└─┴─┴─┴─┘	└─┴─┴─┴─┘	T14c/ T14cw
	Betel, quid (with tobacco)	└─┴─┴─┴─┘	└─┴─┴─┴─┘	T14d/ T14dw
	Other	└─┴─┴─┴─┘ └─┴─┴─┴─┘ If Other, go to T14other, if T13=No, go to T16, else go to T17		T14e/ T14ew
	Other (please specify):	└─┴─┴─┴─┴─┘ If T13=No, go to T16, else go to T17		T14other/ T14otherw

Question	Response			Code
In the **past**, did you **ever use** smokeless tobacco products such as *[snuff, chewing tobacco, or betel, quid with tobacco]*?	Yes	1		T15
	No	2	If No, go to T17	
In the **past**, did you **ever use** smokeless tobacco products such as *[snuff, chewing tobacco, or betel, quid with tobacco]* **daily**?	Yes	1		T16
	No	2		
During the past 30 days, did someone smoke **in your home**?	Yes	1		T17
	No	2		
During the past 30 days, did someone smoke in closed areas **in your workplace** (in the building, in a work area or a specific office)?	Yes	1		T18
	No	2		
	Don't work in a closed area	3		

Questionnaire: Personal Behavioral Measurements (Drinking status)

Alcohol Consumption

The next questions ask about the consumption of alcohol.

Question	Response		Code
Have you **ever** consumed any alcohol such as beer, wine, Hard drinks, ara, changkoe, bangchang, shingchang etc.? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to A16*		A1
Have you consumed any alcohol within the **past 12 months**?	Yes 1 *If Yes, go to A4* No 2		A2
What are the reasons for not drinking any alcohol in the past 12 months? [Multiple response]	Health reasons	1 go to AP1	A3x / A3xOther
	Family pressure	2 go to AP1	
	Cannot afford/no money to buy	3 go to AP1	
	Just wanted to stop	4 go to AP1	
	Spiritual/religious reasons	5 go to AP1	
	Advice of doctor/health worker	6 go to AP1	
	Other (Specify)	7 go to AP1	
During the past 12 months, **how frequently** have you had at least one **standard alcoholic drink**? *(USE SHOWCARD)*	Daily	1	A4
	5-6 days per week	2	
	3-4 days per week	3	
	1-2 days per week	4	
	1-3 days per month	5	
	Less than once a month	6	
Have you consumed any alcohol within the **past 30 days**?	Yes 1 No 2 *If No, go to A13*		A5
What is the alcohol type that you <u>usually</u> or most often drink? [single response]	Beer	1	A5x
	Wine	2	
	Spirit (whisky / Vodka / Gin)	3	
	Ara	4	
	Changkoe	5	
	Bangchang	6	
	Shingchang	7	
	Others (Specify)		
During the past 30 days, on how many **occasions** did you have at least one standard alcoholic drink?	Number Don't know 77 └─┴─┘ *If Zero, go to A8*		A6
During the past 30 days, when you drank alcohol, how many **standard drinks on average** did you have during one drinking occasion? *(USE SHOWCARD)*	Number Don't know 77 └─┴─┘		A7
During the past 30 days, what was the **largest number** of standard drinks you had on a single occasion, counting all types of alcoholic drinks together?	Largest number Don't Know 77 └─┴─┘		A8
During the past 30 days, how many times did you have **six or more** standard drinks in a single drinking occasion?	Number of times Don't Know 77 └─┴─┘		A9
During the past 12 months, how often do you have six or more standard drinks on one occasion?	Never		A9a
	Less than monthly		
	Monthly		
	Weekly		
	Daily or almost daily		

