SMOKELESS TOBACCO IN SOUTH ASIA – THE MEASUREMENT OF DEPENDENCE, SOCIOCULTURAL INFLUENCES AND CARDIOVASCULAR CONSEQUENCES

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Abstract

Introduction: Despite very high smokeless tobacco (ST) consumption in South Asia (SA), there are significant gaps in our knowledge regarding the measurement of ST dependence, sociocultural influences, and consequences associated with the use of South Asian ST products.

Aim: To improve our understanding of ST use and dependency, sociocultural determinants and consequences associated with their use in South Asia.

Methods: My thesis comprised of three empirical studies. I carried out psychometric assessments of three ST dependency scales, using data collected from a convenience sample of adult ST users in India. In the same sample, I quantitatively measured selected sociocultural variables and assessed their association with ST use and quit practices. Finally, I conducted meta-analyses of longitudinal observational studies to examine causal associations between ever use of ST and cardiovascular outcomes, both globally and by geographical subgroups.

Results: Among the scales, internal consistency was highest for Oklahoma Scale for Smokeless Tobacco Dependence (OSSTD). The scales were significantly correlated with each other, and showed positive associations with heaviness and consistency of ST use. Based on exploratory factor analyses (EFA), OSSTD was a unidimensional measure of ST dependence in an Indian context. The sociocultural survey showed that having ST users as close peers and no household restrictions on use adversely influenced quit attempts and quit intentions respectively, in adjusted models. In the meta-analyses, ever use of ST was associated with a 40% increased risk of incident ischaemic health disease (IHD) in SA, which was not found in other geographical regions.

Conclusions: South Asian ST products are likely highly addictive, and sociocultural factors may be associated with fewer quit attempts made. In addition to cancer, ST use also increases the risk of cardiovascular disease outcomes. More research relevant to ST control is needed from SA, particularly given the adverse health consequences associated with use.

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List of Abbreviations

AJOL	African Journals Online
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CFA	Confirmatory Factor Analysis
CHD	Coronary Heart Disease
CPS	Cancer Prevention Studies
CVD	Cardiovascular Disease
DALY	Disability Adjusted Life Years
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECG	Electrocardiogram
EFA	Exploratory Factor Analysis
FCTC	Framework Convention on Tobacco Control
FTND-ST	Fagerström Test for Nicotine Dependence – Smokeless Tobacco
FTQ	Fagerström Tolerence Questionnaire
GATS	Global Adult Tobacco Survey
HR	Hazard Ratio
HT	Hypertension
IARC	International Agency for Research on Cancer
ICD	International Statistical Classification of Diseases and Related Health Problems
IHD	Ischaemic Heart Disease
IMEMR	Index Medicus of the Eastern Mediterranean Region
IMSEAR	Index Medicus of the South-East Asian Region
INR	Indian Rupees
IV	Inverse Variance
KMO	Kaiser-Meyer-Olkin
LILACS	Latin American and Caribbean Health Sciences Literature
LMIC	Low and Middle Income Countries
MI	Myocardial Infarction
MRFA	Minimum Rank Factor Analysis
NCI	National Cancer Institute
NOS	Newcastle-Ottawa Scale
OR	Odds Ratio
OSSTD	Oklahoma Scale for Smokeless Tobacco Dependence
PA	Parallel Analysis
PAH	Polycyclic Aromatic Hydrocarbons

PDM	Primary Dependence Motives
RBCS	Reasons for Betel quid Chewing Scale
RCT	Randomised Controlled Trial
RR	Relative Risk
SA	South Asia
SD	Standard Deviation
SDM	Secondary Dependence Motives
SE	Standard Error
ST	Smokeless Tobacco
TAPS	Tobacco Advertising, Promotion, and Sponsorship
TDS-ST	Tobacco Dependence Screener – Smokeless Tobacco
TSNA	Tobacco-Specific Nitrosamines
UK	United Kingdom
USA	United States of America
USDHHS	United States Department of Health and Human Services
WISDM	Wisconsin Inventory of Smoking Dependence Motives
WHO	World Health Organization

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Author's Declaration

I declare that this thesis is a presentation of original work and I am the sole author. This work has not previously been presented for an award at this, or any other University. All sources have been acknowledged as References.

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Chapter 1. Literature Review

1.1 The use of Smokeless Tobacco (ST) in South Asia (SA)

Smokeless tobacco (ST) describes a diverse group of tobacco-containing products consumed either orally or nasally in their unburnt form. The use of ST is globally widespread, with estimates of over 350 million adult users, who reside across at least 130 countries world over (Mehrotra et al., 2017). In 2010, using data from 113 countries, it was estimated that ST use led to a loss of 1.7 million disability adjusted life years (DALYs) from cancers of the mouth, pharynx and oesophagus, and 4.7 million DALYs from ischaemic heart disease (IHD) (Siddiqi et al., 2015). In another more recent publication, over 650,000 deaths from all-cause mortalities were attributed to the use of various ST products across 133 countries world over (Sinha et al., 2018b). In the coming years, as a result of many countries making progress with cigarette regulations and achieving reductions in smoking rates, the use and global health impact of ST can be expected to intensify (National Cancer Institute (NCI) and Centers for Disease Control and Prevention (CDC), 2014). Activities of the tobacco industry, such as major cigarette companies making their way into ST markets, and employing strategies to promote ST use in smoke-free areas, additionally suggest the high likelihood of this projected trend.

Although the use of ST is spread world over, the highest rates of prevalence and greatest disease burden attributable to ST use can be found within the South Asia (SA) region. Countries in SA are home to over 250 million ST users aged 15 years and older, and users in India and Bangladesh alone make up at least 80% of global consumers of various ST products (NCI and CDC (2014)). Although both countries are major producers and consumers of tobacco products in multiple smoked and smokeless varieties, ST products are the dominant form of tobacco consumption, with higher prevalence of use than smoked tobacco products. This is reflected in the most recent figures from the nationally representative Global Adult Tobacco Survey (GATS), which show that 21.4% of all adults currently use ST products in India compared to 10.7% of adults who use smoked tobacco products (2016). Correspondingly, estimates from Bangladesh show overall use of 20.6% for ST products among adults aged 15 years and over, compared to 18.0% for smoked tobacco (2017). Furthermore, it has been estimated that countries in SA shoulder more than 80% of the global burden of disease and attributable mortality from ST consumption (Siddiqi et al., 2015, Sinha et al., 2018b).

Within the SA region, the prevalence of ST use is higher among certain sub-populations, namely those in higher age groups, and those with lower levels of education and income (Sreeramareddy et al., 2014). Additionally, these education and wealth-related inequalities in ST use may vary according to whether people reside in rural compared to urban areas. For example, in a recent

analysis of GATS data, educational inequalities in ST use were found to be higher in urban areas of India and in rural areas of Bangladesh, whereas wealth inequalities in ST use were higher in urban areas in both the countries (Bandyopadhyay and Irfan, 2019). With regard to gender, while tobacco smoking is generally much higher among adult men than among adult women within the region (e.g. 19.0% of men vs 2.0% of women in India (2016), and 36.2% of men vs 0.8% of women in Bangaldesh (2017)), the gender gap for ST is considerably narrower in India, and in the opposite direction in Bangladesh – higher ST prevalence recorded among adult women compared to adult men in the country. In India, 29.6% of men and 12.6% of women currently use ST, whereas in Bangladesh, 16.2% of men and 24.8% of women are current users of ST products. In both countries, ST use is perceived to be more socially acceptable than tobacco smoking, especially among women (Sansone, 2014); and the gender differences in ST use between the two countries may be due to differences in levels of social acceptability of female ST use in the two settings, likely linked to a range of factors such as culture, tobacco industry practices, and tobacco control policies. In addition, the use of ST among youths in the region is higher than smoking, unlike findings from other geographical regions. Furthermore, ST use among adolescents has markedly increased in few of the countries in SA, which may be an indicator of future trends regarding adult ST use within the region (Mehrotra et al., 2017).

1.2 Reasons for high prevalence

Among the key reasons for the higher prevalence of ST use in SA compared to other geographical regions are – (i) the wide variety of ST products consumed in the region with likely high addiction potential, (ii) the sociocultural factors that are specific to ST use within the region, and (iii) the anti-tobacco policies within the region, which tend to have a greater focus on cigarette smoking. These factors will be considered in turn in the following subsections.

1.2.1 ST products with high potential for dependence

While a variety of ST products are consumed around the world, the greatest diversity in types and forms of use can be found within the SA region (NCI and CDC (2014)). Moreover, the number and variety of South Asian ST products have expanded in recent years beyond traditional handmade forms (e.g. betel quid (paan) with tobacco), to more commercially manufactured products (e.g. gutkha) that are pre-packaged and marketed on a larger scale. Some of popular forms currently used in the region include betel quid with tobacco, zarda, gutkha, khaini, gul, mishri, and tobacco water. Their descriptions and methods of use are summarised in Table 1.1.

Table 1.1 Summary of South Asian ST Products

Name of product	Product description and method of use
Betel quid (paan) with tobacco	Contains tobacco, areca nut, slaked lime (calcium hydroxide) or other alkaline agents, betel leaf, and usually catechu (*Acacia catechu* tree extract). Additional ingredients can vary regionally according to local preference. It is chewed/held in mouth.
Creamy snuff	Contains tobacco, clove oil, glycerine, spearmint, menthol, camphor, and water. It is applied to teeth and gums like regular toothpaste.
Dohra	Contains tobacco, areca nut, and other ingredients such as catechu, slaked lime, peppermint, and cardamom. It is chewed.
Gudakhu	Contains tobacco powder, molasses, red soil, lime, and water. It is applied to teeth/gums, and left in the mouth.
Gul	Contains burned and decomposed tobacco leaves, molasses, and other unknown ingredients. It is applied to teeth/gums, and used as a dentifrice.
Gutkha	Contains tobacco, areca nut, slaked lime, catechu, and other condiments, sweeteners, and flavourings. It is chewed/held in mouth.
Khaini	Contains dried tobacco leaves, slaked lime, and sometimes areca nut. It is sucked/chewed/held in mouth.
Kiwam	Contains tobacco, spices, and other additives such as musk. It is chewed/held in mouth or chewed in betel quid.
Mainpuri	Contains tobacco, slaked lime, areca nut, camphor, and cloves. It is chewed/held in mouth or chewed in betel quid.
Mawa	Contains tobacco, slaked lime, and areca nut. It is chewed.
Mishri	Contains dried and powdered tobacco. It is applied to teeth/gums, or sucked.
Red toothpowder	Contains fine red tobacco powder, herbs, and flavourings. It is applied to teeth/gums, and used as a dentifrice.
Tapkeer	Contains dried and powdered tobacco – similar to mishri. It is applied to teeth/gums, and left in the mouth.
Tobacco leaf	Contains raw dried tobacco leaf. It is chewed by itself/in betel quid/ or other custom-made product.
Tuibur	Contains tobacco smoke, and water. It is gargled or held in mouth
Zarda	Contains tobacco, lime, spices, vegetable dyes, and sometimes areca nut and silver flecks. It is chewed by itself/in betel quid/or other custom-made product.

Source: NCI and CDC (2014)

Dependence to tobacco, often used interchangeably with addiction, may be understood as a construct or state that manifests itself through repeated and compulsive use of tobacco, alongside other characteristics such as impaired control over use, high motivation to seek the drug, and experiencing effects of withdrawal and tolerance (NCI, 2009). Dependence or addiction has been described as the fundamental reason that individuals persist in using any tobacco product including smokeless forms, leading to chronic exposure to different harmful constituents contained in the products (U.S. Department of Health and Human Services (USDHHS), 2010).

Consequently, any effort to reduce tobacco-related morbidity and mortality must take the addiction potential of tobacco products into account.

Although tobacco products contain thousands of non-nicotine chemicals, some of which could contribute to dependence, it is widely accepted that nicotine is primarily responsible for this effect (USDHHS, 1988). Nevertheless, the addiction potential of tobacco products can additionally be influenced by other related factors such as the amount of nicotine contained in the product, its design and speed of nicotine delivery, as well as other ingredients included, making it essential to study tobacco dependence associated with the use of specific product types. With regard to ST dependence, there are additional complexities that arise from differences across various types of ST products. For instance, nicotine content in different ST products have been found to vary between 0.20 – 40.10 mg/g, compared to the standard 16.3 mg/g of nicotine contained in commercially manufactured cigarettes (Malson et al., 2001). In addition, vast variations have been reported in the rate and amount of nicotine absorbed from different ST products (Fant et al., 1999), likely linked with variations in pH – higher levels of pH result in higher levels of free nicotine available for absorption, and consequently higher potential for developing ST addiction (Stanfill et al., 2010).

On biochemical testing, some of the South Asian ST products have been found to have among the highest levels of nicotine compared to ST products consumed in Western countries, as well as very high levels of alkalinity (Stanfill et al., 2010). Many products consumed in the region include areca nut as an added ingredient, which is itself recognised as an addictive substance (International Agency for Research on Cancer (IARC), 2004). In addition, South Asian ST products tend to be made with *Nicotiana rustica*, a species of tobacco with higher concentrations of nicotine and other alkaloids compared to *N. tabacum*, which is used in most other commercial tobacco products worldwide (IARC, 2007). Furthermore, the findings of very low quit rates for ST in SA, as shown in the GATS data from India and Bangladesh, suggest that the ST products consumed in the region are highly addictive and contribute to high rates of prevalence (NCI and CDC (2014)).

1.2.2 Sociocultural factors

Sociocultural aspects of health behaviours have been described as "the social and cultural patterns within the human community that affect health behaviours, including such factors as shared belief systems, family structures, and social contracts" (Gupta et al., 2016). Across countries in SA and the South Asian diaspora, there is a strong sociocultural dimension to ST use, which has been described as 'unique' to these communities. This is also reflected in the coining of the term "culturally-specific tobacco products" to denote South Asian ST products that have historical and

behavioural specificity to both resident and migrant South Asian populations (Mukherjea and Modayil, 2013).

The cultural significance accorded to ST use within SA has been linked to the age-old practice of betel quid or paan chewing (betel leaf rolled with areca nut and spices), which has existed within this geographical region for over 2000 years. Following its introduction in SA in the 1600s, tobacco became an important additive to this traditional product, and chewing betel quid with tobacco gradually became a convenient method of consuming ST within the region (Reddy and Gupta, 2004). Product preference information from the most recent GATS data for Bangladesh (2017) shows that betel quid with tobacco is still the most commonly used ST product in the country, while it is the third most commonly consumed ST product in India (2016). Migrant populations from SA have also been reported to carry on these ST use practices in countries where they have settled, in order for them to maintain what is viewed as traditional practices within new settlements (Messina et al., 2012, Mukherjea et al., 2012).

Unlike tobacco smoking, there is a social acceptance of ST in SA, which can be seen through a characteristic pattern of widespread use within the region not only among men, but even among vulnerable groups such as children, teenagers, and women of reproductive age (Gupta and Ray, 2003). Also, it would be generally acceptable for younger users to chew tobacco in the presence of elders, whereas tobacco smoking in a similar context would be considered as taboo (Gupta et al., 2016). In many South Asian communities, chewing tobacco is often regarded as a shared activity to be performed with friends and family members. It may also be offered to visitors and guests within homes, or at social gatherings such as festivals and weddings, as a means of welcoming people and facilitating social interaction (Anwar et al., 2005, Messina et al., 2012). Users in the region can consider ST to be a ‘part of life’ (Gunaseelan et al., 2007) and a ‘birth right’ (Sorensen et al., 2005), which may be passed on from generation to generation as a cultural tradition within families (Kakde et al., 2012).

Because ST has such a long history of use within South Asian culture, many people in the region do not associate ST use with serious adverse health consequences. Compared with smoking, the levels of awareness about the harmful effects of ST tend to be lower within the region. Although evidence from GATS in India and Bangladesh suggest that the vast majority of adults in both these countries are generally aware that ST products can be harmful, their knowledge of the specific health risks associated with use are limited (Sansone, 2014). In addition, there are misconceptions that ST products are relatively safe to use, and that they may even provide health benefits such as improvements in oral hygiene, aiding with digestion, and relieving tooth pain, headaches, abdominal pain, and nausea in pregnancy (Messina et al., 2012, Begum et al., 2015). Linked with sociocultural factors, this lack of full awareness of harmful effects, as well as

misconceptions relating to ST use are among the key reasons for high prevalence in South Asian contexts. Previous research done in India has demonstrated that differences in levels of knowledge about health effects are significantly linked with ST users' quit intentions and practices, (Raute et al., 2011), suggesting that it is important to improve levels of awareness regarding ST-related health risks to improve cessation rates and reduce prevalence.

1.2.3 Lack of ST control policies

In addition to the factors described previously, the lack of strongly enforced ST control policies in the South Asian region contributes to high rates of prevalence, as detailed below.

In response to the globalisation of the tobacco epidemic, the Framework Convention on Tobacco Control (FCTC) was developed by the World Health Organization (WHO) in 2003 and entered into force in 2005 (WHO, 2003). The FCTC is celebrated as one of the most widely adopted global public health treaties, with 181 Parties as of May 2018 (WHO, 2018). It provides a comprehensive strategy, using a broad range of evidence-based measures to reduce both the demand and supply of all tobacco products. But while almost all provisions of the FCTC have direct and distinct implications for ST products, it is only following the fourth conference of the FCTC parties (WHO, 2010a) that the global threat from ST has come to be formally recognised. Since efforts to include ST in tobacco control policies under the WHO FCTC have begun, there has been considerable progress in its compliance, especially with Parties defining ST products and including them in surveillance measures. However, very little progress has been made with regard to the other policy areas, and ST prevention has received much less attention than smoking prevention overall (Mehrotra et al., 2017).

While countries in SA have ratified the FCTC, ST control policies tend to be limited when compared to smoking control policies, despite the scale of ST use within the region. For example, policies in relation to tobacco taxation show lower tax rates for ST products compared to cigarettes, and higher rates of tax evasion (Khan et al., 2014a). In addition, all provisions of the FCTC articles tend not to be covered with regard to policies relevant to ST control. For example, despite the availability of guidelines for comprehensive bans on ST advertising, promotion, and sponsorship (TAPS), very few Parties have framed comprehensive policies relating to ST TAPS bans (Mehrotra et al., 2017). This is particularly important, given that there is evidence that partial policies are not very effective for tobacco control (Nagler and Viswanath, 2013). Finally, even where there are wide-ranging policies on ST, often they are not effectively implemented, as found in a recent review of existing ST control policies within the South Asian region (Khan et al., 2014a). This is true even in instances where some ST related policies are stricter than smoking policies, such as the gutkha ban in India. A general lack of political will to address the issue, and

the growing influence of tobacco companies within the region contribute to a lack of comprehensive and strongly enforced ST control policies in SA (Khan et al., 2014a). Additionally, a wide range of heterogeneous products, which are often manufactured and sold in informal and unorganised settings pose considerable challenges for developing and implementing effective regulatory policies. Taken together, these factors mean that ST products are widely accessible and easily affordable for the majority of the population in South Asian countries, contributing to high rates of prevalence within the region.

In Table 1.2, I summarise the FCTC demand- and supply-reduction policy measures that are relevant to the regulation of ST products, along with other regulatory initiatives undertaken in some South Asian countries, such as imposing varying levels of restrictions on the manufacture, import, and/or sale of ST products, and implementing bans on spitting and using ST products in public places.

Table 1.2 FCTC and non-FCTC policy measures for ST control

Article	**Description**
Demand-reduction measures	
Article 6	Price and tax measures to reduce demand for ST
Articles 9 & 10	Regulation of ST product contents and disclosures
Article 11	Packaging and labelling of ST
Article 12	Education, communication, training and public awareness on ST
Article 13	Ban on ST advertisement, promotion and sponsorship
Article 14	Demand reduction measures concerning ST dependence and cessation
Supply-reduction measures	
Article 15	Illicit trade in ST
Article 16	Access and availability of ST to minors
Article 17	Economically viable alternatives to ST
Other ST policy measures not included in FCTC	
-	Prohibition on import, manufacture and sale of ST
-	Ban on spitting and ST use in public places

1.2.4 Summary

In summary, countries in SA have the maximum diversity in ST products, with correspondingly wide variations in added ingredients, manufacturing processes and patterns of use. These factors contribute to commonly used South Asian ST products being amongst those with the highest addiction potential. There is also a high social acceptance of ST use within the region, which has itself been identified as a key barrier to the formulation and implementation of effective ST control policies in SA (Khan et al., 2014a). Together, these factors explain the high prevalence of

ST use in the region, resulting in populations facing > 80% of the global burden of disease and deaths due to ST use.

Having considered the reasons for high prevalence of ST use within South Asian contexts, I will focus on explaining the research gaps within each of these areas in the following sections.

1.3 ST dependence and its measurement

From the evidence presented in the previous section, we know that ST products in SA have a high addiction potential, likely resulting in high levels of dependence among users in the region. However, little is known about ways to measure ST dependence in general, and particularly within South Asian contexts, as detailed in the following subsections.

1.3.1 The need to measure ST dependence

Measurement is the cornerstone of science, and given that tobacco dependence research spans the gamut from fields including neuroscience and genetics to prevention, treatment and services, the concept of tobacco dependence and its measurement are directly relevant to many researchers and clinicians working across these multiple fields. More specifically, the measurement of dependence forms the basis for studies to determine the extent and nature of the problem, its causation, prevention and management, in addition to establishing whether and what kind of medical treatment or care may be appropriate for people affected by the condition (West and Miller, 2011). However, robust definitions form a pivotal role in developing meaningful measures of a construct, and disagreements over the definition and nature of tobacco dependence have in turn slowed innovations in this field (Piper et al., 2004). Nevertheless, as the field continues to progress, further studies on the measurement of tobacco dependence will be needed to aid the evolution and refinement of its understanding (USDHHS, (2010)).

Till date, there is a general acceptance of the core features or manifestations of tobacco dependence associated with its use in different forms. These include repeated and compulsive self-administration of tobacco, impaired control over use, high motivation to seek the drug for various reasons (e.g. cravings, to ease a depressed mood, for relaxation or stimulation, etc.), judgment of greater value from the use of tobacco over other activities, and manifesting signs of physical dependence such as withdrawal or tolerance (USDHHS, (2010)). But despite this, there are other issues limiting the measurement of tobacco dependence, which stem from uncertainties regarding the nature of the construct. For example, it is not yet clear whether tobacco dependence should be viewed as categorical (diagnosing dependent vs. non-dependent users), dimensional (unidimensional vs. multidimensional), or emergent (changing over time), and whether it should

be measured accordingly (NCI, 2009). Nevertheless, there seems to be value in dependence measures that are based on these different conceptualisations. For instance, diagnostic measures might be needed for clinical practice and in epidemiological research for identifying rates of dependence, but might be less than optimal when it comes to genetic research, or for informing primary prevention efforts, where other types of dependence measures might be needed (Conway et al., 2010).

While is it important to focus on these aspects of dependence measurement, it is equally important to consider ways of measuring tobacco dependence associated with its use in different forms, particularly in settings where multiple forms of non-cigarette tobacco are widely consumed. In this regard, there are two alternative strategies that have been suggested. Some researchers propose using the same scales across different tobacco products for measuring dependence. For example, DiFranza et al. (2012) demonstrate high cross-product reliability for measures of dependence among adolescent users of cigarettes and ST products, finding no meaningful differences between the two groups at comparable levels of lifetime use. Based on these findings, they argue that this approach has potential value for measuring dependence in contexts where tobacco is used in multiple forms. On the other hand, others point out that behaviours related to each product play a critical role in tobacco dependence, so product-specific scales may be needed (Fagerström and Eissenberg, 2012). As summarised by De Leon et al. (2013) both these approaches may be equally valid for measuring tobacco dependence linked with different product types, with each having distinct applications depending on whether one's primary goal is surveillance or the development of tobacco control interventions that integrate specific behavioural elements related to the use of different product types.

With regard to ST, the peak level of blood nicotine reached among habitual users of ST products seems to approximate that observed in habitual cigarette smokers (Benowitz, 1988, Holm et al., 1992). Although these findings are based on studies limited to snus use, they support the idea that ST users can develop a dependency similar to that seen in cigarette smokers. On the other hand, nicotine absorption kinetics of ST products may differ from those of cigarettes – while nicotine levels tend to fall rapidly after cigarette smoking, they have been found to fall more slowly after the use of ST, consistent with continuous absorption of nicotine even after the tobacco is removed from the mouth (Benowitz et al., 1988). This, in addition to findings of variations in nicotine absorption based on the pH of ST products (Pickworth et al., 2014), suggest that ST dependence should be assessed distinctly from dependence linked with the use of other forms of tobacco.

However, this has come to be more widely recognised by tobacco researchers only in recent years, and only a limited number of studies focus on ways to measure dependence linked with ST use till date. Nevertheless, as noted previously, these include both cross-product and ST-specific

assessments of dependence. In the case of the former, the utility of both complete scales (DiFranza et al., 2012), as well as selected items or item groups from dependency scales (Post et al., 2010, Strong et al., 2015, Strong et al., 2017), have been assessed among users of different forms of tobacco, including ST. On the other hand, there are ST-specific scales, which have been developed to measure dependence exclusively associated with the use of ST products. The available evidence from these studies are considered in more detail below.

1.3.2 ST dependence scales

Given the advances in cigarette dependence measurements, existing ST dependence scales typically tend to be adaptations or modifications of cigarette-based scales, developed either by rewording items to fit ST use practices (e.g. smoking reworded to chewing or dipping), or by including items on features unique to some ST products that could affect nicotine absorption (e.g. swallowing of tobacco juices). Even the cross-product dependence measures tend to be items and scales originally developed for cigarette smoking, and subsequently modified for non-cigarette applications (including ST). Therefore, it follows that classifications of cigarette dependence scales may be applied to ST scales as well, particularly given that progress in the field of ST dependence measurement, albeit slow, has resulted in ST-specific scales currently existing across the scope of cigarette-based dependency scales.

As suggested by Piper et al. (2008a) for cigarette scales, the existing ST dependency scales may also be classified into: (1) global or traditional scales, which tend to focus on direct assessments of the end-products of dependence, and (2) newer multidimensional scales, which have been designed to provide greater insight into the nature or mechanisms underlying the development of tobacco dependence. The traditional scales in turn include (a) diagnostic scales based on clinically defined dependence criteria (e.g. WHO's Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (1992), and American Psychiatry Association's (APA) Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (1994)), as well as (b) Fagerström scales of tobacco dependence. Similar to the development of cigarette scales, newer ST dependence scales try to address some of the limitations posed by earlier ones.

Diagnoses of tobacco dependence are typically made in clinical settings by trained professionals, using structured and semi-structured interviews that are based on the DSM and ICD criteria indicated above. However, itemised paper-and-pencil scales developed on the basis of diagnostic criteria allow for more widespread administration of measures through surveys and self-report. But despite their utility, one of the key limitations of diagnostic scales is that, by providing a dichotomous classification of tobacco users (dependent or non-dependent), they fail to capture

dependence that may vary in degrees and may be insensitive to any differences among those persons diagnosed as being tobacco dependent (Piper et al., 2004). On the other hand, Fagerström measures can be used to determine the degree of dependence among tobacco users (Fagerström, 1978). However, these are based on the limited assumption that the most important component of dependence is physical dependence (e.g. the need to use tobacco within a certain time of awakening so as to alleviate withdrawal, the need to consume high quantities of tobacco each day, etc.), and that this single dimension is adequate to capture any meaningful individual differences in dependence severity (Piper et al., 2004). Another limitation of the Fagerström measures is that they show poor internal consistency on psychometric assessments (Heatherton et al., 1991, Etter et al., 1999). Nevertheless, Fagerström measures are among the most widely used measures of tobacco dependence, likely due to their brevity, ease of administration, and ability to predict dependence criteria such as relapse following a cessation attempt (Piper et al., 2008a).

In time, it was pointed out that tobacco dependence has several dimensions, including physical, behavioural, and psychological components, suggesting that it should be assessed and quantified accordingly (Piper et al., 2004, Shiffman et al., 2004). Therefore, multidimensional dependence scales were developed by focusing on the different components or dimensions of tobacco dependence, and their potentially discrete relationships with dependence criteria such as heaviness of use, cessation outcomes, withdrawal severity and likelihood of relapse. In addition, unlike the other types of dependency scales, the development of multidimensional scales tend to be well-grounded in psychometric theory. However, a likely limitation could be their greater utility in research, rather than clinical settings (Piper et al., 2008a).

1.3.3 Application of ST dependence scales in SA

Although the summary of evidence relating to ST-dependency scales suggests a degree of progress within this area of research, it is important to recognise that all the existing scales have been developed and validated exclusively in Western settings. Moreover, the scales have all been developed in the English language and culturally aligned to the measurement of ST dependence among Western users. Besides the ST-dependence scales, two product-specific scales for measuring betel quid dependence, have been developed and validated in Taiwan (Betel Quid Dependence Scale, Lee et al. (2012)) and Guam (Reasons for Betel Quid Chewing Scale, Little et al. (2014)). However, the application of these scales to other forms of ST may be limited, given that betel quid is often consumed without tobacco in those study settings.

In South Asian countries, despite the widespread use of different ST products, scales to measure ST dependence have not been developed till date. In addition, cross-cultural validation of existing scales have hardly been attempted. This represents a significant research gap, particularly given

the linguistic and cultural differences between ST users in different geographical settings, as well as the likelihood that expressions of ST dependence may vary across different cultures (Mushtaq et al., 2019). Furthermore, the literature shows that different types of research studies from SA include existing ST dependency scales within their methodologies, as presented below. Given this situation, limited attempts at scale validation within South Asian settings can mean inaccurate conclusions regarding the presence and degree of ST dependence assessed by these studies.

The large majority of South Asian studies that incorporate ST dependency scales come from India and apply Fagerström-based measures. Examples of study types, as well as their reasons for using the scales include: intervention studies (e.g. Jain et al. (2013)) – to allow controlling for ST dependence while assessing the effectiveness of cessation interventions; observational studies, including follow-up studies – for setting inclusion criteria based on a certain cut-off scores on dependency scales (e.g. Jena et al. (2016)), and case-control studies – to assess ST dependence as an exposure variable for developing particular health outcomes (e.g. Swaroop et al. (2014)); large cross-sectional surveys – to measure the prevalence of ST dependence and study its determinants (e.g. Manimunda et al. (2012)); and smaller surveys – to measure ST dependence in specific patients or work-based participant groups (e.g. Priyanka et al. (2016)), as well as study the association between ST dependence and specific ST use behaviours such as quitting (e.g. Islam et al. (2014)). These applications demonstrate the need for accurate scales to measure ST dependence in SA, specifically to aid progress in other areas of ST-related research and control.

1.4 Sociocultural factors

So far, we know that sociocultural factors represent an important dimension of ST use in SA, and that they serve to explain the widespread use of ST products within the region. However, little is known about which sociocultural factors are relevant to measure, whether their distribution patterns vary according to sociodemographic characteristics of ST users, or whether they influence any ST use characteristics among South Asian users.

From studies conducted across South Asian countries, we know of the pervasive use of ST among close friends, family members, and other significant contacts of study participants (Kakde et al., 2012). For example, in some cross-sectional studies, participants report ST use in up to 98.1% of close friends (Shah et al., 2008), and up to 100% of close family members (Anwar et al., 2005). Similarly, studies conducted at workplaces and educational institutions report a high degree of ST use among co-workers and teachers of study participants (e.g. Shah et al. (2008), Sreeramareddy et al. (2008)). These sociocultural factors are important to measure, given that studies from SA have found that ST use by parents and peers are strongly associated with ST use among both adolescent (Hussain et al., 2017), and adult participants (Madathil et al., 2015) in the

region. Several studies from India have found that the initiation and acquisition of ST habits can occur at very young ages, as children and adolescents pick up the practice from close family members, according to the patterns of product preference established by adults within their households (Gupta and Ray, 2003). Particularly in the Indian subcontinent, peer pressure is also a well-known reason for ST initiation and continuation (Kakde et al., 2012), as well as for resuming the practice following a cessation attempt (Sorensen et al., 2005).

But while these measures provide important information about the social environments in which individuals live within South Asian settings, they fail to capture whether users show a preference for consuming ST mainly when they are alone or in the company of other people, thereby limiting our ability to appreciate any social patterns of ST use that might exist among user groups. Studies conducted among cigarette (Moran et al., 2004) and water pipe smokers (Maziak et al., 2004) suggest that this can be an important aspect to measure, with more intensive smokers showing an increasingly individual pattern of tobacco smoking. However, we do not know if these findings also apply to ST users in South Asian settings. Similarly, while we know that ST products may be readily available within people's homes in SA (Prabhu et al., 2001), we do not know the extent to which ST use is restricted within households in this region. As with the measure relating to social use of tobacco, cigarette studies suggest that household tobacco restrictions might be important to quantify, as they can influence tobacco use characteristics such as smoking intensity and intentions to quit (Owusu et al., 2017, Owusu et al., 2020).

Overall, the literature relating to ST-linked sociocultural factors in South Asian settings is limited, and only a subset of these studies attempt to quantify associations between sociocultural factors and ST use practices (Ray et al., 2016). Given that a greater understanding of this field can provide valuable insights towards designing and implementing more effective ST control strategies for South Asian populations (Sansone, 2014, Gupta et al., 2016), the lack of evidence represents a significant research gap.

1.5 Research relevant to ST control policies in SA

The write-up in this section is based a series of targeted reviews conducted on both FCTC and non-FCTC policy measures relevant to the control of ST products, the aim being to summarise the recent literature and identify research gaps relevant to the development and implementation of ST-specific policies for South Asian settings. The review methodologies followed are as follows.

In setting the criteria for study selection, only articles written in the English language, and published in 2012 or later were considered for inclusion. While the review was limited to studies

conducted in South Asian countries, this limit was applied at the stage of study selection rather than forming a part of the search strategies. All investigations published in peer-reviewed journals that related to ST control policies were considered eligible for selection. These included policy areas set out under the demand- or supply-reduction measures of the WHO FCTC, as well as other non-FCTC policy measures, such as prohibition on import, manufacture and sale of ST, and ban on spitting and using ST in public places. Studies relating to dual use or use of ST for harm reduction were not selected for inclusion.

The MEDLINE database was searched from January, 2012 to June, 2017, with searches rerun in December, 2018. The search terms included keywords for ST such as "smokeless tobacco" OR "chewing tobacco" OR "snus" OR "snuff", combined with operationalised keywords for each of the FCTC demand-reduction Articles 6, 9 – 14 (e.g. "tax", "price", "content", "disclosure", "packaging", "labelling", "warning", "education", "media", "campaign", "marketing", "advertising", "bans" and "cessation"), and supply-reduction Articles 15 – 17 (e.g. "illicit trade", "youth access", "sale to minors", and "alternatives"). As keywords such as "bans" were included in the FCTC search strategies, separate searches were not run for the non-FCTC policy measures (bans on import, manufacture and sale of ST, and bans on spitting and using ST in public places).

In Table 1.3, I present one of the MEDLINE searches conducted for Article 6 (price and tax measures to reduce demand for ST), along with the number of studies retrieved. Similar details for searches targeting other policy areas can be found in Appendix 1.1. In addition to the MEDLINE searches conducted, other strategies to identify potential studies included the screening of reference lists of eligible studies, as well as scanning the titles of all papers citing the included studies.

Table 1.3 MEDLINE search strategy related to FCTC Article 6

Database (search platform): **MEDLINE (OvidSP)**		
Search date: **24/06/2017**		
Search terms		**Number of studies**
1.	smokeless tobacco.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] or exp Tobacco, Smokeless/	3783
2.	chew* tobacco.mp.	552
3.	oral tobacco.mp.	65
4.	(snus or snuff or dip* tobacco or betel quid or pan masala or gutk*a or khaini).mp.	2301
5.	1 or 2 or 3 or 4	5069
6.	(price or pricing or price elasticity).mp.	20832

7.	(tax* or taxation or excise tax* or tax elasticity).mp.	108218
8.	(economy or economics or economic evaluation).mp.	86125
9.	6 or 7 or 8	210142
10.	5 and 9	110
11.	limit 10 to (english language and humans and yr="2012 - Current")	**42**

References identified from all the searches were imported into a single EndNote file, and duplicate references were identified and removed. A two-step study selection process was employed, by which titles and abstracts were first screened, followed by retrieval and screening of full-text articles. Elimination of studies to geographically limit inclusions from countries in SA was performed at the stage of full-texts screening. Following these steps, studies that fit the selection criteria were retained and sorted, using EndNote reference groups for each of the FCTC Articles and non-FCTC policy measures. On the other hand, studies that did not fit the inclusion criteria were excluded at this stage, noting the reasons for exclusion. No formal assessment of study quality was performed.

The findings based on a narrative synthesis of global studies relevant to ST demand-reduction measures have been published in a paper titled "A Policy Perspective on the Global Use of Smokeless Tobacco" (2017). The results relevant to ST policy research from countries in SA are presented below.

1.5.1 Overview of included studies

Following the two-step selection process, a total of 43 studies were found to be relevant to the various policy areas considered. Among these, six papers were relevant to FCTC Article 6 (price and taxation), eight to Articles 9 and 10 (regulation of ST contents and disclosures), six to Article 11 (packaging and labelling of ST products), three to Article 12 (education, communication, training and public awareness), seven to Article 13 (ST advertising, promotion and sponsorship), nine to Article 14 (policies related to ST cessation), one to Article 15 (illicit trade in ST products), three to Article 16 (sales of ST to and by minors), two to Article 17 (support for economically viable alternative activities), and seven to the non-FCTC policy areas considered. Details of the study selection process, as well as the data extraction table of all included studies can be found in Appendix 1.2 and 1.3.

The vast majority of included studies were conducted in India (36/43), four in Pakistan (Saeed et al., 2012, Arain et al., 2015a, Arain et al., 2015b, Siddiqi et al., 2016a) and one in Bangladesh (Nargis et al., 2014). The two remaining studies were conducted in more than one South Asian country – Bangladesh and India (Mutti et al., 2016), and Bangladesh, Pakistan, and Nepal (Siddiqi

et al., 2016b). There were wide variations in the study types and methodologies employed. Some studies relevant to ST policies on product content involved biochemical testing of ST products (e.g. Saeed et al. (2012)), whereas studies relevant to packaging and marketing policies involved the purchasing of ST products and assessing their labels for health warnings or disclosures (e.g. Sharma et al. (2015)). There were experimental studies that tested different types of interventions for ST cessation (e.g. Jain et al. (2013), and observational studies that either involved primary data collection (e.g. Siddiqi et al. (2016b)), or secondary analyses of large datasets such as GATS (e.g. Kostova and Dave (2015)). The majority of studies that involved the participation of human subjects were conducted among adults, with youth comprising the study population in five studies (Joseph and Chaloupka, 2013, Lal et al., 2015, Mistry et al., 2015, Sardana et al., 2015, Harrell et al., 2016). Gender wise, most papers reported mixed samples, with data from female-only samples reported in three studies (Mishra et al., 2014b, Panda et al., 2015b, Jhanjee et al., 2017). Study participants were male-only or mostly male in three further studies (Pimple et al., 2012, Dhumal and Gupta, 2013, Jain et al., 2013).

In what follows, I will present a summary of my review results in context, and highlight the research gaps across different policy areas for ST control in South Asia.

1.5.2 Demand-reduction measures

1.5.2.1 Article 6 – Price and tax measures to reduce demand for ST

Although studies on pricing and taxation could serve as key motivating factors for governments and decision-makers to support stronger policy measures for ST control, very few ST-specific studies relevant to this policy area are available from South Asian countries. Globally, pricing and taxation measures are considered among the most effective demand-reduction policy tools for ST control (Near et al., 2013, Timberlake et al., 2014). However, evidence on the impact of such measures in South Asian contexts is limited to only one small Indian study, which reports a 38% reduction in average sales of ST, and a 21% reduction in ST consumption, following a 68% rise in ST prices (Singh et al., 2012).

Nevertheless, based on four other South Asian studies (3 – India, 1 – Bangladesh) that report negative price elasticities for ST products (Joseph and Chaloupka, 2013, Nargis et al., 2014, Kostova and Dave, 2015, Selvaraj et al., 2015), there is consistent evidence to suggest that ST pricing and taxation policies could be effective measures for deterring the use of ST among both youth and adult populations in the region, while simultaneously benefitting the countries implementing such measures by increasing their tax revenues. Similarly, studies from European and American regions also estimate price elasticities for ST products to be in the inelastic range

(Huang and Chaloupka IV, 2012, Near et al., 2013, Levy et al., 2016). In SA, the estimated price elasticities of ST products range from -0.21 (Kostova and Dave, 2015) to -0.64 (Nargis et al., 2014) for adults, indicating that a 10% rise in the price of ST would reduce consumption by 2.1% – 6.4%. The estimated price elasticity for youth (13 – 15 years), based on nationally representative survey data in India, also falls within this range (-0.58) (Joseph and Chaloupka, 2013). Reports from India additionally suggest likely differences in responsiveness to ST pricing and taxation policies according to gender and socioeconomic status of users – girls compared to boys (Joseph and Chaloupka, 2013), adult men compared to adult women (Kostova and Dave, 2015), and poorer households compared to wealthier households (Selvaraj et al., 2015), are likely to show greater responsiveness to ST tax and price rises.

On the other hand, studies on the implementation of ST tax policies in the region suggest considerable room for improvement. In India, ST tax rises tend to be small when compared with the price increase of other commodities and per capita income of the population during the same timeframes. This has meant an increase in the general affordability of ST products in India from 2006 – 2012 (Rout and Arora, 2014), with similar findings previously reported for the period 2001 – 2007 (John et al., 2010). In addition, none of the South Asian countries have total ST tax incidence at or above 70% (Mehrotra et al., 2017), despite WHO recommendations that excise taxes alone should account for at least 70% of tobacco retail prices (WHO, 2010b). In Bangladesh and Nepal, tax incidence for ST is lower than cigarettes, whereas it is higher in India. Nevertheless, retail prices for ST are lower than cigarette prices in all three countries, suggesting the need for a minimum floor price on the lowest unit of consumption that is equalised across all tobacco products in the region (Mehrotra et al., 2017). In India, the speed of ST packaging machines has recently been incorporated as a factor for determining the deemed production and excise duty payable by manufacturers under a Compounded Levy Scheme. However, to my knowledge, research studies relating to the implementation or impact of this taxation measure has not been carried out till date.

Based largely on cigarette literature, Van Walbeek et al. (2012) list the following broad areas as research gaps in relation to Article 6, especially for low- and middle-income countries (LMICs): (1) monitoring tobacco consumption, prices, and taxes, (2) assessing the effectiveness of the tax structure in generating revenue and reducing tobacco use, (3) strengthening the tax administration system in order to reduce tax evasion and tax avoidance, and (4) improving understanding of the political economy of tobacco tax policies. Although the evidence from SA makes a reasonable case for increasing taxes to control ST use in the region and enhance government revenues, the overall lack of studies suggests that for the development and implementation of effective ST taxation policies, more research is needed across all the above mentioned areas.

1.5.2.2 Articles 9 & 10 – Regulation of ST product contents and disclosures

Regulating the content of any tobacco product represents an effort to mitigate harm, without hindering any efforts to reduce or eliminate tobacco consumption among populations. Based on this understanding, a sequence of broad research questions to inform policies on regulating the contents of tobacco products are listed by Gray and Borland (2012): (1) what is in the tobacco product, (2) what is absorbed into the body from consumption of the product, and (3) how much of this is harmful, addictive or increases the product's attractiveness.

Seven (4 – India and 3 – Pakistan) of the eight identified studies relating to FCTC Articles 9 and 10, are reports of product testing for contents and disclosures, and provide evidence for the first of these research questions. While two studies test different brands or samples of the same type of ST (naswar – Saeed et al. (2012) and chaini khaini – Stepanov et al. (2015)), others test a range of products available in the market (Prabhakar et al., 2013, Arain et al., 2015a, Arain et al., 2015b, Sharma et al., 2015, Stepanov et al., 2017). The results show higher levels of chemical carcinogens in South Asian ST products than the upper limits set by the WHO Study Group on Tobacco Product Regulation (WHO, 2009). The reports also show wide variations in nicotine and pH levels, for which the setting of upper limits has been suggested (WHO, 2015). Two of these studies (Arain et al., 2015b, Arain et al., 2015a), also report higher levels of nickel and arsenic via ST use in biological samples of oral cancer patients compared to controls, providing some evidence from the region for the two other research questions listed above. However, biochemical testing does not extend to all available ST products within the region, and the products are not analysed on a periodic basis. There are also no studies relating to the implementation or impact assessment of content regulation policies.