Questionnaire: Personal Behavioral Measurements (Drinking status) contd

During each of the **past 7 days**, how many standard drinks did you have each day? *(USE SHOWCARD)* *Don't Know 77*	Monday ⎿⊥⏌	A10a
	Tuesday ⎿⊥⏌	A10b
	Wednesday ⎿⊥⏌	A10c
	Thursday ⎿⊥⏌	A10d
	Friday ⎿⊥⏌	A10e
	Saturday ⎿⊥⏌	A10f
	Sunday ⎿⊥⏌	A10g
I have just asked you about your consumption of alcohol during the past 7 days. The questions were about alcohol in general, while the next questions refer to your consumption of homebrewed alcohol, alcohol brought over the border/from another country, any alcohol not intended for drinking or other untaxed alcohol. Please only think about these types of alcohol when answering the next questions.		
During the **past 7 days**, did you consume any **homebrewed** alcohol (e.g. ara, changkoe, bangchang), any alcohol **brought over the border/from another country**, any alcohol **not intended for drinking** or other **untaxed** alcohol? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to A13*	A11
On average, **how many standard drinks** of the following did you consume **during the past 7 days**? *(USE SHOWCARD)* *Don't Know 77*	Homebrewed spirits, e.g: Ara, changkoe, bangchang, shingchang etc. ⎿⊥⏌	A12a
	Homebrewed beer or wine, e.g. palm or fruit wine ⎿⊥⏌	A12b
	Alcohol brought over the border/from another country ⎿⊥⏌	A12c
	Alcohol not intended for drinking, e.g. alcohol-based medicines, perfumes, after shaves ⎿⊥⏌	A12d
	Other untaxed alcohol in the country ⎿⊥⏌	A12e
During the **past 12 months**, how often have you found that you were not able to stop drinking once you had started? (if A2=1)	Daily or almost daily 1 Weekly 2 Monthly 3 Less than monthly 4 Never 5	A13
During the **past 12 months,** how often have you failed to do what was normally expected from you because of drinking? (if A2=1)	Daily or almost daily 1 Weekly 2 Monthly 3 Less than monthly 4 Never 5	A14
During the **past 12 months,** how often have you needed a first drink in the morning to get yourself going after a heavy drinking session? (if A2=1)	Daily or almost daily 1 Weekly 2 Monthly 3 Less than monthly 4 Never 5	A15
During the **past 12 months**, have you had family problems or problems with your partner due to **someone else's** drinking?	Yes, more than monthly 1 Yes, monthly 2 Yes, several times but less than monthly 3 Yes, once or twice 4 No 5	A16

Questionnaire: Individual Health Status (Raised Blood Pressure)

History of Raised Blood Pressure

Question	Response		Code
Have you ever had your blood pressure measured by a doctor or other health worker?	Yes 1		H1
	No 2	If No, go to H6	
Have you ever been told by a doctor or other health worker that you have raised blood pressure or hypertension?	Yes 1		H2a
	No 2	If No, go to H6	
Were you first told in the past 12 months?	Yes 1		H2b
	No 2		
Have you **ever been told** to **take a medicine** by a doctor or health workers **for raised blood pressure**? (If H2a=yes)	Yes 1		H2c
	No 2		
Have you ever taken drugs/medications for raised blood pressure prescribed by a doctor/health worker? (If H2c=yes)	Yes 1		H2d
	No 2	[If No and H1=yes, go to H3x1]	
In the past two weeks, have you taken any drugs (medication) for raised blood pressure prescribed by a doctor or other health worker? (If H2d=yes)	Yes 1		H3
	No 2		
Where do you usually go for <u>treatment</u> or advice for your raised blood pressure? [Multiple Response] [Appear only If H2a=yes]	Regional Referral Hospital 1		H3x1
	Hospital 2		
	BHU-I 3		
	BHU-II/Sub-post 4		
	Outreach/Mobile Clinic 5		
	Private 6		
	Other (Specify)		
	Don't know 77		
Where do you usually get your drugs for raised blood pressure? [Multiple Response] [Appear only If H2d=yes or H3=yes]	Regional Referral Hospital 1		H3x2
	Hospital 2		
	BHU-I 3		
	BHU-II/Sub-post 4		
	Outreach/Mobile Clinic 5		
	Private 6		
	Medical shops/Pharmacies 7		
	Other (Specify)		
	Don't know 77		
What is the most important reason for which you are not currently taking medications for raised blood pressure or hypertension? [Appear only if H2a=yes and (H2d=no or H3=no)]	Don't think drug is necessary 1		H3x3
	Got side effects 2		
	Afraid of side effects 3		
	Too expensive 4		
	Blood pressure got normal 5		
	Medicine not available 6		
	Medicine not advised by doctor 7		
	Fear of being dependent for lifetime 8		
	Other (specify)		
Have you ever seen a local healer like Tsip/ Jhakri/ Neyjom/ Lama/ Pow for raised blood pressure or hypertension? (if H2a=yes)	Yes 1		H4
	No 2		
Are you currently taking any herbal or traditional remedy for your raised blood pressure? (if H2a=yes)	Yes 1		H5
	No 2		