Article 10 of the FCTC requires ST manufacturers and importers to disclose the contents of products to governments and public, and the evidence from two studies in SA show inadequate regulation of ST products' disclosures in the region. Among samples of gutkha, khaini, and tambakku from India, only some of the products tend to list ingredients, although the presence or effects of nicotine are not included (Sharma et al., 2015). Furthermore, the non-implementation of disclosure requirements often go unquestioned by relevant authorities, during regulatory inspections of manufacturing sites and retail venues (Siddiqi et al., 2016b).

Overall, there is a lack of documentation of the ingredients of various ST products and their toxic effects as a result of product testing not extending across the range of ST products consumed across the SA region. While upper limits have been set for the regulation of carcinogens in ST products, such as Tobacco-Specific Nitrosamines (TSNAs) and benzo[a]pyrene, standards are not yet available for quantifying and regulating other constituents, including additives and flavouring

agents. The overall lack of research within this policy area has been linked to the limited availability of independent laboratory facilities for testing tobacco products, with even lesser focus on smokeless products (Mehrotra et al., 2017). Within the SA region, tobacco testing laboratories are present only in India and Pakistan. Correspondingly, the availability of reports on ST product testing are limited to these countries.

1.5.2.3 Articles 11 & 12 – ST packaging and public awareness campaigns

The findings relevant to Articles 11 and 12 are considered together in this section, given that health warning messages on ST packaging can also serve as communication tools to raise public awareness about the harms associated with ST use. Based on cigarette literature, Hammond et al. (2012) had summarised the research priorities for implementation of the two FCTC Articles as follows: (a) identify information needs and gaps among current users, (b) research to create effective content for health warnings and media campaigns, (c) research on how messages are processed by different groups of people, and (d) research to identify the most cost-effective and best practices for sustaining health communications over time. Although the South Asian ST literature includes studies relevant to each of these priority areas, they are very few in number and largely limited to India.

With regard to Article 11, there is evidence from India and Bangladesh that graphic pictorial warnings are perceived as the most effective form of health warnings for ST products in the region, albeit based on results of one large randomised study conducted across the two countries (Mutti et al., 2016). Further analysis of the collected data shows that the effectiveness of pictorial health warnings are enhanced by images that prompt negative reactions and are perceived as credible by study participants (Mutti-Packer et al., 2017). Experimental studies from other geographical regions report comparable findings, whereby those exposed to graphic warnings perceive greater harm associated with ST use (Popova and Ling, 2014), and are more likely to recall health warning messages (Klein et al., 2017), compared to those exposed to other forms of warning labels.

On the other hand, there are relatively more studies on policy implementation and impact assessment relevant to this FCTC Article. The majority of these studies come from India, where complete policies are in place with regard to health warning labels on ST packages (Mehrotra et al., 2017). While the results of a large study identified in the review suggest that graphic pictorial warnings introduced in 2011 are largely ineffective (Gravely et al., 2016), a further requirement of bigger images that cover up to 85% of the display area on both sides of ST packages has since been incorporated, and results from the most recent GATS (2016) suggest greater impact of these policy changes on ST users' motivations to quit. Nevertheless, other studies report evidence of

inadequate implementation of policy requirements in many parts of India, with some ST products not having pictorial warnings, and some products sold without any health warnings altogether (Sharma et al., 2015, Vidhubala et al., 2016, Shekhawat et al., 2017). Among the other South Asian countries, Bangladesh and Nepal also have complete laws on ST packaging, but yet to be implemented in the case of the former (Mehrotra et al., 2017). However, evidence from these countries also reveal several issues with the implementation of health warning policies, such as very few pictorial warnings (0 – 13.5%), low visibility of warning labels, use of English-only texts, and misleading warnings that tend to be tactfully hidden (Siddiqi et al., 2016b).

With regard to Article 12, all three included studies from the SA region are from India. Of these, two are evaluation studies of mass media campaigns against ST use (Murukutla et al., 2012, Hamill et al., 2015) and one provides information specific to the formulation of anti-ST media campaigns in the country (Singh et al., 2018). The available evidence suggests that mass media campaigns can be highly effective for raising public awareness regarding the harms of ST and impacting greater cessation-oriented intentions and behaviours among ST users in the region. Similar potential for mass media campaigns to reduce ST consumption has also been documented in other geographical regions (Near et al., 2013). A further cost-benefit analysis of the Indian campaign finds it to be highly cost effective (Murukutla et al., 2018), which would justify sustained investments in similar evidence-based policy measures for ST control in South Asian settings. The global evidence on the cost effectiveness of tobacco control mass media is also comparable (Atusingwize et al., 2015). Additionally, ST control advocates could make use of the digital media for running awareness campaigns, as shown by the promising process metric outcomes of ChewOnThis.in, an online media campaign to increase advocacy against ST use (Hamill et al., 2015). However, more is needed to be done regarding anti-ST messages in the media, as greater proportion of all adults seem to notice anti-smoking rather than anti-ST information in India (Singh et al., 2018). The same study also reports that adult men are more likely to notice anti-ST information compared to adult women, suggesting the need for further research on ways to reach women ST users in SA through mass media campaigns. Furthermore, it has been suggested that mass media campaigns could play a role in addressing myths around the presumed benefits of ST use in South Asian settings (Jhanjee et al., 2016), but no studies relevant to this area have been conducted till date.

1.5.2.4 Article 13 – Ban on ST advertisement, promotion and sponsorship (TAPS)

Globally, strong evidence links tobacco products marketing with increased consumption (Davis et al., 2008), as also found in this review for ST advertising and promotions in South Asian settings. Findings from two studies from India show that any exposure to ST advertising is associated with higher probability of use (Sinha et al., 2014, Kostova and Dave, 2015).

Additionally, Sinha et al. (2014) report greater levels of ST use with increasing exposure to ST-related TAPS, whereas Kostova and Dave (2015) report that exposure to ST advertising is more likely to affect use in adult women compared to adult men in India. In one study limited to 15 – 24 year-olds, exposure to ST-related TAPS is reported to influence initiation in this age group (Sardana et al., 2015).

However, studies relating to the implementation of Article 13 in SA reveal several inadequacies, particularly with regard to ST forms (Schensul et al., 2013, Bansal-Travers et al., 2014, Mistry et al., 2015, Balappanavar et al., 2017). For example, despite the ban on advertising and sale of ST within 100 meters of educational institutes in India, studies report clear evidence of non-compliance, with shops creatively displaying ST products at points of sale. While Mistry et al. (2015) report at least one ST advert within 100 meters of schools in up to 54% of surveyed institutes, Balappanavar et al. (2017) report that displays and promotions for ST forms tend to be more common around educational institutes than smoking forms of tobacco.

Nationally-representative data from India also suggest that exposure among adults to ST advertising and promotions tend to be higher than for smoked tobacco products (Mehrotra et al., 2017). But despite this, comparisons between two rounds of GATS in the country reveal overall reductions in exposure to all forms of ST advertisements and promotions, other than at points of sale. This finding highlights that it is important for advertising bans to be comprehensive, as partial bans can lead to redirected marketing efforts to non-banned areas, such as at points of sale (Nagler and Viswanath, 2013). To my knowledge, there are no studies till date on the evaluation of TAPS policies for ST control from India or any other country in South Asia. Similarly, no studies relating to ST marketing surveillance have been conducted, another key research gap for effective implementation of TAPS restriction policies (Nagler and Viswanath, 2013).

1.5.2.5 Article 14 – Demand reduction measures concerning ST dependence and cessation

None of the studies relevant to this policy area describe the implementation or assess the impact of ST cessation policies in South Asian settings. But this is not unexpected, as cessation support policies are reported to be the most poorly implemented FCTC measures worldwide (Nilan et al., 2017). Moreover, implementation largely tend to be limited to the provision of smoking cessation support in high-resource settings (Mehrotra et al., 2017). Although a national-level, bilingual, mCessation programme (mobile phone-based support for tobacco cessation) has reportedly launched in India in 2016, with an average quit rate of about 7% among both smokers and ST users within six months of enrolment (WHO, 2017), no peer reviewed publication of this evaluation exists till date.

On the other hand, some studies report the testing of different types of interventions for ST cessation. These include community-based, worksite-based, and clinic-based studies, which test different types of behavioural support therapies, as well as pharmacotherapies. Overall, the results based on randomised controlled trial (RCT) designs show slightly better cessation outcomes for Varenicline compared to placebo in a sample of daily ST-using adults (mostly male) (Jain et al., 2013), and brief intervention compared to simple advice in a sample of 100 women living in a low-income neighbourhood in New Delhi, India (Jhanjee et al., 2017). A community-based cluster randomised trial of a 2-year multiple-component intervention for youths (10 – 19 years) found no difference in ST use between intervention and control conditions (Harrell et al., 2016). Other studies based on non-randomised designs report that 17% of participants had quit tobacco following a worksite-based intervention involving individual and group behavioural therapy (Pimple et al., 2012), and up to 33.5% of participants had self-reported abstinence following a community-based intervention comprising health education, games and counselling sessions (Mishra et al., 2014b).

Based on RCTs conducted in European and American settings, the Cochrane review of interventions for ST cessation concludes that behavioural interventions, and some pharmacotherapies such as Varenicline and nicotine lozenges might assist ST users to quit (Ebbert et al., 2015). Although not based on RCT evidence, the UK National Institute for Health and Care Excellence (2012) also recommends behavioural support for ST cessation among South Asian communities living in the UK, with the need for further research on the role of pharmacotherapies within this user group. In this review, while there is some evidence that behavioural support therapies might play a role in aiding ST cessation within the SA region, the findings are based on a limited number of studies with varied interventions and study designs. The results of one feasibility study suggests that a culturally appropriate behaviour change intervention could be acceptable to use among South Asian ST users (Siddiqi et al., 2016a), but this remains to be tested in a full-fledged trial. There is very limited research on the use of pharmacotherapies for ST cessation in the region.

Relevant to the setting up of ST cessation services in the region, there is evidence from India that healthcare providers likely have low levels of preparedness for providing ST cessation, suggesting the need for cessation training (Panda et al., 2013, Panda et al., 2015b). This is supported by national evidence from India and other South Asian countries like Bangladesh and Pakistan, where healthcare providers advise greater percentages of smokers to quit compared to ST users (Mehrotra et al., 2017). Additionally, analysis of GATS data from India shows demographic differences in the utilisation of different types of cessation services – male and younger (15 – 24 years) users show significantly lower odds of using counselling for ST cessation compared to female and older users, respectively (Ruhil, 2016). This suggests that demographic factors should

be considered while implementing ST cessation policies in the region.

1.5.3 Supply-reduction measures

Since 2012, only four research studies from SA seem to have focussed on supply-reduction policy measures for ST control in the region (Schensul et al., 2013, Lal et al., 2015, Mistry et al., 2015, Siddiqi et al., 2016b), and none of them are impact assessment studies of any implemented policies. Of the three supply-reduction policy areas, Article 16 (access and availability of tobacco products to minors) has received relatively greater research attention, both historically and in recent years. Although not specific to ST, the prohibition of tobacco sales to and by minors is based on strong evidence that these measures can reduce youth tobacco use (Nagler and Viswanath, 2013). However, none of the South Asian countries with high ST burdens have adopted all provisions of the ban (Mehrotra et al., 2017), and evidence from this review suggests that even the adopted provisions are not adequately implemented. Similar to earlier evidence from India (McKay et al., 2015), it remains easy for minors to purchase ST products in the country (Lal et al., 2015, Mistry et al., 2015), as well as other countries in SA (Siddiqi et al., 2016b). Using a nationwide sample of daily tobacco users aged 15 – 17 years, Lal et al. (2015) estimate that underage users in India alone spend nearly 271 million US dollars per year on various ST products. Despite existing bans, the products are easily accessible to minors near education institutions (Mistry et al., 2015), and shopkeepers seem to justify their sales to minors on the basis that they are purchasing the products for adult users (Siddiqi et al., 2016b).

With regard to supply-reduction Articles 15 and 17, there is clear evidence of illicit trade in ST products in many South Asian countries (Siddiqi et al., 2016b), and that ST production and sale can form an important part of income generation for manufacturers and traders in the region (Schensul et al., 2013, Siddiqi et al., 2016b). Although based on a limited number of studies, these findings suggest the need for effective policy measures relating to Articles 15 and 17 within South Asian settings. However, more studies are needed to understand the magnitude of these issues, as well as for informing the formulation and implementation of supply-reduction policies. Based on the wider tobacco literature, Van Walbeek et al. (2012) suggest the need for a multidisciplinary research approach involving public health specialists, political scientists, and policy experts to tackle these aspects.

1.5.4 Non-FCTC measures

Among the South Asian countries, Bhutan, India, Maldives, and Sri Lanka have varying degrees of bans on ST products (Mehrotra et al., 2017). While Bhutan and Sri Lanka ban all manufacturing, importation and sale of ST products, Maldives prohibits the growing of tobacco

plants, and India has invoked food safety laws to ban the production and sale of specific ST products, namely gutkha and paan masala containing tobacco. However, all the research evidence pertaining to ST bans are limited to India, with studies from across three states in the country – Maharashtra (Nair et al., 2012, Dhumal and Gupta, 2013, Mishra et al., 2014a, Pimple et al., 2014), Telangana (Reddy et al., 2016), and Tamil Nadu (Vidhubala et al., 2016, Deepak et al., 2017).

Overall, the majority of ST users and vendors in India seem to be aware of the ban on gutkha, but there is widespread non-compliance, as a result of poor implementation and lack of robust enforcement. Consequently, several banned products continue to be openly available for purchase. In December 2016, India additionally banned the manufacture and sale of any paan masala sold with nicotine or tobacco, irrespective of whether it was available as one product or a combination of products that needed to be mixed. New research studies are needed to assess the impact of these measures. Similarly, there are gaps in the published literature regarding the impact of ST bans from other countries in South Asia.

In addition to the ban on ST products, several South Asian countries have adopted policies banning public spitting, while some have banned the use of any form of tobacco in public places (Mehrotra et al., 2017). However, there are no studies in relation to these policy measures, suggesting the need for research that can inform policy decisions in these area.

1.5.5 Summary

In summary, the overall research literature from SA pertaining to various policy measures targeting ST use (FCTC and non-FCTC) is limited in content and does not match up to the scale of consumption within the geographical region. Although not systematically reviewed, this summary of evidence is based on clear and pre-defined methods for identifying relevant studies that were recently published. However, grey literature, non-English literature, and articles published before 2012 were not considered. While it is likely that some policy-related evidence was missed due to the limits applied leading to potentially biased results, additional search strategies such as the screening of reference lists, as well as citations of included articles, likely reduced the chances of missed papers. This was also supported by comparisons with other related publications such as the 2017 report on ‘Global ST Control Policies and their Implementation’ (Mehrotra et al., 2017), which suggested that at least the key publications had not been missed.

The findings show that while there is a general lack of research, the gaps are particularly pronounced for measures relating to ST cessation (FCTC Article 14), as well as supply-reduction measures. Furthermore, the majority of studies are from India, pointing toward a need for more

ST-related policy research from other countries in the region. In addition to the lack of evidence within specific policy areas, there are research gaps that are relevant across multiple policy areas, such as gaps in ST surveillance, fostering research communication and collaboration across different organisations and countries, and tracking ST industry activities within the region (Mehrotra et al., 2017).

1.6 Health consequences of ST use in SA compared to other geographical regions

Thus far, ST dependence, sociocultural factors, and the lack of ST control policies have been considered as factors explaining the high prevalence of ST use in South Asian settings. In addition, the gaps in research within each of these areas have been considered in turn. This section will now focus on the health consequences of ST use.

The need for controlling all tobacco products, including ST, arises from their potential to cause serious morbidity and premature mortality. While evidence of a possible association between ST use and oral cancers was initially reported early in the 20th century (Abbe, 1915), the first epidemiologic study on the topic was not conducted until the 1950s (Moore et al., 1953). Subsequently, researches began investigating other possible disease outcomes associated with the use of ST, and these formed the basis of the first comprehensive report on the adverse health effects of ST products by the U.S. Surgeon General in 1986 (USDHHS, 1986). Similar to conclusions of the earlier Surgeon General's report on the health consequences of cigarette smoking (1964), this report found that smokeless forms of tobacco also represent a significant health risk to human populations, causing various types of cancers and other serious health conditions.

However, in comparison to the cigarette literature, the overall body of evidence on ST-related health risks is clearly limited in both quantity and quality (NCI and CDC (2014)). The studies are often small and fail to adequately control for confounding factors such as tobacco smoking and/or alcohol use. Additionally, we have limited understanding of the variations in different health risks posed by variations in quantity of ST consumption, patterns of use, and types of ST products consumed in different geographical settings. Nevertheless, the evidence from these studies are summarised in the following subsections within different health outcomes, particularly comparing the evidence from SA to that from other geographical regions.

1.6.1 Cancers

Of all the health effects associated with ST use, cancer outcomes have been most widely studied. Periodic reviews of the epidemiological evidence linking ST use to different cancers show that

ST can cause cancers of the oral cavity, oesophagus, and pancreas, as well as precancerous oral lesions (IARC (2007), NCI and CDC (2014)). But the presence and magnitude of risk for different types of cancers tend to vary across geographical regions, with overall higher risks for South Asian users. This is influenced at least in part by differences in ST product types consumed in different regions, their inherent toxicity, and methods of use (Awan and Patil, 2016, Asthana et al., 2018, Gupta et al., 2018).

A recent meta-analysis of global studies on the relationship between ST use and oral cancers has found non-significant associations in both American (Relative Risk (RR) = 4.72, 95% Confidence Interval (CI) = 0.66, 33.62) and European (RR = 0.86, 95% CI = 0.58, 1.29) regions, while significantly increased risk has been found in the Southeast Asian (RR = 4.44, 95% CI = 3.51, 5.61), and Eastern Mediterranean (RR = 1.28, 95% CI = 1.04 to 1.56) regions (Asthana et al., 2018). Besides the risk of oral cancer, pooled evidence from India show significantly increased risk for pharyngeal (RR = 2.69, 95% CI = 2.28, 3.17), laryngeal (RR = 2.84, 95% CI = 2.18, 3.70), oesophageal (RR = 3.17, 95% CI = 2.76, 3.63), and stomach cancers (Odds Ratio (OR) = 1.26, 95% CI = 1.00, 1.60), although the associations for laryngeal and stomach cancers become non-significant in random effects models, suggesting that these cancers are likely weakly associated with ST use in the study settings (Sinha et al., 2016). While there is evidence for increased risk of pancreatic cancer from pooling studies conducted in European and American regions (RR = 1·60, 95% CI = 1.10, 2.20) (Boffetta et al., 2008), this association has not been widely researched within South Asian settings (Sinha et al., 2016).

Further evidence presented in the meta-analyses of ST-related cancers, albeit limited to oral cancer, suggests links between the higher risks found in South Asian studies with the types of products consumed in the region. For example, product-specific risks for oral cancer have been estimated by Asthana et al. (2018) in their global review, with two commonly used South Asian ST products, namely gutkha (RR = 8.67, 95% CI = 3.59, 20.95) and betel quid with tobacco (RR = 7.18, 95% CI = 5.48, 9.41), posing the highest risks to users. These findings may additionally be explained by South Asian ST products having higher levels of chemical carcinogens compared to products consumed in Western settings (Stanfill et al., 2010). Although the carcinogenic effect of areca nut in some South Asian ST products (IARC, (2004)) may contribute to the higher risks of ST-related oral cancer found within the region, an increased risk of close to five-fold (RR = 4.70, 95% CI = 3.10, 7.10) has been reported even among those who chew other types of South Asian ST products that do not include areca nut as an added ingredient (Khan et al., 2014b).

Besides the evidence synthesised in meta-analyses, individual epidemiological studies from countries in SA report significant associations between ST use and penile (Harish and Ravi, 1995), cervical (Rajkumar et al., 2003), breast (Kaushal et al., 2010), lung and liver cancers

(Pednekar et al., 2011), as well as Non-Hodgkin's lymphoma (Balasubramaniam et al., 2013). In addition, significant associations between ST use and prostate cancer have been reported in both Western and South Asian settings (Putnam et al., 2000, Dwivedi et al., 2014). However, more studies are needed to conclusively establish a relationship between ST use and these different cancer types, or assess any geographical variations in associated risk.

1.6.2 Cardiovascular diseases (CVD)

While the research literature on ST-related cancers has allowed for the appreciation of geographical variations in risks for some cancer types, as well as the estimation of certain product-specific risks, the evidence pertaining to ST-related CVD risks is much more limited in comparison. The majority of our existing knowledge regarding the cardiovascular health effects of tobacco comes mainly from studies on cigarette smoking, and implicates chemicals such a nicotine, polycyclic aromatic hydrocarbons (PAHs), and heavy metals, which are also present in ST forms (USDHHS (2010)). Nicotine alone is known to contribute to a range of cardiovascular effects, such as raised blood pressure, endothelial inflammation and dysfunction (Benowitz, 2003). Moreover, substances unique to certain ST products (e.g. punk ash or liquorice) are known to produce endothelial damage among users (USDHHS (2010). But while these findings serve to explain the plausibility of links between ST use and adverse cardiovascular consequences, there are still uncertainties regarding the specific risks posed by ST use for endpoint CVD outcomes such as ischaemic heart disease (IHD) and stroke, as outlined below. More work is needed to clarify these relationships, as even relatively small risk estimates would mean a large number of cases and deaths from CVDs attributable to ST use worldwide (NCI & CDC, (2014)).

Overall, pooled evidence on ST-related CVD outcomes indicate that ST use may be associated with increased risk of fatal myocardial infarction (MI) and fatal stroke, but not with non-fatal disease outcomes (Boffetta and Straif, 2009, Piano et al., 2010). This suggests that ST products tend to reduce the chances of survival following a cardiovascular event, rather than increase the risk of CVD incidence. On the other hand, increased risk of CVD incidence are reported in other studies not included in previous reviews (Teo et al., 2006, Mushtaq et al., 2010, Yatsuya et al., 2010). In the INTERHEART study, a large case-control study conducted across 52 countries, the risk of acute MI is reported to be more than two-fold among exclusive users of ST compared to never tobacco users (RR = 2·23, 95% CI = 1·41, 3·52) (Teo et al., 2006). In this study, the use of ST is also mainly reported from countries within the SA region, which indicates that similar to cancer risks, ST-related cardiovascular risks may also show geographical variations. However, this has not been assessed in previous reviews, given that they have been limited to studies conducted in Western settings. Besides MI and stroke outcomes, a limited number of studies from Western settings have reported preliminary evidence linking ST use with peripheral vascular

disease outcomes such as Buerger's disease (O'dell et al., 1987, Bolinder et al., 1992). However, these associations have not been researched in other geographical regions, to my knowledge.

In addition to the endpoint CVD outcomes, studies have assessed the association between ST use and a range of cardiovascular risk factors that can predict future MI and stroke events – e.g. hypertension (HT), and some biochemical risk factors such as C reactive protein, serum lipids, etc. However, these links have mostly been explored in the United States and Sweden, and suggest that ST use in Western settings may be associated with dyslipidaemias (Piano et al., 2010). With regard to HT, although some ST products used in Western settings can produce acute, transient increases in blood pressure (Benowitz et al., 1988), the overall evidence from American and Swedish studies do not support an increased risk of HT among ST users in the two countries (Piano et al., 2010). Similar to the evidence from Western studies, studies from India report significantly higher levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides in ST users compared to non-tobacco users (Khurana et al., 2000, Gupta et al., 2007). On the other hand, there is some evidence showing higher prevalence of HT among men who exclusively use ST products such as betel quid with tobacco, gutkha and khaini, compared to men who use no tobacco (Gupta et al., 2007, Pandey et al., 2009). These findings additionally support the likelihood of geographical variations in cardiovascular risks, with higher risks for users in South Asian countries.

1.6.3 Other health consequences associated with ST use

1.6.3.1 Precancerous lesions and other oral conditions

Many studies from the United States, Europe, and Asia provide conclusive evidence that ST products are strongly associated with the prevalence of precancerous oral conditions such as leukoplakia, erythroplakia, and submucous fibrosis (IARC, 2007, Kallischnigg et al., 2008, Khan et al., 2017). Within South Asian countries, the inclusion of areca nut in ST products such as betel quid with tobacco and gutkha likely contributes to greater risk for users in the region, given that areca nut is itself a strong independent risk factor for oral premalignant conditions (IARC, (2004)). Moreover, it seems to produce greater inflammation of the oral mucosa when combined with other ingredients contained in ST products (Javed et al., 2010). Pooling evidence from 18 case-control studies conducted across countries in SA, Khan et al. (2017) report a strong association (RR = 15.50, 95% CI = 9.90, 24.20) between ST use and potentially malignant oral disorders, with betel quid with tobacco showing the highest risk (RR = 16.10, 95% CI = 7.80, 33.50) among the ST products considered.

Besides premalignant lesions, Western studies report that the use of ST products can lead to

incidence of gingival recession, commonly adjacent to where the product is held within the oral cavity, as well as tooth loss (Kallischnigg et al., 2008). In addition, prevalence of dental decay and caries may also be associated with the use of ST products in Western settings (Greer, 2011). In comparison, evidence from SA supports similar associations between ST use and periodontal and dental consequences (Vellappally et al., 2008, Singh et al., 2011).

1.6.3.2 Reproductive outcomes

Several constituents in ST products, such as nicotine, areca nut, PAHs, and heavy metals such as arsenic, cadmium, lead, and mercury, can be reproductive and developmental toxicants (IARC (2004), USDHHS (2010)). But while some data from Western settings indicate reproductive effects of ST use during pregnancy, such as preterm birth and stillbirth, firm conclusions cannot be drawn (Ahlbom et al., 2007). On the other hand, systematically reviewed evidence, limited to studies from India, show that the use of ST products during pregnancy can significantly increase the risk of low birth weight (RR = 1.88, 95% CI = 1.38, 2.54), preterm births (RR = 1.39, 95% CI = 1.01, 1.91) and stillbirths (RR = 2.85, 95% CI = 1.62, 5.01). This amounts to an annual estimated 0.87 million babies born with low birth weight, 0.19 million preterm births, and 0.12 million stillbirths attributable to ST use in India (Suliankatchi and Sinha, 2016). In addition, ST use during pregnancy is also found to be associated with lower haemoglobin levels (RR =1.70, 95% CI = 1.20, 2.50) in a population-based cohort of 918 pregnant women in Mumbai, India (Subramoney and Gupta, 2008). While these findings suggest geographical variations in risk of reproductive outcomes, with higher risks for women in SA, further studies in this field are required to generate more conclusive evidence.

1.6.3.3 Miscellaneous conditions

Given that ingredients in ST can increase insulin resistance (USDHHS, (2010)), a few studies explore the association between ST use and risk of type 2 diabetes, albeit limited to Scandinavian settings. Based on pooled data from prospective studies of Swedish men, heavy use of moist snuff appears to increase the risk of developing type 2 diabetes (Carlsson et al., 2017). The notion that this effect may be mediated by nicotine, suggests that ST users in South Asian settings likely face a similarly increased risk. However, studies are needed to establish any association.

Although some ST product types are inhaled nasally, including some forms in India, their use is considerably less widespread compared to orally-consumed products, and limited information is available regarding their health effects (Narake and Gupta, 2014). From South Asian countries, there are clinical and histopathological observations of nasal obstruction and mucosal oedema among regular snuff users (Sreedharan et al., 2005), as well as isolated reports on snuff induced

malignancy (Sreedharan et al., 2007). Overall, nasal use of snuff has been associated with oedema of the nasal mucosa, atrophy of the middle and inferior turbinates, and chronic rhinitis (Sapundzhiev and Werner, 2003). Although the products contain substances that are potentially carcinogenic, existing studies have not provided conclusive evidence of a relationship with head and neck, or other malignancies till date.

ST use and its relation to a range of mental health outcomes including anxiety disorders, panic disorders, major depression, and posttraumatic stress disorders, have been assessed in a limited number of studies within Western settings, using either nationally representative samples (Fu et al., 2014), or specific participant groups such as American Indians (Sawchuk et al., 2012) and US military personnel (Hermes et al., 2012). The findings of these studies suggest that psychiatric correlates differ depending on the type of ST products used. However, they are derived from cross-sectional data, and causal relations between ST and psychiatric disorders cannot be determined on their basis. Associations between ST use and mental health outcomes have not been assessed in SA to the best of my knowledge.

Finally, within the context of South Asian ST use, it has been suggested that patients with asthma may find their condition aggravated by the use of products such as betel quid with tobacco, as areca nut added to these products can induce contractions of the bronchiolar smooth muscles (Gupta and Ray, 2003).

1.6.4 Summary of research needs in SA

As the ST market in SA continues to evolve and newer products are introduced, some health effects associated with use may only become apparent in the coming years. This implies the need for continued monitoring of ST products and their chemical constituents on the one hand, as well as epidemiological investigations of different health effects associated with their use, on the other (NCI & CDC (2014)). At present, based on a fair amount of research studies from SA (mostly India), the links between ST use and risk of oral, pharyngeal, and oesophageal cancers, as well as oral premalignant conditions, seem to be well established. However, more studies are needed from the region to establish conclusive relationships with other cancer types. Similarly, better quantification of other ST-related health risks are needed from the region, including CVDs, diabetes, and outcomes relating to women's health. Their findings would contribute important information towards better assessments of the public health impact of ST use in South Asia.

Chapter 2. Aims and Objectives

From the literature presented in the first chapter, it is evident that ST use in SA presents a complex public health problem with serious consequences, including morbidity and premature mortality. However, despite knowledge of the scale of use and its propensity to cause harm, several aspects regarding South Asian ST products and their use remain considerably under-researched. Given these circumstances, my overall research goal is to contribute new knowledge to some of the under-researched aspects of ST use in South Asia. The resulting knowledge in these areas, would in turn contribute to more effective control efforts for the prevention and cessation of ST consumption across this geographical region.

Within this thesis, my aims are to carry out three empirical pieces of research in pursuit of the above goal. The areas covered include measurement of ST dependence, sociocultural influences, as well as cardiovascular health consequences associated with ST use. First, I aim to translate, cross-culturally adapt, and validate existing measures of ST dependence within a South Asian setting. This can help determine which scales developed in Western settings are effective for application among South Asian ST users, who are culturally different and use distinct ST products. Second, I aim to explore sociocultural factors relating to ST use in South Asian settings, by describing their distribution across sociodemographic characteristics of ST users, and studying any association between the factors and ST use practices. This can help generate hypotheses for further study and potentially inform ST control interventions targeting sociocultural factors for testing in future studies. Finally, I aim to investigate the relationship between ST use and the risk of CVD according to geographical regions, including South Asia. This will help a better understanding of ST-related CVD risks for South Asian users, and whether there are any geographical variations in these associated risks.

In the following subsections, I will describe each of the study aims and their specific objectives in turn.

2.1 Aim 1 – Validation of ST dependency scales in a South Asian setting

In Chapter 1, I have discussed that dependence to tobacco drives its continued use, and makes it difficult for users to quit. However, almost all our understanding of tobacco dependence is based on cigarette studies. On the other hand, there is evidence to suggest that ST dependence might be physiologically and behaviourally different from cigarette dependence, needing separate assessment. This is particularly relevant for South Asian countries like India and Bangladesh, where tobacco is primarily consumed in smokeless forms. While there is evidence to suggest that

South Asian ST products are highly addictive, it is not clear how ST dependence can be accurately measured among users in the region, as almost all ST dependency scales have been developed and validated exclusively in Western settings till date. This represents an obvious knowledge gap for countries in South Asia. Nevertheless, the existence of a range of ST dependency scales from Western settings makes it possible to adapt the existing measures to study dependence among South Asian ST users, and appreciate any differences in aspects of dependence across different geographical regions and cultures.

The following are my objectives for the validation of ST dependency scales:

- To translate and cross-culturally adapt existing ST dependency scales that represent the range of available measures
- To test the feasibility of using the ST dependency scales in primary research in a South Asian setting
- To determine the internal consistency, and carry out criterion and construct validation of the ST dependency scales
- To investigate the underlying dimensions of ST dependence that the scales can capture

2.2 Aim 2 – Exploration of sociocultural factors and their association with ST use in a South Asian setting

Existing research has measured some sociocultural factors such as ST use among close friends and family members, and acknowledged their widespread prevalence. However, little is known about other sociocultural measures, how they operate, and whether they impact ST use behaviours such as frequency of use, quantity of use, and quitting. Moreover, these aspects are not adequately covered in nationally representative surveys on tobacco (e.g. GATS) conducted in countries within South Asia. Given the deep-rooted social and cultural acceptance of ST use in SA, greater understanding of these factors and their association with ST use practices among South Asian users may be crucial for ensuring effective ST control in the region.

The following are the objectives within this aim to address specific gaps recognised in the literature:

- To quantify a selected range of sociocultural measures relating to ST use among adult users in a South Asian setting
- To describe the distribution of these measures according to sociodemographic characteristics of ST-using adults in a South Asian setting
- To explore the associations between these measures and ST use practices, including initiation, current use, and quit practices, among ST-using adults in a South Asian setting

2.3 Aim 3 – Investigation of the association between ST use and risk of CVDs by geographical regions

Cardiovascular diseases, such as IHD and stroke, have been recognised as major and growing contributors to both morbidity and mortality among South Asian populations (Ghaffar et al., 2004). In addition, these diseases have been found to manifest almost 10 years earlier on average within the SA region compared to the rest of the world, which can likely result in a projected loss of 17.9 million years of productive life by 2030 in India, compared to less than ten times that value for populations in the United States (Goyal and Yusuf, 2006). The focus of my final area in this thesis is therefore on the extent to which ST use contributes to CVD morbidity and mortality in South Asian settings.

The available evidence points to ST use being an important risk factors for CVD outcomes such as IHD and stroke. As summarised in Chapter 1, pooled evidence from Swedish and American studies has found significantly increased risk for fatal IHD and fatal stroke among ever ST-users compared to non-tobacco users, but not for overall CVD incidence (Boffetta and Straif, 2009). In a related meta-analysis of Asian studies, authors assess the cardiovascular risks associated with the consumption of all chewed substances, some of which do not contain tobacco in them (Zhang et al., 2010).

In a subsequent publication, Rahman et al. (2011) include studies from Asia in a systematic review of global evidence linking ST use and coronary heart disease (CHD). However, this is a narrative review, which does not include cerebrovascular disease outcomes on the one hand, and includes cross-sectional study designs on the other, which tend to limit certainties regarding the temporal relationship between exposure and outcome.

On the whole, this means that global estimates of ST-related CVD risks do not include results from South Asian studies. More importantly, it is not clear whether the overall evidence from SA points towards an increased risk for CVDs among South Asian ST users, as summary estimates from the region are not available.

Specific objectives are, therefore:

- To systematically review the global evidence on the risk of IHD and stroke associated with ST use among adults, including studies from South Asia
- To estimate region-specific risks for each disease outcome, and ascertain any variations by geographical regions

2.4 Summary of aims and objectives

Table 2.1 Aims and objectives of presented studies

Aims	Objectives
1. To cross-culturally adapt and validate measurement scales of ST dependence among South Asian users (Chapter 3)	• To translate and cross-culturally adapt existing ST dependency scales that represent the range of available measures • To test the feasibility of using the scales in primary research in a South Asian setting • To determine the internal consistency, and carry out criterion and construct validation of the scales • To investigate the underlying dimensions of ST dependence that the scales can capture
2. To explore sociocultural influences of ST use among South Asian users (Chapter 4)	• To quantify a selected range of sociocultural measures relating to ST use among adult users in a South Asian setting • To describe the distribution of these measures according to sociodemographic characteristics of ST-using adults in a South Asian setting • To explore the associations between these measures and ST use practices, including initiation, current use, and quit practices, among ST-using adults in a South Asian setting
3. To investigate the relationship between ST use and CVD by geographical regions, including SA (Chapter 5)	• To systematically review the global evidence on the risk of IHD and stroke associated with ST use among adults, including studies from South Asia • To estimate region-specific risks for each disease outcome, and ascertain any variations by geographical regions

Chapter 3. Translation and Validation of ST Dependence Scales within a South Asian setting

"Progress in tobacco research may depend on improved measurement" (Piper et al., 2006)

"As with all measurements, we have to decide whether it measures what we want it to measure, and how well" (Bland and Altman, 2002)

Both the development and cross-national validation of itemised scales for measuring ST dependence have hardly been undertaken in South Asian settings. In this chapter, I present the methodology and results of a validation study of ST dependence measures among adult ST users in India. The chapter also includes exploratory findings on the dimensionality of ST dependence, my interpretations of the study findings within context, and implications for future research on ST dependence, ST cessation practice and policy.

3.1 Methodology

A protocol was set out a priori, detailing the anticipated methods for achieving the study objectives (Appendix 3.1). The methodologies set out in the protocol were strictly adhered to in carrying out the different steps of translation, cross-cultural adaptation, and data collection. However, the protocol included additional provisions for the identification and recruitment of eligible participants from more number of study settings than were required for the current study (e.g. from hospital and workplace-based settings).

3.1.1 Research design

For the validation of ST dependence scales in a South Asian setting, I used a cross-sectional research design, which involved participant data collection at one point in time. This approach allowed for all the required information to be obtained concurrently, and the subsequent assessment of associations between the different measures collected. Cross-sectional study designs have been mentioned in a number of research articles on scale validation as an efficient way of testing and validating measurement tools (Arafat et al., 2016). However, given that the steps in scale validation studies often involve procedures such as translation and cross-cultural adaptation, as well as some distinctive statistical analyses such as reliability and validity testing, it has been argued that validation studies should be described as separate study designs in themselves rather than cross-sectional studies (Arafat, 2016).

3.1.2 Inclusion criteria for study participants

The research participants for this study were adults who were 18 years of age or older, and were residents in New Delhi, India between February, 2015 and March, 2015. To be eligible for participation, they had to be fluent in spoken Hindi, and self-reported as current and exclusive users of ST products. Current use of ST was defined as the consumption of any ST product or products for the past one-year at least, and consumption of at least one can or pouch of ST per week at the time of enrolment. This definition of current use not only allowed for the enrolment of regular ST users, but participants with a range of ST consumption patterns in order to guard against the likelihood of homogeneous measurements. On the other hand, strict definitions regarding the exclusivity of ST use meant that participants had to be never-smokers, or former-smokers who had not consumed smoked tobacco in the past 30 days. This was to ensure that data collected on the dependence measures were not based on other forms of tobacco. Other exclusion criteria included participation in any type of cessation treatment to help quit ST in the past 30 days, and history of psychiatric illness.

3.1.3 Sampling methodology

A nonprobability-based convenience sampling technique was used for selecting study participants. Although existing studies on cross-cultural adaptation and psychometric validation of measurement scales have used both probability and non-probability sampling techniques, they have tended to deviate towards non-probability sampling techniques as the preferred method (Arafat et al., 2016). The use of non-probability sampling techniques has also been described as more suitable for these types of studies, given that the research aim is not to establish population estimates, but rather to use validation methodologies for examining the relationships between scale items and other relevant variables (Viswanathan, 2005).

3.1.4 Sample size determination

In general, the methods used for sample size estimation and justification tend to be different in validation studies compared to other epidemiological study types (Arafat et al., 2016). Moreover, in the absence of accepted guidelines, validation researchers have used a variety of methods for sample size determination, including adequacy of sample size for performing factor analyses, sample size estimations based on regression formulae, and item sample ratio methods for determining sample size, as used in this study. Based on recommended guidelines, it was decided to use an item is to participant ratio of 1:10 for this validation study (Sousa and Rojjanasrirat, 2011). This meant that for each item on the ST dependency scales, at least ten eligible participants would be recruited. The longest of the scales was chosen to determine the study sample – with 23

items on the Oklahoma Scale for Smokeless Tobacco Dependence (OSSTD), a required sample size of at least 230 study participants was estimated. These numbers were also in line with other published recommendations to reach an absolute minimum of 100 to 250 participants for this type of study (Anthoine et al., 2014).

3.1.5 Measures

While some of the study measures were specifically developed for the current validation study, the large majority were selected from items included in existing large-scale tobacco surveys. The questionnaire construct sheet for this study, including the sources for each of the survey items can be found in Appendix 3.2.

3.1.5.1 Sociodemographic and general health measures

The data collected on sociodemographic and general health characteristics served to describe the sample of ST users recruited for the validation study.

Sociodemographic measures: The variables included were age in completed years, gender – with 'Male' and 'Female' response options, highest level of completed education – with 'No formal school', 'Less than primary school' (equivalent to < 4 years), 'Primary school' (4 years), 'Less than secondary school' (4 – 8 years), 'Secondary school' (8 years), 'Less than higher secondary school' (8 – 12 years), 'Higher secondary school' (12 years), 'College or university', and 'Post-graduate degree' (> 12 years) response options, and ownership of any of the following household facilities/assets – electricity, flush toilet, fixed telephone, cellular telephone, television, radio refrigerator, car, scooter/motorcycle, and washing machine. The age reported by study participants was categorised into the following groups for description of the sample: 18 – 29 years, 30 – 39 years, 40 – 54 years, and 55+ years; education level reported was grouped into three categories: 'No formal schooling completed' (equivalent to 0 years in formal education), 'Up to secondary schooling completed' (1 – 8 years), and 'More than secondary schooling completed' (> 8 years); and wealth status was ascertained based on number of household facilities/assets grouped into three categories: 'Up to 3 assets owned', '4 – 7 assets owned' and 'More than 7 assets owned'.

General health characteristics: The measures of general health included the presence of any diagnosed health condition (heart attack, HT, asthma, or cancer), the presence of any diagnosed teeth or gum problems, self-rated health, servings of fruit and vegetable consumed per day on average in the past week, number of days in the past month in which participants engaged in any physical activity besides work, and number of alcoholic drinks consumed in the past month. The

response options for the presence of health and dental problems were ‘Yes’ or ‘No’, whereas participants rated their current health condition as being ‘Poor’, ‘Fair’, ‘Good’, ‘Very good’, or ‘Excellent’. Responses to servings of fruit and vegetable consumed per day were categorised into ‘No servings’, ‘1 or 2 servings’ and ‘3 or more servings’; engagement in physical activity and alcohol consumption in the past month were categorised into ‘No’, and ‘Yes’ response options.

Past smoking history: Besides practices relating to ST forms of tobacco, enquiries were made into participants’ past smoking histories, for all participants who reported smoking at least 100 times in their lifetime. Questions on smoking history included age when they started smoking, their preferred product of use, and the number of times they smoked per day on average during maximum use of smoked tobacco. As current smokers would not meet the study’s inclusion criteria, the questions on smoking history included: ‘How long has it been since you stopped smoking’, ‘Why did you stop smoking?’, and ‘Did you use any of the following methods to help you quit smoking?’, with switching to ST included amongst the response options.

3.1.5.2 Measures relating to ST products and use characteristics

ST products: Questions on products included the types of ST products ever used, and those currently used by study participants. In addition, the questionnaire included measures related to the buying and carrying of ST products, in order to describe these measures within the context of their current ST use practices. Participants were asked: ‘Do you usually carry ST with you?’ with ‘Yes and ‘No’ response options. They were also asked for details relating their most recent purchase of ST – where they made the purchase, how many cans/pouches were purchased, how much was paid for the purchase, and how long the purchase was meant to last.

ST use characteristics: The ST use practices of particular relevance to the scale validation analyses included frequency (chews/dips per day), quantity (cans/pouches per week), and duration (years) of use. For those using multiple ST products, the data reflected the overall use characteristics, combined across all product types reported. The question on quantity was framed as ‘How many cans/pouches of ST do you use per week?’ with response options that ranged from one to more than three cans/pouches per week. Given the diversity of ST products that could be sold in cans or pouches of varying sizes, the responses to this question were combined with the information on the sizes of commonly sold ST cans and pouches (noted separately). This process allowed for the estimation of the amount of ST consumed in grams, by each participant, during one week on average. Participants were also asked ‘How much of the time have you felt the urge to use ST in the past 24 hours?’, with the following response options: ‘Not at all’, ‘A little of the time’, ‘Some of the time’, ‘A lot of the time’, ‘Almost all the time’, and “All the time”; as well as ‘How strong have the urges been?’, with response options ranging from ‘No urges’ to ‘Extremely strong urges’.

3.1.5.3 Measures relating to ST dependence

ST dependency scales: For the validation study, I selected three itemised scales, specific to measuring ST product dependence – (a) the Tobacco Dependence Screener for ST users (TDS-ST), (b) the Fagerström Test for Nicotine Dependence for ST users (FTND-ST), and (c) the Oklahoma Scale for Smokeless Tobacco Dependence (OSSTD). These scales were selected in order to cover the range of existing types of ST dependence measures, i.e. diagnostic measures, Fagerström measures, and multidimensional measures. I have justified my selection of these specific scales as opposed to other available scales in each category, along with the scale descriptions below.

Scale 1: The TDS-ST (Mushtaq and Beebe, 2015) served as a diagnostic measure of tobacco dependence among ST users, and included 10 items based on clinical definitions of tobacco dependence set out under the ICD-10 (1992) and DSM-IV (1994) diagnostic criteria. It was originally developed as a self-administered screening questionnaire for tobacco dependence and validated in a sample of cigarette smokers (Kawakami et al., 1999). Having demonstrated associations with other measures of dependence such as heaviness of smoking, Fagerström measures, and exposure biomarkers including cotinine and carbon monoxide, the scale was subsequently used in further tobacco dependence studies (e.g. Piper et al. (2008b)) for screening smokers according to clinically-defined diagnostic criteria. The TDS-ST was adapted for measuring ST dependence by changing the references for smoking to ST use (Mushtaq and Beebe, 2015). To my knowledge, the TDS-ST is the only available diagnostic measure to screen for tobacco dependence among ST users. All ten items on the scale had two response options: 'Yes' – assigned a score of 1, and 'No/not applicable' – assigned a score of 0. This meant a total possible score that ranged from 0 to 10, which was calculated as the sum of individual item scores.

Consistent with the results of smoking studies, the TDS-ST had demonstrated acceptable reliability and concurrent validity among ST users in America. Using data collected from a community-based sample of exclusive ST users in Oklahoma, it was also found that a cut-off score of 5+ would be optimal for making a diagnosis of tobacco dependence among adult ST users (Mushtaq and Beebe, 2015). This meant that the TDS-ST could be used to classify ST users according to their dependence status (dependent or not dependent) in addition to providing a continuous score for measuring dependence. Furthermore, unlike other tobacco dependence measures based on clinical definitions of dependence (e.g. Composite International Diagnostic Interview and Diagnostic Interview Schedule) that tended to be long and needed administrations by trained professionals in face to face interviews, the TDS-ST could be administered with greater ease in different research settings while covering the same aspects of tobacco dependence.

Scale 2: Historically, the Fagerström measures (e.g. Fagerström Tolerence Questionnaire (FTQ) and Fagerström Test for Nicotine Dependence (FTND)) have been the most commonly used measures of tobacco dependence among smokers and ST users. These scales were originally developed to assess physical dependence among cigarette smokers (Fagerstrom and Schneider, 1989, Heatherton et al., 1991), and subsequent validation studies have demonstrated that the scales can predict smoking cessation outcomes (Fagerström et al., 2012). Till date, a few different variants of Fagerström measures have been adapted for measuring dependence among ST users, with considerable overlap between them (Mushtaq and Beebe, 2012). Among these are two ST-modified FTQ measures (Boyle et al., 1995, Thomas et al., 2006), one ST-modified FTND measure (Ferketich et al., 2007), as well as the FTND-ST measure, developed by Ebbert et al. (2006). Unlike the other Fagerström measures for ST dependence, the FTND-ST does not require a rating for the nicotine content of ST products, as this data was found to be scarce or non-existent. This version has also been the most widely applied measure in ST dependence research till date, and selected for inclusion in this validation study. In a sample of exclusive ST users from Oklahoma, the FTND-ST demonstrated good psychometric properties and a unidimensional structure, indicating physical dependence (Mushtaq and Beebe, 2017b). The scale included six-items, and offered a continuous measure of tobacco dependence among ST users. The response options varied from item to item and total scores ranged from 0 to 10, with higher scores indicating greater levels of tobacco dependence.

Scale 3: The ST dependency scale with the most number of items was the OSSTD (Mushtaq et al., 2014), a multidimensional measure with items based on different motivational processes leading to compulsive ST use and dependence. The scale was developed based on the Wisconsin Inventory of Smoking Dependence Motives (WISDM), one of the most comprehensive scales for measuring smoking dependence (Piper et al., 2004). Specifically, a ST-adapted version of WISDM was administered to a sample of exclusive ST users, and only the items and subscales relevant to measuring ST dependence were retained from the original scale, based on the findings of correlation and factor analyses. In the same study, the newly developed scale was found to be highly internally consistent, and demonstrated significant correlations with other measures of ST dependence. Besides OSSTD, two other scales included diverse items that measured additional dimensions of ST dependence in combination with physical dependence (Ebbert et al., 2012) – the Glover-Nilsson Smokeless Tobacco Behavioural Questionnaire (GN-STBQ), and the Severson Smokeless Tobacco Dependency Scale (SSTDS). However, the OSSTD appeared to have greater content coverage and better psychometrics, and was therefore selected for inclusion.

The OSSTD scale included 23 items that belonged in seven subscales. Among the subscales, two comprised primary dependence motives (PDM) and five comprised secondary dependence

motives (SDM) for compulsive ST use and dependence. The PDM subscales mainly assessed physical dependence and included 'Loss of control & Craving' and 'Tolerance & Automaticity', with four items in each, while the SDM subscales were 'Affective enhancement', 'Affiliative attachment', 'Cognitive enhancement', 'Weight control', and 'Cue exposure', with three items in each. The response options for each item ranged from 'Not true of me at all' to 'Extremely true of me' on a 7-point Likert scale. Table 3.1 summarises the OSSTD subscales along with the evidence-based rationale for each subscale, i.e. how each of the underlying motivational processes can lead to tobacco dependence. These data are reproduced from the NCI monograph titled 'Phenotypes and Endophenotypes –Foundations for Genetic Studies of Nicotine Use and Dependence' (2009).

Table 3.1 OSSTD subscales and rationale

Subscale	Construct rationale
Loss of control & Craving	Strong dependence motivation is related to the perception of loss of volition; Craving reflects not only magnitude of physical dependence but also error signals indicative of conflict over drug-use decisions in such structures as the anterior cingular cortex
Tolerance & Automaticity	Rate of tobacco clearance and tolerance to nicotine actions may permit high levels of self-administration; may be linked to nicotine metabolism or distributional tolerance in the brain; Drug self-administration and supportive information processing becomes automated
Affective enhancement	Drug use is motivated by desire to experience mood enhancement (rush, high) even in the absence of distress; drug use is motivated by strong negative affect occurring via either withdrawal or stressor
Affiliative attachment	Use of addictive drugs, including nicotine, is motivated by the impact of the drug on social affection systems and is manifest as emotional attachment to the drug; drug use is inversely proportional to constraints on access to drug and to other reinforces
Cognitive enhancement	Nicotine enhances cognitive processing via suppression of withdrawal
Weight control	Nicotine appears to lower body weight set-point, and this may motivate nicotine self-administration, especially among those seeking weight loss; may be related to nicotine's effects on hypothalamic weight regulatory centres or to systems that affect taste hedonics
Cue exposure	Conditioned responses to drug cues activate drug motivational processing and encourage self-administration

Source: NCI (2009)

Self-rated ST addiction: In addition to the three ST dependence scales, the study questionnaire included a self-rated ST addiction measure, which was scored on a 7-point Likert scale (similar to the OSSTD), with response options ranging from 1 = 'I am not addicted to ST at all' to 7 = 'I am extremely addicted to ST'. Similar measures have been used in other studies of cigarette, alcohol, and illicit drug use, and performed well on tests of validity (Etter et al., 2003).

Salivary cotinine: For the validation of ST dependency scales, levels of salivary cotinine were selected as the primary criterion measure. Given that nicotine in tobacco products is primarily responsible for the development of dependence, cotinine, a major metabolite of nicotine, has been recommended as a biomarker for assessing the severity of tobacco dependence (Society for Research on Nicotine and Tobacco (SRNT), 2002). Although the recommendations were largely based on studies conducted among cigarette smokers, ST dependence studies have also reported significant associations with cotinine concentrations (Ebbert et al., 2004, Mushtaq et al., 2011), supporting its use as criterion measure for nicotine dependence among ST users.

3.1.6 Translation and cross-cultural equivalence of ST dependency scales

Recognising translation and achieving cross-cultural equivalence as key steps for validation, I followed rigorous processes to produce Hindi versions of all the ST dependency measures used in this study, based on standard methodologies (Sousa and Rojjanasrirat, 2011). The recommended steps were themselves based on reviews of published literature on translation and validation of itemised scales used in health care research.

In brief, the steps of translation included the involvement of two sets of bilingual translators for the two stages of translation and back-translation, as well as an independent reviewer for synthesising both translated versions. In addition to their linguistic background, educational and cultural backgrounds of translators were considered during selection, so that areas such as familiarity with technical terminology, and colloquial use of the target language were not missed during the translation processes. I also carried out a joint committee review with all four translators and independent reviewer to reach consensus on the pre-final Hindi versions of the scale items, and ensure cross-cultural equivalence of the translations produced. I then pretested the translations in a sample of 10 ST users in New Delhi to arrive at the final versions of the ST dependency scales. Each of these steps are described in further detail below.

3.1.6.1 Forward translation

Forward translations of the scales from English (source language) to Hindi (target language) were carried out by two independent translators (Forward Translators 1 & 2), so that two preliminary

Hindi versions of the scales were initially produced. The translators were both bilingual, and their educational and cultural backgrounds were considered during selection, so that one translator (Forward Translator 1) was familiar with the technical terminology used in the field of tobacco use and health, while the second translator (Forward Translator 2) was more familiar with the colloquial use of the target language (Hindi). Instructions were provided to both translators so that conceptual translations rather than literal ones were produced, keeping typical respondents for the scales in mind.

3.1.6.2 Independent review

Next, the two preliminary Hindi versions of each scale were compared against one another and to the original English versions by a third bilingual individual (Independent Reviewer). Following this step, a meeting was arranged between the three bilingual individuals (Forward Translators 1 & 2 and Independent Reviewer), so that discrepancies in translations could be discussed and resolved through consensus. At the end of this step, one combined forward-translated version of each ST dependency scale was produced in Hindi.

3.1.6.3 Back translation

Back translation of each scale to the source language (English) was carried out by a second set of independent bilingual translators from distinct backgrounds (Back Translators 1 & 2), who were both either native speakers of English or spoke English since early childhood. The back translators were also blind to the original English versions of the scales. On completion, this step resulted in two independently back-translated versions of each ST dependency scale in English.

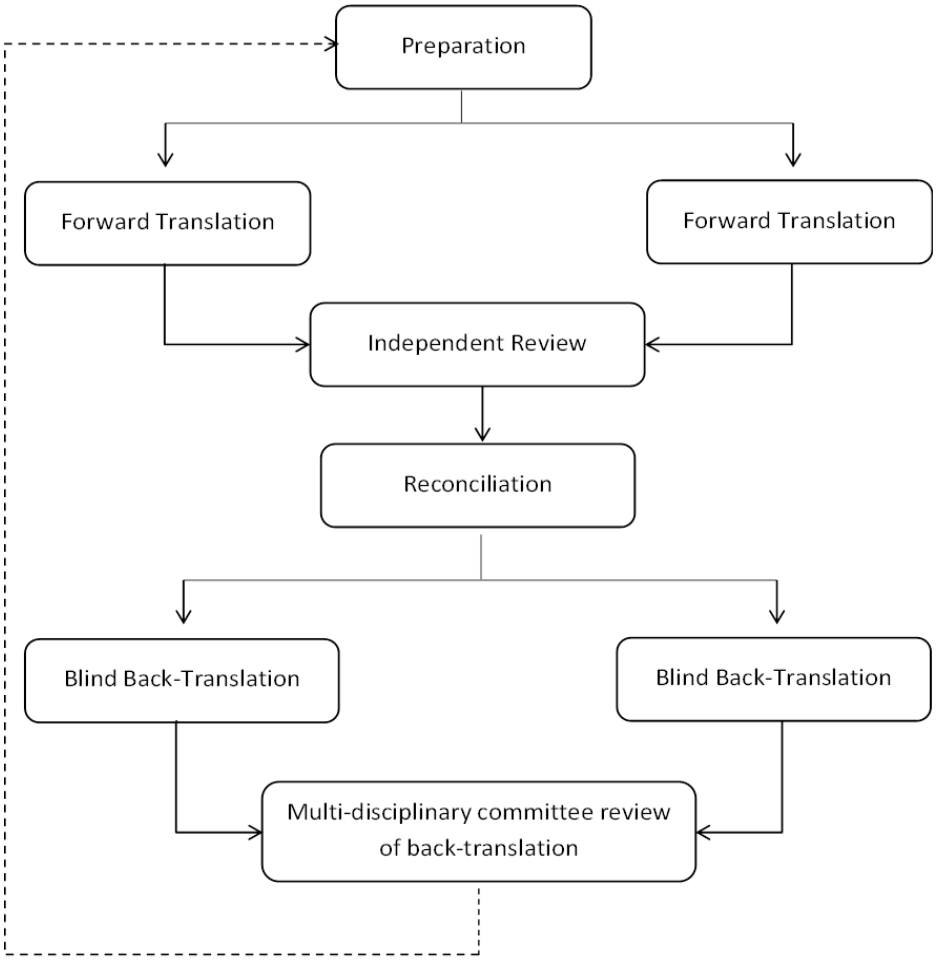
Further details regarding the specific eligibility criteria for selecting the four translators (Forward Translators 1 & 2, and Back Translators 1 & 2) and independent reviewer can be found within the study protocol included as Appendix 3.1.

3.1.6.4 Joint review and adaptation

Next, the back-translated English versions were compared with the original English versions of each scale, by a joint committee which comprised of all four translators and independent reviewer. I was also a part of this committee in my role as someone who was familiar with the content areas covered by the scales. Any discrepancies in translations identified during this meeting were discussed by the committee and resolved through consensus, and one pre-final version of each scale was produced in Hindi (termed Pre-Final Target-Language version – PF-TL). As overall agreements on translations were achieved for all the scale items during this meeting, we did not

have to repeat the steps of translation and back-translation for any of them, using a different set of bilingual translators. In addition to reviewing the translations, the discussions during this committee meeting also served to evaluate and achieve some initial conceptual, semantic and content equivalence of the PF-TL versions between the source and target cultures. Figure 3.1 depicts the various steps of translation described thus far.

Figure 3.1 Steps followed for English to Hindi translation of ST dependence scales



3.1.6.5 Pre-testing of scales

The PF-TL versions of the dependency scales were then pre-tested in a sample of 10 ST users in a dental setting in New Delhi, to better assess the linguistic and cross-cultural equivalence of the translated scales, before full psychometric testing in a community-based sample. The respondents for this stage were native speakers of Hindi, and they were administered all the instructions, response formats and items, just as things would be done during actual data collection. At the end of each interview, respondents were asked if any of the instructions, response formats or items were unclear, as well as suggestions on how to rewrite any unclear statements in order to make

them more understandable. Some minor revisions were made to the translations based on these suggestions, but the scales themselves were not modified. Final versions of the translated scales were prepared for data collection on completion of pre-testing, and the scale data collected from these respondents were not stored or used in any later analyses.

3.1.7 Participant recruitment and data collection procedures

Ethical approval for the study was obtained from the Research Governance Committee, based in the University of York. Approval was also sought and obtained from the Institutional Ethics Committee of the Indian Institute of Public Health – Delhi. The approved versions of the participant information sheet, consent form, and study questionnaires have been included as Appendix 3.3.

To select a community-based sample from the target population, I approached Children's Hope Prayas, a volunteer-led organisation, working to improve the lives of children and families in the Kathputli Colony of New Delhi, India. More specifically, the organisation is based in Pandav Nagar, a low-income community within the Kathputli Colony, which covers an area of nearly 10 square kilometres. The organisation has worked previously with researchers on Project ACTIVITY (Stigler et al., 2010), a group randomised intervention trial for tobacco control among young persons living in low-income communities in India. Following the finalisation of arrangements in February, 2015, data for the current study were collected in March, 2015. Through existing links that the organisation had with the people living in the community they served, I was able to obtain references of some ST users in the area. I was also able to approach additional potential participants by visiting some houses in the area, as well as ST-selling shops, and explaining my study objectives and sharing the information sheet developed for the study. Those who expressed an interest to participate were invited to the community centre for eligibility screening and recruitment. Further candidates were identified through word-of-mouth community referrals and snowballing techniques, and recruited for participation after eligibility screening. A screening questionnaire was used for assessing participant eligibility based on the study inclusion and exclusion criteria. All study procedures, including screening, recruitment, and data gathering were carried out within the office areas of the community organisation. After providing information about the study to eligible candidates, consent was obtained from willing participants, whereas individuals who expressed uncertainty were asked to return to the study setting after having thoroughly considered all the information provided. I conducted face-to-face interviews with consenting participants to collect the study data, given the greater likelihood of participants understanding spoken Hindi compared to reading. Each interview took about 40 minutes to complete and a voucher for 100 Indian Rupees (roughly 1 British pound sterling at the time of data collection) was provided to respondents as compensatory costs for their time.

In addition to the questionnaire data, I collected saliva samples from all study participants for measuring levels of cotinine, given that salivary cotinine was selected as the criterion variable for validation of the ST dependency scales. On completion of the interview, unstimulated saliva samples were collected by placing a sterile cotton swab under each participant's tongue and leaving it in place until the swab became fully soaked. Participants were asked to rinse their mouths before starting the interview. I then collected the soaked swabs in storage tubes and transported them in ice boxes to an accredited laboratory in New Delhi at the end of each day, where the samples were immediately frozen at -20 degree Celsius and subsequently thawed before biochemical testing.

The samples were analysed through a high sensitivity enzyme immunoassay technique using Salimetrics cotinine kits, as previously used by Mushtaq et al. (2011) among ST users in America. The test provided quantitative measurements of cotinine, which have been found to be highly correlated with chromatographic assessments of cotinine among cigarette smokers, while avoiding the need for specialised laboratories to carry out the analyses (Salimetrics, 2009). The technique allowing the detection of cotinine levels as low as 1 ng/mL. Each kit contained a 96-well microtiter plate, along with a standard solution of cotinine (200 ng/mL) to allow for internal validation of test procedures. The test itself involved the addition of collected saliva samples to each well in the microtiter plate along with the rabbit antibody and conjugate solutions provided. After incubation and washing away of unbound components, the amount of bound components (cotinine and antibody) were measured using their optical density. Cotinine levels in saliva samples were subsequently calculated from the optical density measurements, using the guidelines provided for such computations (Salimetrics, 2009).

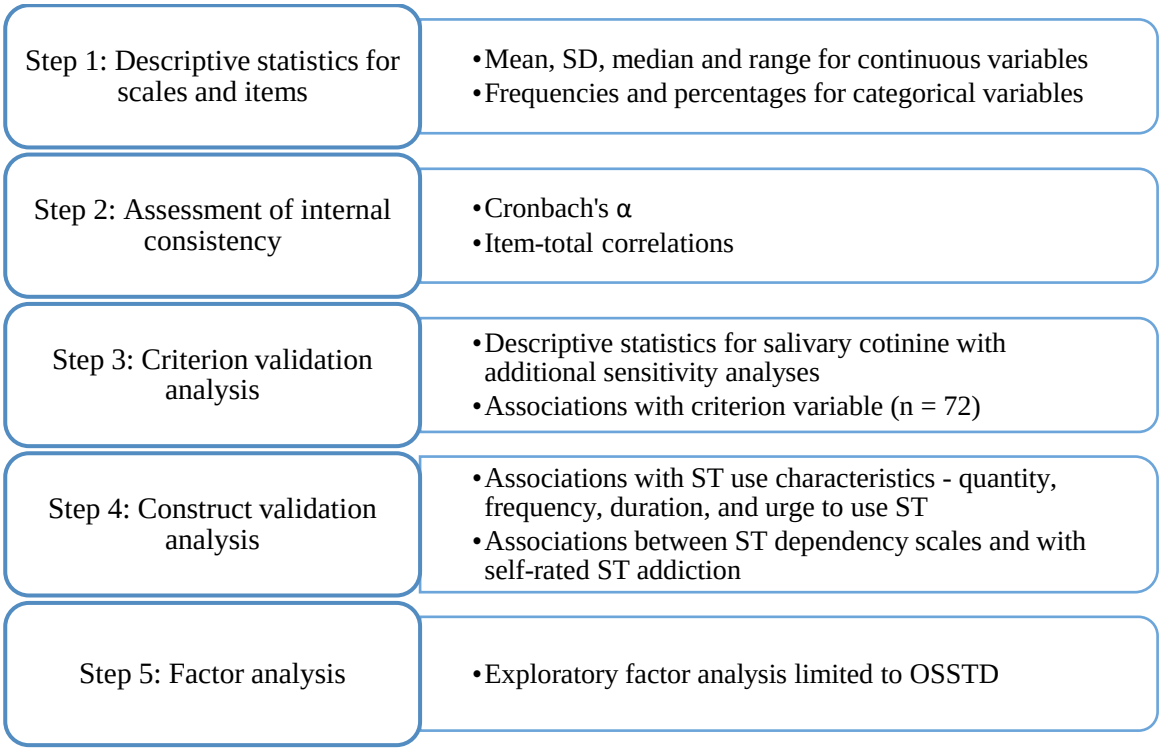
3.1.8 Data management

As all the questionnaire data and laboratory results were available in paper formats, the transfer of study data involved the scanning and uploading of all documents in a secure manner onto my personal computer, before electronically transferring the data to a secure data storage folder provided by the University of York. The personal computer used for storing the data was password protected and no personally identifiable data from study participants were collected or stored. The paper questionnaires were couriered to the University of York using a standard international courier service, where they were securely stored in a locked cupboard. Using the codebook developed for the study questionnaire, I manually entered the data twice, with subsequent data comparisons to create a final dataset for analyses. The codebook used for data entry can be found along with the questionnaire construct sheet in Appendix 3.2.

3.1.9 Description of analyses

The data analyses for the validation of ST dependency scales centred on the assessment of their psychometric (reliability and validity) and structural (underlying factors or subscales) properties. However, the initial steps involved the generation of descriptive statistics based on the sociodemographic, tobacco use, and general health characteristics of study participants. These results were summarised in tables, using frequencies and percentages for categorical variables, and means, standard deviations (SDs), and ranges for continuous variables. In addition, these analyses also served to describe if there were any differences in tobacco use behaviours across the sociodemographic characteristics of study participants. Having familiarised myself with the sample characteristics, I moved on to the validation analyses of ST dependency scales, the steps of which have been summarised in Figure 3.2.

Figure 3.2 Overview of validation analyses of ST dependency scales



3.1.9.1 Descriptive statistics for ST dependency measures

For each of the ST dependency scales, I first generated item-wise and scale-wise descriptive statistics, using means, SDs, medians and ranges for continuous measures (TDS-ST, FTND-ST, OSSTD items, and total scores on OSSTD scale and subscales), and frequency counts and percentages for categorical measures (individual items on TDS-ST and FTND-ST scales). Summary tables were produced based on these descriptive statistics.

3.1.9.2 Internal consistency

Next, internal consistency or the degree of homogeneity of the ST dependency scales was evaluated by calculating Cronbach's alpha (α) coefficient (Cronbach, 1951) for each of the scales and the OSSTD subscales. Also, in order to establish the contribution of individual items to each scale/subscale, the change in Cronbach's α was noted following the deletion of each scale item. No other tests of reliability such as test-retest were undertaken as part of this study.

3.1.9.3 Criterion validation analyses

While reliability assessments are a necessary step in establishing the usefulness of measures, accurate conclusions regarding the presence and degree of any attribute (dependence, in this instance) can only be made using 'valid' measurement scales (Streiner et al., 2015). One way of assessing the scale validity is to correlate the scale data with data from another accepted criterion or 'gold standard' measure of the attribute under study. As previously stated, salivary cotinine levels were selected as the 'gold standard' for criterion validation of ST dependency scales. In accordance with earlier studies on ST dependence (Ebbert et al., 2004, Mushtaq et al., 2011), it was expected that cotinine levels would show meaningful variations across different levels of dependence measured by the scales used in the study.

As a first step, descriptive analyses of the cotinine data were carried out. The subsequent steps planned for criterion validation included the assessment of correlations between ST dependence scales and subscales on the one hand and salivary cotinine measurements on the other. In addition, simple linear regression analyses of cotinine values on ST dependence scales and subscales were to be carried out using data from the entire sample. Standardized regression coefficients (beta) and p-values would be reported from the analyses, and an alpha level of 0.05 would be used for all tests of significance. However, preliminary analysis of the cotinine data showed some unexpected results, which in turn, affected the plans for conducting criterion validation analyses.

Sensitivity analysis: Although all survey participants reported regular use of ST products, the laboratory results showed non-detectable levels of cotinine in 35.2% (n = 82) of collected samples (reported as < 0.8 ng/mL). Given that the analysis of salivary samples was carried out in three separate batches, I first explored the distribution of cotinine values according to the batch of analysis and tabulated these results. I then carried out a series of sensitivity analyses to examine if those with non-detectable cotinine values differed from the rest of the study sample with regard to their ST use characteristics, as well as other variables that may have likely influenced their cotinine measurements. Comparisons between groups with non-detectable and detectable cotinine

levels were carried out using t-tests for continuous variables, and either Pearson's Chi-square or Fisher's exact tests for categorical variables, with a p-value of 0.05 (adjusted for multiple hypotheses testing) for inferring statistical significance. Based on the results of the sensitivity analyses (Section 3.2.3.3), it was decided to carry out the steps of criterion validation using data from a limited sample of 72 participants whose saliva samples were all analysed in one of the three cotinine batches. However, the results were interpreted with some reservations.

3.1.9.4 Construct validation analyses

Construct validation of ST dependence can be viewed as an on-going process of learning more about the construct, making new predictions, and testing them. Convergent validation, a type of construct validation, suggests that measures of theoretically similar constructs should be substantially correlated (Streiner et al., 2015). For the construct validation analyses of ST dependency scales, I applied these principles to study how closely the TDS-ST, FTND-ST, and OSSTD scores matched up to other related measures such as frequency (number of times ST used per day), quantity (grams per week), duration of ST use (years), and the urge to use ST products, using both correlation and regression methodologies. For the correlation analyses, bivariate correlations between each of the ST dependency scales and ST use characteristics were performed, and the results were tabulated. Linear regression analyses based on the ST use characteristics were limited to duration, quantity, and frequency, as the measures of urge were not truly continuous in nature. Square root transformations were applied to all three ST use characteristics to meet the assumptions of regression models, and multivariate models adjusted for potential confounding from age and gender of study participants.

Furthermore, to examine the extent to which the scores on ST dependency scales related to one another, I performed correlation analyses using total TDS-ST scores, diagnosis of ST dependence (derived from TDS-ST), total FTND-ST scores, total OSSTD scores, and OSSTD subscale scores. In addition, simple linear regression analyses were conducted to evaluate the association of individual OSSTD subscales with total TDS-ST and FTND-ST scores, whereas multiple regression analysis was used to assess the joint association of all OSSTD subscales on the other measures of ST dependence. Univariate logistic regression analyses were performed on the diagnosis of ST dependence, using FTND-ST, and OSSTD scale and subscales as independent variables. Correlation and regression analyses were also conducted for the validation of ST-dependency scales against the self-rated ST addiction measure.

All the analyses described so far were performed using IBM SPSS, Version 24.0 (2016)

3.1.9.5 Exploratory factor analysis

Of the three ST dependency scales included in this study, only the OSSTD was developed as a multidimensional measure of ST dependence. For this reason, factor analysis was limited to the OSSTD scale, in order to assess its underlying structure. Given that the OSSTD had not been previously subjected to psychometric testing within South Asian settings, the following steps of my analyses were exploratory in nature, as I had no firm a priori expectations regarding the factor structure of the scale. To conduct the exploratory factor analysis (EFA), I used the Factor program, Version 10.8.04 (Lorenzo-Seva and Ferrando, 2013).

Conditions necessary for performing EFA: Data are said to be factorable if there are substantial number of meaningful relationships between the scale items, noted by low-moderate to strong correlation coefficients in inter-correlation matrices, usually r = 0.300 or greater (Pallant, 2013). I checked this prerequisite by visually inspecting the correlation matrices of the OSSTD scale items, and by using Bartlett's test of sphericity (significance assessed using p-value < 0.05) and Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (minimum value of 0.60) (Mvududu and Sink, 2013). Other conditions for performing EFA were assessed based on the descriptive statistics and figures previously generated for the OSSTD scale items. These included missing data, outliers, linearity, normality, and multicollinearity (Tabachnick and Fidell, 2011).

In this study, there were no missing data in the OSSTD scale items. Outlier points, linearity and normality of responses to scale items were assessed by examining the box plots (outliers emerge as circles with identifying number), scatterplots (scores fall in a roughly straight line), and histograms (normality curve is roughly symmetrical), respectively. Presence of multicollinearity was assessed by looking for high correlations (r = 0.900 and above) between independent variables. These findings were used for making subsequent decisions regarding the analytical methods applied for factor extraction.

Factor extraction: In order to determine the smallest number of factors that were needed to best represent the interrelations between scale items, I applied the principles of principal factors to identify any underlying factors or dimensions that reflected what the scale items might have in common (Tabachnick and Fidell, 2011). Given that the OSSTD items were scored on ordinal scales and the observed data distribution deviated from normality, I used the Parallel Analysis (PA) approach for assessing the dimensionality of the dataset or in other words, the number of factors that is thought to best describe the underlying correlations between the scale items (Timmerman and Lorenzo-Seva, 2011). In PA, a random dataset is created with the same numbers of observations and variables as the original data. A correlation matrix is computed from the randomly generated dataset and its eigenvalues are computed. True dimensions or factors are

those with eigenvalues that are larger than the ones derived using the randomly generated dataset (Horn, 1965). For my analysis, the PA was configured to produce 500 permutated random correlation matrices.

As recommended by Timmerman and Lorenzo-Seva (2011), I ran the PA based on Minimum Rank Factor Analysis (MRFA) (Ten Berge and Kiers, 1991) for factor extraction, so as to minimise the amount of common variance left unexplained after extracting a fixed number of common factors. Also, the eigenvalues obtained from MRFA could be used to estimate the amount of common variance explained for each extracted factor.

Factor rotation: Having identified the number of factors to be extracted, the next step was to interpret them, by applying a factor rotation technique. While factor rotation does not change the results, it presents the loading patterns in a way that can be better interpreted (Tabachnick and Fidell, 2011). There are different methods of factor rotation, depending on whether the underlying factors are thought to be correlated (oblique rotation techniques) or uncorrelated (orthogonal rotation techniques). For this study, I employed Promin rotation (Lorenzo-Seva, 1999), the default method implemented in the Factor program and tabulated the factor loadings obtained. Promin is an oblique rotation technique, and better suited to deal with situations where all variables may not be pure measures of a single underlying construct (Lorenzo-Seva, 2013).

In assessing the factor loadings, I looked for item communalities of > 0.400, several items or variables loading strongly on each factor, and absence of any cross-loadings (Costello and Osborne, 2005). Allowing for a 10% overlap of variance with the other items in that factor, Tabachnick and Fidell (2011) have cited ± 0.320 as a rule of thumb for minimum loading of each item, with cross-loading referring to items that load at 0.320 or higher on two or more factors. Factor loadings below 0.320 were ignored.

3.2 Results

These results are based on a total of 233 surveys, completed from 9th to 27th March, 2015. The general characteristics of the study sample, including sociodemographic and health-related profiles are described below. Missing data were minimal, with a maximum missing value of three on only one study variable (health risks of smoking compared to ST), missing values of two on variables relating to general health characteristics (including alcohol use) and self-rated ST addiction, and a missing value of one on amount spent on most recent ST purchase.

3.2.1 Characteristics of the study sample

The sociodemographic and general health characteristics of the sample are summarised in Table 3.2. Participants ranged in age from 18 to 72 years with a mean of 30.5 years (SD = 11.39), the average male participant (n = 118, mean = 29.5 years, SD = 10.10) being only slightly younger than the average female participant (n = 115, mean = 31.6 years, SD = 12.54). Although no stratified sampling was carried out on the basis of gender, nearly half the sample comprised women (49.4%), five of whom were pregnant (4.3%), and 12 breastfeeding (10.4%) at the time of interview.

Overall, 51.1% of participants had had no formal education, 41.2% had completed up to secondary schooling, and the remaining 7.7% of participants were high school graduates, six among them having attended or graduated from undergraduate studies. Wealth status, assessed by the number of household assets, showed that nearly 60% of participants owned up to 3 assets, 33.9% reported owning 4 – 7 assets, and 6.4% owned 8 or more household assets. The younger survey respondents (18 – 29 years) had completed higher levels of education and owned more assets compared to older participants (30+ years) in the sample. Similarly, male respondents were more educated and owned more household assets compared to female respondents in the sample.

Table 3.2 Sociodemographic and general health characteristics of study sample

Categories	**N (%)**				
	Total 233 (100)	Non-daily ST users 5 (2.1)	Non-smokers 197 (84.5)	Former smokers 23 (9.9)	Current smokers 13 (5.6)
Sociodemographic characteristics					
Age group					
18 – 29 years	133 (57.1)	5 (100)	119 (60.4)	8 (34.8)	6 (46.2)
30 – 39 years	51 (21.9)	-	38 (19.3)	8 (34.8)	5 (38.5)
40 – 54 years	39 (16.7)	-	32 (16.2)	5 (21.7)	2 (15.4)
55+ years	10 (4.3)	-	8 (4.1)	2 (8.7)	-
Gender					
Male	118 (50.6)	5 (100.0)	86 (43.7)	19 (82.6)	13 (100.0)
Female	115 (49.4)	-	111 (56.3)	4 (17.4)	-
Education					
No formal schooling	119 (51.1)	-	109 (55.3)	5 (21.7)	5 (38.5)
Up to secondary schooling	96 (41.2)	4 (80.0)	75 (38.1)	15 (65.2)	6 (46.2)
> secondary schooling	18 (7.7)	1 (20.0)	13 (6.6)	3 (13.0)	2 (15.4)
Assets					
Up to 3 assets owned	139 (59.7)	1 (20.0)	128 (65.0)	6 (26.1)	5 (38.5)
4 – 7 assets owned	79 (33.9)	3 (60.0)	57 (28.9)	15 (65.2)	7 (53.8)
> 7 assets owned	15 (6.4)	1 (20.0)	12 (6.1)	2 (8.7)	1 (7.7)

General health characteristics*					
Diagnosed with illness					
No	213 (91.4)	5 (100.0)	179 (91.8)	21 (91.3)	13 (100.0)
Yes	18 (7.7)	-	16 (8.2)	2 (8.7)	-
Teeth and gum problems					
No	132 (56.7)	2 (40.0)	115 (59.0)	10 (43.5)	7 (53.8)
Yes	99 (42.5)	3 (60.0)	80 (41.0)	13 (56.5)	6 (46.2)
Self-rated health condition					
Poor	7 (3.0)	-	5 (2.6)	0 (0.0)	2 (15.4)
Fair	54 (23.2)	1 (20.0)	46 (23.6)	7 (30.4)	1 (7.7)
Good	96 (41.2)	3 (60.0)	81 (41.5)	8 (34.8)	7 (53.8)
Very good	54 (23.2)	-	47 (24.1)	5 (21.7)	2 (15.4)
Excellent	20 (8.6)	1 (20.0)	16 (8.2)	3 (13.0)	1 (7.7)
Vegetables per day					
None	9 (3.9)	-	9 (4.6)	-	-
1 or 2 servings	210 (90.1)	3 (60.0)	178 (91.3)	21 (91.3)	11 (84.6)
3 or more servings	12 (5.2)	2 (40.0)	8 (4.1)	2 (8.7)	2 (15.4)
Fruits per day					
None	121 (51.9)	1 (20.0)	106 (54.4)	11 (47.8)	4 (30.8)
1 or 2 servings	106 (45.5)	4 (80.0)	87 (44.6)	11 (47.8)	8 (61.5)
3 or more servings	4 (1.7)	-	2 (1.0)	1 (4.3)	1 (7.7)
Physical activity besides work					
No	195 (84.4)	3 (60.0)	171 (87.7)	14 (60.9)	10 (76.9)
Yes	36 (15.6)	2 (40.0)	24 (12.3)	9 (39.1)	3 (23.1)
Alcohol consumption in past month					
No	179 (76.8)	3 (60.0)	163 (83.6)	12 (52.2)	4 (30.8)
Yes	52 (22.3)	2 (40.0)	32 (16.4)	11 (47.8)	9 (69.2)

* Missing values = 2

A small number of participants (n = 18, 7.7%) indicated having medical conditions such as coronary heart disease, HT, or asthma, while a little over 40.0% of the sample reported dental problems (n = 99, 42.5%). Overall, health conditions were self-rated positively, with only 3.0% of the sample reporting 'poor' health. Nearly all participants reported consuming at least one serving of vegetable per day in the past week (96.1%), while per day fruit consumption in the past week was less widely reported (47.6%). Few participants reported engaging in any physical activities besides work (15.6%). Alcohol consumption in the past 30 days was reported by 52 (22.5%) participants, nearly all being male (n = 48). The average number of alcoholic drinks consumed in the past month was 5.98 (SD = 5.03).

Despite using a broad criteria to define current use of ST for scale validation (i.e. any use of ST in the past week, and at least once-a-week consumption in the past six months), almost all the recruited participants consumed ST products on a daily basis (n = 228, 97.9%) and reported daily

consumption for at least six months duration. The five non-daily ST users were all male and belonged in the youngest age group (18 – 29 years). In the week prior to the interview, the number of days on which they had consumed ST products ranged from two to six days. Most of the study participants were non-smokers, having smoked less than 100 times in their entire lifetime (n = 197, 84.5%),

Among ever smokers (n = 36, 15.5%), 32 were male and four were female respondents. Their mean age of smoking initiation was 17.2 years (SD = 4.75), and the majority of them (n = 26, 72.2%) reported having smoked daily for six months or longer. With regard to smoking products, cigarettes were used by 23 participants (9.9%), and bidis by 20 participants (8.6%), with seven participants (3.0%) reporting the use of both cigarettes and bidis. No other forms of smoked tobacco were reported to be used by the study sample. While 23 of the ever smokers reported cessation of smoking practices (10.0% of study sample), 13 members continued to smoke at the time of participation. The current smokers were all male and made up 5.6% of the final sample. The quit duration among past smokers ranged from < 1 year to 20 years, with a mean of 6.5 years (SD = 5.87). Thirteen participants reported switching to ST to aid with smoking cessation, while the other past smokers (n = 10) reported quitting on their own. In general, the former and current smokers in the sample appeared to have completed higher levels of education and owned greater number of household assets compared to the non-smokers. A greater proportion of them also reported alcohol consumption in the past month.

3.2.2 Tobacco products and use characteristics

Table 3.3 Tobacco products used and ST use characteristics reported by study sample

ST products, n (%)	
Types of ST products currently used*	
Zarda	2 (0.9)
Betel quid (paan) with tobacco	24 (10.3)
Gutkha	137 (58.8)
Khaini	115 (49.4)
Snus	7 (3.0)
Gul	9 (3.9)
Number of ST products currently used	
1 product	174 (74.7)
> 1 product	59 (25.3)
Duration, quantity, and frequency of ST use, mean (SD)	
Duration of ST use in years	12.6 (10.11)
Quantity of ST consumed in grams per week	86.6 (62.61)
Number of times ST used per day	17.0 (14.17)
Frequency during maximum use	20.4 (16.32)

Urge and strength of urge to use ST, n (%)	
Urge to use ST in past 24 hours	
None of the time	2 (0.9)
A little of the time	24 (10.3)
Some of the time	34 (14.6)
A lot of the time	67 (28.8)
Almost all the time	64 (27.5)
All the time	42 (18.0)
Strength of urge felt	
No urges	2 (0.9)
Slight	37 (15.9)
Moderate	45 (19.3)
Strong	48 (20.6)
Very strong	47 (20.2)
Extremely strong	54 (23.2)
Buying and carrying ST, n (%)	
Amount spent on most recent ST purchase**	
0 – 10 INR	109 (46.8)
11 – 50 INR	103 (44.2)
51 – 100 INR	16 (6.9)
>100 INR	4 (1.7)
Place of most recent ST purchase	
Street vendor	147 (63.1)
Store	84 (36.1)
From another user	2 (0.9)
Carrying ST	
Yes	173 (74.2)
No	60 (25.8)

* Some participants used > 1 tobacco product, ** Missing values = 1, further details of how long this purchase was meant to last are provided in the text below.

3.2.2.1 Tobacco products

The various types of ST consumed by survey respondents included zarda, betel quid (paan) with tobacco, gutkha, khaini, snus, and gul, as well as different combinations of these ST products. Among these products, gutkha was the most commonly used (n = 137, 58.8%), followed by khaini (n = 115, 49.4%), with 39 participants (16.7%) reporting the use of both products in the past 7 days. This was despite an existing state-wide ban on gutkha manufacture and sale since 2012 in New Delhi. In March 2015, when the study was being carried out, the ban was made stricter and extended to all ST products (including twin-packs). Nearly 75% of participants (n = 174) reported the current use of only one type of ST, while 58 participants (24.9%) used two products in combination. Only one person reported the current use of four different ST product types (paan with tobacco, gutkha, khaini, and gul). No notable variations were found regarding the number or types of ST products used according to sociodemographic characteristics of study participants.

Nearly three quarters of study participants reported carrying their ST products on person, with male participants in the sample being more likely than female participants to report this practice. The large majority of users made their most recent purchase from a street vendor or store, while two participants (0.9%) reported making their purchases from other ST users. The mean amount in Indian Rupees (INR) spent on the last purchase was 24.8 (SD = 39.89), with a median of 12.0, and values ranging from INR 0.0 – 450.0. No notable variations in amount spent were found by age or gender of study participants. The majority of participants reported that their last purchase was meant to last 1 – 2 days (n= 159, 68.5%); 3 – 10 days for 30.1% (n = 70) of respondents, and > 10 days for the remaining study sample (n = 3, 1.3%).

3.2.2.2 ST use characteristics

Total duration of ST use in years: The mean duration of ST use for the entire sample was 12.6 years (SD = 10.11), with women in the sample having chewed for slightly longer on average (mean = 13.5, SD = 10.78) compared to male participants (mean = 11.8, SD = 9.39). As would be expected, the mean duration of ST use was lower for younger participants, and given that the mean age of study participants reduced with increasing levels of education and wealth, the mean duration of ST use also followed the same trend. Mean duration was 15.2 years (SD = 11.21) in those with no formal education, 10.6 years (SD = 8.19) in those who had completed up to secondary schooling, and 6.4 years (SD = 6.14) in those with greater than secondary schooling. Similarly, ST use was consumed on average for 14.5 years (SD = 11.04) by those owning 0 – 3 assets, 10.8 years (SD = 8.16) by those owning 4 – 7 assets, and 5.4 years (SD = 3.60) by those owning 8 or more household assets.

Weekly quantity of ST use in grams: Data on quantity consumed in the form of number of cans/pouches of ST consumed per week showed that the majority of surveyed participants (n = 182, 78.1%) consumed more than 3 cans/pouches, 17.2% consumed 2 – 3 cans/pouches, while 4.7% reported consuming up to 1 can/pouch per week. In terms of grams of ST consumed per week, the average calculated for the entire sample was 86.6 grams (SD = 62.61), with a range of 4.0 – 350.0 grams. While the weekly mean weight of consumption in grams did not vary notably by age group, the results showed that female participants (mean = 94.6, SD = 67.63) in the sample chewed greater quantities per week on average compared to male participants (mean = 78.8, SD = 56.50). The mean weekly consumption in grams was also found to reduce with higher levels of education and wealth, with the differences being more noticeable in the case of the former. Mean quantity consumed was 97.9 grams (SD = 65.15) in those with no formal education, 78.2 grams (SD = 58.30) in those who had completed up to secondary schooling, and 56.5 grams (SD = 52.79) in those who had completed greater than secondary schooling.