Questionnaire: Individual Health Status (CVD)

History of Cardiovascular Diseases			
Have you ever had a heart attack or chest pain from heart disease (angina) or a stroke (cerebrovascular accident or incident)?	Yes 1		H17
	No 2		
Are you currently taking aspirin regularly to prevent or treat heart disease?	Yes 1		H18
	No 2		
	Don't know 77		
Are you currently taking statins (Lovastatin/Simvastatin/Atorvastatin or any other statin) regularly to prevent or treat heart disease?	Yes 1		H19
	No 2		
	Don't know 77		

Questionnaire: Individual Health Status (Oral Health Status)

Oral Health		
The next questions ask about your oral health status and related behaviours.		
Question	Response	Code
How long has it been since you last **saw a dentist/health worker** for any dental/oral health issues?	Less than 6 months 1 6-12 months 2 More than 1 year but less than 2 3 2 or more years but less than 5 years 4 5 or more years 5 Never received dental care 6 *go to O9*	O7
What was the **main reason for your last visit** to the dentist?	Consultation / advice 1 Pain or trouble with teeth, gums or mouth 2 Treatment / Follow-up treatment 3 Routine check-up treatment 4 Other 5 *go to O8other*	O8
	Other (please specify) ⌞ ⌞ ⌞ ⌞ ⌞	O8other
How **often do you clean** your teeth?	Never 1 *go to O13a* Once a month 2 2-3 times a month 3 Once a week 4 2-6 times a week 5 Once a day 6 Twice or more a day 7	O9
Have you **experienced any of the following problems** during the past 12 months because of the **state of your teeth, gums or mouth**? (RECORD FOR EACH)		
Difficulty in chewing foods	Yes 1 No 2	O13a
Difficulty with speech/trouble pronouncing words	Yes 1 No 2	O13b

Mouth feels dry	Yes 1 No 2	O13c
Have a persistent wound and/or swelling in the mouth for more than three weeks	Yes 1 No 2	O13d
Have a red or red and white patch in the mouth	Yes 1 No 2	O13e
Days not at work because of teeth or mouth	Yes 1 No 2	O13f
Difficulty doing usual activities	Yes 1 No 2	O13g
Reduced participation in social activities	Yes 1 No 2	O13h

Annex 2:   QUESTIONNAIRE: DEPENDENT VARIABLE

Betel or areca nut		
Do you **currently use** betel or areca nut (Doma, Paan, Supari, other betel nut products)? *(USE SHOWCARD)*	Yes 1 No 2 If No, go to B4	B1
Do you **currently use** betel or areca nut products **daily?**	Yes 1 No 2	B2
On average, how many **times a day/week** do you use betel or areca nut products *(IF LESS THAN DAILY, RECORD WEEKLY)*	DAILY↓ WEEKLY↓ Betel nut (Doma and Paan) �L_L_L_L⌐ ⌐L_L_L_L⌐	B3a/ B3aw
(RECORD FOR EACH TYPE, USE SHOWCARD) *Don't Know 7777*	Supari and other products ⌐L_L_L_L⌐ ⌐L_L_L_L⌐	B3b/ B3bw
In the past, did you ever use betel or areca nut products?	Yes 1 No 2 go to A1	B4
In the past, did you ever use betel or areca nut products daily?	Yes 1 No 2	B5