Number of times ST used per day: On average, participants reported 17.0 times of ST use per day (SD = 14.17), with male participants (mean = 15.7, SD = 13.66) using ST less frequently than female participants (mean = 18.3, SD = 14.61). Mean frequency of ST use per day showed a decreasing trend with increasing age, education levels, and wealth status of study participants. However, the observed differences were most noteworthy for highest levels of completed education. Mean frequency of ST consumption was 19.5 times per day (SD = 15.32) in those with no formal education, 15.4 (SD = 12.53) in those who had completed up to secondary schooling, and 9.2 (SD = 10.35) in those who had completed greater than secondary schooling.

Urge to use ST products: The urge to use ST in the past 24 hours was felt 'some of the time' or less by about half the study participants (n = 127, 54.5%), while the rest of the participants reported feeling urges 'a lot of the time' or more (n = 106, 45.5%). The strength of these urges were reported to be moderate or less by 36.1% (n = 84), and strong or more by 63.9% (n = 149) of study participants. Both measures did not show much variation by age group, but female participants tended to report greater strength of urge compared to male participants in the sample. Also, while both measures did not show any variation by household asset ownership, those with lower levels of completed education were more likely to report greater frequency of urge and strength of urge to use ST products.

3.2.2.3 Distribution of ST use characteristics by number and types of ST products consumed

Some ST use characteristics, such as frequency and quantity of use, were found to vary with number and type of products currently used. In general, those who reported the current use of more than one ST product chewed more frequently (mean = 25.9 times per day, SD = 16.42 vs. mean = 13.9, SD = 11.92) and in greater quantities (mean = 121.1 grams per week, SD = 66.89 vs. mean = 74.8, SD = 56.66) than those currently using any single ST product. The mean frequency and quantity of ST use were also higher among never smokers compared to ever smokers in the study sample. On the other hand, average duration of ST consumption, urge to use ST, and strength of urge, did not show any notable variations according to the number of ST products consumed, or ever use of smoked tobacco.

Among the single product users of ST, both mean frequency of use and quantity were highest among gul users, although this result was based only on two survey responses. Among users of the two most common types of ST (gutkha and khaini), greater quantities of khaini was reported to be consumed per week (mean = 89.1 grams per week, SD = 54.5 for khaini vs. mean = 65.4, SD = 51.28 for gutkha), while gutkha was consumed with greater frequency on average (mean = 15.3 times per day, SD = 13.49 for gutkha vs. mean = 13.3, SD = 9.62 for khaini).

3.2.3 ST dependence

The results for ST dependence are presented in the order corresponding to the description of analyses – descriptive results of ST-dependency scales, internal consistency measurements, results of criterion, construct, and concurrent validation, and EFA results limited to the OSSTD measure.

3.2.3.1 Descriptive statistics for ST-dependency scales

There were no missing data within the ST dependency scales or entries outside the range of expected values. As summarised in Table 3.4 below, the mean scores and SDs were 6.5 ± 2.29 for TDS-ST, and 5.7 ± 2.11 for FTND-ST, with total possible scores ranging from 0 to 10 on both dependency scales. For the TDS-ST scale, the lowest and highest possible scores were recorded for one (0.4%) and 18 (7.7%) study participants, respectively. For the FTND-ST scale, these corresponding scores were recorded for one (0.4%) and two (0.9%) survey respondents from the entire sample.

Table 3.4 Descriptive statistics for ST dependency scales and subscales

Scales	**Mean (SD)**	**Median (min – max)**
TDS-ST[1]	6.5 (2.29)	7.0 (0 – 10)
FTND-ST[1]	5.7 (2.11)	6.0 (0 – 10)
OSSTD[2]	31.6 (8.60)	33.2 (9.8 – 46.0)
OSSTD Subscales		
PDM[3]	4.9 (1.33)	5.1 (1.2 – 7)
Loss of control & Craving[4]	5.1 (1.45)	5.5 (1 – 7)
Tolerance & Automaticity[4]	4.6 (1.49)	4.7 (1 – 7)
SDM[5]	4.4 (1.26)	4.7 (1.3 – 6.60)
Affective enhancement[4]	4.9 (1.47)	5 (1 – 7)
Affiliative attachment[4]	4.6 (1.69)	5 (1 – 7)
Cognitive enhancement[4]	4.6 (1.70)	5 (1 – 7)
Weight control[4]	2.9 (1.47)	2.67 (1 – 7)
Cue exposure[4]	5.0 (1.53)	5.33 (1.3 – 7)

[1] Minimum and maximum possible scores for TDS-ST and FTND-ST were 0 and 10

[2] OSSTD dependence scores were calculated as the sum of the means of the seven subscales

[3] PDM scores were calculated as (Loss of control & Craving + Tolerance & Automaticity)/2

[4] Minimum and maximum possible scores for OSSTD and self-rated ST addiction were 1 and 7

[5] SDM scores were calculated as (Affective enhancement + Affiliative attachment + Cognitive enhancement + Weight control + Cue exposure)/5

The item-level descriptive statistics for all the ST dependency scales can be found in Appendix 3.4. The results pertaining to TDS-ST items showed that the most and least number of 'Yes' responses were obtained for the following two items, respectively: 'Did you continue to use tobacco after you knew that it caused you health problems?' (n = 218, 93.6%) and 'Have you ever given up work or social activities so you could use tobacco?' (n = 54, 23.2%). Otherwise, around 55 – 78% of study participants answered 'Yes' to the remaining TDS-ST items. Applying a score of 5+ on the total TDS-ST scores to diagnose ST dependence as recommended (Mushtaq and Beebe, 2015), 66.5% (n = 155) of study participants were categorised as dependent users, whereas 33.5% (n = 78) were found to be non-dependent.

Based on the FTND-ST scale, item-level data showed that the majority of participants placed their first chew within 30 minutes of awakening (n = 175, 75.1%), compared to 7.3% (n = 17) and 17.6% (n = 41) of participants who reported placing their first chew between 31-60 minutes or after 60 minutes of awakening. The majority of participants also reported that the first chew in the morning would be the one they would hate to give up most (n = 175, 75.1%). However, less than half the sample reported chewing more frequently during the first hours after awakening (n = 114, 48.9%) than during the rest of the day (n = 119, 51.5%). Most participants did not intentionally swallow tobacco juices (n = 168, 72.1%), and less than half of them reported chewing ST if they were so ill that they were in bed for most of the day (n = 104, 44.6%).

The mean dependence score calculated using the OSSTD scale was 31.6 ± 8.60. Within the OSSTD subscales, the mean scores were highest for the 'Loss of control & Craving' subscale (5.1 ± 1.45), and lowest for the 'Weight control' subscale (2.9 ± 1.47). The PDM scores (4.9 ± 1.33) were slightly higher than SDM scores (4.9 ± 1.26), on average. Item-level data for the OSSTD scale items showed that the mean values ranged from 1.8 (SD = 1.41) for 'Weight control is a major reason that I chew/dip' to 5.6 (SD = 2.02) for 'I chew/dip within the first 30 minutes of awakening in the morning'.

The distribution of dependency scores across sociodemographic characteristics did not show notable variations by age groups for any of the scales. However, mean scores on the 'Weight control' subscale of the OSSTD were slightly higher among younger (18 – 29 year olds = 3.1 ± 1.47) compared to older participants (30+ years = 2.6 ± 1.44). On the other hand, distribution of dependency scores by gender showed that female participants had higher mean scores on the OSSTD scale and all subscales, as well as on the FTND-ST measure. With regard to education, those with higher levels of completed education, scored lower on all ST dependence measures on average. Similarly, those who owned more household assets had lower mean ST dependence scores on average. The diagnosis of ST dependence (based on the TDS-ST scores) did not show any sociodemographic variations. Further results of these analyses can be found in Appendix 3.5.

3.2.3.2 Internal consistency

The Cronbach's α coefficients were 0.693 for TDS-ST, 0.522 for FTND-ST, and 0.924 for OSSTD. The coefficients for the PDM and SDM items were 0.825 and 0.886, respectively. Internal consistency scores for each of the OSSTD subscales are listed in Table 3.5. The lowest of these were found for the 'Weight control' subscale (α = 0.523), and the highest for the 'Cognitive enhancement' subscale (α = 0.812).

For the TDS-ST scale, the variations in Cronbach's α ranged between 0.605 – 0.706, following the deletion of each item. Similar analyses for the FTND-ST scale showed variations between 0.360 – 0.573. With regard to OSSTD, Cronbach's α varied between 0.917 – 0.925 for each item in the entire scale. Within the subscales, item deletions resulted in values that varied between 0.674 – 0.762 for 'Loss of control & Craving', 0.546 – 0.691 for 'Tolerance & Automaticity', 0.428 – 0.693 for 'Affective enhancement', 0.409 – 0.722 for 'Affiliative attachment', 0.720 – 0.759 for 'Cognitive enhancement', 0.237 – 0.575 for 'Weight control', and 0.478 – 0.613 for 'Cue exposure'. Further details of these results have been included along with the item-level descriptive statistics in Appendix 3.4.

Table 3.5 Cronbach's coefficients for ST dependency scales and subscales

Scales	**Cronbach's α coefficient**
TDS-ST	0.693
FTND-ST	0.522
OSSTD	0.924
OSSTD Subscales	
PDM	0.825
Loss of control & Craving	0.775
Tolerance & Automaticity	0.692
SDM	0.886
Affective enhancement	0.652
Affiliative attachment	0.688
Cognitive enhancement	0.812
Weight control	0.523
Cue exposure	0.647

3.2.3.3 Criterion validation

Descriptive results: The mean cotinine level for the entire sample (n = 233) was 156.4 ng/mL, with a SD of 310.56. Median score was 19.0 ng/mL, with a range of measurements from min = 0.4 ng/mL to max = 3175.9 ng/mL. However, as previously stated, the reports relating to non-

detectable cotinine in 35.2% (n = 82) of analysed samples were unexpected, and the results of the sensitivity analyses performed to further explore these findings are presented below.

Results of sensitivity analyses: The analyses of the 233 saliva samples were carried out in three separate batches, using a different kit for each batch. In accordance with this, the first step of the sensitivity analysis looked at the distribution of cotinine results by batch of analysis. The results showed that all the non-detectable cotinine values belonged in the first two batches, comprising 35.0% of batch one (28 of 80 samples) and 66.7% of batch two samples (54 of 81 samples) Therefore, wide variations were found in mean cotinine levels, with values of 194.4 ng/mL (SD = 470.80) for samples analysed in batch one, 33.5 ng/mL (SD = 71.88) for batch two, and 252.9 ng/mL (185.04) for batch three, respectively. In the same order, the three median scores with minimum and maximum values were 9.4 ng/mL (0.4 – 3175.9 ng/mL) for batch one, 0.4 ng/mL (0.4 – 278.4 ng/mL) for batch two, and 233.8 ng/mL (0.9 – 720.6 ng/mL) for batch three, respectively (Table 3.6).

Table 3.6 Distribution of cotinine measurements by batch of analysis

Categorised cotinine	**Analysis batch**			
	Batch 1, n (%)	Batch 2, n (%)	Batch 3, n (%)	Total n (%)
< 0.8 ng/mL	28 (35.0)	54 (66.7)	0 (0.0)	82 (35.2)
>= 0.8 ng/mL	52 (65.0)	27 (33.3)	72 (100.0)	151 (64.8)
Total	80 (100.0)	81 (100.0)	72 (100.0)	233 (100.0)

Assuming the cotinine reports are accurate, we would expect the data in the detectable and non-detectable cotinine groups (< 0.8 ng/mL and >= 0.8 ng/mL) to vary on some of the other study variables recorded, such as duration, quantity, and frequency of ST consumption, number and type of ST product consumed, and use of any other forms of tobacco. However, the sensitivity analyses failed to show any significant differences between the two groups for the entire study sample. Next, given that all the non-detectable results were obtained from samples analysed in batches one and two, and that some ST use characteristics (such as quantity and frequency of use) were significantly different in batch three compared to batches one and two, additional analyses included the comparison of detectable and non-detectable groups, by limiting the data to samples analysed in the first two cotinine batches (n = 161). The results of these additional tests showed significant variations in frequency of ST use between the two groups, after adjusting for multiple hypotheses testing. However, the mean frequency of ST use was higher in the non-detectable cotinine group, showing that the sensitivity analyses did not offer any logical explanations for the existence of non-detectable values within the study sample. All the results of these analyses have been included as tables in Appendix 3.6.

It was considered if another likely explanation for the non-detectable cotinine measurements could be from the inclusion of a large number of non-tobacco users, who ended up forming a part of the final study sample despite self-reporting ST use. However, measurement errors resulting from the misclassification of about a third of the study sample was considered highly unlikely, with some evidence in support of this being offered by data collected on ST carrying practices of study participants. Nearly 75% (n = 173) of survey respondents reported carrying their ST products on person, which I was able to verify at the time of the interview. Taken together with the results of the sensitivity analyses, these findings led me to conclude that the cotinine values reported from batches one and two were inaccurate, and were therefore excluded from any further analyses. On the other hand, given that none of the cotinine values were non-detectable in batch three (as would be expected for this study sample), and that I personally observed the laboratory analyses being performed on this batch of saliva samples, I decided to carry out the steps of the criterion validation analyses limited to this reduced sample (n = 72).

Descriptive results for limited sample (n = 72): The mean salivary cotinine concentration was 252.9 ng/mL (SD = 185.04), and the median was 233.8 ng/mL (min = 0.9 ng/mL, max = 720.6 ng/mL). The distribution of cotinine levels according to sociodemographic variables showed higher mean values for participants who were older (30+ years = 302.3 ± 202.80) and male (300.2 ± 161.32), compared to those who were younger (18 – 29 years = 208.8 ± 157.43) and female (224.5 ± 194.10), respectively. No notable variations were noted according to education levels completed or number of household assets owned. Mean cotinine did not vary much between those who reported the current use of one (259.1 ± 188.19), or more than one (240.6 ± 181.90) ST product. However, ever-smokers (287.8 ± 189.79) appeared to have slightly higher mean cotinine measurements compared to never-smokers (245.2 ± 184.74), on average. Mean cotinine levels were also higher in those who never swallowed tobacco juices (264.6 ± 206.82), compared to those who reported swallowing the juices sometimes (257.8 ± 127.75) and always (174.9 ± 157.45). Similarly, the values were higher in those who consumed ST within five minutes of waking up (252.9 ± 185.04), compared to average values in other response categories (6 – 30 minutes: 255.5 ± 188.47, 31 – 60 minutes: 194.8 ± 250.56, and > 60 minutes: 193.3 ± 180.71).

As cotinine values were skewed, square root transformations were applied to the data. Correlation analyses between transformed cotinine and ST use characteristics showed positive correlations with duration ($r = 0.175$, $p = 0.141$), quantity ($r = 0.085$, $p = 0.480$), and frequency ($r = 0.151$, $p = 0.205$) of ST use. Similarly, positive correlations were found with urge to use ST ($r = 0.318$, $p = 0.007$) and strength of urge felt ($r = 0.161$, $p = 0.177$).

Criterion validation results for limited sample (n = 72): No evidence of statistically significant correlations were found between the transformed cotinine variable and any of the ST dependency

scales in the reduced dataset – TDS-ST (r = 0.177, p = 0.137), FTND-ST (r = 0.068, p = 0.571), or OSSTD (r = 0.230, p = 0.052). However, some of the individual items on the FTND-ST scale showed significant correlations, albeit without adjustments of p-values for multiple hypotheses testing. While cotinine values were positively correlated with ST use soon after awakening rather than later (r = 0.248, p = 0.036), they were negatively correlated with greater frequency of use during the first hours of awakening (r = –0.272, p = 0.021). In addition, some OSSTD subscales showed significant positive correlations – both PDM subscales: 'Loss of control & Craving' (r = 0.247, p = 0.037), 'Tolerance & Automaticity' (r = 0.233, p = 0.049), and one SDM subscale: 'Cognitive enhancement' (r = 0.249, p = 0.035). The correlation coefficients for the other OSSTD subscales ranged from r = 0.077 to r = 0.209, and none of them were statistically significant. There was also no significant difference in mean cotinine levels for those who had TDS-ST based dependence diagnosis and those who did not (p = 0.355).

Table 3.7 Linear regression of ST dependency scales with transformed cotinine

Scales	**Univariate model**				**Multivariate model***			
	β	SE	t-value	p-value	B	SE	t-value	p-value
TDS-ST	0.575	0.382	1.505	0.137	0.570	0.388	1.469	0.146
Dependence diagnosis	2.231	1.833	1.217	0.228	3.049	1.856	1.643	0.105
FTND-ST	0.261	0.459	0.569	0.571	0.566	0.453	1.251	0.215
OSSTD	0.198	0.100	1.980	0.052	0.202	0.097	2.078	0.042
OSSTD Subscales								
Loss of control & Craving	1.183	0.556	2.128	0.037	1.154	0.538	2.145	0.036
Tolerance & Automaticity	1.405	0.700	2.007	0.049	1.472	0.680	2.164	0.034
Affective enhancement	1.064	0.594	1.792	0.077	0.966	0.580	1.665	0.101
Affiliative attachment	0.328	0.505	0.648	0.519	0.542	0.493	1.101	0.275
Cognitive enhancement	1.128	0.524	2.154	0.035	1.019	0.527	1.932	0.058
Weight control	0.454	0.570	0.797	0.428	0.791	0.567	1.395	0.168
Cue exposure	0.973	0.552	1.762	0.082	0.816	0.552	1.479	0.144

Note: Square root transformation of cotinine data applied; *Model adjusts for age, gender, and ever-smoking.

The results of linear regression analyses using transformed cotinine measurements showed that the associations with ST dependency scales had slight changes after adjusting for potential confounding from age, gender, and ever-smoking status of study participants (Table 3.7). The assumptions of normality and uniform variance seemed to be supported in all the regression models using transformed cotinine measurements. Although the p-value for FTND-ST was not statistically significant in the adjusted model, the β coefficient showed a change from 0.261 to

0.566. The associations that remained statistically significant in both unadjusted and adjusted models were for the two PDM subscales of OSSTD – 'Loss of control & Craving' and 'Tolerance & Automaticity'. On the other hand, the statistical significance of associations for total OSSTD and 'Cognitive enhancement' subscale changed as follows in adjusted models. The total OSSTD score was significantly associated with transformed cotinine in the adjusted model ($p = 0.042$), but not in the unadjusted model ($p = 0.052$). However, the value of the β coefficient did not vary greatly (adjusted $\beta = 0.202$ vs. unadjusted $\beta = 0.198$). The change in p-value for 'Cognitive enhancement' indicated that the subscale was not significantly associated with transformed cotinine measurements in the adjusted model ($p = 0.058$).

3.2.3.4 Construct validation – ST use characteristics

Table 3.8 Correlation between dependency scales and ST use characteristics

Scales	**Correlation coefficient, r (p-value)**				
	Duration	Quantity	Frequency	Urge	Strength of urge
TDS-ST	0.173 (0.008)	0.459 (<0.001)	0.422 (<0.001)	0.511 (<0.001)	0.483 (<0.001)
FTND-ST	0.128 (0.050)	0.374 (<0.001)	0.405 (<0.001)	0.525 (<0.001)	0.507 (<0.001)
OSSTD	0.068 (0.301)	0.371 (<0.001)	0.404 (<0.001)	0.634 (<0.001)	0.704 (<0.001)
OSSTD Subscales					
Loss of control & Craving	0.094 (0.153)	0.343 (<0.001)	0.394 (<0.001)	0.537 (<0.001)	0.579 (<0.001)
Tolerance & Automaticity	-0.037 (0.570)	0.369 (<0.001)	0.427 (<0.001)	0.574 (<0.001)	0.617 (<0.001)
Affective enhancement	0.044 (0.508)	0.260 (<0.001)	0.227 (<0.001)	0.379 (<0.001)	0.531 (<0.001)
Affiliative attachment	0.076 (0.248)	0.278 (<0.001)	0.301 (<0.001)	0.523 (<0.001)	0.587 (<0.001)
Cognitive enhancement	0.037 (0.570)	0.326 (<0.001)	0.314 (<0.001)	0.541 (<0.001)	0.541 (<0.001)
Weight control	0.050 (0.445)	0.247 (<0.001)	0.288 (<0.001)	0.455 (<0.001)	0.519 (<0.001)
Cue exposure	0.162 (0.013)	0.266 (<0.001)	0.304 (<0.001)	0.508 (<0.001)	0.542 (<0.001)

The TDS-ST and FTND-ST scores were significantly correlated with all the components of ST use characteristics used for construct validation – duration (years of ST use), quantity (grams per week), frequency (dips/chews per day), urge to use ST (in the past 24 hours), and strength of urge felt. However, the coefficients were much lower for duration of use compared to other ST use

characteristics. On the other hand, the OSSTD scale and subscales did not show significant correlations with duration of ST use, with the exception of 'Cue exposure', which showed a small positive correlation which was statistically significant (r = 0.162, p = 0.013). Apart from duration, all other ST use characteristics were significantly correlated with the OSSTD scale and subscales, as summarised in Table 3.8.

The ST use characteristics also showed significant variations between those diagnosed as dependent and non-dependent, based on TDS-ST scores. While the mean duration of ST use was higher among dependent users (13.3 years ± 9.88) compared to non-dependent users (11.4 ± 10.51), this difference was not statistically significant (p = 0.178). The mean values of all other ST use characteristics were significantly higher in those diagnosed with dependence, as shown in Table 3.9.

Table 3.9 ST use characteristics by diagnosis of ST dependence

ST use characteristic	**Overall (n = 233),** Mean (SD)	**Dependent users (n = 155),** Mean (SD)	**Non-dependent users (n = 78),** Mean (SD)	**p-value**
Duration (years)	12.6 (10.11)	13.3 (9.88)	11.4 (10.51)	0.178
Quantity (grams per week)	86.6 (62.61)	102.7 (65.01)	54.6 (42.42)	<0.001
Frequency (chews per day)	17.0 (14.17)	20.4 (15.16)	10.4 (8.81)	<0.001
Urge (in the past 24 hours)	3.3 (1.25)	3.7 (1.09)	2.4 (1.13)	<0.001
Strength of urge	3.1 (1.42)	3.5 (1.28)	2.3 (1.31)	<0.001

The results of linear regression analyses showed that the associations with quantity and frequency remained significant for all ST dependency scales and subscales in both unadjusted and adjusted models. On the other hand, with regard to duration, the unadjusted models indicated that TDS-ST, FTND-ST and the 'Cue exposure' subscale of the OSSTD were significantly associated. However, in the adjusted models, only the 'Tolerance & Automaticity' subscale of the OSSTD failed to show significant associations with transformed duration of ST use. The detailed results of these analyses can be found in Appendix 3.7.

3.2.3.5 Concurrent validation – ST dependency scales, including self-rated ST addiction

Table 3.10 Correlation between ST dependency scales, including self-rated ST addiction

Scales	**Dependence diagnosis**	**TDS-ST**	**FTND-ST**	**Self-rated ST addiction***
	Correlation coefficient, r (p-value)			
Dependence diagnosis	1			
TDS-ST	0.845 (<0.001)	1		

FTND-ST	0.432 (<0.001)	0.507 (<0.001)	1	
Self-rated ST addiction*	0.512 (<0.001)	0.516 (<0.001)	0.473 (<0.001)	1
OSSTD	0.504 (<0.001)	0.543 (<0.001)	0.572 (<0.001)	0.701 (<0.001)
OSSTD Subscales				
Loss of control & Craving	0.540 (<0.001)	0.585 (<0.001)	0.519 (<0.001)	0.730 (<0.001)
Tolerance & Automaticity	0.417 (<0.001)	0.440 (<0.001)	0.546 (<0.001)	0.642 (<0.001)
Affective enhancement	0.389 (<0.001)	0.403 (<0.001)	0.413 (<0.001)	0.506 (<0.001)
Affiliative attachment	0.403 (<0.001)	0.462 (<0.001)	0.457 (<0.001)	0.563 (<0.001)
Cognitive enhancement	0.377 (<0.001)	0.402 (<0.001)	0.443 (<0.001)	0.476 (<0.001)
Weight control	0.293 (<0.001)	0.282 (<0.001)	0.346 (<0.001)	0.475 (<0.001)
Cue exposure	0.389 (<0.001)	0.450 (<0.001)	0.461 (<0.001)	0.532 (<0.001)

* Missing values = 2

Based on the results of the simple linear regression models presented in Table 3.11, it was found that the TDS-ST and FTND-ST scales shared a common variance of 25.7%. The total OSSTD scores accounted for 29.5% and 32.7% of the variability in TDS-ST and FTND-ST scales, respectively. With regard to the OSSTD subscales, it was found that individual subscales accounted for 7.9% ('Weight control') to 34.2% ('Loss of control & Craving') of the variability in TDS-ST scores, and 12.0% ('Weight control') to 29.9% ('Tolerance & Automaticity') of the variability in FTND-ST scores. The self-rated ST addiction measure accounted for 26.6%, 22.4% and 49.2% of the variability in total TDS-ST, FTND-ST, and OSSTD scores, respectively.

Table 3.11 Linear regression analyses using ST dependency scales

Scales	**TDS-ST**		**FTND-ST**		**Self-rated ST addiction***	
	β (SE)	p-value	β (SE)	p-value	β (SE)	p-value
OSSTD	0.145 (0.482)	<0.001	0.141 (0.013)	<0.001	0.128 (0.009)	<0.001
OSSTD Subscales						
Loss of control & Craving	0.924 (0.084)	<0.001	0.757 (0.082)	<0.001	0.790 (0.049)	<0.001
Tolerance & Automaticity	0.673 (0.090)	<0.001	0.772 (0.078)	<0.001	0.674 (0.053)	<0.001
Affective enhancement	0.625 (0.094)	<0.001	0.593 (0.086)	<0.001	0.545 (0.061)	<0.001
Affiliative attachment	0.626 (0.079)	<0.001	0.571 (0.073)	<0.001	0.528 (0.051)	<0.001
Cognitive enhancement	0.541 (0.081)	<0.001	0.551 (0.073)	<0.001	0.440 (0.054)	<0.001

Weight control	0.438 (0.098)	<0.001	0.497 (0.089)	<0.001	0.509 (0.062)	<0.001
Cue exposure	0.673 (0.088)	<0.001	0.637 (0.081)	<0.001	0.544 (0.057)	<0.001

* Missing values = 2

The results of univariate logistic regression analyses (Table 3.12) showed that the odds ratio (OR) for being diagnosed with dependence that corresponded to a unit increase in total FTND-ST scores was 1.62 (95% CI = 1.39, 1.90). The ORs found for total OSSTD scores and self-rated ST addiction were 1.15 (95% CI = 1.11, 1.20) and 2.21 (95% CI = 1.77, 2.77), respectively. For the OSSTD subscales, the ORs ranged from 1.61 (1.30 – 1.99) for 'Weight control' to 2.60 (1.11 – 1.20) for 'Loss of control & Craving'.

Table 3.12 Logistic regression analyses based on dependence diagnosis

Scales	**Odds Ratio (OR)**	**95% CI**
FTND-ST	1.62	1.39 – 1.90
Self-rated ST addiction*	2.21	1.77 – 2.77
OSSTD	1.15	1.11 – 1.20
OSSTD Subscales		
Loss of control & Craving	2.60	1.99 – 3.39
Tolerance & Automaticity	1.91	1.54 – 2.37
Affective enhancement	1.81	1.47 – 2.24
Affiliative attachment	1.72	1.43 – 2.07
Cognitive enhancement	1.63	1.37 – 1.95
Weight control	1.61	1.30 – 1.99
Cue exposure	1.76	1.44 – 2.15

* Missing values = 2

3.2.3.6 Exploratory factor analysis

Exploratory factor analysis limited to the OSSTD scale showed the following results. Correlation matrix of the OSSTD items (Table 3.13) showed that inter-item coefficients were all positive and ranged from 0.030 to and 0.624. Item-total correlations were all significant at the 0.01 level, and ranged from 0.271 (item 11: "Weight control is a major reason that I chew/dip") to 0.751 (item 20: "Chewing/dipping helps me think better"). All the OSSTD subscales were also significantly correlated with each other (Table 3.14).

The various tests performed for assessing the conditions of EFA showed the following results. As there were no missing data, all 233 survey questionnaires were used for factor analysis. The data were considered factorable, as every variable on the OSSTD was significantly correlated with at

least one other variable (Table 3.13). Except for one item (item 11: "Weight control is a major reason that I chew/dip"), whose minimum significant coefficient with another item was r = 0.281, all other variables met the recommended criteria for factorability (minimum value of r = 0.300 in the inter-correlation matrix). In addition, Bartlett's test of sphericity was statistically significant (Chi square = 2413.2, df = 253, $p < 0.001$), and the overall measure of sampling adequacy yielded a high value (KMO = 0.913). Inspection of the boxplots for individual OSSTD items (Appendix 3.4) showed outliers for items 11, 14, 18, and 22. However, all the values fell within the range of permissible values and were therefore retained for analysis. Scatterplots showed that the linearity of items was satisfactory, while frequency histograms of variable distribution showed that some items deviated from the normality assumption. No correlation was greater than 0.900, which indicated the absence of multicollinearity between the scale variables.

Applying factor extraction methods that were most suited to ordinal data that did not follow a normal distribution, the results of EFA suggested that up to two factors could be extracted from the OSSTD variables. This was supported by Kaiser's criterion (factors with eigenvalue values greater than 1.0 – the eigenvalues obtained for the two factors were 8.5 and 1.5, respectively), and the percentage of variance explained by the extracted factors (satisfactory cut-off point of 60% – the two extracted factors accounted for 60.87% of the common variance). Omitting all factor loadings lower than an absolute value of 0.320, the two-factor model produced loadings that ranged from 0.327 – 0.910 (Table 3.15).

In this model, all item communalities were greater than 0.400, ranging from 0.495 to 0.888. Ten of the scale items loaded on the first factor, whereas 19 loaded on the second factor, with six cross-loading items. All the cross-loading items belonged in SDM subscales, with each SDM subscale having at least one cross-loading item. These were distributed as follows: one in 'Affective enhancement' – item 21 ("Chewing/dipping really helps me feel better if I've been feeling down"), one in 'Affiliative attachment' – item 15 ("I would feel alone without my chew/dip"), two in 'Cognitive enhancement' – item 5 ("I chew/dip when I really need to concentrate") and item 20 ("Chewing/dipping helps think better"), one in 'Weight control' – item 11 ("Weight control is a major reason that I chew/dip"), and one in 'Cue exposure' – item 17 ("Some things are very hard to do without chewing/dipping"). Among the cross-loading items, one item ("Weight control is a major reason that I chew/dip") showed a strong loading on one factor (0.743) compared to the second (-0.451), while the other items showed low loadings on both extracted factors.

Not considering the low-loading items on the two factors, the first factor appeared to relate to the 'Weight control' and 'Automaticity' subscales, while the second factor to the remaining OSSTD subscales ('Loss of control & Craving', 'Tolerance', 'Affective enhancement', 'Affiliative

attachment', 'Cognitive enhancement' and 'Cue exposure'). However, the presence of six cross-loading items, and high levels of correlation between the two factors (inter-factor correlation = 0.703), suggested that extracting more than one factor might not be necessary for the data collected in this study. In the one-factor model (Table 3.15), the item communalities ranged from 0.488 to 0.886, and all items except one showed factor loadings > 0.320 (factor loading for item 11 = 0.195). Not considering item 11, the factor loadings in the one-factor model ranged from 0.472 for item 8 ("There are particular sights and smells that trigger strong urges to chew/dip") to 0.743 for item 12 ("I'm really hooked on chew/dip") on the OSSTD scale. The one-factor solution accounted for 51.47% of the common variance.

Table 3.13 Inter-item and item-total correlation coefficients for OSSTD

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	Item total
1	1																							0.586
2	0.492	1																						0.602
3	0.396	0.471	1																					0.558
4	0.322	0.424	0.325	1																				0.592
5	0.378	0.354	0.310	0.408	1																			0.634
6	0.296	0.225	0.321	0.163*	0.332	1																		0.559
7	0.387	0.357	0.440	0.420	0.399	0.421	1																	0.703
8	0.276	0.270	0.283	0.336	0.206	0.238	0.397	1																0.497
9	0.314	0.336	0.351	0.386	0.597	0.345	0.377	0.247	1															0.634
10	0.441	0.459	0.376	0.484	0.433	0.309	0.412	0.390	0.494	1														0.701
11	**0.083**	**0.098**	**0.056**	**0.030**	0.281	0.153*	0.133*	0.129*	0.141*	0.178	1													0.271
12	0.515	0.392	0.378	0.443	0.379	0.347	0.540	0.360	0.441	0.621	**0.067**	1												0.717
13	0.181	0.299	**0.090**	0.247	0.268	0.289	0.222	0.226	0.212	0.355	0.245	0.322	1											0.496
14	0.470	0.373	0.358	0.432	0.314	0.264	0.420	0.323	0.263	0.509	**0.066**	0.585	0.266	1										0.624
15	0.312	0.386	0.257	0.443	0.311	0.305	0.566	0.291	0.347	0.456	0.136*	0.414	0.360	0.418	1									0.664
16	0.478	0.315	0.367	0.362	0.422	0.412	0.415	0.315	0.368	0.506	0.140*	0.539	0.279	0.435	0.380	1								0.678
17	0.300	0.397	0.381	0.398	0.342	0.411	0.400	0.378	0.435	0.475	0.133*	0.481	0.319	0.462	0.512	0.474	1							0.731
18	0.329	0.209	0.256	0.361	0.337	0.363	0.353	0.163*	0.341	0.330	**0.108**	0.412	0.158*	0.444	0.382	0.426	0.562	1						0.587
19	0.226	0.283	**0.115**	0.253	0.385	0.284	0.340	0.207	0.364	0.355	0.297	0.384	0.624	0.291	0.437	0.366	0.450	0.293	1					0.600
20	0.408	0.447	0.423	0.422	0.563	0.355	0.476	0.273	0.612	0.522	0.206	0.443	0.290	0.353	0.486	0.484	0.544	0.480	0.416	1				0.751
21	0.243	0.275	0.236	0.254	0.365	0.225	0.462	0.276	0.415	0.330	0.186	0.343	0.257	0.280	0.510	0.323	0.463	0.370	0.348	0.517	1			0.593
22	0.333	0.375	0.360	0.319	0.315	0.255	0.468	0.280	0.381	0.375	**0.075**	0.469	0.224	0.420	0.345	0.345	0.482	0.407	0.310	0.534	0.531	1		0.625
23	0.172	0.193	0.191	0.213	0.273	0.404	0.436	0.247	0.210	0.262	0.229	0.335	0.335	0.195	0.319	0.385	0.444	0.263	0.473	0.376	0.329	0.328	1	0.543

* Correlations were significant at 0.05 level (2-tailed), Unmarked correlations were significant at 0.01 level (2-tailed), Figures in bold were non-significant

Table 3.14 Correlations between OSSTD subscales

Subscales	PDM1	PDM2	SDM1	SDM2	SDM3	SDM4	SDM5
PDM1	1						
PDM2	0.623**	1					
SDM1	0.624**	0.551**	1				
SDM2	0.664**	0.545**	0.662**	1			
SDM3	0.631**	0.592**	0.619**	0.579**	1		

SDM4	0.388**	0.597**	0.398**	0.491**	0.468**	1	
SDM5	0.684**	0.623**	0.609**	0.635**	0.510**	0.465**	1

** Correlations are significant at the 0.01 level (2-tailed)

Table 3.15 Results of EFA for OSSTD

Item No.	Subscales and variables	Two-factor solution			One-factor solution	
		Factor 1	Factor 2	Communality	Factor 1	Communality
PDM1: Loss of Control & Craving						
1	Chew/dip controls me	-	0.742	0.691	0.564	0.688
4	It's hard to ignore an urge to chew/dip	-	0.766	0.732	0.621	0.731
10	I frequently crave chew/dip	-	0.690	0.689	0.696	0.689
12	I'm really hooked on chew/dip	-	0.838	0.842	0.743	0.842
PDM2: Tolerance & Automaticity						
13	I find myself reaching for chew/dip without thinking about it	0.774	-	0.715	0.461	0.715
16	Other chewers/dippers consider me a heavy chewer/dipper	-	0.559	0.651	0.670	0.652
18	I chew/dip within the first 30 minutes of awakening	-	0.783	0.888	0.660	0.886
19	Sometimes I am not aware that I am chewing/dipping	0.910	-	0.805	0.577	0.794
SDM1: Affective enhancement						
2	Chewing/dipping improves my mood	-	0.543	0.676	0.559	0.678
21	Chewing/dipping really helps me feel better if I've been feeling down	0.327	0.327	0.771	0.596	0.773
22	Chewing/dipping makes me feel good	-	0.571	0.603	0.611	0.604
SDM2: Affiliative attachment						
3	Very few things give me pleasure each day like chew/dip	-	0.629	0.568	0.529	0.570

7	Chew/dip keep me company, like a close friend	-	0.556	0.847	0.725	0.851
15	I would feel alone without my chew/dip	0.363	0.379	0.865	0.677	0.865
SDM3: Cognitive enhancement						
5	I chew/dip when I really need to concentrate	0.323	0.341	0.735	0.607	0.739
9	Chewing/dipping helps me stay focused	-	0.460	0.719	0.619	0.722
20	Chewing/dipping helps think better	0.335	0.456	0.781	0.729	0.789
SDM4: Weight control						
6	I rely upon chewing/dipping to control my hunger and eating	0.508	-	0.721	0.539	0.727
11	Weight control is a major reason that I chew/dip	0.743	-0.451	0.495	-	0.488
23	Chewing/dipping keeps me from over eating	0.855	-	0.745	0.503	0.736
SDM5: Cue exposure						
8	There are particular sights and smells that trigger strong urges to chew/dip	-	0.339	0.428	0.472	0.430
14	I crave chew/dip at certain times of the day	-	0.900	0.714	0.633	0.709
17	Some things are very hard to do without chewing/dipping	0.351	0.451	0.847	0.738	0.855

3.3 Discussion

The findings of this validation study are important because research in the field of ST dependence measurement is scarce, particularly from South Asia. To my knowledge, this is among the first comprehensive attempts at scale validation for measuring ST dependence within a South Asian setting. In this discussion section, I summarise the main findings based on validation of three ST dependency scales and interpret the findings of my analyses within the context of other research literature on the topic. I then present the strengths and limitations of the different methodologies applied for collecting and analysing the study data. Finally, I consider the implications of my findings for practice, policy, and future research on ST dependence within the study settings.

3.3.1 Summary of main findings and their interpretation within context

"Assessing tobacco dependence is difficult and is made even more so in population-based epidemiologic research by the need for efficient assessment (valid and brief). Ideally, a measure should reflect the nature or domain of the construct of interest (i.e. tobacco dependence), predict important outcomes (e.g. likelihood of quitting, problems encountered through use), and be relatively brief to assess." – IARC (2008)

The primary objective of my study was to carry out a comprehensive validation of a range of itemised scales for measuring dependence among adult ST users within a South Asian context. Given the strengths and limitations of the different types of dependency scales and their variations in potential for application in different clinical and research settings, it was decided to include a range of ST dependence measures in this validation study. For example, traditional measures such as the diagnostic and Fagerström measures, have been shown to predict clinically important dependence criteria such as heaviness of use and relapse among smokers (Fagerstrom and Schneider, 1989, Kawakami et al., 1999). In addition, their brevity and ease of administration have been recognised as factors linked with their widespread application. On the other hand, it has been pointed out that tobacco dependence has several dimensions, including physical, behavioural, and psychological components, whereas the traditional measures tend to place a heavier emphasis on limited psychiatric and physical symptoms (NCI, 2009). In line with this view, newer scales had been developed, specifically to assess and quantify tobacco dependence as a multidimensional construct. As scales for measuring ST dependence had been developed across the three approaches described above, it was decided to carry out a validation study that could make a comprehensive assessment based on all three available approaches. Moreover, given that all the ST dependence scales had been developed and validated in western countries, their relevance to ST users who are culturally different and use diverse ST products was tested in the current study.

Till date, only two other studies have carried out similar comprehensive assessments of ST dependency scales, none in India. The first was based on a sample of 100 adults living in Oklahoma, USA (Mushtaq et al., 2014), while the second was based in Dhaka, Bangladesh and included a sample of 200 adult participants (Mushtaq et al., 2019). The eligibility criteria regarding the exclusivity and regularity of ST consumption in both studies were comparable with my validation study, although the final recruited sample in Oklahoma comprised only male ST users. Since the ST dependency measures were all originally developed in the English language, there were additional steps of translation and cross-cultural adaptation to produce Hindi (my study) and Bangla versions of the scales, for use in New Delhi and Dhaka, respectively.

Comparisons across the three studies showed further differences in some of the methods used for data collection. While all the study material including questionnaires and saliva collection tubes were mailed out to eligible participants in the American study, this approach was not considered as feasible within my study context. Instead, face-to-face interviews were conducted with consenting participants, and questionnaires were filled out according to the received responses, similar to the approach used in Bangladesh. On the other hand, the laboratory methods used for analysing saliva samples differed between the Bangladesh and India studies. While Salimetrics (2009) immunoassay kits were used to analyse saliva samples in India (similar to the Oklahoma study), the samples from Bangladesh were shipped to UK, for testing based on a validated liquid chromatography-tandem mass spectrometry method. In Table 3.16 I summarise the main results based on the psychometric assessments of the three ST dependency scales in three different study settings – New Delhi, Oklahoma, Dhaka.

Table 3.16 Comparison of psychometric results of ST dependency scales

Psychometric assessments	**New Delhi, India – results from my study (n = 233*)**	**Oklahoma, USA** (n = 100)**	**Dhaka, Bangladesh*** (n = 200)**
Internal consistency, Cronbach's α			
TDS-ST	0.693	0.765	0.857
FTND-ST	0.522	0.696	0.640
OSSTD	0.924	0.925	0.921
Correlations with transformed cotinine, Pearson's r (p-value)	n = 72		
TDS-ST	0.177 (0.137)	0.241 (0.018)	NS
FTND-ST	0.068 (0.571)	0.610 (< 0.001)	0.220 (0.002)
OSSTD	0.230 (0.052)	0.267 (0.009)	NS
Correlations with ST use duration, Pearson's r (p-value)			
TDS-ST	0.173 (0.008)	Positive (<0.050)	0.353 (< 0.001)

FTND-ST	0.128 (0.050)	Positive (< 0.001)	0.258 (< 0.001)
OSSTD	0.068 (0.301)	0.297 (0.003)	0.126 (0.078)
Correlations with ST use quantity****, Pearson's r (p-value)			
TDS-ST	0.459 (<0.001)	0.143 (NS)	0.042 (0.558)
FTND-ST	0.374 (<0.001)	0.656 (<0.050)	0.559 (<0.001)
OSSTD	0.371 (<0.001)	0.294 (0.003)	0.213 (0.003)
Correlations with ST use frequency, Pearson's r (p-value)			
TDS-ST	0.422 (<0.001)	0.255 (<0.050)	−0.022 (0.764)
FTND-ST	0.405 (<0.001)	0.592 (<0.050)	0.400 (< 0.001)
OSSTD	0.404 (<0.001)	0.281 (0.005)	0.288 (< 0.001)
Correlations between ST scales, Pearson's r (p-value)			
TDS-ST & FTND-ST	0.507 (<0.001)	0.430 (< 0.001)	0.369 (<0.050)
TDS-ST & OSSTD	0.543 (<0.001)	0.594 (< 0.001)	0.207 (<0.050)
FTND-ST & OSSTD	0.572 (<0.001)	0.515 (< 0.001)	0.469 (<0.050)
Total scores on ST dependence scales, Mean (SD)			
TDS-ST	6.5 (2.29)	5.4 (2.61)	4.8 (3.08)
FTND-ST	5.7 (2.11)	3.8 (2.54)	4.7 (2.47)
OSSTD	31.6 (8.60)	26.5 (8.44)	35.6 (7.24)

NS – Not Significant (p > 0.050, actual p-values not available)

*For the India study n = 233, except for correlations with transformed cotinine, where n = 72, ** Results obtained from 3 different publications – Mushtaq et al. (2014), Mushtaq and Beebe (2015), and Mushtaq and Beebe (2017b), *** Pearson's correlation coefficients were adjusted for gender, **** Quantity measured as cans/pouches per week in Oklahoma and Dhaka, and grams per week in New Delhi

3.3.1.1 Internal consistency

Across the three studies, the Cronbach's α coefficients were uniformly high for OSSTD (> 0.900), with lower coefficients for the other two dependency scales. The coefficients for FTND-ST were lowest among the dependency scales in all study settings. With regard to the OSSTD subscales, although coefficients were not available from the Bangladesh study for comparisons (Mushtaq et al., 2019), some differences were noted between my study and the Oklahoma study. In the original validation (Mushtaq et al., 2014), the α coefficients for all of the subscales were more than 0.860, except for 'Cue exposure' (α = 0.662) and 'Tolerance & Automaticity' (α = 0.785). In comparison, my study found lower coefficients for all OSSTD subscales in general (range = 0.523 – 0.812), with the lowest values found for the 'Weight control' subscale. The coefficients for TDS-ST and FTND-ST were also lower in my study compared to the other assessments.