Annex 3:   ADMINISTRATIVE CLEARANCE, MOH

དཔལ་ལྡན་འབྲུག་གཞུང་། **ROYAL GOVERNMENT OF BHUTAN**
MINISTRY OF HEALTH
གསོ་བ་སྨན་ལས། **THIMPHU BHUTAN**
P.O BOX: 726

MoH/PPD/ADM.CL/9/2023/*2023023*   12/05/2023

Mr. Tashi Penjor
Chief Planning Officer
Policy and Planning Division
Ministry of Health

Subject: **Administrative Clearance**

Dear Tashi,

The Ministry of Health is pleased to issue Administrative Clearance for the study titled "**Prevalence of betel or Areca Nut (AN) use and its associated factors among Bhutanese population aged 15-69 years old: an analysis of national health data of non-communicable disease (NCD) survey in 2019**" after reviewing its purpose, objectives, and intended outcome(s). However, the following conditions needs to be fulfilled in order for the clearance to be valid:

1. Obtain technical and ethical clearance from Research Ethics Board of Health (REBH) or KGUMSB Institutional Review Board (*if the sites of the study are confined to KGUMSB or its affiliated teaching hospitals*) prior to the conduct of study and ensure strict adherence to its requirements, terms and conditions.
2. Abide by national policies and laws applicable to the study;
3. Seek approval from work site(s) prior to the conduct of study;
4. Ensure no interference with routine delivery of health services at the study site(s);
5. Concurrence for movement of health staff (if any) for the purpose of the study from Department of Medical Services and study sites from the concerned authorities at least one month prior to the conduct of the study;
6. Respond within 10 working days to queries (if any) from the Ministry of health with regard to the implementation of the study: and
7. Share a signed copy of the report with Planning and Policy Division, Ministry of Health

Thanking you.

Yours sincerely,

(Mr. Kinga Jamphel)
Offtg. Acting Secretary

Annex 4: DATA USE AGREEMENT

UNDERTAKING (for Data Use)

I, Mr./Mrs./Ms. _TASHI PENJOR_ CID/Passport number _11410005067_ from _BIKHAR_ bearing _Samkhar_ Gewog under _TASHIGANG_ Dzongkhag ("mention your permanent address") presently _MOTITHANG, THIMPHU_ ("mention what you are doing/occupation/name of office"), hereby accept to access a de-identified dataset of _NCD STEPS 2019_ ("name of survey or data source") , from Ministry of Health Bhutan, for use in secondary data analyses relating to _PREVALENCE OF BETEL-NUT AREA NUT USE IN BHUTAN AND ITS ASSOCIATED FACTORS AMONG BHUTANESE POPULATION AGE 15-69YRS OLD_ ("name of the research"). _AN ANALYSIS OF NATIONAL HEALTH DATA OF NON-COMMUNICABLE DISEASE (NCD) SURVEY IN 2019._

I do hereby undertake:

1. To use the de-identified dataset only for the above-mentioned research project and to seek separate approval for other research projects, if any being planned;
2. To seek prior ethical clearance from Research Ethics Board of Health (REBH), Bhutan, for the research;
3. Not to redistribute the data to another third party without the written consent from Ministry of Health, Bhutan;
4. To use appropriate safeguards to prevent use or disclosure of the de-identified dataset; this includes storing the data securely where they cannot be accessed by an unauthorized user;
5. To report to the Ministry of Health, Bhutan, any use or disclosure of the de-identified dataset of which it becomes aware, that is not permitted or required by laws of Bhutan including the presence of identifiers in the dataset;
6. Not to use the information in the de-identified dataset, alone or in combination to identify or contact the individuals who are data subjects;
7. To cite and acknowledge the dataset used and the data creators and the Ministry of Health, Bhutan in any publication or report of work derived in whole or in part from the de-identified dataset;
8. To provide a hard or electronic copy of any publication or report resulting from analysis of the de-identified dataset to the Policy and Planning Division, Ministry of Health, Bhutan;
9. To require any of its subcontractors or agents that receive or have access to the data to agree to the same restrictions and conditions on the use and/or disclosure of the de-identified dataset that applies to the Recipient;
10. To take responsibility for destroying the dataset soon after the requirement of the research project is fulfilled; and informing the Health Information Management System, Ministry of Health.