To an extent, a high value of Cronbach's α was expected for OSSTD, given the scale's length (23 items), and its development as a multidimensional measure of ST dependence with seven subscales. Nevertheless, coefficients > 0.900 in three different study settings and in samples ranging between 100 – 200+ suggested 'good' internal consistency, based on standards that explicitly considered the influence of both scale length and sample size on α coefficients (Ponterotto and Ruckdeschel, 2007). Within the subscales, some of the coefficients showed increases after deleting certain items – the coefficient changed from 0.652 to 0.693 for 'Affective enhancement' after deleting "Chewing/dipping improves my mood", from 0.688 to 0.722 for 'Affiliative attachment' after deleting "Very few things give me pleasure each day like chewing/dipping", and from 0.523 to 0.575 for 'Weight control' after deleting "Weight control is a major reason that I chew/dip". However, the increases were not substantial, and did not serve to explain the lower subscale coefficients found in my study.

With regard to the other dependency scales, although it is possible that the number of scale items may be linked with the lower α values found (10 items in TDS-ST and 6 items in FTND-ST), α coefficients of at least 0.700 are generally desired during validation (Streiner et al., 2015). In this study, the Cronbach's α for TDS-ST was close to this acceptable value (0.693), although it was lower than values obtained from other administrations of the scale among study samples comprising ST users (Mushtaq and Beebe, 2015, Mushtaq et al., 2019) and cigarette smokers (Kawakami et al., 1999). Only one item showed an increase in Cronbach's α after deletion – the coefficient increased from 0.693 to 0.706 after deleting "Did you continue to use tobacco after you knew that it caused you mental problems". However, the increase was not substantial.

Similar to the findings of my study, it appears that all administrations of the FTND-ST have found Cronbach's coefficients to be less than 0.700 (Mushtaq and Beebe, 2012, Mushtaq et al., 2014, Mushtaq et al., 2019), which suggested low levels of correlation between the scale items. The deletion of two scale items ("How often do you intentionally swallow tobacco juice?" and "How many cans/pouches per week do you use?") resulted in increases in the scale's Cronbach's coefficients, but not by much.

3.3.1.2 Criterion validation

In this study, criterion validation using salivary cotinine levels failed to show significant correlations with any of the ST dependency scales in a reduced dataset (n = 72). However, after adjusting for potential confounders (age, gender, and ever-smoking), the associations with transformed cotinine measurements were statistically significant for total OSSTD scores, as well as scores on the two PDM subscales ('Loss of control & Craving' and 'Tolerance &

Automaticity'). While Mushtaq et al. (2014) similarly found these measures to be significantly associated with the criterion variable, they additionally found significant associations with total TDS-ST and FTND-ST scores as well. The Bangladesh study (Mushtaq et al., 2019), on the other hand, found that significant associations were limited to the FTND-ST scale ($r = 0.220$, $p = 0.002$). However, results from an earlier publication based on this data suggested that these associations did not remain significant in adjusted models (Huque et al., 2016). A few other studies from India have assessed the correlation between FTND-ST scores and cotinine measurements – while four of five identified studies found poor correlation between the two measures, based on testing of urine (Balhara et al., 2012, Jain et al., 2015) or saliva samples (Asha and Dhanya, 2015, Patel et al., 2017), significant correlations were found in one study of drug-dependent persons who were seeking treatment for addiction to other drugs besides tobacco (Jain et al., 2012).

Overall, criterion validation against salivary cotinine levels could not be established for the ST dependency scales in this study, which could be a type 2 error resulting from a small sample size. However, the reasons for this finding, as well as comparisons with other validation studies were difficult to interpret, given that the results from my study were based on a reduced dataset. This was recognised as a major drawback, and will be considered later under study limitations (Section 3.3.2). Additionally, comparisons between the other study results were also made difficult due to differences in study samples, as well as biochemical testing methods used for obtaining cotinine measurements.

3.3.1.3 Construct validation

For the FTND-ST, the results of construct validation analyses were comparable across the three study settings (Oklahoma, Dhaka, and New Delhi), and showed significant positive correlations with all three ST use characteristics measured (duration, quantity, and frequency). On the other hand, while TDS-ST was found to be significantly correlated with duration in all three study settings, correlations with quantity were only found to be significant in my study, whereas correlations with frequency were found to be significant in both my study and the Oklahoma study. With regard to the OSSTD, all three studies found significant correlations with quantity and frequency, whereas a significant association with duration was only found in the Oklahoma study. While the association between OSSTD and duration of ST use became significant after adjusting for age and gender in the current study, the associations presented in the Dhaka study had only adjusted for differences in gender and remained non-significant in adjusted models. One other study conducted in India also found FTND scores to be a significant predictor of duration of tobacco use, although the findings were based on a sample that comprised both smokers and ST users (Saha et al., 2017). To my knowledge, no other studies have published construct validation results for the TDS-ST and OSSTD scales.

Despite some differences in associations between individual validation studies, the overall findings suggested significant positive associations between ST dependency scales and measures relating to heaviness and consistency of ST use across time, in different study settings. The finding of significant associations between FTND-ST and measures relating to heaviness of ST use was expected to some extent, given that the FTND-ST itself directly assessed heaviness of use (item 4 – "How many cans/pouches per week do you use?"). However, in the current study, this scale item was not directly used as a measure of quantity of ST consumed, unlike the Oklahoma and Dhaka studies. Instead, quantity consumed in grams per week was used for construct validation of the scales, and this difference likely explained why the finding of significant association between TDS-ST and quantity was limited to the current study. Similar to the links between FTND-ST and heaviness, the significant associations found between the ST dependency scales and measures of urge in my study could be explained by the presence of some items in all three scales that directly focussed on feelings of urge or on similar constructs (e.g. craving). These correlations were not tested in the other two validation studies.

The results pertaining to the construct validation of OSSTD subscales showed some variations across the three studies. In the Oklahoma study, Mushtaq et al. (2014) found variations in correlation patterns between the OSSTD subscales and ST use characteristics – duration of ST use was significantly correlated with 'Loss of control & Craving' ($r = 0.427$, $p < 0.001$), 'Tolerance & Automaticity' ($r = 0.447$, $p < 0.001$), and 'Affiliative attachment' ($r = 0.359$, $p = 0.0002$), quantity of ST use was significantly correlated with 'Cue exposure' ($r = 0.261$, $p = 0.009$), 'Tolerance & Automaticity' ($r = 0.541$, $p < 0.001$), and 'Loss of control & Craving' ($r = 0.250$, $p = 0.012$) and frequency of ST use was significantly correlated with both PDM subscales ($r = 0.381$, $p < 0.001$ for 'Loss of control & Craving' and $r = 458$, $p < 0.001$ for 'Tolerance & Automaticity'). Overall, the findings from Oklahoma showed that both the PDM subscales were significantly associated with all three ST use characteristics, while there were no observable patterns with regard to the associations with SDM subscales. These results were likely comparable with the results of WISDM-based studies, which found that primary motives explained the most significant share of a range of dependence criteria in validation models (Piper et al., 2008a).

On the other hand, more homogenous patterns of associations were observed between the OSSTD subscales and ST use characteristics in Dhaka and New Delhi. In the Dhaka study (Mushtaq et al., 2019), none of the subscales were associated with duration; all subscales except 'Weight control' were significantly associated with quantity; and all subscales except 'Weight control' and 'Cue exposure' were significantly associated with frequency of ST use. In the current study, all the subscales showed significant correlations with frequency and quantity of ST use with low to moderate correlation coefficients, while all subscales except 'Tolerance & Automaticity'

showed significant associations with duration of ST use in models adjusting for age and gender. These findings suggested that the various OSSTD subscales did not have any distinct associations with ST dependence criteria within my study settings.

Based on the overall construct validation results, it also appeared that quantity and frequency were more relevant as ST dependence criteria, rather than duration of ST use in years. In the current study, much lower coefficients were found for duration compared to other ST use characteristics on all three dependency scales (Table 3.16). The finding appeared to be true for Dhaka as well, where the OSSTD scale and subscales failed to show any association with duration of ST use, in addition; some of the coefficients for duration were not available from the Oklahoma study for comparison. Furthermore, additional analyses conducted using data collected in my study suggested that duration of daily ST use might be more suited as a validation criteria relating to consistency of heavy use (Appendix 3.7). However, associations with this measure were not available from the other validation studies for comparison.

3.3.1.4 Concurrent validation

Correlations between the ST dependency scales were all statistically significant across the three validation studies. However, the correlation coefficients were lower in the Bangladesh study (Mushtaq et al., 2019), particularly the ones involving the TDS-ST measure. In the current study, all the OSSTD subscales also showed significant positive correlations with the other ST dependency scales, with the lowest coefficients found for the 'Weight control' subscale. The results of regression analyses also showed that the 'Weight control' subscale accounted for the least variability in TDS-ST and FTND-ST scores. Similarly, all the subscales showed significant correlations with TDS-ST in the Oklahoma study, but for FTND-ST the 'Affective enhancement' subscale was not significantly correlated ($r = 0.160$, $p = 0.111$). On the other hand, all the subscales showed significant correlations with FTND-ST in the Dhaka study, whereas 'Loss of Control & Craving' ($r = -0.034$, $p > 0.050$), 'Tolerance & Automaticity' ($r = -0.018$, $p > 0.050$), and 'Affective enhancement' ($r = 0.086$, $p > 0.050$) subscales were not significantly correlated with TDS-ST.

The overall results of concurrent validation indicated that all the scales used in this study were measures of ST dependence with some level of substitutability. Although there were some variations with regard to the OSSTD subscales, the results of concurrent validation were largely comparable across the three studies. However, the results pertaining to TDS-ST in Dhaka appeared to vary from the other results, based on construct and concurrent validation.

3.3.1.5 Factor analysis

Although factor analysis was carried out for both OSSTD and FTND-ST scales in the Oklahoma and Dhaka studies, it was limited to the OSSTD scale in my study. This was because only the OSSTD was intentionally developed as a multidimensional measure among the three ST dependency scales included for validation. In this subsection, the results pertaining to OSSTD from Oklahoma and Dhaka will be compared with the FA results from the current study.

Overall, the conditions for factorability were met by the OSSTD scale data in all three studies. However, the item-total correlations were generally lower in this study (range = 0.271 – 0.751), with the lowest coefficient found for item 11 ("Weight control is a major reason that I chew/dip") within the 'Weight control' subscale. The item-total correlations ranged between 0.390 and 0.760, and between 0.380 and 0.750 in Oklahoma and Dhaka, respectively. Item 11 was also found to have the lowest item-total correlation in Oklahoma (r = 0.390), whereas this information was not available from the Dhaka study.

The factor analyses methodologies used in the three studies differed from one another. In the Oklahoma study, two EFAs were computed to separately assess the dimensionalities underlying PDM and SDM measures. Given that the OSSTD was adapted from the WISDM scale, the decision to carry out two EFAs during initial validation was based on the finding that WISDM comprised two distinct categories of subscales (PDM and SDM), with notable variations in their ability to predict relapse, withdrawal and other dependence criteria among smokers (Piper et al., 2008a). However, it was considered that the relative importance of different motives for ST dependence might be distinct from those for smoking. It was therefore decided to carry out a single EFA in the current study, which did not distinguish between PDM and SDM measures. This approach nevertheless allowed the possibility of finding a multi-factor solution for the OSSTD scale, with factors that might correspond with the PDM and SDM subscale categories. While no EFA was performed in the Dhaka study, confirmatory factor analysis (CFA) was undertaken based on the scale's originally intended factor structure (7 first-order freely correlating factors i.e., 2 PDM and 5 SDM), with subsequent assessments of model fit (Mushtaq et al., 2019).

The results of EFAs differed between the two assessments in Oklahoma and New Delhi. Unlike the results of the original OSSTD study, which identified two-factor and five-factor solutions underlying the PDM and SDM measures, my study found a single underlying factor for all OSSTD scale measures within an Indian context. Based on their EFA findings, and results of construct validation analyses (which showed diverse patterns of relationships between the OSSTD subscales and ST use indices), Mushtaq et al. (2014) recognised OSSTD to be a multidimensional measure of ST dependence. This was further examined by means of CFA,

which compared a single factor model with a two factor model, based on PDM and SDM factors forming two distinct dimensions of ST dependence. The CFA results from Oklahoma showed that a two-factor model provided a better fit for their data compared to a single factor solution. However, the findings of the current study did not support the conclusions of the original study. In addition to a single factor extracted from the EFA, fairly homogenous patterns were discernible between the various OSSTD subscales and ST use characteristics. No CFA was undertaken in the current study. Similar to the findings of my study, the study in Dhaka could not replicate the seven-factor structure of OSSTD found in the initial assessment (Mushtaq et al., 2019).

These findings indicated that the scale performed differently in different study settings, and likely served as a unidimensional measure of ST dependence within South Asian settings. However, it was difficult to draw firm conclusions regarding the scales' dimensionality, particularly given the differences across study settings in language, participant characteristics, ST products, and modes of scale administration.

3.3.1.6 Scores on ST dependency scales

The total scores on all the ST dependency scales used in this study were on average higher than the total scores found in the Oklahoma evaluations (Mushtaq et al., 2014, Mushtaq and Beebe, 2015, Mushtaq and Beebe, 2017b) (Table 3.16). The total FTND-ST and OSSTD scores from Dhaka (Mushtaq et al., 2019) were also higher than average values obtained from Oklahoma. While the mean OSSTD score in this study was slightly lower than values from Dhaka, the mean TDS-ST and FTND-ST scores were higher in comparison. The lowest total TDS-ST scores were found in Dhaka, on average. Based on a TDS-ST cut-off of 5+, about a third of study participants (n = 155, 66.5%) were categorised as dependent users in this study, compared to 47.0% in Dhaka (Mushtaq et al., 2019), and 50.5% in Oklahoma (Mushtaq and Beebe, 2015). Although the Fagerström measures have been used to classify cigarette smokers according to their levels of dependence, similar criteria have not been previously assessed for ST users based on scores on the FTND-ST scale. While some studies have used the smoking cut-offs to classify ST users as having low, moderate, and high levels of dependence (e.g. Asha and Dhanya (2015)), this technique was not pursued in the current study.

Overall, the findings based on ST dependence scores indicated higher dependence among South Asian ST users compared to ST users in the United States, likely linked with differences in ST product types used in different regions. Results of biochemical analyses of ST products have found that some product types used in SA have amongst the highest total and free nicotine concentrations. For example, gul powder used in SA was found to have significantly higher levels of free nicotine (29.1–31.0 mg/g) compared to products used in other regions (<10 mg/g) (Stanfill

et al., 2010). Moreover, high pH levels have been documented in widely used South Asian ST products such as khaini (Stepanov et al., 2015) and naswar (Saeed et al., 2012), which can determine the amount of nicotine absorbed from the product and in turn influence their addiction potential.

Sociodemographic variations of ST dependency scores suggested that women had higher levels of dependence compared to men, based on significant differences by gender found in FTND-ST and OSSTD scores. While average scores on the TDS-ST was also higher in female participants, the difference was not statistically significant. These findings were comparable with the Dhaka study, although score variations by gender were statistically significant across all three ST dependency scales (Mushtaq et al., 2019). In addition, the findings suggested that lower levels of education and wealth were associated with higher levels of ST dependence, as found in other studies of tobacco dependence among cigarette smoking (Siahpush et al., 2006). With regard to age, none of the ST dependency scaled showed significant variations between younger and older users in the sample. However, mean score on the 'Weight control' subscale of the OSSTD was slightly higher among younger compared to older participants, and the difference was statistically significant ($p = 0.020$). These findings suggested that while 'Weight control' might not be an important motivating factor for ST use and dependence among adult users, it may be relevant to younger ST users.

3.3.1.7 Other ST dependency measures

Items from the FTND-ST (item 1 – time to first chew/dip of the day, and item 4 – number of cans of ST used per week) have been combined with measures of ST use frequency (number of dips/chews per day) to develop brief measures of ST dependence, such as the heaviness of ST use index, ST dependence index, and ST quantity frequency index. These indices have been subjected to psychometric evaluations in the United States and found to be effective substitutes for FTND-ST (Mushtaq and Beebe, 2017a), similar to the Heaviness of Smoking Index in smoking dependence studies (Heatherton et al., 1989). The low internal consistency of FTND-ST found in this study suggested a role for the brief indices. However, the psychometrics of these measures were not explored in analysis.

One further measure of ST dependence used in this study was the self-rated ST addiction measure. This was scored on a 7-point Likert scale, with an average score of 5.11 (SD = 1.57, missing values = 2). The validation analyses using this measure showed significant associations with all three ST use characteristics and with the other dependency scales used in the study (Appendix 3.7). This suggested that users in the study settings were aware of their dependence to ST products to some extent.

3.3.1.8 Overall summary

Based on measures relating to heaviness of ST use, construct validation was established for all three ST dependency scales in a South Asian setting. The scales were all significantly correlated with each other, establishing concurrent validation. However, criterion validation based on salivary cotinine levels could not be established within the study settings. Similar to other studies, internal consistency assessments showed good, acceptable, and low scores for OSSTD, TDS-ST, and FTND-ST measures, respectively. Overall scores on the ST dependency scales suggested high levels of dependence associated with the use of South Asian ST products.

Factor analyses of the OSSTD failed to replicate its original factor structure, and suggested that the scale was a unidimensional measure of ST dependence within the study settings. Furthermore, results suggested that the scale could be modified for better assessment of ST dependence in this population. In particular, the 'Weight control' subscale appeared to be a weak measure based on almost all analyses performed, and suggested that it may not be among the important motivating factors for developing ST dependence among adult users within the study settings. Results from Dhaka also showed that this particular subscale was not associated with any of the ST use characteristics in their sample, leading the authors to consider if this aspect of dependence might vary between South Asian and Western ST users (Mushtaq et al., 2019). However, the subscale did not appear to be a particularly strong motivating factor even in the Oklahoma sample, based on low mean scores obtained and low correlation coefficients found with other validators used in their study (Mushtaq et al., 2014). An earlier study among adult women who used ST in America also reported that few participants acknowledged the role of ST for the purposes of weight control (Gerend et al., 1998). Taken together, these findings suggested a limited role for ST use in weight management among adult users in varied geographical settings at present, although the reasons for this are as yet unclear given the limited number of studies on the topic. With regard to the other OSSTD subscales, although they demonstrated acceptable psychometric properties, they did not show any distinctive roles in the measurement of ST dependence in this study sample.

3.3.2 Strengths and limitations

One of the key strengths was the attention given to translation processes. All the scales used in the study were originally developed in English and translated into Hindi using rigorous methodologies. Given that they were used across cultures, in settings different from where they were originally developed, cross-cultural adaptation was also given due consideration. This was to maintain the content validity of the scales at a conceptual level, including its original structure and items, across different cultural contexts (Beaton et al., 2000). At the stage of joint review with

all four translators and independent reviewer, different areas of equivalence between the source and target versions of the scales were discussed and consensus reached. In addition, the pre-final versions were field tested among ST users in the study setting before finalisation of the scale items in Hindi. Other strengths of the study included the use of a range of measures to study ST dependence, an adequate sample size with nearly equal representation of male and female ST users, and meticulous data collection methodologies that resulted in very little missing data. However, the following limiting factors must be considered in the interpretation of results, and during any application of the ST dependence scales evaluated in this study.

The screening criteria set for selecting study participants intended the inclusion of a range of dependence-related features that was exclusive to the use of ST products. But the final recruited sample predominantly comprised daily ST users (97.9%), which possibly attenuated coefficients in the correlation analyses and factor loadings in the EFA to some extent. However, it was considered unlikely that this aspect had a large impact on the results, as a range of variations was recorded with regard to the types of ST products consumed, as well as frequency and quantity of consumption. In addition, despite screening, there were some current smokers in the final sample, as well as some former smokers. Although all the survey items made specific references to ST products, it is possible that at least some of the responses from the current and former smokers in the sample were related to other forms of tobacco. However, these participants comprised a small proportion of the sample and their use of smoking tobacco was largely occasional, as opposed to the regular use of ST products.

To ensure that participants understood the items as intended, they were also screened for fluency in Hindi at the time of recruitment. However, it is possible that Hindi was not the primary language for some participants, which was not recorded. In addition, the step-by-step translation and cultural adaptation methodologies did not extend to the entire questionnaire and this meant that some items were not adequately prepared for use in a different geographical and cultural context. For example, the items relating to servings of fruit and vegetable were merely ‘translated’ rather than ‘adapted’ for use, and likely not interpreted as intended by study participants. The offer of a financial compensation for time spent during the interview could have influenced the participation of those who were motivated to receive this award. However, the value of the compensation was not large and unlikely to have resulted in a selection bias.

Almost all the information in this study was collected through self-report, and at a single point in time. The concurrent gathering of all measures used in the validation analyses raised the possibility that the correlations found could be related to respondents guessing the study hypotheses and providing answers that were consistent with one another. However, a wide range of measures used in the study likely reduced the chances of this occurrence. More importantly,

the laboratory data pertaining to biological markers of ST dependence (salivary cotinine levels) could not be utilised in analyses. This was one of the major limitations of the study, as levels of salivary cotinine were meant to serve as the criterion variable. However, it was not the only dependence measure used for validation of the scales, and very few studies from SA had assessed cotinine levels among ST users in the region – the results from these studies seemed to suggest that dependence scales such as the FTND-ST and salivary cotinine were likely measuring distinct phenomena (Asha and Dhanya, 2015, Patel et al., 2017), which raised questions regarding the utility of cotinine as a criterion variable for validation of ST dependence scales in the study settings. Similarly, no association between salivary cotinine and certain ST-specific characteristics such as the swallowing of tobacco juices was found in Bangladesh (Huque et al., 2016), whereas swallowing of tobacco juices was significantly associated with higher cotinine concentrations in America (Mushtaq et al., 2011).

The following were some of the limitations with regard to the analytical techniques applied in this study. There were no measures of scale reliability such as test-retest, as all the data were collected in a single sitting by one interviewer. However, internal consistency using Cronbach's alpha coefficients were estimated, which were among the most commonly estimated forms of reliability assessments for this type of study (Arafat et al., 2016). An optimum cut-off score for using the TDS-ST to make a diagnosis of ST dependence was not calculated for the study settings. Rather, a previously used score of 5+ was used to categorise participants as 'dependent' and 'not dependent' ST users (Mushtaq and Beebe, 2015). Although this approach might be questioned, given the differences in study settings, it was not the only measure of validation used, and the categorisation was used alongside total TDS-ST scores in all instances. Finally, the findings regarding the dimensionality of the OSSTD scale were based on exploratory rather than confirmatory analyses, which meant more tentative outcomes as opposed to conclusive ones. However, the use of this approach was considered to be appropriate because this was the first administration of the scale in India, and the existing evidence regarding its structure suggested the lack of a well-developed hypothesis for confirmatory analyses. Moreover, the EFA techniques applied were most suited for the type of data collected using the OSSTD scale items, which added further credibility to the findings. However, additional studies are required to further explore and confirm this factor structure and other psychometric properties of the OSSTD scale in different settings.

Limitations relating to the generalisability of findings from the use of a convenience sample was not a major concern, considering the study objectives. Instead, the inclusion of male and female participants who used a range of ST products available in the study settings meant a wider application of the validation findings. On the other hand, there might be limitations to generalisability over time, alongside likely variations in ST dependence motives among study

participants, which was not assessed in this study. Finally, the research design used was cross-sectional, and concerns may be raised about the temporality of relationships between dependence and ST use practices. However, most of the analyses were correlational in nature, with no claims of causality.

3.3.3 Implications of findings

Based on a range of validation analyses, the findings of this study suggest that measures relating to physical aspects of ST dependence demonstrate comparable psychometric properties in both Western and South Asian contexts. However, scales developed to capture some of the other dimensions of ST dependence (psychological, behavioural, social, etc.), appear to perform differently in different study settings. Given that these findings likely have more direct implications for continuing research on ST dependence compared to ST control practice or policy within South Asian settings, the research implications will be considered first.

3.3.3.1 For future research

The focus of this section will be on the following aspects – the need for additional studies that specifically address some of the limitations of the current study, and the need for modified or newer scales for the measurement of ST dependence, particularly within South Asian contexts.

It is important for future validation studies of ST dependence scales to incorporate measures of reliability beyond internal consistency such as test-retest reliability, to assess the stability of scale responses between two time points, during which it can be reasonably assumed that things have not changed. While the FTND has demonstrated adequate test-retest reliability among cigarette smokers in the past (Pomerleau et al., 1994), this function has not been assessed for any ST-based scales till date to the best of my knowledge. Similarly, validation against other dependence criteria beyond heaviness of ST use are needed. As with studies on smoking dependency scales (Piper et al., 2008a), these could include validation against criteria such as the ability to maintain abstinence, magnitude of increase in craving post-quit, withdrawal severity, as well as relapse latency, and would require the follow-up of participants over time. These associations would also be particularly important to assess for ST dependency scales, given that they have been mostly adapted from cigarette-based scales, and the availability of evidence that nicotine pharmacokinetic profiles of at least some ST products are different from that of cigarettes (Benowitz et al., 1988).

To my knowledge, predictive validation assessments (the extent to which a measure can predict a future variable or outcome) of ST dependency scales have only been performed in one study

using the modified 9-item FTQ scale (Thomas et al., 2006). While the scale predicted significant three-month abstinence (OR = 0.76, 95% CI = 0.61, 0.96), it failed to predict abstinence at six months (OR = 0.86, 95% CI = 0.69, 1.00). Although there was no follow-up for predictive validation in this study, the average scores on all the dependence scales were higher among those who had no intention to quit using ST within six months of the interview, compared to those who intended to quit (Appendix 3.7). This suggested that the scales might be able to predict cessation outcomes within South Asian settings. However, follow-up studies over time will be needed to confirm this finding. Validation of scales against biological markers of ST dependence is another area for future research studies to explore, particularly because poor correlations have been reported between cotinine levels and behavioural scales among South Asian studies. It might also be important to consider the methodologies used for cotinine measurements, as the majority of reports till date are based on qualitative assessments of cotinine levels.

Although it seems that a consensus has emerged in which tobacco dependence is viewed as a multidimensional construct, and should therefore be assessed and quantified accordingly (NCI, 2009), there are few multidimensional scales in existence, specific to the measurement of ST product dependence. Furthermore, in this study, the OSSTD has failed to adequately distinguish between different sub-phenotypes of ST users within a South Asian setting, unlike the results of the original validation assessment in Oklahoma. This may likely be due to differences in the cultural and social factors relating to ST use, ST use behaviours, and products used in the different settings. While this suggests that the scale could be revised for use in these populations, there might also be a role for developing newer multidimensional scales for studying ST dependence within different study settings, as has been previously recommended (De Leon et al., 2013). Among the existing ST scales, items relating to heaviness of consumption may also need modification. Specifically, the FTND-ST item on the number of cans/pouches of ST consumed per week does not directly extend to products such as betel quid with tobacco, which are commonly consumed in South Asian settings.

Finally, the finding that ST dependence in SA is likely higher than other geographical regions is supported by evidence relating to the contents of ST products from different regions, and therefore considered plausible. However, reliable and valid measures of ST dependence must be administered across a representative sample of users from the study setting, to obtain population-based estimates of dependence linked with the use of South Asian ST products.

3.3.3.2 For practice and policy

Although some of the dependency scales, such as TDS-ST, are based on psychiatric diagnostic criteria of tobacco dependence, they will need further assessments in the form of reliability testing

and predictive validation before they can be applied as effective tools in clinical settings for diagnosing ST dependence. Some of the brief indices might similarly find applications in ST cessation practice, following further study. From a policy perspective, the most relevant findings are the likely high levels of dependence associated with the use of South Asian ST products, supported by evidence related to the chemical composition of products, as well as high prevalence of use within the region. This warrants effective policies to regulate the manufacture and sale of ST products within the region, as well as policies to help ST cessation and prevention.

Chapter 4. Sociocultural Influences on ST Use and Cessation Practices within a South Asian Setting

While sociocultural factors are often amongst the reasons cited for the widespread acceptability and high prevalence of ST use among South Asian communities, the overall research evidence on this topic is very limited, with considerable knowledge gaps in the understanding of their influence on ST-related practices, particularly quitting behaviours. In this chapter, I present descriptive findings relating to some sociocultural aspects of ST use within a South Asian setting. In addition, I present some exploratory findings on the association between different sociocultural factors and a range of ST use practices among adult users. I then discuss my study findings in relation to the literature, along with their implications for practice, policy, and future research.

4.1 Methodology

4.1.1 Background information on study setting and data collection

All the data for this study were collected at the same time as the validation study (presented in Chapter 3), from the same sample of participants, who were recruited through community-based convenience sampling from a low-income neighbourhood in New Delhi, India. The study setting may be described as an urban slum, and the socioeconomic disadvantage of living in the setting may itself be linked to several behaviours that influence health, including tobacco use (Jarvis and Wardle, 1999). High rates of tobacco have in fact been reported among adults and adolescents living in similar urban, low-socioeconomic areas in India, and regular use of ST have been reported in children as young as six years of age in urban slum dwellings in New Delhi (Arora et al., 2010). Respondents in this study stated that they had started using ST after their friends or family members offered it to them, and in many cases, parents and other close family members also consumed tobacco, both in chewed and smoked forms.

The research design for this study was cross-sectional in nature, and respondents included adults who were regular and exclusive users of ST forms of tobacco. The sample size estimations from the validation study were retained for these analyses. The survey questionnaires were developed in English and then translated into Hindi, and surveys were conducted using face-to-face interviewing techniques in the local language. Informed consent was obtained from each respondent before completing the survey, and respondents who completed the survey were given a token of appreciation for their time. Each survey took about 40 minutes to complete. The study was approved for ethics by the following institutions: the Research Governance Committee at the University of York (York, UK), and the Institutional Ethics Committee at the Indian Institute of Public Health – Delhi (New Delhi, India). In the following subsections, I describe the measures

included in the survey instrument that are relevant to the analyses presented in this chapter (sociocultural factors and ST use practices), as well as the statistical techniques applied for the analyses.

4.1.2 Measures

Sociodemographic variables (age, gender, highest level of education completed, and asset ownership) were explored and controlled for in the regression analyses of associations between dependent and independent variables in this study. The survey measures used to collect sociodemographic data have already been described in the last chapter (Section 3.1.5.1).

4.1.2.1 Sociocultural variables

Two primary measures of ST use by close friends and family members were included: "How many of your five closest friends use ST", and "How many of your five closest relatives use ST". The response options for both questions ranged from none to all five. These items have been previously used in tobacco research, including ST research (e.g. Sansone (2014)), and further details of their original sources can be found in the questionnaire construct sheet (Appendix 3.2). As a follow-up to the second item, participants with one or more ST-using family members were asked to specify this relationship using the following response options: "Parents, Grandparents, Parents-in-law", "Siblings (including sister- or brother-in-law)", "Partners", "Children (including son- or daughter-in-law)", and "Any other relatives living in the same household". As described in Chapter 1, these two aspects have previously been assessed among South Asian populations, with significant associations found with ST use prevalence among both male and female participants in the region (e.g. Ray et al. (2016)). However, little is known about how these factors are associated with ST use practices among current users, including practices related to quitting.

Two other sociocultural measures were included in the study. Participants were asked if in the past 7 days they used ST mainly when they were alone, mainly when they were with people, or as often by themselves as in the company of other people. In addition, they were asked which statement best described ST use within their household, with three possible response options – "ST use is never allowed", "ST use is allowed during special occasions or when there are visitors", and "ST use is allowed at all times". Similar measures have been studied among cigarette and water pipe smokers, and found to significantly influence characteristics such as quit practices (e.g. Moran et al. (2004)). Although it seems that these factors are at least equally, if not more important to study with regard to ST use in South Asian settings, particularly given the social and cultural acceptance of the practice within these populations, they have not been previously measured.

4.1.2.2 ST use practices

The dependent variables in this study were behaviours relevant to ST use – age of first ST use, current use practices such as duration, quantity, and frequency, and behaviours relevant to quitting ST use, including current attempts to cut down on ST use, any quit attempts made in the past 12 months, as well as intentions to quit using ST products in the future. To measure age of first use, participants were asked "How old were you when you first used ST", with responses recorded in years. The variables relating to current use practices of duration, quantity and frequency were used in the validation analyses in Chapter 3, and have been previously described (Section 3.1.5). In addition, participants were asked if they were trying to cut down on their ST use in relation to their current practices. To measure quit attempts, survey respondents were asked if during the past 12 months they had tried to quit using ST completely. Those who answered "Yes" were then asked how many times they had stopped using ST for one day or longer because they were trying to quit. The responses to these two questions were turned into a derived binary variable to represent making a quit attempt in the past 12 months that lasted at least one day or longer versus no attempt to quit using ST in the past year. To measure ST quit intentions, participants were asked about their plans to quit using ST in the future. They were asked to pick from the following four options on what best described their intentions to stop using ST completely – "Never expect to quit", "May quit in the future, but not in the next 6 months", "Will quit in the next 6 months", and "Will quit in the next 30 days". The first two responses and the last two responses were combined to create a binary variable representing any intention to completely stop using ST in the next 6 months. Studying individual-level quit predictors among cigarette smokers, Hyland et al. (2006) found both these measures (quit attempts in the past 12 months and quit intentions) to be significant predictors of making a quit attempt in the future.

4.1.2.3 Other measures

Besides sociodemographic variables, the other study measures that were considered as likely to confound the relationship between different sociocultural measures and ST use behaviours (particularly quit practices) included ST dependence, perceptions of health risks associated with ST use, and having received advice from a doctor or health care provider to stop using ST in the last 12 months. A diagnosis of dependence was made based on total TDS-ST scores of greater than five, as explained in the previous chapter (Section 3.1.5). Perceptions regarding ST-related health risks were measured for oral cancer and heart disease, by asking participants about their likelihood of developing these conditions if they continued using ST products. On the other hand, "Yes" and "No" response options were used to measure if participants were advised to stop using ST products during any visit to a doctor or health care provider in the past 12 months.

4.1.3 Description of analyses

All the analyses were performed using IBM SPSS, Version 24.0 (2016). Descriptive analyses were performed to explore all the study variables, as well as their distribution across sociodemographic characteristics of study participants. The results were summarised in tables and figures. Responses to the four primary items were dichotomised, so that the measures included in further analyses were as follows: having at least one individual among their closest friends who used ST versus none, having at least one individual among their closest family members who used ST versus none, using ST mainly in company versus not, and ST use being allowed at home versus never being allowed. Next, crosstabs analyses were used to further examine how the sociocultural factors related to sociodemographic variables, as well as with each other. Chi-square tests were performed to look for any significant differences in distribution patterns across these analyses. To examine the relationships between different sociocultural factors and ST use practices, a series of unadjusted and adjusted, linear and logistic regression analyses were performed. Separate models were run for each of the ST use practices as outcome variables, and the different sociocultural variables as independent variables. Demographic variables and other potential confounders (ST dependence diagnosis, perceptions of health risks associated with ST use, and doctor's advice to stop using ST in the last 12 months) were controlled for in adjusted analyses, and model diagnostics were run to assess if the assumptions of regression were met.

4.2 Results

As described in Chapter 3, the survey respondents (n = 233) were mostly daily (n = 228) and exclusive (n = 220) users of ST products. Further descriptions of sample characteristics and some tobacco use practices relating to duration, quantity, and frequency of ST consumption, as well as buying and carrying of ST products, can be found in Sections 3.2.1 and 3.2.2. In Table 4.1, I have summarised the descriptive results for the variables relevant to this study, not previously described.

Table 4.1 Descriptive results for dependent and independent variables

Variable	Categories	N	%
Sociocultural factors			
ST use among five closest friends	None use ST	32	13.7
	One	15	6.4
	Two	31	13.3
	Three	38	16.3
	Four	17	7.3
	All five use ST	100	42.9
ST use among five closest	None use ST	82	35.2

family members	One	54	23.2
	Two	49	21.0
	Three	16	6.9
	Four	9	3.9
	All five use ST	23	9.9
ST use among parents/grandparents	No	171	73.4
	Yes	62	26.6
ST use among siblings	No	137	58.8
	Yes	96	41.2
ST use among partners	No	163	70.0
	Yes	70	30.0
ST use among children	No	215	92.3
	Yes	18	7.7
ST use among other close relatives within household	No	222	95.3
	Yes	11	4.7
ST use alone/in company during past 7 days	Used ST mainly when alone	99	42.5
	As often alone as with others	94	40.3
	Used ST mainly when with other people	40	17.2
ST use permissibility within household	Never allowed	110	47.2
	Allowed only during special occasions	12	5.2
	Allowed at all times	111	47.6
ST use practices			
Age of first ST use	<18 years	125	53.6
	18+ years	108	46.4
Currently trying to cut down ST use	No	109	46.8
	Yes	124	53.2
Quit attempts in past 12 months	No	149	63.9
	Yes	84	36.1
Intention to quit using ST in 6 months	No	154	66.1
	Yes	79	33.9
Other measures			
Diagnosis of ST dependence	No	78	33.5
	Yes	155	66.5
Likelihood of developing oral cancer*	No chance	23	9.9
	Very unlikely	26	11.2
	Unlikely	14	6.0
	Moderate chance	23	9.9
	Likely	42	18.0
	Very likely	67	28.8
	Certain to happen	36	15.5
Likelihood of developing heart disease*	No chance	53	22.7
	Very unlikely	39	16.7
	Unlikely	28	12.0
	Moderate chance	33	14.2
	Likely	38	16.3
	Very likely	31	13.3
	Certain to happen	9	3.9
Health risk of ST	More health risks	95	40.8

compared to smoking**	Less health risks Same health risks Do not know	75 55 5	32.2 23.6 2.1
Received advice from doctor to quit ST in past 12 months	No Yes	201 32	86.3 13.7

* Missing values = 2, ** Missing values = 3

4.2.1 Results of descriptive analyses

4.2.1.1 Sociocultural factors

When asked how many of their five closest friends used ST, a small number of survey respondents (n = 32, 13.7%) reported having no ST-users amongst their five closest friends. While 100 respondents (42.9%) said that all five of their closest friends used ST, 15 (6.4%), 31 (13.3%), 38 (16.3%), and 17 (7.3%) participants reported having one to four ST-users amongst their closest friends in the increasing order. Taken together, participants had an average of 3.26 (SD = 1.83) closest friends who used ST products, with the value being slightly higher for younger (18 – 29 years) compared to older (30+ years) (mean = 3.4, SD = 1.71 vs. mean = 3.05 SD = 1.98), and male compared to female participants (mean = 3.5, SD = 1.70 vs. mean = 3.0, SD = 1.94). Those with higher levels of completed education also appeared to have more numbers of ST-using friends on average (mean ± SD = 3.2 ± 1.86 vs. 3.2 ± 1.83 vs. 4.0 ± 1.53, with increasing education levels), similar to those reporting greater ownership of household assets (3.2 ± 1.91 vs. 3.2 ± 1.78 vs. 4.0 ± 1.19, with increasing household assets).

With regard to family members, 82 (35.2%) participants reported no ST use amongst their five closest relatives. Contrary to results for closest friends, only 23 (9.9%) participants reported ST use among all five closest relatives, with 54 (23.2%), 49 (21.0%), 16 (6.9%), and 9 (3.9%) participants having one to four ST users amongst their five closest relatives. The average for this variable was 1.5 (SD = 1.59) for the entire sample, with the age and gender distribution of the mean showing that older (mean = 1.6, SD = 1.65) and female respondents (mean = 1.9, SD = 1.59) reported slightly higher numbers of ST-users amongst their closest relatives compared to younger (mean = 1.4, SD = 1.54) and male respondents (mean = 1.1, SD = 1.48). The average number of closest relatives using ST was found to reduce with increasing levels of completed education (mean ± SD = 1.9 ± 1.60 vs. 1.3 ± 1.54 vs. 0.2 ± 0.43) and household asset ownership (mean ± SD = 1.8 ± 1.62 vs. 1.2 ± 1.50 vs. 0.3 ± 0.49). Sixty two (26.6%) participants reported ST use among parents, parents-in-law, or grandparents, 96 (41.2%) among siblings, 70 (30.0%) among partners, 18 (7.7%) among their children, and 11 (4.7%) among other family members they considered as being amongst their closest relatives. The large majority of those who reported

ST use among partners were women (61 of 70).

When asked about using ST mainly when they were alone or in the company of others, about 40.0% of survey respondents reported ST use mainly when they were alone (n = 99, 42.5%), another 40.3% of participants (n = 94) said they used ST as often by themselves as in the company of others, and the remaining participants (n = 40, 17.2%) reported ST use mainly when they were with other people. The distribution of sociodemographic characteristics were comparable among lone consumers and those who reported no preference for using ST either alone or in the company of other people, and no distinct patterns were observed in their distributions. These two response categories were combined, so that 82.8% of all participants used ST alone or as often alone as in the company of others. On the other hand, participants who reported using ST mainly in the company of others were more likely to be younger, male, to have completed higher levels of education, and own greater number of household assets.

With regard to final sociocultural measure, nearly half the sample reported that ST use was 'never allowed' (n = 110, 47.2%) within their households, while a similar number reported that it was 'allowed at all times' (n = 111, 47.6%). A small number of survey respondents reported that ST use was only allowed in their homes during special occasions or when they had visitors (n = 12, 5.2%). The latter two response categories were combined, so that 52.8% of participants reported ST use as being allowed within their households, compared to 47.2% of participants who said that it was never allowed. Across the sociodemographic characteristics measured, those who reported ST use permissibility within their households tended to be older, female, completed lower levels of education, and owned fewer household assets.

4.2.1.2 ST use practices

On average, the study participants started using ST around 18 years of age (mean = 17.9 years, SD = 6.13), the earliest reported age of first use being 6 years. The mean age of surveyed men (mean = 17.7 years, SD = 5.55) when they started using ST was about the same as the surveyed women (mean = 18.1 years, SD = 6.69), while younger participants started using ST earlier (mean = 15.6 years, SD = 3.84 for 18 – 29 age group) than older participants in the sample (mean = 20.9 years, SD = 7.22 for 30+ age group). No notable differences were found in age of first ST use by education level completed or household asset ownership. Descriptive results for the other ST use practices (duration, quantity and frequency) have already been summarised in Section 3.2.2.

With regard to whether participants were currently trying to cut down on their ST consumption, the results showed a roughly equal distribution between those who responded "Yes" (n = 124, 53.2%) and "No" (n = 109, 46.8%). More number of male participants, and those with higher

levels of education and household assets were trying to cut down on their ST use, compared to female participants, and those with lesser education and fewer number of household assets. No notable differences were observed by age group for this study measure.

Across the sample, fewer participants reported having made a quit attempts in the past 12 months (n = 84, 36.1%), compared to no quit attempts (n = 149, 63.9%). Among those who had made a quit attempt, 53 participants (22.7%) reported less than 5 attempts in the past 12 months, 23 (9.9%) had made 5-10 attempts, whereas 8 (3.4%) had made more than 10 quit attempts. Overall, those who had made quit attempts had tried 5.02 times on average (SD = 3.84), with a mean quit duration of 10.4 days (SD = 17.88) on their longest attempt. While four participants reported having used counselling services or some form of medication to aid with cessation, the large majority of participants did not use any method to aid with their ST cessation attempts. The results of ST quit intentions were similar to quit attempts, with 33.9% (n = 79) intending to quit, and 66.1% (n = 154) not intending to quit using ST within the next six months. There were no obvious variations across sociodemographic characteristics for both quit attempts and quit intentions.