I do hereby confirm that I undertake to abide by clauses hereinabove stated having understood each clauses, including the implication and consequences of deviating from them. In particular, I understand that in the event that I do not adhere to any one of the hereinabove stated conditions, I shall be liable for prosecution in the Court of Law as per Laws of the Land.

(Affix Legal Stamp)

Name: _TASHI PENJOR._
Place: _THIMPHU_
Date: _01/06/2022._

Annex 5: RESEARCH ETHICS BOARD OF HEALTH: WAIVER

ROYAL GOVERNMENT OF BHUTAN
MINISTRY OF HEALTH
RESEARCH ETHICS BOARD OF HEALTH
THIMPHU : BHUTAN
P.O. BOX : 726

Ref. No. REBH/PO /2023/011   Date: 15/06/2023

EXEMPTION LETTER

Protocol No: PO2023011

Protocol Title: PREVALENCE OF BETEL OR ARECA NUT (AN) USE AND ITS ASSOCIATED FACTORS AMONG BHUTANESE POPULATION AGED 15-69 YEARS OLD: AN ANALYSIS OF NATIONAL HEALTH DATA OF NON-COMMUNICABLE DISEASE (NCD) SURVEY IN 2019.

Principal Investigator: Mr. Tashi Penjor
Institute: MoH
Co-Investigator (s):

This is to state that Research Ethics Board of Health (REBH) has determined that the above protocol, submitted to REBH for ethical approval, qualify for exemption from ethics review based on the criteria specified in the Standard Operating Procedures (SOP) of REBH.

Therefore, the need for REBH approval is exempted for the protocol. Nonetheless, the investigator(s) shall be responsible to;

1. Seek all other clearances/approvals required by law/policy including permission from the study sites before conducting the study/project,
2. Report any major changes on the protocol or related documents to REBH before implementation. The changes can be implemented only after receiving approval from REBH.
3. Submit Final Report of the study/project, at the end of the study/project, for review and protocol file closure.

Note: Technical and ethical soundness of protocols are not assessed by REBH for the protocols that qualify for exemptions of REBH review.

(Dr. Chhabi Lal Adhikari)
Chairperson

For further information please contact: *REBH Secretary:* at *Tel: +975-2-32260*2 or email at
rebhsecretary@gmail.com

PABX: + 975-2-322602, 322351, 328091, 328092, 328093 (Extension 333) Fax: 324649

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จุฬาลงกรณ์มหาวิทยาลัย

CHULALONGKORN UNIVERSITY

VITA

NAME	Tashi Penjor
DATE OF BIRTH	07 November 1979
PLACE OF BIRTH	Bhutan
INSTITUTIONS ATTENDED	1. Sherubtse College affiliated to Delhi University, India
	2. Royal Institute of Management, Bhutan.
	3. Lal Bahadur Shastri National Academy of Administration, Mussoorie, India.
	4. Lee Kuan Yew School of Public Policy, National University of Singapore.
HOME ADDRESS	Building no. 29 (B) , Motithang, Thori Lam, Thimphu Bhutan, 11001
AWARD RECEIVED	1. Lee Kuan Yew Scholarship, National University of Singapore, Singapore
	2. Director's Gold Medal, Lal Bahadur Shastri National Academy of Administration, India