4.2.1.3 Other measures

Using the TDS-ST scores of study participants, a diagnosis of dependence was accorded to 66.5% (n = 155) of the sample, whereas 33.5% (n = 78) were categorised as non-dependent users. The distribution of dependence diagnoses did not show notable variations across any of the sociodemographic variables measured. Results on perceptions of health risks with continued ST use showed that the majority of survey respondents felt they were likely to develop oral cancer (n = 168, 72.1%), whereas likelihood of developing heart disease was reported by less than half the study sample (n = 111, 47.6%). Ninety five (40.8%) participants felt that ST use had greater health risks compared to tobacco smoking, whereas 75 (32.2%) respondents perceived less health risks with ST use, and 55 (23.6%) respondents reported similar health risks for both types of tobacco. Five (2.1%) participants said they did not know which form of tobacco was more harmful to health. In the past 12 months, few survey respondents had received any advice from a doctor or health care provider to stop ST use (n = 32, 13.7%). None of these variables showed any notable differences in distribution across sociodemographic characteristics of study participants.

4.2.2 Distribution of sociocultural measures by demographic variables and across each other

The results of significance testing using crosstabs analyses for any differences in distribution of sociocultural factors across demographic variables, and across each other, have been summarised below. More details of these results can be found in Appendix 4.1.

4.2.2.1 Associations with sociodemographic variables

Only for some of the sociocultural factors measured a difference was observed by age group. Pearson's chi-square was significant for ST use among closest friends and ST use being allowed within participants' households. Younger users (18 – 29 years) were more likely to have at least one ST user among their closest friends, whereas older users (30+ years) were more likely to report no ST users among their closest friends ($\chi^2 = 5.806$, $p = 0.016$). On the other hand, younger users were significantly more likely to report that ST use was never allowed within their households, while older users felt that the practice was allowed either during special occasions or at all times ($\chi^2 = 4.738$, $p = 0.029$). There were no significant differences by age group on whether participants had any ST users among their five closest relatives overall ($\chi^2 = 1.351$, $p = 0.245$). However, younger users were significantly more likely to report ST use among their parents and grandparents ($\chi^2 = 14.263$, $p < 0.001$), whereas older users tended to report ST users among their partners ($\chi^2 = 4.034$, $p = 0.045$) or children ($\chi^2 = 21.140$, $p < 0.001$). Although a greater proportion of participants who used ST mainly in company belonged in the younger age group compared to the rest of the sample, this difference in distribution was not found to be statistically significant ($\chi^2 = 3.290$, $p = 0.070$).

Chi-square analyses by gender were significant for the following sociocultural measures – ST use by closest relatives, ST use permissibility within households, and ST use in company. Women users were significantly more likely to have at least one ST user among their five closest relatives compared to men ($\chi^2 = 20.427$, $p < 0.001$). In particular, they were significantly more likely to report ST use among partners ($\chi^2 = 57.158$, $p < 0.001$) and children ($\chi^2 = 12.196$, $p < 0.001$). Women were also more likely to report ST use permissibility within households, whereas men tended to report that it was 'never allowed' ($\chi^2 = 28.368$, $p < 0.001$). With regard to ST use in company, men were significantly more likely to report ST use mainly in the company of other people, whereas more women reported using ST mainly when they were alone or as often alone as in the company of others ($\chi^2 = 13.934$, $p < 0.001$).

Differences in the distribution of sociocultural factors by highest level of completed education and asset ownership were statistically significant for the same three variables as gender – ST use by closest relatives, ST use being allowed within households, and ST use in company. Those with higher levels of completed education tended to report not having any ST users among their closest family members ($\chi^2 = 24.847$, $p < 0.001$), not having ST use allowed within their households ($\chi^2 = 34.420$, $p < 0.001$), and using ST mainly in the company of other people ($\chi^2 = 41.697$, $p < 0.001$). With regard to familial relationships, those with higher levels of completed education were significantly less likely to report ST use among siblings ($\chi^2 = 11.139$, $p = 0.004$), partners ($\chi^2 = 29.218$, $p < 0.001$), and children ($\chi^2 = 11.256$, $p = 0.004$). The findings with regard to number

of household assets were largely similar to education levels. Those with higher number of household assets tended to report no ST users among their closest family members ($\chi^2 = 15.508$, $p < 0.001$), particularly among siblings ($\chi^2 = 8.153$, $p = 0.017$) and partners ($\chi^2 = 23.762$, $p < 0.001$). In addition, they tended to report no ST use permissibility within their households ($\chi^2 = 20.280$, $p < 0.001$), and using ST mainly in the company of other people ($\chi^2 = 16.733$, $p < 0.001$).

4.2.2.2 Associations between sociocultural measures

Further crosstabs analyses to examine how the sociocultural factors related to each other showed the following results. There were no significant differences in distribution between ST use among closest friends and ST use among closest family members ($\chi^2 = 0.087$, $p = 0.769$), or between ST use among closest friends and ST use being permitted within households ($\chi^2 = 0.116$, $p = 0.734$). However, Pearson's chi-square was significant for those having at least one ST-user amongst their closest family members and reporting ST use as being allowed within their households ($\chi^2 = 52.177$, $p < 0.001$). These associations were significant for reported ST use by parents ($\chi^2 = 7.578$, $p = 0.006$), siblings ($\chi^2 = 16.688$, $p < 0.001$), partners ($\chi^2 = 47.382$, $p < 0.001$), and children ($\chi^2 = 13.581$, $p < 0.001$).

Pearson's chi-square was also significant for the 'ST use in company' variable with having ST users among closest friends ($\chi^2 = 5.144$, $p = 0.023$), as well as permissibility of ST use within households ($\chi^2 = 6.132$, $p = 0.013$). Compared to the rest of the study sample, those who used ST mainly in company were significantly less likely to report that none of their closest friends used ST products, and significantly more likely to report non-permissibility of ST use within their households. No association was found between ST use in company and having ST users among closest family members ($\chi^2 = 0.113$, $p = 0.737$).

4.2.3 Association between sociocultural measures and ST initiation, duration, quantity, and frequency of use – results of linear regression analyses

The results of linear regression analyses have been summarised in Table 4.2, with further details provided in Appendix 4.2. The dependent variables used in analyses were age at first ST use, and duration, quantity, and frequency of current consumption. The dependent variables were all transformed using the square root function for more effective application in linear regression analyses, and the assumptions of normality and uniform variance appeared to be supported in subsequent regression models. Collinearity statistics based on variance inflation factors also showed the absence of multicollinearity between independent variables.

Table 4.2 Association between sociocultural measures and ST initiation, duration,

quantity, and frequency of use – results of linear regression analyses

Measures	Univariate model			Multivariate model*		
	β	95% CI	p-value	β	95% CI	p-value
Age of first ST use						
ST use among closest friends (Ref=No)	-0.355	-0.618 – -0.091	0.009#	-0.126	-0.377 – 0.124	0.321
Among closest relatives (Ref=No)	0.004	-0.189 – 0.197	0.970	-0.061	-0.248 – 0.125	0.516
Among parents/ grandparents (Ref=No)	-0.342	-0.545 – -0.138	0.001#	-0.164	-0.358 – 0.030	0.097
Among siblings (Ref=No)	-0.125	-0.312 – 0.061	0.187	-0.116	-0.289 – 0.056	0.184
Among partners (Ref=No)	-0.010	-0.211 – 0.191	0.922	-0.103	-0.313 – 0.107	0.336
Among children (Ref=No)	0.708	0.375 – 1.040	<0.001#	0.166	-0.201 – 0.533	0.373
Among other close relatives (Ref=No)	0.080	-0.354 – 0.514	0.717	0.080	-0.314 – 0.475	0.689
ST use mainly in company (Ref=No)	0.038	-0.206 – 0.282	0.757	0.242	-0.005 – 0.488	0.054
Permissibility within households (Ref=No)	0.017	-0.168 – 0.201	0.858	-0.123	-0.309 – 0.063	0.193
Duration of ST use						
ST use among closest friends (Ref=No)	-0.620	-1.125 – -0.116	0.016#	0.159	-0.150 – 0.468	0.311
Among closest relatives (Ref=No)	0.470	0.107 – 0.833	0.011#	0.107	-0.123 – 0.336	0.361
Among parents/ grandparents (Ref=No)	-0.309	-0.705 – 0.087	0.126	0.210	-0.030 – 0.449	0.085
Among siblings (Ref=No)	0.244	-0.112 – 0.600	0.178	0.147	-0.065 – 0.360	0.174
Among partners (Ref=No)	0.570	0.194 – 0.947	0.003#	0.194	-0.064 – 0.452	0.140
Among children (Ref=No)	1.826	1.212 – 2.441	<0.001#	-0.344	-0.795 – 0.108	0.135
Among other close relatives (Ref=No)	-0.328	-1.157 – 0.500	0.435	-0.089	-0.575 – 0.398	0.720
ST use mainly in company (Ref=No)	-1.004	-1.452 – -0.556	<0.001#	-0.423	-0.725 – -0.122	0.006#
Permissibility within households (Ref=No)	0.658	0.316 – 0.999	<0.001#	0.137	-0.092 – 0.367	0.238
Quantity of ST use						
ST use among closest friends (Ref=No)	0.481	-0.764 – 1.727	0.447	0.577	-0.710 – 1.864	0.378
Among closest relatives (Ref=No)	0.541	-0.354 – 1.437	0.235	0.056	-0.900 – 1.013	0.908

Among parents/ grandparents (Ref=No)	-0.330	-1.300 – 0.640	0.503	-0.459	-1.460 – 0.542	0.367
Among siblings (Ref=No)	0.305	-0.566 – 1.176	0.490	0.045	-0.843 – 0.933	0.920
Among partners (Ref=No)	0.696	-0.236 – 1.628	0.142	0.177	-0.903 – 1.256	0.747
Among children (Ref=No)	0.552	-1.053 – 2.158	0.499	-0.116	-2.003 – 1.771	0.904
Among other close relatives (Ref=No)	-0.217	-2.240 – 1.806	0.833	-0.053	-2.079 – 1.972	0.959
ST use mainly in company (Ref=No)	-1.390	-2.513 – -0.266	0.016#	-1.023	-2.291 – 0.244	0.113
Permissibility within households (Ref=No)	0.857	0.004 – 1.709	0.049#	0.356	-0.599 – 1.311	0.464
Frequency of ST use						
ST use among closest friends (Ref=No)	0.371	-0.210 – 0.952	0.210	0.373	-0.221 – 0.966	0.217
Among closest relatives (Ref=No)	0.466	0.050 – 0.882	0.028#	0.295	-0.145 – 0.735	0.188
Among parents/ grandparents (Ref=No)	-0.143	-0.596 – 0.311	0.535	-0.244	-0.706 – 0.218	0.299
Among siblings (Ref=No)	0.148	-0.259 – 0.555	0.475	0.014	-0.396 – 0.424	0.945
Among partners (Ref=No)	0.401	-0.033 – 0.836	0.070	0.261	-0.236 – 0.759	0.302
Among children (Ref=No)	0.351	-0.398 – 1.101	0.357	0.285	-0.585 – 1.156	0.519
Among other close relatives (Ref=No)	0.299	-0.646 – 1.243	0.534	0.369	-0.565 – 1.303	0.437
ST use mainly in company (Ref=No)	-0.590	-1.116 – -0.063	0.028#	-0.395	-0.981 – 0.192	0.186
Permissibility within households (Ref=No)	0.586	0.192 – 0.981	0.004#	0.448	0.010 – 0.886	0.045#

Note: Square root transformations applied to all dependent variables;

* Multivariate model adjusts for age (continuous variable), gender (male as ref. cat.), highest level of education completed (no formal schooling as ref. cat.), household asset ownership (0 – 3 assets as ref. cat.), and ever-smoking (never-smoking as ref. cat);

Statistically significant results.

4.2.3.1 Age of first ST use

In unadjusted analysis, ST use among closest friends was significantly associated with age of first ST use (F = 7.036, p = 0.009), whereby those with at least one ST user among their five closest friends were more likely to have first used ST at a younger age compared to those with no ST users among their closest friends. Although ST use among closest family members was not

significantly associated overall (F = 0.001, p = 0.970), ST use among parents/grandparents, as well as ST use among children were significantly associated with age of first ST use – those whose parents/grandparents used ST were significantly younger (F = 10.946, p = 0.001), and those whose children used ST were significantly older (F = 17.595, p < 0.001) when they first used ST themselves. Use of ST mainly in the company of others (F = 0.096, p = 0.757), as well as permissibility of ST use within households (F = 0.032, p = 0.858), did not show significant associations with age of first use in unadjusted analyses.

After adjusting for demographic variables and ever-smoking status, none of the sociocultural measures showed significant associations with age of first ST use. However, in a model that additionally controlled for the effects of other sociocultural factors, 'ST use in company' was significantly associated with age of first ST use (p = 0.038). Those who used ST mainly in the company of others were significantly likely to report higher ages of first ST use, compared to the rest of the sample. In all adjusted models, participant age was significantly associated with age of first ST use, whereby younger users were more likely to report first use of ST considerably earlier than older users in the sample.

4.2.3.2 Duration of ST use

In univariate analyses, having ST users among closest friends (F = 10.946, p = 0.001), and using ST mainly in the company of others (F = 19.517, p < 0.001), were significantly associated with lesser duration of ST use. On the other hand, having ST users among closest family members was significantly associated with greater duration of ST use (F = 6.499, p = 0.11), particularly if the users were partners (F = 8.900, p = 0.003) or children (F = 34.267, p < 0.001). Similarly, permissibility of ST use within households was also significantly associated with greater duration of ST use (F = 14.362, p < 0.001).

In multiple regression analyses controlling for demographic variables and ever-smoking, only the measure relating to 'ST use in company' remained significantly associated with duration of ST use. The results were the same after adjusting for the effects of other sociocultural factors. Those who used ST mainly in the company of others were significantly likely to have lower durations of use, compared to the rest of the sample. Participant age was the only other significantly associated factor, with younger users more likely to report lesser durations of ST use compared to older users in the sample.

4.2.3.3 Quantity of ST use

The use of ST by closest friends (F = 0.581, p = 0.447) or family members (F = 1.419, p = 0.235) were not significantly associated with quantity of ST use in univariate models. On the other hand, variables relating to ST use in company (F = 5.941, p = 0.016) and household permissibility (F = 3.923, p = 0.049) showed significant associations with quantity of consumption. Those who used ST mainly in company consumed lesser quantities of ST per week compared to the rest of the sample, while permissibility of ST use within households was significantly associated with greater quantities of consumption.

None of the sociocultural measures showed significant associations with quantity of ST consumed in adjusted models. However, education was significantly associated in all adjusted models, whereby higher levels of completed education were associated with lower quantities of ST consumed. These findings remained in a combined regression model of ST use quantity that included all the sociocultural measures.

4.2.3.4 Frequency of ST use

In univariate regression, the use of ST by closest friends (F = 1.583, p = 0.210) was not significantly associated with daily frequency of ST consumption. However, ST use by closest family members was significantly associated with greater frequency of use (F = 4.878, p = 0.028). Similar to the findings for quantity, ST use mainly in company was significantly associated with lesser frequency (F = 4.873, p = 0.028), whereas household permissibility was associated with greater frequency of ST consumption (F = 8.569, p = 0.004).

In multivariate regression models adjusting for demographic variables and ever-smoking status, only the household permissibility measure remained significantly associated with ST use frequency. However, none were significantly associated with frequency in a model that included all sociocultural measures. Higher levels of completed education were significantly associated with lower frequency of consumption in all adjusted models.

4.2.4 Association between sociocultural measures and ST reduction, quit attempts, and quit intentions – results of logistic regression analyses

The results of logistic regression analyses between sociocultural factors and ST control and quit practices have been summarised in Table 4.3. Further details are included in Appendix 4.3. The dependent variables used were whether participants were currently trying to cut down on ST use, whether they had made any quit attempts in the past 12 months, and whether they had any intention to stop using ST in the next 6 months.

Table 4.3 Association between sociocultural measures and ST reduction and quit practices – results of logistic regression analyses

Measures	Univariate model		Multivariate model*	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Currently trying to reduce ST use				
ST use among closest friends (Ref=No)	0.55 (0.25 – 1.20)	0.134	0.49 (0.21 – 1.12)	0.090
ST use among closest relatives (Ref=No)	0.61 (0.36 – 1.06)	0.081	0.77 (0.42 – 1.42)	0.405
ST use among parents/grandparents (Ref=No)	0.92 (0.51 – 1.64)	0.767	1.04 (0.55 – 1.97)	0.893
ST use among siblings (Ref=No)	0.86 (0.51 – 1.45)	0.577	0.98 (0.56 – 1.72)	0.951
ST use among partners (Ref=No)	0.65 (0.37 – 1.41)	0.134	0.99 (0.51 – 1.93)	0.974
ST use among children (Ref=No)	0.68 (0.26 – 1.80)	0.440	0.78 (0.24 – 2.54)	0.684
ST use among other close relatives (Ref=No)	0.49 (0.14 – 1.71)	0.260	0.36 (0.09 – 1.46)	0.153
ST use mainly in company (Ref=No)	0.97 (0.49 – 1.91)	0.920	0.73 (0.32 – 1.68)	0.463
ST use permissibility within households (Ref=No)	0.68 (0.41 – 1.15)	0.152	0.85 (0.46 – 1.55)	0.594
Quit attempts in past 12 months				
ST use among closest friends (Ref=No)	0.38 (0.18 – 0.81)	0.012[#]	0.39 (0.17 – 0.89)	0.025[#]
ST use among closest relatives (Ref=No)	0.82 (0.47 – 1.43)	0.486	0.92 (0.50 – 1.71)	0.798
ST use among parents/grandparents (Ref=No)	1.06 (0.58 – 1.94)	0.841	1.29 (0.67 – 2.46)	0.448
ST use among siblings (Ref=No)	1.30 (0.75 – 2.23)	0.384	1.48 (0.83 – 2.64)	0.180
ST use among partners (Ref=No)	0.62 (0.34 – 1.13)	0.121	0.55 (0.27 – 1.14)	0.108
ST use among children (Ref=No)	0.66 (0.23 – 1.93)	0.449	0.57 (0.16 – 2.01)	0.379
ST use among other close relatives (Ref=No)	1.51 (0.45 – 5.10)	0.508	1.24 (0.35 – 4.36)	0.738
ST use mainly in company (Ref=No)	0.62 (0.29 – 1.32)	0.219	0.47 (0.19 – 1.18)	0.110
ST use permissibility within households (Ref=No)	0.58 (0.34 – 0.99)	0.046[#]	0.57 (0.31 – 1.07)	0.080
Intentions to quit using ST				
ST use among closest friends (Ref=No)	0.53 (0.25 – 1.13)	0.099	0.46 (0.20 – 1.04)	0.063

ST use among closest relatives (Ref=No)	0.65 (0.37 – 1.14)	0.133	0.97 (0.52 – 1.82)	0.929
ST use among parents/grandparents (Ref=No)	0.90 (0.49 – 1.68)	0.749	1.02 (0.52 – 2.00)	0.941
ST use among siblings (Ref=No)	1.42 (0.82 – 2.45)	0.212	1.98 (1.08 – 3.62)	0.026
ST use among partners (Ref=No)	0.42 (0.22 – 0.81)	0.009[#]	0.59 (0.28 – 1.27)	0.178
ST use among children (Ref=No)	0.53 (0.17 – 1.68)	0.282	0.73 (0.19 – 2.81)	0.643
ST use among other close relatives (Ref=No)	0.72 (0.19 – 2.79)	0.635	0.67 (0.16 – 2.71)	0.575
ST use mainly in company (Ref=No)	1.38 (0.68 – 2.77)	0.372	0.76 (0.32 – 1.83)	0.546
ST use permissibility within households (Ref=No)	0.37 (0.21 – 0.65)	0.001[#]	0.51 (0.27 – 0.97)	0.039[#]

*Multivariate model adjusts for age (continuous variable), gender (male as ref. cat.), highest level of education completed (no formal schooling as ref. cat.), household asset ownership (0 – 3 assets as ref. cat.), and ever-smoking (never-smoking as ref. cat)

[#]statistically significant results.

4.2.4.1 Reduction in ST use

For reduction in current ST use, none of the sociocultural measures showed significant associations in both unadjusted and adjusted logistic regression models (Table 4.3). Among the demographic variables included in multivariate analyses, only number of household assets was significantly associated, whereby those with higher number of household assets were more likely to report trying to cut down on their current levels of ST use (ORs for the demographic variables can be found in Appendix 4.3).

4.2.4.2 Quit attempts in the past 12 months

In unadjusted analyses, two of the sociocultural measures were found to be significantly associated with ST quit attempts. Those who had at least one ST-user among their closest friends (OR = 0.38, 95% CI = 0.18, 0.81), as well as those who reported ST use permissibility within their households (OR = 0.58, 95% CI = 0.34, 0.99), were significantly less likely to have made a quit attempt in the past 12 months, compared to those who had no ST users among their closest friends and those who said ST use was never allowed within their households, respectively. However, in models adjusting for demographic variables and ever smoking exposure, only having a ST user among their closest friends was significantly associated with participants' not having made a quit attempts in the past 12 months (aOR = 0.39, 95 % CI = 0.17, 0.89). The significant

inverse relationship between these two variables held in a model that included all sociocultural factors and demographic variables entered together (aOR = 0.41, 95% CI = 0.17, 0.98).

In most of the adjusted models, education was significantly associated with quit attempts (Appendix 4.3). Those with higher levels of completed education were significantly more likely to have made a quit attempt in the past 12 months, compared to those with no formal schooling. None of the other sociodemographic variables showed any notable associations with ST quit attempts in adjusted models.

4.2.4.3 Quit intentions

In unadjusted analyses with ST quit intentions as the dependent variable, ST use permissibility within households was significantly associated, whereby those who reported permissibility were less likely to report quit intentions (OR = 0.37, 95% CI = 0.21, 0.65). Even in adjusted analysis, those with permitted ST use within their households showed significantly lesser odds of intending to quit within six months of the interview (aOR = 0.51, 95% CI = 0.27, 0.98), and the association held in a model that included all sociocultural factors and demographic variables entered together. With regard to close family members, while ST use among partners was significantly associated with lower odds of quit intentions in unadjusted analysis (OR = 0.42, 95% CI = 0.22, 0.81), the association was not statistically significant after adjusting for demographic variables. On the other hand, sibling ST use was significantly associated with positive quit intentions in adjusted analysis (aOR =1.98, 95% CI = 1.08, 3.62).

Similar to quit attempt models, education was significantly associated with quit intentions in analyses that included sociodemographic variables (Appendix 4.3). Those with higher levels of completed education were significantly more likely to report intentions to quit using ST, compared to those with no formal schooling. None of the other demographic variables in adjusted models showed significant associations with ST quit intentions.

4.2.4.4 Other measures

Additional models of ST control and quit practices with sociocultural measures that controlled for ST dependence diagnosis (reference = not dependent), perceptions of ST-related health risks (reference = not likely to develop oral cancer/heart disease), and doctor's advice to quit ST use (reference = no advice received), showed the following results. With regard to trying to cut down on current ST use, diagnosis of dependence was significantly associated in all models – the odds of trying to reduce ST consumption were significantly lower in dependent users compared to non-dependent users (aOR = 0.54, 95% CI = 0.29, 0.99 in a fully adjusted model that controlled for

sociodemographic, sociocultural, and other measures). On the other hand, perceptions of ST-related health risks and doctor's advice to quit using ST were not significantly associated. As found in earlier models, none of the sociocultural measures showed significant associations with ST use reductions after controlling for the additional factors.

With regard to ST quit attempts, having received advice from a doctor or healthcare provider in the past 12 months was significantly associated in all models with additional variables. Compared to those who had not received any advice, those who received advice to quit using ST were significantly more likely to have made quit attempts (aOR = 3.24, 95% CI = 1.39, 7.56 in fully adjusted model). On the other hand, dependence diagnosis and perceptions of ST-related health risks did not show significant associations. Even after controlling for additional factors, ST use among friends remained significantly associated, with lower odds of making a quit attempt among those who had ST-users among their closest friends (aOR = 0.35, 95% CI = 0.14, 0.85 in fully adjusted model).

Similar to what was found with ST quit attempts, doctor's advice was significantly associated with quit intentions in all models with additional controlling factors (aOR = 2.54, 95% CI = 1.11, 5.80 in fully adjusted model). Besides this, diagnosis of ST dependence or perceptions of ST-related health risks did not show any significant associated with ST quit intentions in multivariate logistic regression. The sociocultural measure relating to household permissibility remained significantly associated with quit intentions even after additional adjustments (aOR = 0.51, 95% CI = 0.26, 0.99 in fully adjusted model).

4.3 Discussion

The findings of this study are important because of the dearth of evidence relating to sociocultural influences on various aspects of ST use within South Asian settings, particularly given the scale of use within the region and the widespread recognition that ST use is culturally ingrained and often considered to be a shared social activity.

In this discussion section, I summarise the main findings from the survey conducted in New Delhi, India and interpret the findings of my analyses within the context of other research findings on the topic. I then work through the strengths and limitations of this study and consider the implications of my findings for practice, policy, and future research in this field.

4.3.1 Summary of main findings

Overall, three main findings emerged from the analyses of ST-related sociocultural factors

presented in this chapter. The first was that ST users in the study had a considerable number of other ST users among their close contacts, including friends and family members. Nearly 90% of the sample had at least one close friend who used ST, with 42.9% of participants reporting ST use among all five of their closest friends. In addition, the majority of participants (64.8%) also had at least one ST user among their five closest relatives, although only 9.9% of participants reported ST use among all five of their closest relatives. Among the family members, ST use was most commonly reported among siblings (41.2%), partners (30.0%), and parents/grandparents (26.6%), with women comprising the large majority of those reporting ST use among partners. For both these variables, significant differences were found across participants' sociodemographic characteristics. Younger users (18 – 29 years) were significantly more likely to have ST users among their five closest friends compared to older users (30+ years). On the other hand, having ST users among closest family members was significantly associated with female gender, lower levels of completed education, and owning fewer number of household assets.

Second, the associations between particular sociocultural factors, as well as their demographic distributions, suggested some distinct patterns of ST use within the study settings. Across sociocultural measures, chi-square tests were significant between 'ST use in company' and 'ST use among closest friends', whereby those who mainly used ST in company were significantly less likely to report no ST users among their closest friends. In terms of numbers, of the 32 participants who had no ST users among their closest friends, only one person reported using ST mainly in the company of other people. Those who mainly used ST in company also had more ST-using peers on average (mean = 3.8, SD = 1.51), compared to the rest of the sample (mean = 3.1, SD = 1.88). Furthermore, the distribution of sociodemographic variables across these two sociocultural measures showed similarities between those who had more number of ST users among their closest friends and those who mainly used ST in the company of others. Participants in both these categories tended to be younger, male, more educated, and wealthy. This likely suggested a social pattern of ST use, whereby ST was consumed on routine basis by some adult users mainly in the company of other ST-using peers.

Similarly, significant positive associations were found between ST use permissibility within households and having ST users among closest relatives. Those who reported ST use as allowed within their households had more number of ST-using relatives on average (mean = 2.1, SD = 1.56), compared to those who reported ST use as never allowed (mean = 0.8, SD = 1.30). Similar to the previously described pattern of use, the distribution of sociodemographic variables was comparable across these two categories. But in contrast to the previous section, participants who had more number of ST-using relatives and those who reported permissibility of ST use within their households tended to be older, female, less educated, and less wealthy. In addition, participants in both these categories were also more likely to report no preference for using ST

products either alone or in the company of others. These findings likely suggested a second distinct social pattern of ST use, whereby routine consumption of ST by some adult users was more domestic, linked with household permissibility and familial use of ST products.

Finally, the third main finding that emerged from this study was that sociocultural factors likely played a significant role in influencing a variety of ST use practices, including initiation, heaviness of current use, and quit practices. In the linear regression model of duration, the 'ST use in company' variable showed a significant association, whereby those who used ST mainly in company were significantly likely to have consumed ST for lesser duration than the rest of the sample. On the other hand, household permissibility was found to be significantly associated with frequency of ST use in adjusted linear regression analysis. In logistic regression models of quit attempts, 'ST use among closest friends' and 'ST use within households' showed significant associations, whereby having at least one ST user among closest friends, and being allowed ST use within households, were significantly associated with reduced odds of attempting to quit using ST products. The association held for 'ST use among closest friends' in adjusted models. In regression models predicting quit intentions, 'ST use within households' and 'sibling use of ST' were significantly associated factors – those who reported ST use as being allowed within their households were significantly less likely to report quit intentions in both unadjusted and adjusted analyses, whereas sibling use of ST was associated with greater odds of intending to quit in adjusted models.

Findings related to additional measures included in multivariate models showed that education levels were significantly associated with quantity and frequency of ST consumption, as well as quit attempts and quit intentions. Those with higher levels of completed education were more likely to consume ST products in lesser quantities and frequencies. They were also significantly more likely to have made quit attempts and report intentions to quit using ST within 6 months of the interview. In regression models of quit attempts and intentions, having received doctor's advice in the past 12 months were significantly associated with positive outcomes. In regression models of trying to cut down on ST use, diagnosis of ST dependence was significantly associated.

4.3.2 Interpretation of findings within context

4.3.2.1 Widespread ST use among close contacts of ST users

The high prevalence of ST use among the closest friends and family members of study participants meant that ST users in the study likely spent a considerable amount of time with other ST users. These findings were expected, given that tobacco use behaviours have been found to cluster within social networks (Mead et al., 2014). Other studies from across various countries in SA,

such as Nepal (Sreeramareddy et al., 2008), Pakistan (Shah et al., 2008), and Bangladesh (Sansone, 2014), have also consistently reported high peer and familial use of ST products. More recent evidence from a bigger and more representative sample of adult ST users from across four states in India also supported these findings (Ray et al., 2016). Although no specific data were collected in the present study regarding other forms of tobacco used by close associates of study participants (e.g. cigarettes or bidis), related evidence from studies conducted in similar settings suggest that the use of ST would be more likely among the closest associates of ST users, rather than other forms of tobacco (Sansone, 2014, Ray et al., 2016).

4.3.2.2 Social use of ST with peers

This study was the first to explore aspects related to adult ST users mainly consuming the products in the company of other people. The findings suggested that, on a usual basis, ST was mainly consumed alone by regular users. Nonetheless, it appeared that there were some ST users (~20% of participants) who mainly consumed ST products in the company of other people even on a routine basis. Although not specifically asked, this was most likely with other ST users. Moreover, significant associations found between this response category and having ST users among close friends suggested a pattern of routine ST consumption by some adult users in the company of other ST-using peers. Compared to rest of the sample, this group tended to be younger, male, more educated and wealthy.

This pattern of consumption was distinct from the practice of shared ST use with friends and family members reported in previous studies (Anwar et al., 2005, Mukherjea et al., 2012), which involved specific social situations such as having guests or attending social gatherings. Instead, it was more akin to the pattern of social smoking described by Moran et al. (2004) among US college students, which was based on students who stated that they smoked mainly with others rather than alone or equally by themselves and others. Moreover, in the American study, regression analysis showed significant associations between social use of tobacco and lower consumption and higher social support scores, similar to the findings of this study. Other studies from South Asian settings have documented the role of peer influence on ST initiation and continuation (Kakde et al., 2012), with one study from India finding that younger and male participants were significantly more likely to report ‘peer pressure’ as a motivating factor for ST initiation (Danawala et al., 2014). However, the practice of using ST in the company of other users, or the potential of this factor to influence ST use practices have not been previously assessed.

4.3.2.3 Domestic use of ST within households

Permissibility of ST use within households has also not been previously assessed within South

Asian settings to my knowledge. Although nearly half the sample reported that ST use was allowed within their households at all times, this was considerably lower than the proportion of participants reporting smoking permissibility within households (75.8%) based on GATS data from 14 LMICs, including India and Bangladesh (Owusu et al., 2017). However, estimates limited to countries from the SA region were not separately available from that study for comparison. Besides, my findings were based on a convenience sample unlike the nationally-representative GATS data, further limiting comparability. On the other hand, the finding that younger users were significantly more like to report non-permissibility of ST use within their households, was comparable to findings of cigarette studies from the region (Bush et al., 2003). Users reporting non-permissibility also tended to be male, completed higher levels of education, and owned greater household assets than those who reported ST use permissibility within their households at all times. Very few participants in the current study reported that ST use was allowed within their households only during special occasions. This was likely linked to the overall lower socioeconomic status of the study sample.

A significant positive association was found between household ST use permissibility and having ST users among closest relatives. These findings were considered likely because having ST users among close family members likely made the use of ST products within their households more acceptable. Or inversely, having no household restrictions influenced more number of close family members to use ST products. While both explanations seemed plausible, further clarity regarding the direction of association could not be provided due to the cross-sectional nature of the study design employed. Nevertheless, similarities in the distribution of sociodemographic variables across these two categories suggested a distinct social pattern of ST use within the study settings. The findings that women ST users were more likely to report greater number of ST-using relatives, as well as greater permissibility of ST use within their households, were likely linked to greater ST use among their partners. The large majority of those reporting ST use among their partners were women in this study. Gender differences in tobacco use by partners have been previously reported in South Asian settings, with greater likelihood of female spouses being non users of tobacco (Sansone, 2014).

4.3.2.4 Sociocultural influences on ST use practices

Overall, very few South Asian studies have assessed the influence of sociocultural factors on specific ST use behaviours such as initiation and cessation. In some (e.g. Narain et al. (2013)), despite the inclusion of ST users in the study sample, the authors report the risk of any or all tobacco use associated with peer and parental tobacco use, rather than the specific risk for taking up the use of ST products. Also, the exact type of tobacco used by peers and family members had not been explicitly stated. Specific to ST use, one study of adult women in Mumbai found

significant links between resistance to quitting ST and holding positive beliefs and norms about ST use (Schensul et al., 2018). While some of the specific measures of norms were related to the measures in this study (e.g. whether husband used ST, whether ST should be used in weddings), others were different (e.g. use of ST for toothaches). Nevertheless, the findings of significant inverse relations between overall positive norms regarding ST and its quit practices were comparable to the findings of this study.

One other study of sociocultural influences on ST quit practices in India and Bangladesh failed to find significant associations between the study variables (Sansone, 2014). However, the measures used in this study related to societal disapproval of ST use and acceptability of female ST use, which were different from the sociocultural measures assessed in my study. On the other hand, studies on cigarette smoking have reported comparable findings to those presented in this thesis. With regard to peer smoking, it has been found that smokers with greater number of smoking friends were significantly less likely to intend to quit, make a quit attempt, or to be successful in their future attempts (Hitchman et al., 2014). Similarly, smoking restrictions within households were significantly associated with increased odds of intending to quit smoking (Owusu et al., 2017).

4.3.2.5 Other influences on ST use practices

Other South Asian studies specific to ST use practices have also found education to be a significant influencing factor (Sansone, 2014), as have reports that included tobacco smokers within their study samples (Sarkar et al., 2013, Dhumal et al., 2014, Pradhan and Patel, 2019). The findings regarding advice from healthcare providers were comparable to the results of other larger surveys from India (Panda et al., 2015a, Pradhan and Patel, 2019), and suggested that healthcare providers played an important role in influencing ST quit practices in the study settings. However, opportunities for tobacco use screening and cessation advice were frequently missed during health visits, more so for ST users than tobacco smokers (Pradhan and Patel, 2019).

With regard to dependence, although some studies from India have reported findings of non-significant associations with ST quit practices (Panda et al., 2014, Parashar et al., 2017), others have found dependence to be a key determinant of quitting tobacco (Islam et al., 2014). In this study, diagnosis of ST dependence was only significantly associated with trying to cut down ST use. However, the measures of dependence used in the different studies were different.

4.3.3 Strengths and limitations

At the outset, it must be stated that the study objectives were not to make a comprehensive

epidemiological study of different sociocultural factors surrounding ST use and how they influenced ST use practices in the study settings. Rather, they were more focussed on describing some sociocultural aspects and exploring their likely associations with different ST use practices. The findings were nevertheless important, particularly for generating research hypotheses for further study. Recognising that some of the sociocultural aspects measured in this study had not been previously explored among ST users, particularly in a non-English speaking study setting, careful procedures were followed during the translation process to ensure that the English version of each question was appropriately understood in Hindi by the study participants. The study data were gathered from a fair-sized, community-based sample of largely exclusive ST users, who lived in a high burden setting. There was very little missing data overall.

Among the limitations, face-to-face interviews conducted to gather the study data likely meant that some respondents felt uncomfortable about answering questions regarding the sociocultural factors, which likely affected their survey responses. Other studies in similar settings additionally found that specific groups of respondents were shyer about answering questions pertaining to tobacco use and sociocultural factors, such as female respondents in the presence of other household members (Sansone, 2014). However, individual interviews conducted in relative privacy in a community setting rather than a household setting likely protected against potential biases arising from these factors.

On the topic of information gathering, another limitation was the small number of survey items relating to sociocultural factors, which did not extend to measures of injunctive or subjective norms surrounding ST use. It is possible that even if many close contacts within one's social network use ST products, indicating a positive descriptive norm towards ST use, there could be an opposing pattern with regard to subjective norms. People most important to users may actually disapprove of their habit and want them to quit using tobacco. This pattern has been reported among tobacco users in Bangladesh and India, with even less approval from close contacts for female tobacco users compared to males (Sansone, 2014). However, given the more descriptive and exploratory nature of the study objectives, and that the survey was also designed to collect data on various measures of ST dependency, brevity was chosen over gaining a complete understanding of sociocultural factors surrounding ST use and how they were associated with ST use practices in the study settings. This also meant that the regression analyses of association between sociocultural factors and ST use practices only controlled for some potential confounders such as ST dependence and knowledge of health risks, whereas the influence of other factors such as policy awareness was not controlled for in analyses.

Also among the limitations, no formal sample size was calculated for studying the associations presented, and analyses based on cross-sectional data meant limitations in interpreting the

direction of associations. Furthermore, convenience sampling techniques employed limited the overall generalisability of study findings.

4.3.4 Implications of findings

The findings of this research have important implications for ST control strategies, by suggesting that interventions that target sociocultural factors can be effective approaches for influencing ST use behaviours within the study settings. In addition, the finding of gender differences in the social patterns of ST use suggests the need to consider gender in the design and implementation of ST control strategies in South Asian settings, as has been previously highlighted (Sansone, 2014). The impact of a ST user as a close friend appears to be greater than that of having ST users among close relatives in adult males, whereas the vice versa appears to be true for adult females in the study settings. The interventions could also be at the policy-level, such as anti-ST campaigns, which can target the social norms surrounding ST use. In fact, recent studies using large, nationally representative samples in different countries have demonstrated that tobacco control policies are associated with social norms. However, the findings are limited to tobacco smoking and largely from outside the SA region (Thrasher et al., 2009, Rennen et al., 2014).

In addition to the implications for ST control interventions and policies, the findings support the need for further studies on sociocultural factors related to ST use in South Asian settings. This could extend to specific groups of ST users, such as pregnant women, in whom some sociocultural factors have been linked to ST initiation and onset of daily use (Begum et al., 2015). It is also important that future studies exploring these associations apply robust methodologies, but with more representative sample selections and formal calculations of sample size, so that the findings are more generalisable. In addition, larger studies with more data on potential confounders could better establish the link between sociocultural factors and ST use behaviours. These studies could also likely assess the underlying mechanisms of influence linking specific sociocultural factors to ST use practices using mediation analyses, as has been carried out in studies of cigarette smoking (Li et al., 2018). Finally, it would also be beneficial for more studies in future to expand to other types of social norms surrounding ST use, such as the work by Sansone (2014), which covers areas of descriptive, injunctive, and subjective norms surrounding ST use in high-burden countries such as Bangladesh and India.

Chapter 5. A Systematic Review of Longitudinal Observational Studies on ST Use as a Risk Factor for IHD and Stroke

To find out if the geographical differences observed with ST-related risks of cancers might also extend to CVD outcomes, I systematically reviewed the global evidence linking ST use to IHD and stroke outcomes. In this chapter, I report the strategies used for systematically identifying, retrieving and analysing the available data on the subject (Section 5.1). In the results section, I present four separate meta-analyses of studies linking ever use of ST with incident and fatal IHD and stroke, both globally and by grouping studies according to geographical subgroups (Section 5.2). Finally, in the discussion section, I summarise and interpret my findings in relation to the broader literature, reflect on the strengths and limitations of the research methodologies used, and discuss the implications of my findings for practice, policy, and future research (Section 5.3).

5.1 Methodology

The methodologies that would be used in the systematic review were set out in a study protocol. Although the review and analytical processes were carried out exactly as per the steps detailed in this predetermined protocol, the document was neither registered nor published.

5.1.1 Study selection criteria

The following list of criteria were used for selecting studies to include in the systematic review.

5.1.1.1 Population and timeframe

All populations were considered as eligible, including community-based participants or patients recruited in health care settings. Age or gender of study participants were not considered for decisions regarding inclusion or exclusion of studies. No restrictions were imposed regarding the timeframe of studies, either on the basis of date of data collection or publication.

5.1.1.2 Language and geographical settings

The review did not exclude studies based on language or geographical setting. Any paper not published in the English language was translated into English at each stage of screening, as was required. In practice, this was required for two studies identified via electronic searches, both published in the German language.

5.1.1.3 Exposure

Studies were eligible for inclusion if they reported ever (current or past) use of any ST product. Exposure could have been measured through self-report or the use of biochemical markers (e.g. cotinine levels in samples of saliva, plasma, urine, or hair). The type of measure used for exposure ascertainment did not constitute a criterion for exclusion.

If a study recruited users of both smoked and smokeless forms of tobacco, then to be eligible for inclusion, it should have either presented risks for a subsample of exclusive ST users, or clearly controlled for smoking exposure in the analysis. This was to control for any confounding effect of smoking on CVD outcomes.

5.1.1.4 Outcome

To meet the inclusion criteria, studies had to report at least one of the following disease outcomes:

- Incident or fatal IHD (ICD-10 codes I20 – I25)
- Incident or fatal stroke (ICD-10 codes I60 – I69)

These were decided on the basis of a scoping review to identify ST-related CVD outcomes. However, studies that only reported intermediate cardiovascular outcomes such as blood pressure or lipid levels were excluded from the review, as these factors were likely to be on the causal pathway.

The study outcomes had to be clearly defined according to a recognised system of disease classification such as the WHO ICD-10 (1992) or its previous revisions. It was decided to keep the estimates for fatal outcomes of both diseases separate, due to the increased risk of fatal IHD and stroke reported in a previous meta-analysis of American and European studies on the topic, which was not found for non-fatal disease outcomes (Boffetta and Straif, 2009).

5.1.1.5 Study design

To be eligible for inclusion, studies had to follow a longitudinal observational design, in order to provide information on the temporal relationship between exposure to ST products and risk of CVD outcomes. In addition, studies had to present a quantitative estimate of CVD risk associated with ever use of ST products. For these reasons, cross-sectional study designs were excluded, and only cohort and case-control studies were considered to be eligible for inclusion.

5.1.1.6 Publication type and quality

As a step to minimise publication bias, studies were not excluded on the basis of publication type or status. However, if a study meeting the selection criteria for the review was only available as conference abstracts or theses, then the authors of these studies were contacted to ask if their work was available in other published formats.

In line with published recommendations (Centre for Reviews and Dissemination, 2009), no studies were excluded on the basis of their methodological quality. However, the implications of study quality were explored in analyses using subgroups, as explained in the section on data analysis below.

5.1.2 Search strategies

The search strategy for this review comprised searching of electronic databases, screening the reference lists of eligible studies, and searching through papers citing the included studies.

5.1.2.1 Electronic database searches

For systematic searching of electronic databases, I designed a search strategy in consultation with the academic liaison librarian at the University of York. The strategy was designed to be more sensitive than specific, so as to retrieve as many potentially relevant studies as possible.

a) Sources

A total of sixteen databases were searched up until July 2014, with searches rerun in September 2015 to identify any additional studies of relevance published since the original searches. The following databases were searched:

1. MEDLINE, 1946 – current
2. Embase, 1974 – current
3. PsycINFO, 1967 – current
4. Cumulative Index to Nursing and Allied Health Literature Plus (CINAHL Plus), 1937 – current
5. Web of Science, 1898 – current
6. Cochrane Library, 1898 – current
7. Scopus

In addition, searches were run in the following regional databases:

8. African Journals Online (AJOL)
9. Latin American and Caribbean Health Sciences Literature (LILACS)
10. WHO Index Medicus of the Eastern Mediterranean Region (IMEMR)
11. WHO Index Medicus of the South-East Asian Region (IMSEAR)
12. PakMediNet
13. IndMED

Finally, grey literature was searched using the following three databases:

14. ProQuest Dissertations & Theses Global™
15. Open Grey
16. The British Library electronic theses database (ETHOS)

b) Search terms

My strategy for searching the electronic databases involved combining the ST-related search terms (exposure) with terms for specific CVD outcomes. The exposure-related search terms were selected to reflect the wide variety of ST products with different regional names and practices of use. They were largely based on published systematic reviews on ST products (e.g. Kakde et al. (2012)), as well as the IARC monograph on ST titled 'Smokeless Tobacco and some tobacco-specific N-Nitrosamines' (2007). The outcome-specific terms were also based on other systematic reviews of CVD outcomes (e.g. Matheny et al. (2011)), with some incorporated modifications that were suggested by the information specialist at the University of York. Subject headings and free text words with variations and truncations were incorporated into the search strategy and tailored to suit each database. Terms referring to study design did not form a part of my search strategy.

In Table 5.1, I present an example of the search strategy used in MEDLINE, including the number of studies retrieved by the search. Similar details for the searches conducted using other electronic databases can be found in Appendix 5.1.

Table 5.1 MEDLINE search strategy for systematic review

Database (search platform): **MEDLINE (OvidSP)**	
Search date: **21/07/2014**	
Search terms	**Number of studies**
smokeless tobacco*.mp. or Tobacco, Smokeless/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	3209
(oral* adj3 tobacco*).mp.	526
(chew* adj3 tobacco*).mp.	929
(spit* adj3 tobacco*).mp.	48
(dip* adj3 tobacco*).mp.	62
gutk?a.mp.	79
kiwam.mp.	1
zarda.mp.	20
mawa.mp.	9
tuibur.mp.	3
shamma.mp.	15
gul.mp.	40
snuf*.mp.	1161
snus.mp.	271
chimo.mp.	13
iqmik.mp.	12
toombak.mp.	28
tumbaku.mp.	1
mishri.mp.	7
m?sheri.mp.	24
n?swar.mp.	19
(p?an adj3 (masala or quid)).mp.	85
gudak?u.mp.	4
k?aini.mp.	26
(maras adj3 (powder or tobacco*)).mp.	24
(quid adj3 (betel or tobacco*)).mp.	665
((twist* or plug*) adj3 tobacco*).mp.	11
((loose leaf or toothpaste*) adj3 tobacco*).mp.	13
((pouch* or mix* or powder*) adj3 tobacco*).mp.	223
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	5144
exp Cardiovascular Diseases/ or cardiovascular disease*.mp.	1909655
exp Myocardial Infarction/ or myocardial infarc*.mp.	191342
heart attack*.mp.	3783
exp Heart Arrest/ or heart arrest*.mp.	40876
exp Coronary Disease/ or exp Coronary Artery Disease/ or coronary disease*.mp.	187076
coronary event*.mp.	5067
cardio?vascular mortalit*.mp.	7538

cardiac mortalit*.mp.	1807
cardio?vascular death*.mp.	3791
exp Death, Sudden, Cardiac/ or cardiac death*.mp.	21449
exp Cerebrovascular Disorders/ or cerebrovascular disorder*.mp.	279788
cerebro?vascular accident*.mp.	4911
cerebro?vascular event*.mp.	2762
cerebro?vascular disease*.mp.	13619
exp Stroke/ or stroke*.mp.	193317
brain isch?emia.mp. or exp Brain Ischemia/	83487
exp Intracranial Hemorrhages/ or exp Cerebral Hemorrhage/ or intracranial h?emorrhag*.mp.	58630
31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	1962081
30 and 48	**291**

5.1.2.2 Screening of reference lists

In addition to the electronic searches, the reference lists of all the papers meeting the inclusion criteria were screened to identify any missed articles.

5.1.2.3 Citation searches

Finally, the titles of the included papers were entered into Google Scholar to search the list of articles citing these papers that might be eligible for inclusion in the review.

5.1.2.4 Managing references

All identified studies were imported into a single EndNote file for managing references.

5.1.3 Study selection

As a first step, duplicate articles were identified and removed from the list of references imported into the EndNote library. This was followed by the various steps of screening, as detailed below.

5.1.3.1 Screening of titles and abstracts

Two researchers (Aishwarya Vidyasagaran and Kamran Siddiqi) independently screened all the titles and abstracts, eliminating studies that were unrelated to the topic of study. Any disagreements were resolved through discussion. For those studies that appeared to fit the inclusion criteria after initial screening of titles and abstracts, full texts were retrieved.

5.1.3.2 Screening of full-text articles

In this next step of screening, the same two researchers (AV and KS) independently examined the retrieved full-texts and decided on which studies met the inclusion criteria, using a screening form (Appendix 5.2). Study authors were contacted for clarifications when required, and any disagreements on decisions to include/exclude studies were resolved through discussions between the two researchers. Those studies that did not fit the inclusion criteria were excluded at this stage, noting the reasons for exclusion.

5.1.4 Data extraction

A template was developed for data extraction (Appendix 5.3) and used by one researcher (AV) to extract all the relevant data from included studies. The extracted information was then verified against the original papers by the second researcher (KS). If a study reported several of the outcome measures considered in the review, the results relevant to each outcome measure was extracted separately. Also, if a study used statistical methods to control for potential confounders, the data were extracted from the controlled model. If any data were found missing, the study authors were contacted for the required information.

5.1.5 Assessment of study quality

As recommended by the Cochrane Collaboration (Higgins and Green, 2011), the methodological quality of included studies or the risk of bias was assessed using the Newcastle-Ottawa scales (NOS) for case-control and cohort study designs (Wells et al., 2000).

Using these scales, a maximum of nine points could be assigned to studies with the least risk of bias within three categories of assessments, namely (1) selection of study groups (up to four points), (2) comparability of study groups (up to two points), and (3) ascertainment of exposure and outcomes (up to three points) for case–control and cohort studies, respectively. Similar to data extraction, the quality assessment of included studies was carried out by one researcher (AV) using the NOS templates (Appendix 5.4) and verified by the second researcher (KS).

5.1.6 Data analysis

The included studies were first grouped according to the geographical regions in which they were conducted, and their study characteristics and risk estimates were summarised in a table. The data analysis stage only included papers which reported an effect estimate and standard error (SE) or CI, or from which these measures could be calculated. The effect measures were either reported

as RRs, ORs, or hazard ratios (HR), but given that the event rates were low in the included studies, and the selected populations were not particularly at high-risk for disease incidence, it was decided that the different types of effect measures would be treated alike in analyses. On the other hand, it was anticipated that the effect size magnitudes in the different studies would not be similar, since they were derived from different geographical regions, and investigated CVD risks associated with the use of different types of ST products. Nevertheless, studies were deemed sufficiently similar to warrant aggregation of results, and random effects models were chosen to obtain the pooled estimates, in order to allow for anticipated variations between the included studies.

Separate meta-analyses were performed for each outcome measure under study, i.e. (1) incident IHD, (2) fatal IHD, (3) incident stroke, and (4) fatal stroke. Each forest plot presented an overall pooled estimate based on all the included studies within that outcome category, to answer the broader question of whether exposure to ST was associated with overall increased risk. In addition, the forest plots also presented region-specific risks for each outcome measure considered. The presence of heterogeneity in analyses was assessed using the I^2 statistic, by quantifying the proportion of observed inconsistencies across study results that could not be explained by chance. Where there was evidence of heterogeneity, their potential sources were explored on the basis of pre-defined subgroups which included differences in study design, study setting, participant characteristics, and exposure measurement.

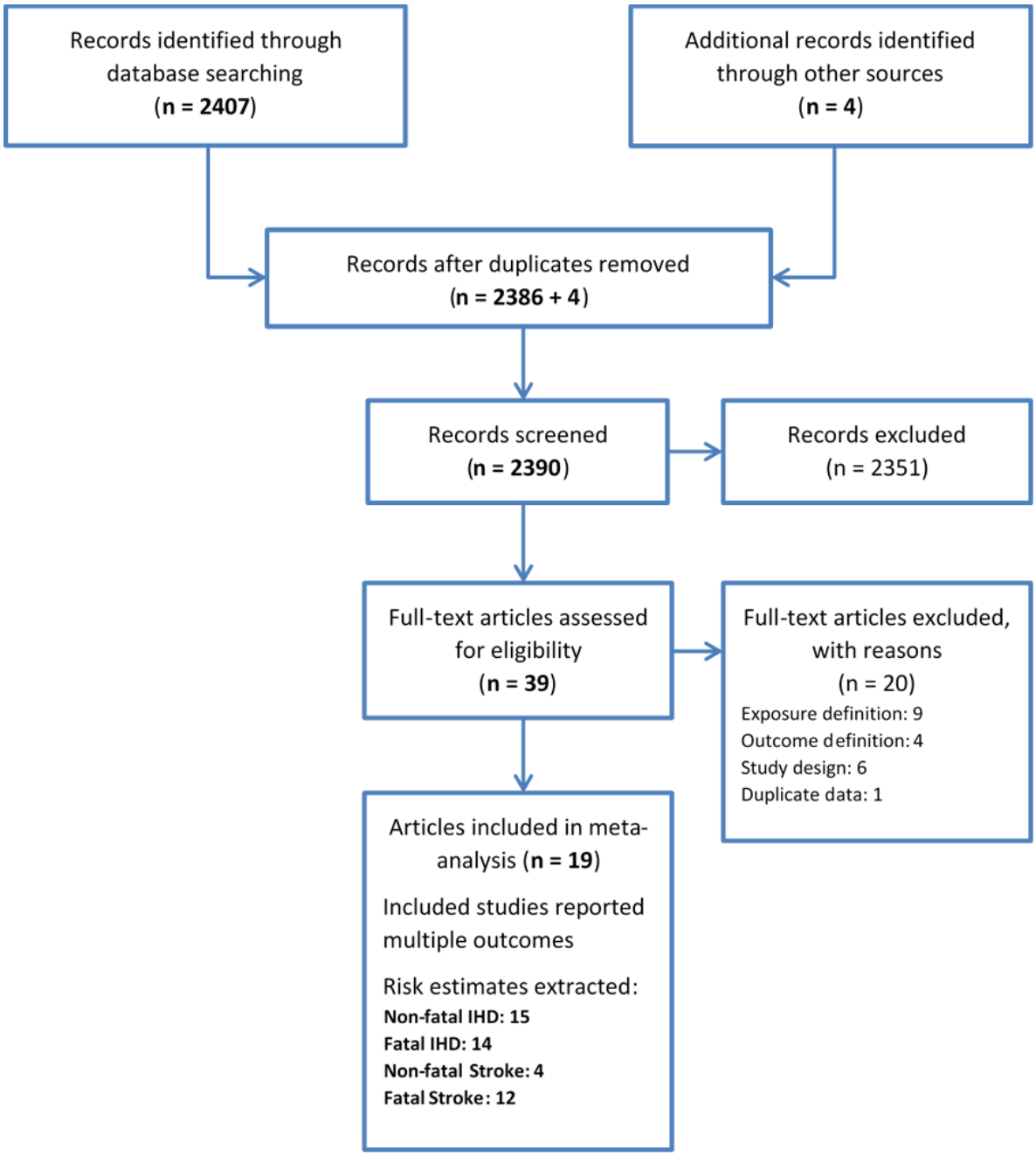
The possibility of publication bias was explored by visually inspecting the funnel plots for asymmetry of distribution. In line with Cochrane recommendations, statistical tests were not performed for assessing any asymmetries, given the limited number of included studies (Higgins and Green, 2011). All the analyses were performed using RevMan version 5.3 (The Cochrane Collaboration, 2014).

5.2 Results

Following the two-stage screening process, a total of 20 studies reported in 19 publications were identified for inclusion in the meta-analyses. From these, 15 risk estimates were extracted for incident IHD, 14 for fatal IHD, 4 for incident stroke and 12 for fatal stroke outcomes. In the following subsections, I present the detailed results of my analyses.

5.2.1 Overview of included studies

Figure 5.1 Flow diagram of study selection process for the systematic review



5.2.1.1 Excluded and included studies

As depicted in Figure 5.1, electronic database searches resulted in 2407 references, with 2386 remaining for stage one screening after removing duplicate inputs. Four additional study titles were identified through the other search strategies employed, and screened for eligibility. On completion of stage one screening of titles and abstracts, a total of 39 references remained for

second stage screening of full-texts. Of these, 20 studies were excluded for one of the following reasons:

- Exposure and outcome definitions (13 studies) – Haldar et al. (2005), Haglund et al. (2007), Henley et al. (2007), Yen et al. (2008), Pyrgakis (2009), Janzon and Hedblad (2009), Mushtaq et al. (2010), Yatsuya et al. (2010), Arefalk et al. (2012), Deoke et al. (2012), Ram and Trivedi (2012), Puri et al. (2013), and Arefalk et al. (2014)
- Study design (6 studies) – Squier and Johnson (2000), Nitzkin (2011), Tully et al. (2011), Yatsuya and Folsom (2011), Hansson et al. (2012), and Hansson et al. (2014)
- Duplication of data (1 study) – Rahman et al. (2012a)

Of the 20 included studies, six were conducted in Asian countries – three in Bangladesh (Rahman and Zaman, 2008, Mateen et al., 2012, Rahman et al., 2012b), two in India (Gupta et al., 2005, Gajalakshmi and Kanimozhi, 2015), and one in Pakistan (Alexander, 2013); 10 were conducted in Europe – all in Sweden (Huhtasaari et al., 1992, Bolinder et al., 1994, Huhtasaari et al., 1999, Asplund et al., 2003, Hergens et al., 2005, Johansson et al., 2005, Hergens et al., 2007, Wennberg et al., 2007, Hergens et al., 2008, Hansson et al., 2009); and three (reported in two papers) were conducted in North America – all in the USA (Accortt et al., 2002, Henley et al., 2005). One was a large case-control study which was conducted across 52 countries world over (INTERHEART study). However, ST use was mainly reported from countries in SA (Teo et al., 2006). All the included studies were written in English and published since 1992.

With regard to study design, there were 11 case-control studies and nine cohort studies with inceptions between 1959 (Henley et al., 2005) and 1998 (Hansson et al., 2009). All reports from North America were of cohort studies, with one article reporting results from two cohorts – Cancer Prevention Studies (CPS) I & II (Henley et al., 2005). Of the Asian studies, only one was a cohort study design – Bombay Cohort Study (Gupta et al., 2005), while the rest were case-control studies. The European studies were an equal mix of cohort and case-control study designs (five each). With the exception of one thesis (Alexander, 2013), all the included studies were published as peer-reviewed journal articles. The study presented in the thesis (PROMIS) was not found in any other published format.

5.2.1.2 Sample size and participant characteristics

The sample sizes ranged from 207 (Rahman and Zaman, 2008) to 451,000 (Gajalakshmi and Kanimozhi, 2015), with a total of 1,102,035 participants aged 18+. While all the European studies reported data limited to male participants, all the Asian studies were based on data collected from mixed samples. Of the three studies from North America (reported in two paper), two included

only male participants (Henley et al., 2005), while one included a mixed sample (Accortt et al., 2002). The INTERHEART study included both male and female participants (Teo et al., 2006).

5.2.1.3 Exposure and outcome

All the included studies measured ST exposure through self-report. There were variations in the exposure statuses reported in the included papers, as well as variations in ST product types. Across the studies, most reported ever use of ST, while some differentiated between current and former use. A few of the European studies specified regular (Huhtasaari et al., 1992, Huhtasaari et al., 1999, Asplund et al., 2003) and daily (Johansson et al., 2005) consumption among the current ST users. With regard to ST product types, one half of the included studies (10/20) considered exposure to any form of ST, while the majority of European studies focused on just snuff dipping. Some of the included papers specifically described exposure to chewing tobacco (Teo et al., 2006), or tobacco powder (Mateen et al., 2012), while one study differentiated between dipping and chewing forms of ST used by study participants (Alexander, 2013).

Some of the included studies reported results of multiple CVD outcomes, explaining the higher number of total risk estimates (45) compared to the number of articles included (19). The various methods used in the studies for outcome ascertainment included the examination of medical records (Huhtasaari et al., 1992, Huhtasaari et al., 1999, Hergens et al., 2005) or municipal records (Gupta et al., 2005), death certificates (Accortt et al., 2002, Henley et al., 2005), verbal autopsy reports (Mateen et al., 2012, Gajalakshmi and Kanimozhi, 2015) or national registers (Bolinder et al., 1994, Asplund et al., 2003, Johansson et al., 2005, Hergens et al., 2007, Wennberg et al., 2007, Hergens et al., 2008, Hansson et al., 2009). In three studies from Asia (Rahman and Zaman, 2008, Rahman et al., 2012b, Alexander, 2013), as well as the INTERHEART study (Teo et al., 2006), cases were identified by doctors based on clinical findings and some relevant investigations such as electrocardiogram (ECG), cardiac enzymes, exercise tolerance, or coronary artery angiogram. In two of these studies (Rahman and Zaman, 2008, Rahman et al., 2012b), angina pectoris was included within the case definition of IHD outcomes.

A summary of study characteristics is presented in Table 5.2.

Table 5.2 Characteristics of studies included in the systematic review

Reference	Country	Study period	Study design (number of participants)	Age and gender of participants	Exposure status	Included smokers/ alcohol users	Outcome	Risk estimate (95% CI)	Comments
INTERHEART study – 52 countries									
Teo et al. (2006)	52 countries (ST use data mainly from countries in South Asia)	1999 – 2003	Case-Control (Cases – 12461, Controls – 14637)	Not available Mixed	Use of chewing tobacco	No/Yes	IHD	OR = 2.23 (1·41, 3.53)	Adjusted for diet, diabetes, HT, exercise, obesity
ASIA									
Gupta et al. (2005)	India	1992 – 1999	Cohort (5470)	> 35 years Mixed	Ever use of ST	No/Not available	Fatal IHD Male Female Fatal Stroke Male Female	RR = 0.89 (0.75, 1.05) 1.25 (1.05, 1.49) 1.32 (0.94, 1.84) 1.15 (0.84, 1.59)	Adjusted for education, age
Rahman and Zaman (2008)	Bangladesh	2006 – 2007	Case-Control (Cases – 69, Controls – 138)	20 – 49 years Mixed	Ever use of ST	No/Not available	IHD	OR = 2.80 (1.10, 7.13)	Adjusted for age, sex, HT

Rahman et al. (2012b)	Bangladesh	2010	Case-Control (Cases – 302, Controls – 1510)	40 – 75 years Mixed	Ever use of ST	No/Not available	IHD	OR = 0.77 (0.52, 1.14)	Adjusted for age, diabetes, psycho-social stress, HT
Mateen et al. (2012)	Bangladesh	2005 – 2008	Case-Control (Cases – 1250, Controls – 246)	20 – 100 years Mixed	Ever use of tobacco powder	Yes/Not available	Fatal Stroke	OR = 1.15 (0.30, 7.64)	Adjusted for age, sex, HT, diabetes, betel nut, smoking, heart disease
Alexander (2013)	Pakistan	2005 – 2011	Case-Control (Cases – 7905, Controls – 7458)	20 – 80 years Mixed	Ever use of dipping ST Ever use of chewing ST	No/Not available	IHD	OR = 1.46 (1.20, 1.77) 1.71 (1.46, 2.00)	Adjusted for age, region, sex, ethnicity
Gajalakshmi and Kanimozhi (2015)	India	1998 – 2001	Case-Control (Cases – 22000, Controls – 429000)	35 – 69 years Mixed	Ever use of ST	No/No	Fatal Stroke	OR = 1.40 (1,20, 1.60)	Adjusted for age, education, urban/rural. sex
EUROPE									
Huhtasaari et al. (1992)	Sweden	1989 – 1991	Case-Control (Cases – 585, Controls – 589)	35 – 64 years All male	Regular use of snuff	Yes/Not available	IHD	OR = 1.01 (0.66, 1.55)	Adjusted for age, education, smoking
Bolinder et al. (1994)	Sweden	1974 – 1985	Cohort (135036)	35 – 65 years All male	Ever use of ST	No/Not available	Fatal IHD 35 – 54 years 55 – 65 years Fatal Stroke 35 – 54 years 55 – 65 years	RR = 2.00 (1.40, 2.90) 1.20 (1.00, 1.50) 1.90 (0.60, 5.70)	Adjusted for age, region of origin

								1.20 (0.70, 1.80)	
Huhtasaari et al. (1999)	Sweden	1991 – 1993	Case-Control (Cases – 687, Controls – 687)	25 – 64 years All male	Former use of snuff	No/Not available	IHD	OR = 1.23 (0.54, 2.82)	Adjusted for age
Asplund et al. (2003)	Sweden	1985 – 2000	Case-Control (Cases – 276, Controls – 551)	25 – 74 years All male	Regular use of ST	No/Not available	Stroke	OR = 0.87 (0.41, 1.83)	Adjusted for diabetes, HT, education, marital status, cholesterol
Hergens et al. (2005)	Sweden	1998 – 2005	Case-Control (Cases – 1432, Controls – 1810)	45 – 70 years All male	Current use of snuff Former use of snuff Current use of snuff Former use of snuff	No/Not available	IHD Fatal IHD	OR = 0.59 (0.25, 1.40) 1.20 (0.43, 3.20) 1.70 (0.48, 5.50) 1.70 (0.21, 13.60)	Adjusted for age, hospital catchment area
Johansson et al. (2005)	Sweden	1988 – 2000	Cohort (3120)	30 – 75 years All male	Daily use of snuff	No/Not available	IHD	HR = 1.41 (0.61, 3.28)	Adjusted for BMI, physical activity, HT, diabetes
Hergens et al. (2007)	Sweden	1978 – 2004	Cohort (118395)	35 – 65 years All male	Ever use of ST	No/Not available	IHD Fatal IHD	RR = 0.91 (0.81, 1.02) 1.28 (1.06, 1.55)	Adjusted for age, BMI, region of residence

Wennberg et al. (2007)	Sweden	1985 – 1999	Case-Control (Cases – 525, Controls – 1798)	30 – 60 years All male	Current use of snuff Former use of snuff Current use of snuff Former use of snuff	No/Not available	IHD Fatal IHD	OR = 0.82 (0.46, 1.43) 0.66 (0.32, 1.34) 1.12 (0.38, 3.29) 0.64 (0.13, 3.18)	Adjusted for BMI, physical activity, education, cholesterol
Hergens et al. (2008)	Sweden	1978 – 2003	Cohort (118465)	35 – 65 years All male	Ever use of ST	No/Not available	Stroke Fatal Stroke	RR = 1.00 (0.89, 1.11) 1.27 (0.92, 1.76)	Adjusted for age, BMI, region
Hansson et al. (2009)	Sweden	1998 – 2005	Cohort (16642)	> 40 years All male	Current use of snuff Former use of snuff Current use of snuff Former use of snuff	No/Not available	IHD Stroke	RR = 0.85 (0.51, 1.42) 1.07 (0.56, 2.04) 1.18 (0.67, 2.08) 1.35 (0.65, 2.80)	Adjusted for age, diabetes, cholesterol, HT
NORTH AMERICA									
Accortt et al. (2002)	USA	1971 – 1992	Cohort (6805)	25 – 74 years Mixed	Ever use of ST	No/Not available	Fatal IHD Male Female Fatal Stroke Male Female	HR = 0.60 (0.30, 1.20) 1.40 (0.80, 2.20) 0.70 (0.20, 2.00)	Adjusted for age, race, HT, poverty index, alcohol, BMI, cholesterol, activity, fruit

								1.00 (0.30, 2.90)	and vegetable intake
Henley et al. (2005)	USA	1959 – 1972	Cohort (77407)	> 35 years All male	Current use of ST	No/Yes	Fatal IHD Fatal Stroke	HR = 1.12 (1.03, 1.21) 1.46 (1.31, 1.64)	Adjusted for age, race, education, fat/ fruit/vegetable intake, alcohol, activity, BMI, aspirin
Henley et al. (2005)	USA	1982 – 2000	Cohort (114809)	> 35 years All male	Ever use of spit tobacco Current Former Current Former	No/Yes	Fatal IHD Fatal Stroke	1.26 (1.08, 1.47) 0.70 (0.52, 0.95) 1.40 (1.10, 1.79) 1.21 (0.83, 1.76)	Adjusted for age, race, education, fat/ fruit/vegetable intake, alcohol, activity, BMI, employment, aspirin

Abbreviations: ST – Smokeless Tobacco, IHD – Ischaemic Heart Disease, HT – Hypertension, BMI – Body Mass Index, OR – Odds Ratio, RR – Relative Risk, HR – Hazard Ratio, CI – Confidence Interval

5.2.2 Quality of included studies

The quality assessment scores of the included studies using NOS measurements (Wells et al., 2000) are presented in Table 5.3. Further details of the scoring can be found in Appendix 5.4.

Table 5.3 Summary scores on methodological quality of included studies

Reference	Study design	NOS categories of quality assessment		
		Selection (4 stars max)	Comparability (2 stars max)	Exposure/ Outcome (3 stars max)
INTERHEART study – 52 countries				
Teo et al. (2006)	Case-control	****	**	*
ASIA				
Gupta et al. (2005)	Cohort	****	**	**
Rahman and Zaman (2008)	Case-control	***	**	*
Rahman et al. (2012b)	Case-control	****	**	*
Mateen et al. (2012)	Case-control	***	**	*
Alexander (2013)	Case-control	****	**	**
Gajalakshmi and Kanimozhi (2015)	Case-control	****	**	***
EUROPE				
Huhtasaari et al. (1992)	Case-control	****	**	*
Bolinder et al. (1994)	Cohort	**	**	***
Huhtasaari et al. (1999)	Case-control	****	**	**
Asplund et al. (2003)	Case-control	****	**	**
Hergens et al. (2005)	Case-control	***	**	**
Johansson et al. (2005)	Cohort	****	**	***
Hergens et al. (2007)	Cohort	**	**	***
Wennberg et al. (2007)	Case-control	****	**	*
Hergens et al. (2008)	Cohort	**	**	***
Hansson et al. (2009)	Cohort	***	**	*
NORTH AMERICA				
Accortt et al. (2002)	Cohort	***	**	***
Henley et al. (2005)	Cohort	***	**	***
Henley et al. (2005)	Cohort	***	**	***

Case-control studies: In all the case-control studies (n = 11), case definitions were adequate and the diagnoses were also independently validated in all but one instance (Hergens et al., 2005). The methods used for case selection had minimum risk of bias in all included studies – either all eligible cases over a defined time period or a representative series of cases were selected. In only one study, the authors described additional efforts made to identify deaths in rural settings in

India, as registration of death was reported to be less than 60% complete (Gajalakshmi and Kanimozhi, 2015). Control selection was limited to hospital controls in only one study (Rahman and Zaman, 2008), and the control participants had no history of disease outcome in general. However, in one study, adult injury deaths were selected as controls for stroke cases, with no mention of history of stroke in control participants (Mateen et al., 2012).

All case-control studies had controlled for potentially confounding variables. However, there were variations in the controlling factors measured. While exposure to smoked tobacco was controlled for in all studies that included smokers, use of alcohol was not measured in many of the studies. The ascertainment of exposure was mostly measured through self-report, and even in studies that used structured interviews, the interviewers were not blinded to the case/control status of study participants. However, in all studies, the same methods were used for exposure ascertainment among both cases and controls. With regard to non-response rates, they were either not mentioned or inadequately described in six studies (Huhtasaari et al., 1992, Teo et al., 2006, Wennberg et al., 2007, Rahman and Zaman, 2008, Mateen et al., 2012, Rahman et al., 2012b). The remaining case-control studies (5/11) either reported low rates of non-response or comparable rates between the two groups.

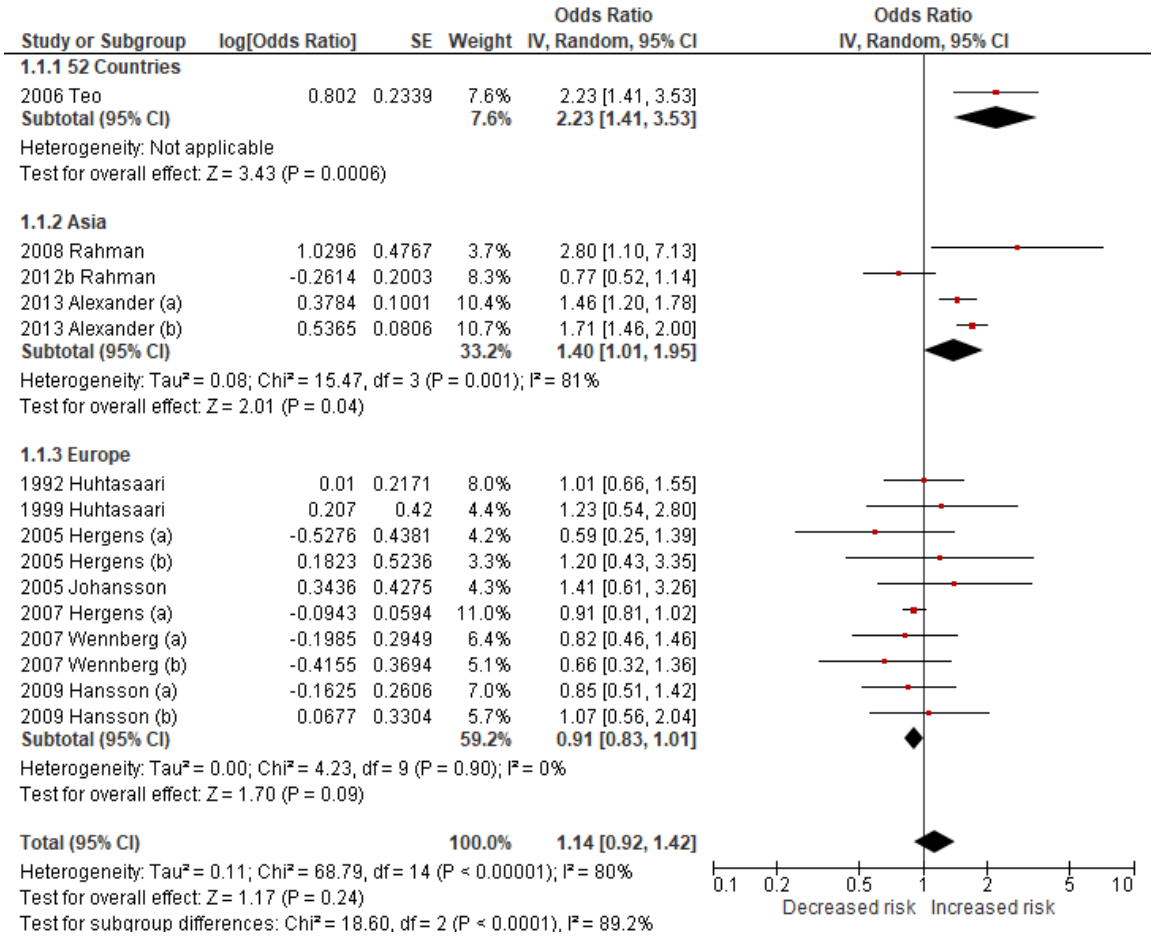
Cohort studies: Of the nine cohort studies included in the review, four drew responses from select participant groups – three from Swedish construction workers (Bolinder et al., 1994, Hergens et al., 2007, Hergens et al., 2008), and one from twins in Sweden (Hansson et al., 2009). The remaining studies were all based on representative cohorts of participants recruited from the community. In all the included studies, non-exposed cohorts were enrolled from the same setting as exposed cohorts. The ascertainment of exposure was through self-report in all but three studies, which used structured interviews for measuring ST consumption (Gupta et al., 2005, Johansson et al., 2005, Hansson et al., 2009). The disease outcomes measured were clearly not present at the start of the study in all included cohorts.

Similar to what was found with the case-control studies, the cohort studies either studied exclusive ST users or controlled for exposure to smoking forms of tobacco; there were wide variations in the adjustments for other potential confounding factors, and inadequate measurement of alcohol consumption. Disease outcomes were assessed through record linkages in all studies and the period of follow-up was 12 years or more in all but two studies (Gupta et al. (2005) – 5-6 years, and Hansson et al. (2009) – 4.9 years on average). While the majority of included studies reported minimal or no loss to follow up, there was no statement about the adequacy of follow-up in one study (Hansson et al., 2009).

5.2.3 Risk of incident IHD

The summary results for incident cases of IHD were based on 15 risk estimates – one from across 52 countries, four from Asia (2 – Bangladesh, 2 – Pakistan), and ten from Europe (10 – Sweden). The forest plot of this analysis is shown in Figure 5.2.

Figure 5.2 Forest plot of comparison: Ever use of ST with incident IHD



2013 Alexander (a) – Dippers, and 2013 Alexander (b) – Chewers

2005 Hergens (a), 2007 Wennberg (a), and 2009 Hansson (a) – Current ST Users

2005 Hergens (b), 2007 Wennberg (b), and 2009 Hansson (b) – Former ST Users

2007 Hergens (a) – Risk of IHD

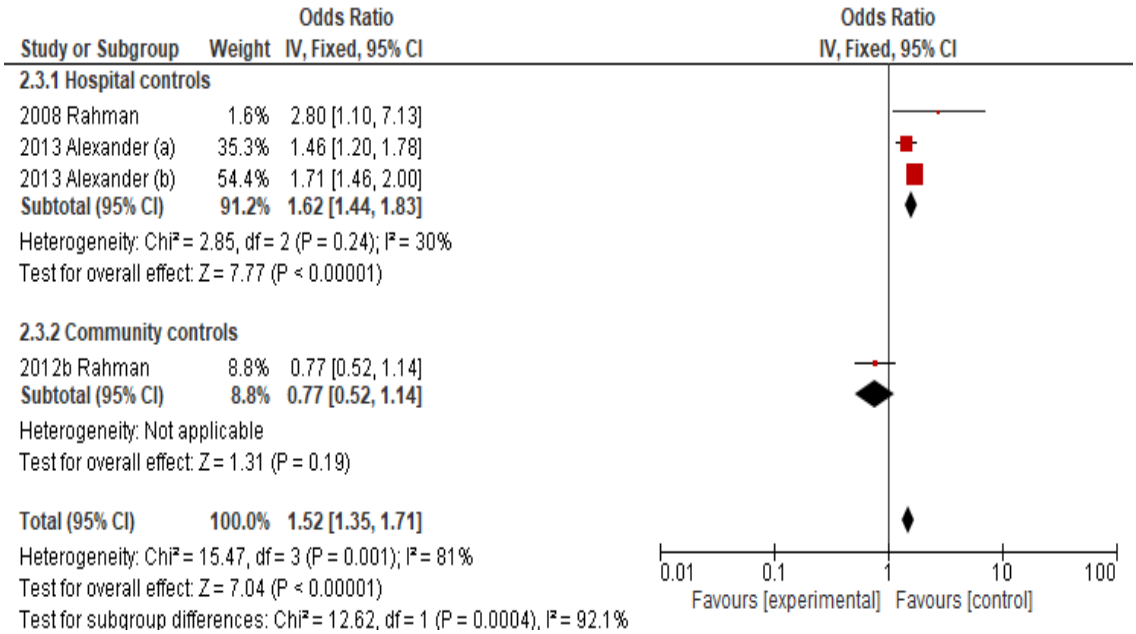
Abbreviations: SE – Standard Error, IV – Inverse Variance, CI – Confidence Interval, ST – Smokeless Tobacco, IHD – Ischaemic Heart Disease

The random-effects meta-analysis for incident IHD comparing ever use of ST to no tobacco use showed an overall risk of 1.14 (95% CI = 0.92, 1.42). Although the overall analysis showed strong evidence of heterogeneity (I^2 = 80%), statistical testing for differences across geographical subgroups was also highly significant (χ^2 = 18.60, df = 2, p < 0.01), which likely explained a considerable amount of the heterogeneity found.

The region-specific risk estimates showed that studies from Europe had no association between exposure and outcome (RR = 0.91, 95% CI = 0.83, 1.01), whereas studies from Asia showed a significantly increased risk of incident IHD among ever ST users compared to non-tobacco users (RR = 1.40, 95% CI = 1.01, 1.95). The risk reported in the INTERHEART study, in which ST use was mainly reported from South Asian countries, was also significantly increased (RR = 2.23, 95% CI = 1.41, 3.53).

Within the regional subgroups considered, there was no evidence of heterogeneity among the European studies (I^2 = 0%). but strong evidence of heterogeneity was found among the studies included from Asia (I^2 = 81%). Further analyses to explore the likely sources of this finding showed that differences in study settings, particularly the settings from which control participants were selected, accounted for at least some of the heterogeneity found among the Asian studies included (χ^2 = 12.62, df = 1, p < 0.01). While all four studies within this geographical subgroup were case-control studies and recruited hospital-based control participants, Rahman et al. (2012b) additionally recruited community-based control subjects to measure the risk of association between exposure and outcome (Figure 5.3). Beyond this, no other factors such as differences in country of research (χ^2 = 0.06, df = 1, p = 0.81), or mean age of study participants (χ^2 = 1.67, df = 1, p = 0.20), were found to account for any of the heterogeneity found (Appendix 5.5).

Figure 5.3 Heterogeneity among Asian studies reporting incident IHD

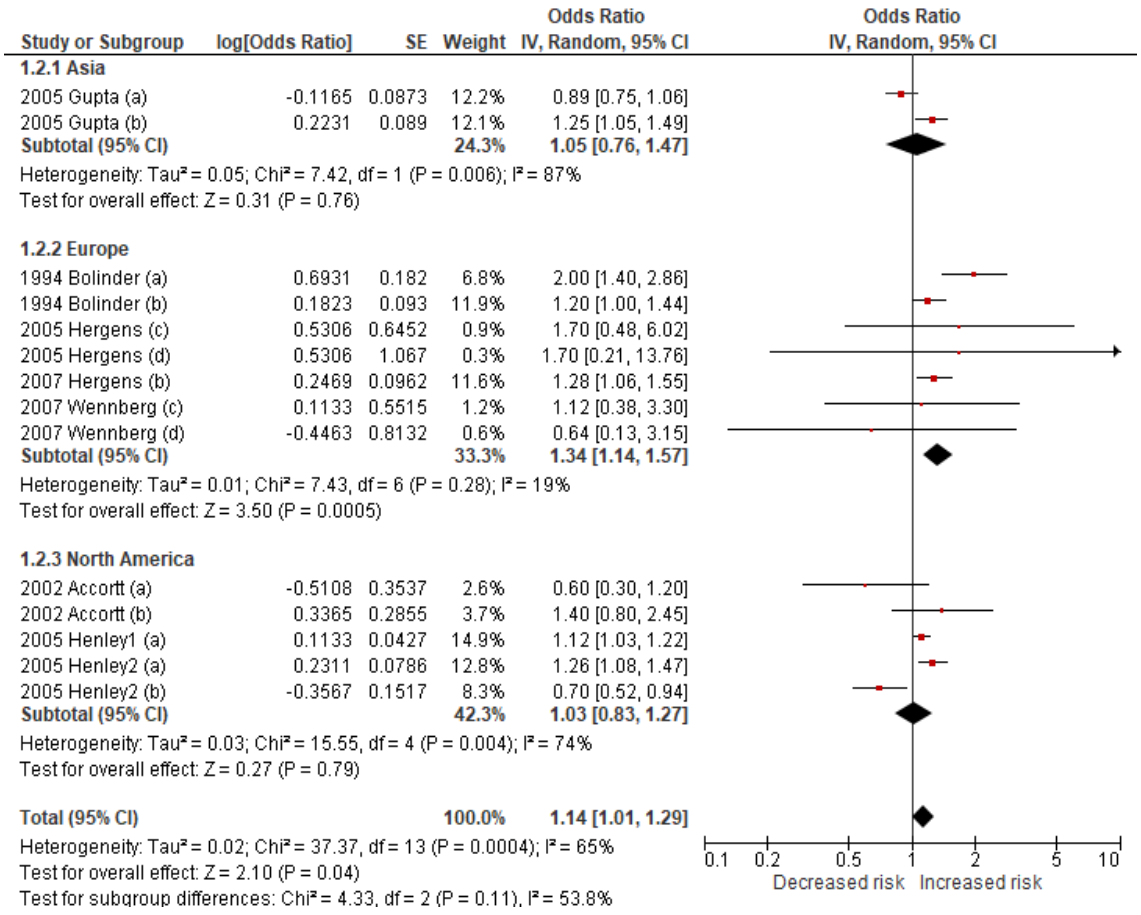


2013 Alexander (a) – Dippers, and 2013 Alexander (b) – Chewers

5.2.4 Risk of fatal IHD

The results for fatal IHD (Figure 5.4) were based on 14 risk estimates – two from Asia (both from India), seven from Europe (all from Sweden), and five from North America (all from USA). These results showed an overall increased risk for fatal IHD associated with the ever use of ST products compared to no tobacco, which was statistically significant (RR = 1.14, 95% CI = 1.01, 1.29). However, there was evidence of considerable heterogeneity among the studies included in this outcome category (I^2 = 63%), which could not be explained on the basis of geographical subgroups (χ^2 = 4.33, df = 2, p = 0.11).

Figure 5.4 Forest plot of comparison: Ever use of ST with fatal IHD



2005 Gupta, 2002 Accortt (a) & (b) – Risk among men and women

1994 Bolinder (a) & (b) – Risk among 35 – 54 and 55 – 65 year olds

2005 Hergens, 2007 Wennberg (c) & (d) – Risk among current and former ST users

2007 Hergens (b) – Risk of fatal IHD

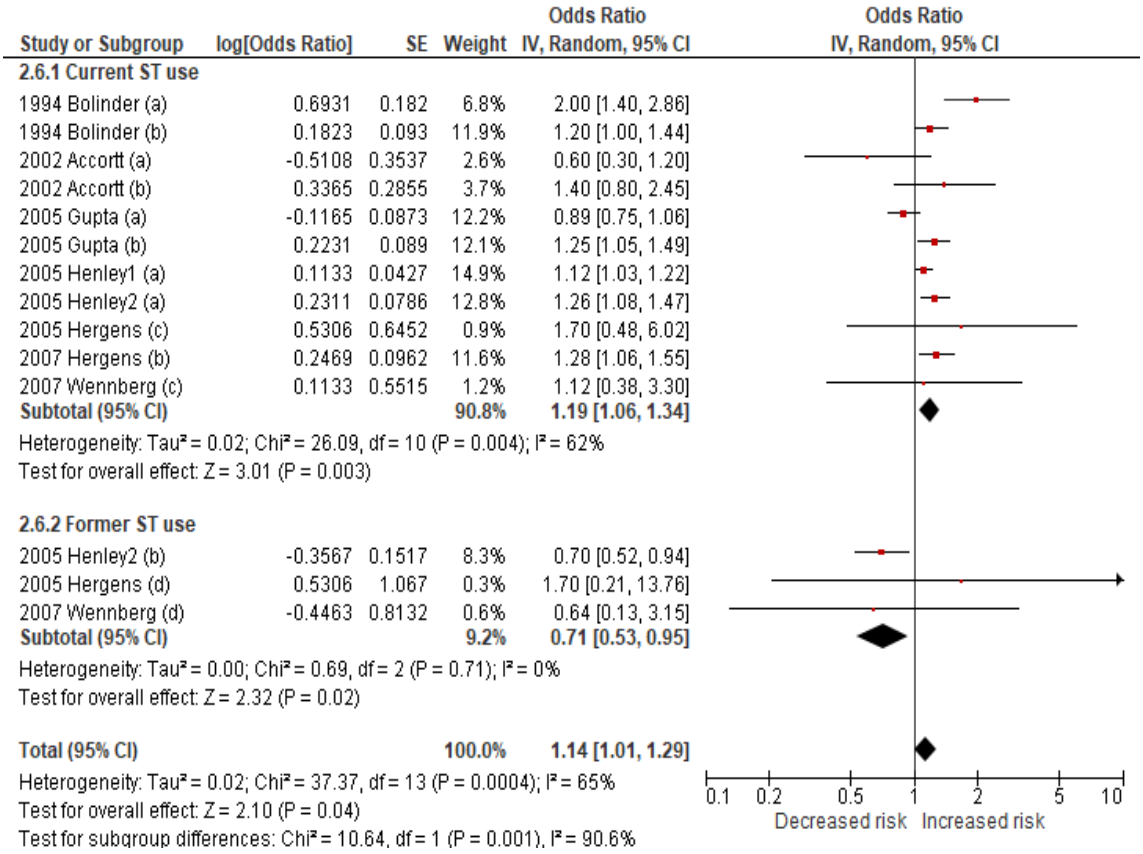
2005 Henley1 (a) – Risk of fatal IHD from CPS-I

2005 Henley2 (a) & (b) – Risk among current and former ST users from CPS-II

Abbreviations: SE – Standard Error, IV – Inverse Variance, CI – Confidence Interval, ST – Smokeless Tobacco, IHD – Ischemic Heart Disease, CPS – Cancer Prevention Study

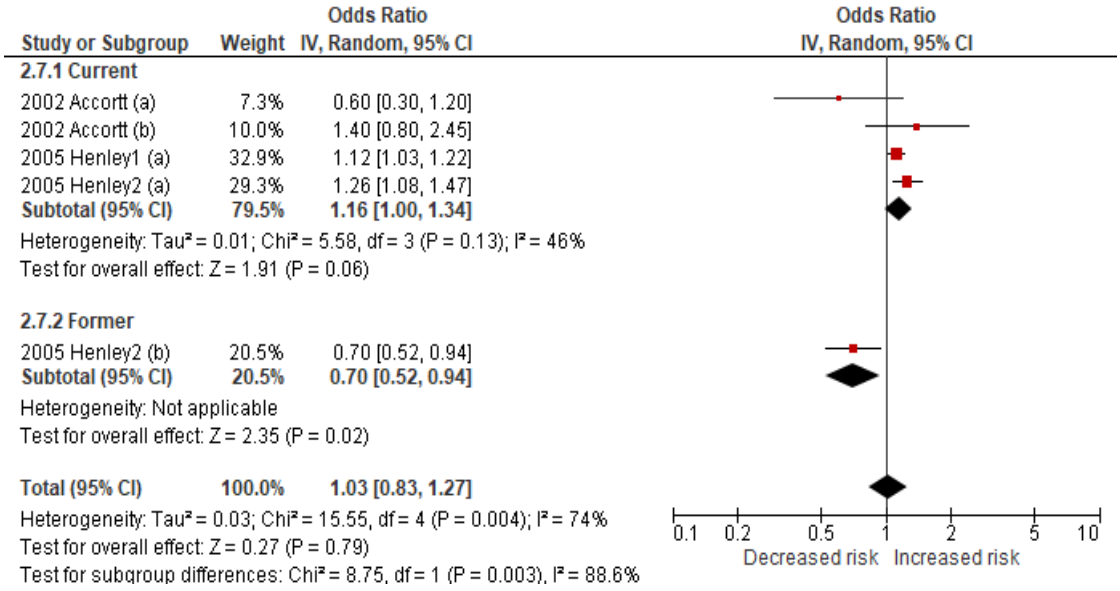
Further analyses to identify other likely sources of heterogeneity showed that subgroup differences were statistically significant for current versus former use of ST products ($\chi^2 = 10.64$, df = 1, $p < 0.01$) (Figure 5.5), but not for other factors considered such as differences in study design ($\chi^2 = 0.02$, df = 1, p = 0.89), or gender of study participants ($\chi^2 = 1.24$, df = 1, p = 0.27) (Appendix 5.5).

Figure 5.5 Heterogeneity among studies reporting fatal IHD



Within the geographical subgroups in this outcome category, significantly increased risk of fatal IHD was only found among the European studies (RR = 1.34, 95% CI = 1.14, 1.57), but not the Asian (RR = 1.05, 95% CI = 0.76, 1.47), or American studies (RR = 1.03, 95% CI = 0.83, 1.27). In addition, there was evidence of minimal heterogeneity among the European studies ($I^2 = 19\%$), but considerable heterogeneity among the Asian ($I^2 = 87\%$) and American studies ($I^2 = 74\%$). While the heterogeneity observed between the Asian studies could likely be explained on the basis of gender (the two included estimates were for male and female participants from a single study), the same was not found for the American studies ($\chi^2 = 1.16$, df = 1, p = 0.26) (Appendix 5.5). However, subgroup analysis according to current versus former ST use resulted in a significant test for difference among the American studies included ($\chi^2 = 8.75$, df = 1, $p < 0.01$) (Figure 5.6).

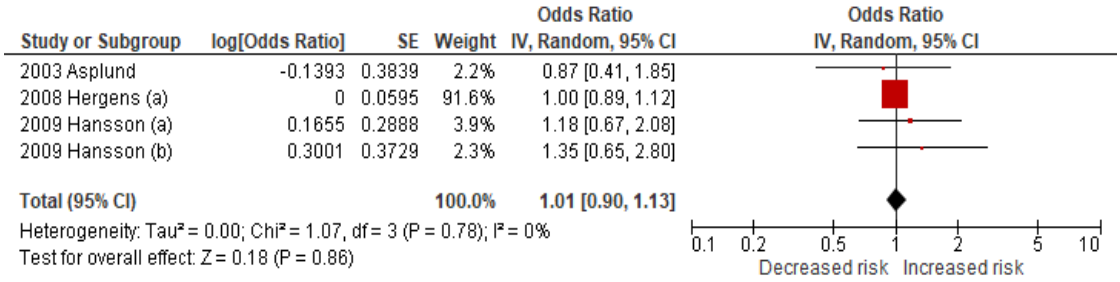
Figure 5.6 Heterogeneity among American studies reporting fatal IHD



5.2.5 Risk of incident stroke

On the basis of four risk estimates from Sweden, the overall RR for incident stroke was 1.01 (95% CI = 0.90, 1.13), with no evidence of heterogeneity between the included studies (Figure 5.7).

Figure 5.7 Forest plot of comparison: Ever use of ST with incident stroke



2008 Hergens (a) – Risk of stroke

2009 Hansson (a) & (b) – Risk among current and former snuff users

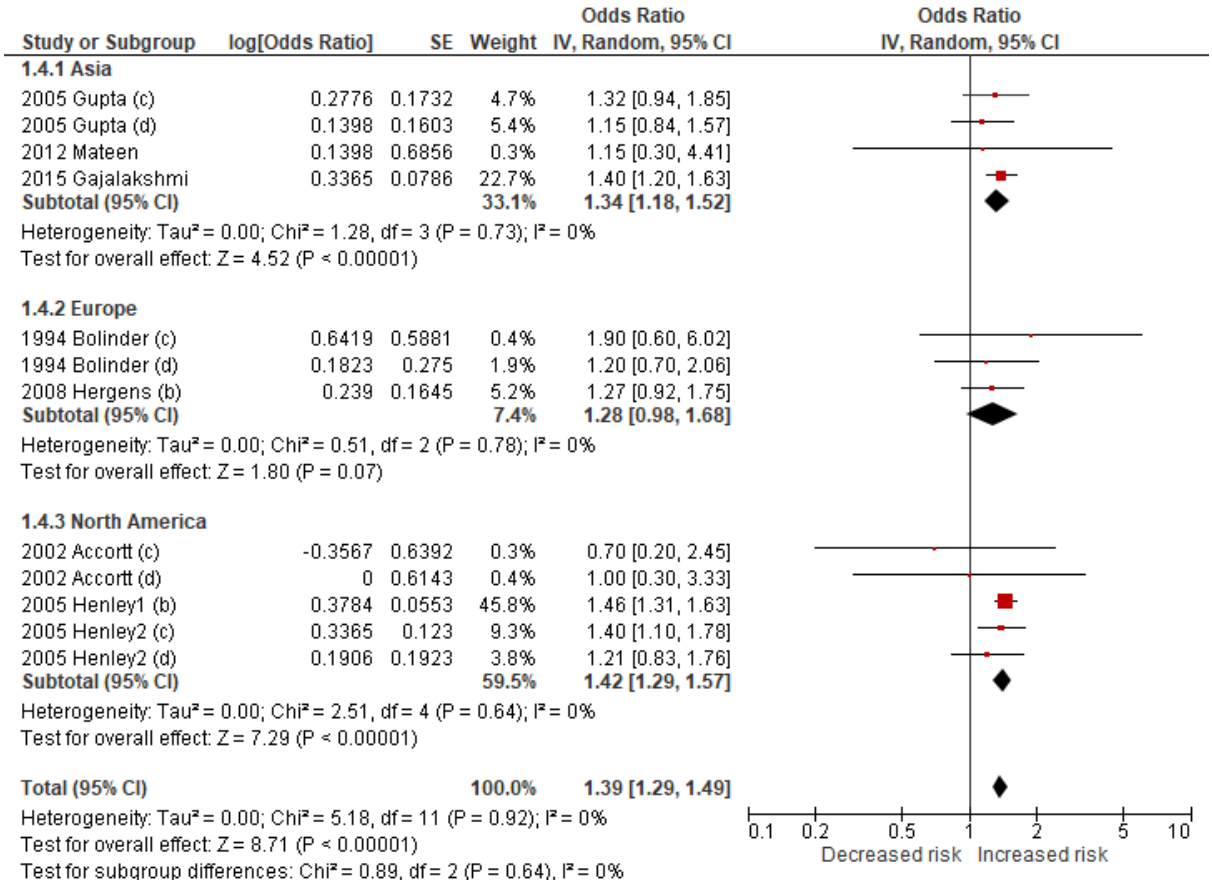
Abbreviations: SE – Standard Error, IV – Inverse Variance, CI – Confidence Interval

5.2.6 Risk of fatal stroke

In the final meta-analysis (Figure 5.8), pooled risk of fatal stroke was calculated from 12 estimates, which included four estimates from Asia (3 – India, 1 – Bangladesh), three from Europe (all from Sweden), and five from North America (all from USA). Similar to the results of fatal IHD, the overall risk of fatal stroke showed a significant positive effect in ever ST users compared to non-tobacco users (RR = 1.39, 95% CI = 1.29, 1.49). Although increased risks were found in

all the geographical subgroups considered, the results were statistically significant among Asian (RR = 1.34, 95% CI = 1.18, 1.52) and American studies (RR = 1.42, 95% CI = 1.29, 1.57), but not among the Europe studies (RR = 1.28, 95% CI = 0.98, 1.68). There was also no evidence of heterogeneity, both overall and within the geographical subgroups.

Figure 5.8 Forest plot of comparison: Ever use of ST with fatal stroke



2005 Gupta, 2002 Accortt (c) & (d) – Risk among men and women

1994 Bolinder (c) & (d) – Risk among 35 – 54 and 55 – 65 year olds

2008 Hergens (b) – Risk of fatal stroke

2005 Henley1 (b) – Risk of fatal stroke from CPS-I

2005 Henley2 (c) & (d) – Risk among current and former ST users from CPS-II

Abbreviations: SE – Standard Error, IV – Inverse Variance, CI – Confidence Interval, ST – Smokeless Tobacco, CPS – Cancer Prevention Study

5.2.7 Risk of publication bias

Visual inspection of funnel plots did not show any obvious evidence of publication bias for any of the study outcomes considered (Appendix 5.6).

5.3 Discussion

The findings of this review are important because to my knowledge, this is the first systematic review and meta-analysis on the topic which included studies from Asia. Additionally, the review found differences by geographical regions for ST-related risks of incident IHD, which had not been previously reported. In the following subsections, I summarise the main findings of my systematic review and meta-analyses and interpret them within the wider context of other published literature on this topic. I then reflect on the strengths and limitations of my review methodologies, and consider the implications of my findings for practice, policy, and future research on the topic.

5.3.1 Summary of main findings and comparisons with previous reviews

This systematic review of global literature on ST-related risk of CVDs found that ever use of ST products was associated with a 14% increased risk of incident IHD (pooled RR = 1.14, 95% CI = 0.92, 1.42), and a 14% increased risk of IHD deaths (pooled RR = 1.14, 95% CI = 1.01, 1.29). However, only the latter association reached statistical significance. With regard to stroke outcomes, ever use of ST was significantly associated with an increased risk of fatal stroke (pooled RR = 1.39, 95% CI = 1.29, 1.49), but not with stroke incidence (pooled RR = 1.01, 95% CI = 0.90, 1.13). With the exception of incident IHD risks associated with ST use, the other findings of this meta-analysis were largely comparable to the only previous meta-analysis on this topic, which was limited to American and European studies (Boffetta and Straif, 2009).

For both fatal disease outcomes (IHD and stroke), the magnitude of excess risk did not differ much between the two meta-analyses, despite the inclusion of additional estimates from Asian studies (two for fatal IHD and four for fatal stroke). The current meta-analysis also excluded one European study reporting fatal IHD outcomes which was included in the previous review (Haglund et al., 2007), because the ST product use reported in this study did not appear to be exclusive, with no control for smoking in their analysis. With regard to incident stroke, only one new estimate from Sweden was identified and included from studies published since the previous review (Hansson et al., 2009). This meant that all the studies in this outcome category were still limited to the European region, and showed no association between ever use of ST and incident stroke within that geographical setting.

On the other hand, the pooled risk estimates for incident IHD differed between the two reviews, with the previous review finding no association with ever ST use (pooled RR = 0.99, 95% CI = 0.89 – 1.10) (Boffetta and Straif, 2009). Although the current meta-analysis included two additional studies from Europe reporting incident IHD outcomes (Johansson et al., 2005, Hansson

et al., 2009), the main reason for the difference in findings appeared to be the inclusion of three studies from Asian countries, specifically SA (Bangladesh – Rahman and Zaman (2008) and Rahman et al. (2012b), and Pakistan – Alexander (2013)), and one study conducted across 52 countries, in which ST use was predominantly reported from South Asian countries (Teo et al., 2006). Within the South Asian subgroup, ever use of ST was found to be associated with a 40% increased risk of incident IHD (pooled RR: 1.40, 95% CI = 1.01, 1.95), while the INTERHEART study also reported a substantially increased risk for this disease outcome (RR = 2.23, 95% CI = 1.41, 3.53). Comparable to the findings reported by Boffetta and Straif (2009), the studies included from the European region showed no association between ever use of ST (mainly snus) and IHD incidence (pooled RR = 0.91, 95% CI = 0.83, 1.01). With regard to the additional studies from Europe included in the current meta-analysis, one was published since the previous review (Hansson et al., 2009), while it is not entirely clear why the second study was not included in earlier estimates (Johansson et al., 2005). There were no American studies identified within this outcome category.

5.3.2 Interpretation of findings

It is likely that the geographical variations in the ST-related risk of incident IHD highlights a truly increased risk for ST users in SA, as supported by the following related evidence. First, it is likely that the increased risk of incident IHD reported in the INTERHEART study reflects the increased risk within SA, as the use of ST in the case-control study was mainly reported from countries within this geographical region (Teo et al., 2006). Second, the methodological quality of all the included studies that were used to arrive at this conclusion appears to be adequate, which adds further credibility to the interpretation. Third, global reviews on the risk of ST-related cancers report similar differences in risk between SA and other geographical regions, with substantially higher risks for South Asian ST users (Asthana et al., 2018). These differences are largely thought to arise from geographical differences in ST product types consumed (Awan and Patil, 2016), and supported by findings of laboratory testing of different ST products for their levels of chemical carcinogens. South Asian ST products such as zarda, khaini, and gutkha, are reported to have some of the highest TSNA levels among various ST products tested from different geographical regions (Stanfill et al., 2010). Finally, the available evidence on increased blood pressure, a strong predictor of developing CVDs including IHD and stroke, also appears to suggest geographical variations in risk, similar to what was found in this review. While the American and European studies fail to show an increased risk of HT among ST users (Piano et al., 2010), South Asian studies from India report significantly higher prevalence of HT among ST users compared to non-tobacco users within the study settings (Gupta et al., 2007, Pandey et al., 2009). Any geographical variations in risk of ST-related stroke incidence could not be assessed due the lack of studies from outside the European region.

Based on overall pooling of study estimates reporting fatal CVD outcomes, the findings suggest that ST products can be a risk factor for poorer prognosis among patients with IHD and stroke, even though they may not be a significant risk for disease incidence in all geographical regions. With regard to fatal stroke, the pooled risk estimates did show a substantial increase in all geographical subgroups considered, although statistical significance was reached only among studies included from Asia (pooled RR: 1.34, 95% CI = 1.18, 1.52) and America (pooled RR: 1.42, 95% CI = 1.29, 1.57), not Europe (pooled RR = 1.28, 95% CI = 0.98, 1.68). The Asian studies showed a 34% increased risk and the American studies showed a 42% increased risk for fatal stroke among ever ST users compared to non-tobacco users within their respective geographical settings. On the other hand, the pooled risks within geographical subgroups for fatal IHD were only significantly increased among European studies (pooled RR = 1.34, 95% CI = 1.14, 1.57), while no association was found among the Asian (pooled RR = 1.05, 95% CI = 0.76, 1.47) and American studies (pooled RR = 1.03, 95% CI = 0.83, 1.27). Nevertheless, the risk associated with ST use for fatal IHD cannot be ruled out within Asian contexts, as the finding reported was only based on one study from India (Gupta et al., 2005).

5.3.3 Plausibility of findings

Several chemical constituents in tobacco products such as nicotine, polycyclic aromatic hydrocarbons (PAHs,) and heavy metals have been implicated in tobacco-related cardiovascular health effects. For example, PAHs have been shown to accelerate atherosclerosis in experimental animals, and heavy metals such as cadmium can catalyse the oxidative processes of cellular proteins and produce components which can then accumulate and injure endothelial surfaces within aortic vessel walls (USDHHS, (2010)).

While these explanations are applicable to all forms of tobacco, discussions around the biological plausibility of ST-specific CVD risks are largely limited to the European literature, and tend to focus on the role of nicotine in increasing CVD risks (Hergens et al., 2007, Hergens et al., 2008, Boffetta and Straif, 2009). More specifically, the studies limit their considerations to how nicotine can increase the severity of IHD and stroke outcomes, and thereby worsen disease prognosis. But other studies on the use of nicotine-only patches in patients with known CVDs have reported improvements in existing disease conditions (Mahmarian et al., 1997). In addition, ST products contain many different chemical constituents besides nicotine, making it much more likely that the increased CVD risks for ST users are due to the combined effect of other chemicals with nicotine, rather than due to nicotine acting alone. Given the wide geographical variations in ST products consumed, including their chemical constituents, additives, and methods of preparation and use, it is highly likely that South Asian ST products contain substances that are more toxic to

cardiovascular health than products consumed in other regions. The available evidence also points to higher levels of total and free nicotine in commonly used South Asian ST products (Brunnemann et al., 1985), with greater levels of alkalinity that can enhance the absorption of nicotine and other harmful chemicals (Stanfill et al., 2010). These factors likely explains some of the geographical differences in the CVD risks associated with the use of ST products, although further characterisation of more ST products are needed to specifically examine the type of toxins in different products that can have an influence on cardiovascular risks.

5.3.4 Strengths and limitations

The strengths of this review include the thoroughness of the search strategies employed, the explicit criteria set out for inclusion of studies with regard to study design, exposure, and outcome, and the adequate methodological quality of all the studies included in the meta-analyses. Only longitudinal studies which provided a clear direction of association between ST use and CVD outcomes were included. Just as importantly, clear definitions regarding exposure to ST products meant that the pooled risks estimated were specific to exclusive consumption of ST products, as opposed to any other forms of tobacco.

But besides the strengths, the following limitations should be considered in interpreting the study findings. First, with regard to exposure, the results were pooled across different types of ST products consumed by study participants. Although analyses based on geographical subgroups likely addressed this limitation to some extent, ST products are known to vary even within geographical regions, particularly in South Asian countries. Apart from some European studies that specified the use of snus, the other included studies measured exposure to all ST products. This meant that pooled risks could not be estimated according to specific types of ST products consumed. Given the different types of ST products measured and other variations between the pooled studies (e.g. study designs), some level of heterogeneity was anticipated. However, evidence of heterogeneity was limited to the two meta-analyses involving IHD outcomes, and largely explained by additional analyses carried out to identify their likely sources. A further limitation with regard to exposure measurement was that information on ST use was collected only at baseline and not updated during follow-up among the cohort studies included.

With regard to study outcomes, the lack of studies on ST-related stroke incidence from outside the European region limited the assessment of risk for this disease outcome from other geographical regions. Specific to fatal outcomes, particularly among the Asian and American studies, the reliance on death certificates or similar record-based information for outcome ascertainment meant that some of the deaths were not necessarily first occurrences of the diseases and did not represent true incidence.

A further limitation could be related to exposure misclassification, particularly because the measurement of ST use was solely through self-report in all the included studies. However, this was most likely non-differential and biased the effect sizes towards the null. The possibility of misclassification bias arising from differences in disease definitions is unlikely, although it cannot be entirely ruled out.

There were additional limitations in relation to controlling for confounding factors between exposure and outcome variables. Although potential confounding by smoking was adequately accounted for by restricting the analysis to never smokers or including only smoking-adjusted estimates of risk, the same cannot be said for alcohol use, as most of the included studies did not measure exposure to alcohol among study participants. Similarly, it was not possible to assess the effects of other potential confounders such as blood pressure, serum lipids, BMI, diabetes, etc., as there was no uniformity among the included studies in adjusting for these variables. Moreover, some of these adjusted factors were likely in the causal pathway, and thereby resulted in conservative estimates of risk. Also, with regard to sociodemographic variables such as age and gender, sufficient data were not available to create distinct groups and assess if the CVD risks associated with ST use differed across different sociodemographic groups. The possibility of further confounding by unmeasured and unknown variables also cannot be ruled out.

Although the methodological quality of the included studies was largely assessed to be adequate using the NOS (Wells et al., 2000), the validity of the quality assessment scale used has been questioned (Stang, 2010). Moreover, differences in NOS scores have been noted between reviewers and authors, suggesting the need to contact authors for details not included in the publications when applying the NOS tool in systematic reviews (Lo et al., 2014). While some study authors were contacted for clarification of methodologies in this review, this was not done in relation to quality assessment of the included studies.

Finally, although the funnel plots for the four meta-analyses showed distributions that were largely symmetrical, it is possible that publication bias accounted for some of the associations within the geographical subgroups considered.

5.3.5 Implications of findings

With the inclusion of risk estimates from SA, the main finding of this review is that ST-related risk of incident IHD shows considerable variations by geographical regions, with increased risks for users in SA, not found in European settings. The use of ST products also appears to worsen prognosis for patients with IHD and stroke, including within South Asian settings.

The implications of these findings, specific to South Asian contexts, are discussed below.

5.3.5.1 For practice

Given the high prevalence of ST use in South Asian countries, health practitioners are highly likely to encounter users within their clinical practices, and have an important role in influencing their ST use behaviours. However, there is a lack of awareness among health professionals about ST forms of tobacco and its associated harms, with many physicians and frontline health workers in India advising smokers to switch from cigarettes to ST products to aid with smoking cessation (Panda et al., 2013, Panda et al., 2015b). The findings of this review support that ST products in SA can have serious cardiovascular consequences for users and cannot be used as a harm reduction tool for smoking cessation.

5.3.5.2 For policy

The policy implications of the review findings can extend to different aspects of policy such as ST prevention and cessation, raising public awareness about the harm of ST use, as well as ST product regulations. The main findings of the review suggest that addressing ST use could contribute to reduced mortality from IHD and stroke, as well as the prevention of IHD incidence within South Asian settings. While these findings have direct implications for ST prevention and cessation policies, the overall evidence from interventions directed at ST forms of tobacco is limited, and further complicated by factors such as ST product heterogeneity and variations in contexts of use (Siddiqi et al., 2016a). World over, tobacco cessation support remains the most poorly implemented policy measure, with poorer countries having lesser cessation support than high-income countries (Nilan et al., 2017). In addition to ST cessation policies, the review findings may also have some implications for policies that aim to raise public awareness, as well as educate health professionals regarding the cardiovascular risks associated with ST use.

Moreover, there is a lack of regulation of South Asian ST products, whereas the Swedish snus products adhere to a voluntary form of industry self-regulation of manufacturing and storage that is intended to reduce the levels of carcinogens and other harmful substances (NCI and CDC (2014)). Although the regulatory standards were only formally introduced in the late 1990s, measures to reduce unwanted substances in Swedish snus have been successively introduced during the past 30 – 40 years (Rutqvist et al., 2011). These regulatory measures likely explain some of the geographical differences found in ST-related CVD risks, and suggest implications for regulating the contents of ST products in other geographical regions, including South Asia.

5.3.5.3 For future research

There is a need for more epidemiological studies on ST use and CVD risks that address some of the key limitations of the studies included in this review. All the included studies measured ST use at a single point in time, suggesting the need for studies that measure exposure to ST products at periodic intervals. This would help to better understand if ST use evolves over time and how that might affect the risk of developing CVD outcomes. In addition, it is important for future studies to adequately control for factors such as alcohol use that may confound or modify the association between ST use and CVD incidence. More studies on the risk of stroke incidence related to ST use are needed, particularly from within South Asian settings, to assess the presence and magnitude of associated risk from this geographical region.

Other implications for future research based on the findings of this review include further investigations into the constituents of South Asian ST products and the likely mechanisms and pathways through which their use can be linked with different CVD outcomes. These studies will help improve our understanding of the roles played by different chemical constituents in disease aetiology that likely need greater regulations.

Chapter 6. Overall Discussion and Conclusions

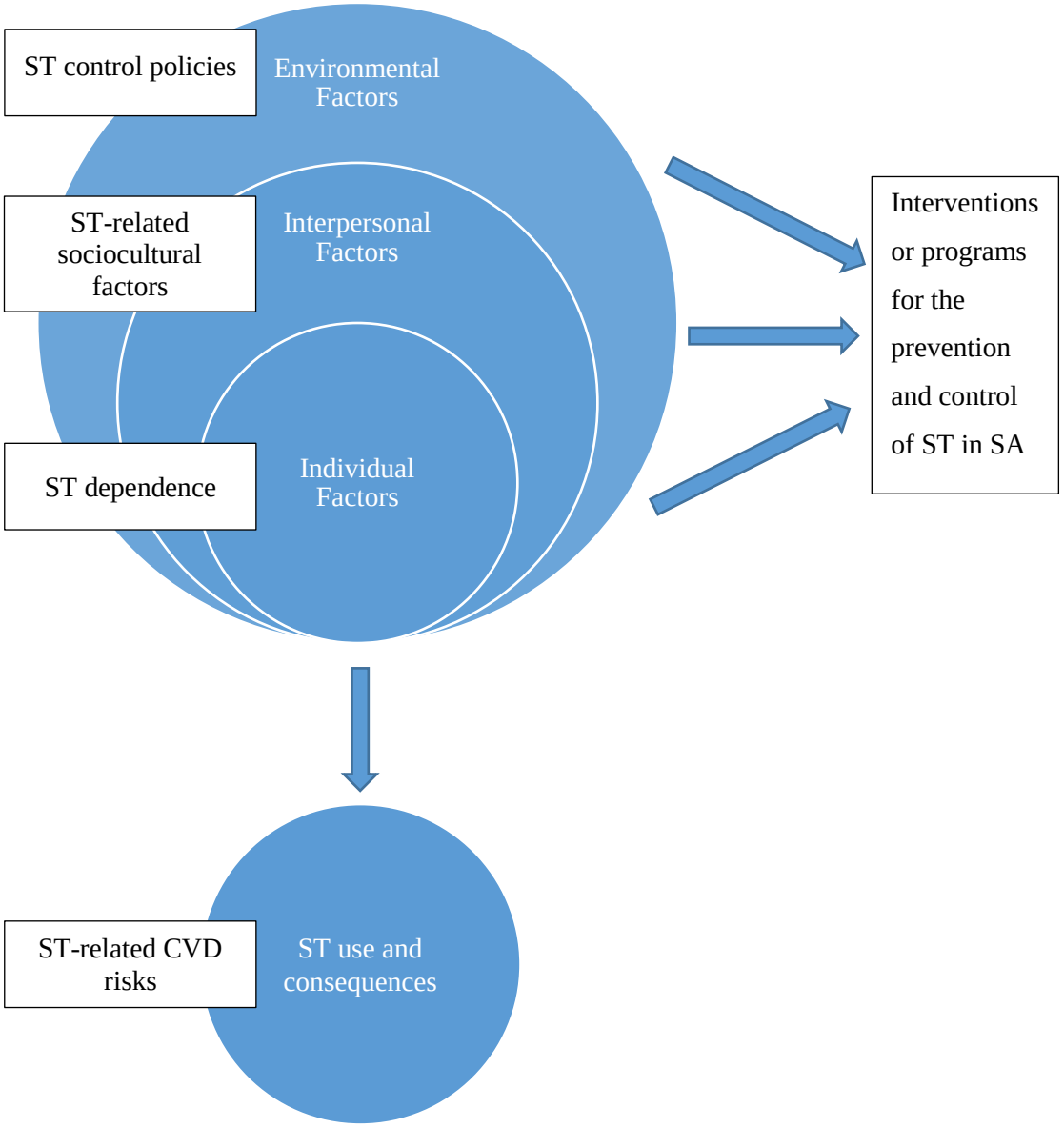
In this final chapter, I present a theory-based summary of the overall evidence from my thesis using the socioecological model of health behaviours (Section 6.1). Next, I discuss the strengths of my research (Section 6.2), including the importance and contributions of each study to ST research and control within South Asian contexts, as well as the originality and rigour of the three pieces of work. Then, I discuss the overall limitations of the research undertaken (Section 6.3), and finally, I end the thesis with some reflections on my learnings and overall conclusions (Section 6.4).

6.1 Summary of evidence using the socioecological model of health behaviours

Determinants of tobacco use are a mix of biological, psychological, sociocultural, and wider environmental factors, and various theories of tobacco use and quitting behaviours differ in the relative importance given to each of these factors and the inter-relationships between them (Greenhalgh, 2016). However, the more widely used theories such as the health belief model and theory of planned behaviour tend to place their emphasis on individual-level factors, while overlooking the ways in which environmental factors can influence tobacco use practices. Socioecological models on the other hand work by emphasising the role of multiple levels of influence on specific health behaviours such as tobacco use; accordingly, explicit consideration of all these different levels are needed to guide the development of comprehensive interventions for changing behaviours in a way that will achieve meaningful reductions in the prevalence of serious public health problems (Sallis et al., 2015). Interventions based on socioecological models would therefore typically be complex, multi-level (individual, interpersonal, organisational, community, and public policy influences), and multi-sectoral, with room for wider application and evaluation in public health research and practice (Glanz and Bishop, 2010).

Multi-level interventions across socioecological models have been recognised as vital for achieving major reductions in tobacco smoking across USA since the 1960s (Brandt et al., 2001). Specific to South Asian contexts, Arora et al. (2013) have developed an evidence-based framework (IMPACT) based on socioecological models for preventing and controlling tobacco use (smoking and smokeless) among children and adolescents in India. Based on extensive literature reviews and syntheses of published research, the IMPACT framework presents both risk factors and interventions at multiple levels, and suggests that implementing these interventions in a coordinated way would work synergistically, particularly in LMIC settings. However, much of the evidence is based on smoking studies, and the model is limited to children and adolescents.

Figure 6.1 Summary of research using a socioecological model of health behaviours



The research presented in this thesis adds evidence to multiple levels of a socioecological model of ST use among adult users in South Asian settings (Figure 6.1), where ST poses a significant threat to public health. At the individual level, results from the validation study showed strong dependence among adult ST users in India. Similar to results from Bangladesh (Mushtaq et al., 2019), relatively higher mean scores were obtained on the dependency scales compared to adult ST users in the United States (Mushtaq et al., 2014). While median cotinine levels were also found to be higher in the Bangladesh study compared to the United States, this was not possible to assess in my sample, due to the reasons described in Chapter 3 (Section 3.2.3.3). At the interpersonal level, ST use was found to be widely prevalent among close friends and family members of adult ST users interviewed in my study. Similar findings have been reported in other studies conducted across South Asian countries (Sreeramareddy et al., 2008, Shah et al., 2008, Sansone, 2014). However, I additionally found significant associations between sociocultural factors and a range

of ST use practices, including initiation, heaviness of current use, and quit practices. These associations have rarely been assessed in other works till date. At the wider environmental level, my review of existing research to inform the development and implementation of different ST control policies within the SA region showed several gaps, most notably for policies relating to ST cessation (FCTC Article 14) and supply-reduction (Section 1.5). Outside of the socioecological model, I also looked at the extent to which ST use contributed to CVD morbidity and mortality in South Asian settings, and found significantly increased risk for outcomes including incident IHD among South Asian ST users (Chapter 5).

6.1.1 Ramifications for public health practice and policy

There are important ramifications of these various findings for public health practice and policy, and those specific to each study have been discussed in previous chapters. In this subsection, I will focus on some additional aspects that may be more generally considered across the different research studies covered in my thesis.

Given the likely high dependence to ST products among users in South Asian settings, cessation interventions will play a vital role in reducing the ST-related public health burden. However, both globally and in SA, there is a dearth in the published literature from ST cessation intervention trials – studies are available from only 3% of WHO-FCTC ratified Parties, i.e. Sweden, Norway, India, United Kingdom and Pakistan, as well as USA (Nethan et al., 2018). Nevertheless, the results from these studies suggest that behavioural interventions would be an efficacious and feasible modality for ST cessation in both high and low resource settings (Ebbert et al., 2015, Nethan et al., 2018). Within this context, the findings from my thesis highlight the need to take account of sociocultural factors in developing and adapting behaviours change interventions for ST cessation among South Asian users. The training needs of healthcare providers and cessation practitioners in delivering these interventions should also be considered, given the low levels of preparedness among South Asian practitioners for providing ST cessation in clinical settings (Panda et al., 2015b).

In addition to individual-level approaches, ST use may also be influenced though community and policy-level approaches. While more research is needed to inform the most appropriate interventions for ST control at all levels of the socioecological model, the evidence presented in the IMPACT framework (Arora et al., 2013) suggests that interventions at each level would contribute to micro-level gains in reducing and preventing tobacco use, and these will in turn significantly reduce morbidity and mortality attributable to tobacco. This is also supported by the mathematical 'SimSmoke' model, which shows greater effectiveness of public polices in reducing tobacco use prevalence when used in combination (Near et al., 2013).

6.1.2 Recommendations for future research

The main areas of future research suggested by this thesis include a) further validation and scale developmental work to measure ST dependence in South Asian settings, b) testing the exploratory findings with regard to the sociocultural factors and their association with ST use and quit practices, c) investigations into the constituents of South Asian ST products and the likely mechanisms through which their use can be linked with different disease outcomes, and d) further research to inform policy development and implementation for ST control in South Asian settings. An interdisciplinary study titled 'ASTRA – Addressing Smokeless Tobacco and Building Research Capacity in South Asia', aiming to reduce the substantial burden of disease caused by ST use in South Asian settings is currently underway (Readshaw et al., 2020). This is a three year programme funded by the National Institute for Health Research, and will address some of the gaps in policy research identified in my thesis. I contribute to the policy study under ASTRA to further the research on this subject.

Overall, there is a need for prospective longitudinal studies on ST use; particularly for the first two points in the paragraph above, as these will help establish predictive validation of dependency scales, and also the direction of association for sociocultural influences on ST use practices. Furthermore, both the validation and sociocultural survey results were based on convenience sampling from a single setting, and should be carried out in other settings and populations to improve the generalisability of findings. Finally, one other additional area of focus would be to articulate and align my findings to models of behaviour such as COM-B, and the PRIME Theory of motivation linked to this model (West and Michie, 2020). This would be of particular use in assisting any future development of behaviour change interventions for ST control in SA that may build on my research findings.

6.2 Strengths of the research

Till date, the large majority of research on tobacco use has focused on cigarette smoking. Consequently, much less is known about ST forms and their use, especially in South Asian countries like Bangladesh and India. The public health problems due to tobacco faced by this geographical region cannot be fully appreciated unless these 'traditional forms' of tobacco are adequately represented in research and control activities. Furthermore, it is important to focus on ST for greater equity in tobacco research with regard to gender and socioeconomic status, given that ST use is more common among women in SA compared to tobacco smoking, and that the poorest of poor face the greatest disease burden from the use of ST products (Sinha et al., 2018a). As stated in Chapter 2, my research goal is to contribute new knowledge to some of the under-

researched aspects of ST use in South Asia. Given that these products represent the dominant form of tobacco in many South Asian settings, the exclusive focus on ST is among the key strengths of this work.

6.2.1 Importance of research and contributions

6.2.1.1 Study 1 – Validation of ST dependency scales

The validation study builds on a long history of research that focuses on the measurement of tobacco dependence. While considerable research continues to utilise traditional scales for measuring the construct, efforts have also been directed toward the development of multidimensional scales in the recent past, so as to better understand possible theories and mechanisms underlying tobacco dependence, which could in turn be used to improve treatment and future research (Piper et al., 2008b). Consequently, there are different types of tobacco dependence scales, with a varying range of clinical and research utility. The assessment of the psychometric properties of tobacco dependence scales that cover the range of available measures from a South Asian setting is an important contribution of this research. The focus was exclusively on ST use, given that the majority of global ST users live within this geographical region.

6.2.1.2 Study 2 – Associations between sociocultural measures and ST use characteristics

Besides gathering information on ST dependence, the survey conducted in New Delhi also covered sociocultural aspects of ST use. The findings based on the descriptive analyses of included items suggest that different sociocultural measures might be important for different demographic groups of ST users in South Asian settings. For example, ST use among close friends and ST use in company appear to be important measures among younger and male users, whereas ST use among family members and ST use within households are likely more important for older and female ST users. Additionally, the findings based on regression analyses demonstrate that sociocultural measures can influence ST use behaviours among adult users in the study settings. It is important to understand these effects, in order to develop interventions and strategies that can reduce ST use by targeting wider sociocultural factors.

6.2.1.3 Study 3 – Systematic review of CVD risks association with ST use

The recognition of ST use as a risk factor for adverse health outcomes is largely limited to oral cancers. However, there appeared to be an increased risk of IHD incidence linked with ST use (Teo et al., 2006), which was not found in existing meta-analysis of studies limited to European and American regions (Boffetta and Straif, 2009). Including studies from SA to better understand

the link between ST use and CVD risk is an important contribution of this research. The studies were identified through a systematic review of the evidence base. This work also contributed important information towards the first estimation of global burden of disease from the use of ST products (Siddiqi et al., 2015). The estimates indicate that in 2010, ST use led to 4.7 million DALYs lost and 204,309 deaths from IHD, with over 85% of this burden found in the South-East Asia region.

6.2.2 Originality

6.2.2.1 Study 1 – Validation of ST dependency scales

This is the first time that a comprehensive validation study of behavioural scales for measuring ST dependence has been carried out in India. Given the progress in ST dependence measurement in Western settings, I was able to identify existing scales, which I translated and cross-culturally adapted for use in my investigation. This approach also allowed the comparison of the scales' psychometric properties and ST dependency scores across different cultural contexts, which has rarely been undertaken till date (De Leon et al., 2013). Based on comparisons of internal consistency and construct validation measures, it may be said that the performance of the three scales in this study is largely comparable to findings from America. In addition, the comparison of scores suggest higher levels of dependence among ST users in India, similar to findings reported from Bangladesh (Mushtaq et al., 2019). However, neither this study, nor the Bangladesh study could replicate the original multifactorial structure model of the OSSTD measure (Mushtaq et al., 2014).

On the one hand, it is possible that this difference is due to the lack of achievement of linguistic equivalence of the translated scales. But similar translation methodologies applied to the FTND-ST items have still resulted in comparable factor structures across different study settings. This suggests other reasons beyond the translation of scale items for the differences in findings related to the OSSTD scale. In my administration of the measures, I found respondents often expressing difficulty in understanding the 7-point Likert scale. It is possible that a 5-point scale as used by Little et al. (2014) in the Reasons for Betel quid Chewing Scale (RBCS) might be better suited. It is also possible that this format does not work similarly when administered in face-to-face interviews, as opposed to respondents filling out self-administered questionnaires.

On the other hand, it is possible that the underlying motives of ST dependence in South Asian settings are different from those covered by the OSSTD measure. Based on the findings of this study, it may be said that the 'Weight control' subscale is weakly related to the construct of interest, at least among adult ST users. In addition, there may be other underlying constructs that

are more relevant to the development of ST dependence among South Asian users. An example of this is the sociocultural construct covered in the RBCS measure, which includes the following items – "All of my friends chew", "My family members chew", "It's rude not to chew", and "People will not respect me if I don't chew" (Little et al., 2014). My findings based on the study of sociocultural measures suggest that this could be an important construct to include in future measurement scales of ST dependence in South Asian settings.

6.2.2.2 Study 2 – Associations between sociocultural measures and ST use characteristics

My analyses of sociocultural measures relating to ST use in SA contributes new knowledge by describing some factors that have not been previously reported from these settings. In studies conducted till date (Ray et al., 2016, Hussain et al., 2017), the focus has been on ST use by close friends and family members, and my findings on these measures are largely comparable to the existing evidence – ST users are significantly more likely to have ST users among their close contacts. However, the questionnaire in this study additionally included two further sociocultural measures, namely 'ST use in company' and 'household permissibility of ST use'. With the inclusion of these measures, this research uncovered that there are likely social users of ST products, similar to social smokers described by Moran et al. (2004). In addition, a significant association was found between ST use among close family members and household permissibility, suggesting a second distinct social pattern of ST use in the study settings.

Recently, some efforts have been made to study the associations between sociocultural measures and quit practices among ST users in South Asian settings (Sansone, 2014, Schensul et al., 2018). Nevertheless, my study is the first to explore the associations with a range of ST use characteristics, including initiation, intensity of current use, as well as quit practices. The findings based on regression analyses indicate that ST use among close friends and household permissibility are significantly associated with fewer quit attempts made and weaker quit intentions among adult users. These findings have important implications for ST cessation strategies and interventions in South Asian settings, which need to account for sociocultural measures in order to be more effective.

6.2.2.3 Study 3 – Systematic review of CVD risks association with ST use

The evidence from SA on ST-related CVD risks had not been systematically reviewed, and the studies from this geographical region were not included in global reviews on the topic. Given this background, I updated the systematic review on the association between ever use of ST and risk of CVDs, with no geographical restrictions on inclusion criteria. To my knowledge, this is the first systematic review to identify geographical variations in ST-related risk of IHD incidence.

While studies from European and American regions did not find an association, a 40% increased risk of incident IHD was calculated from studies conducted in South Asian countries. This also supports evidence from reviews of ST-related cancers, which report higher risks in South Asian countries compared to other geographical regions, likely linked with differences in ST products consumed in different regions.

6.2.3 Rigour

A key strength of my doctoral work is the systematic methods used in each of the studies carried out. Organised methods in data collection and management also ensured no data loss and very little missing data overall.

6.2.3.1 Study 1 – Validation of ST dependency scales

In the case of the validation study, without an informed overview of the existing scales for measuring ST dependence, it would not have been possible to select scales that covered the range of measurement types for inclusion in my analysis. Furthermore, this understanding allowed for the inclusion of scales that are likely to have applications in both clinical and research settings. Although the FTND-ST measure had been previously used in research studies conducted in SA (e.g. Jain et al. (2013)), it is not clear if rigorous steps were followed to achieve linguistic and cross-cultural equivalence of the scale. These steps were given careful consideration in this study. Each of the included measures was evaluated based on its internal consistency and correlation with other included measures. In addition, associations with tobacco dependence criteria such as frequency and quantity of current ST consumption were evaluated, and construct validation of the scales were established. However, criterion validation analyses could not be performed, and should be explored in future research. Similarly, future research must focus on predictive validation of the scales against clinically important dependence criteria such as cessation and withdrawal.

6.2.3.2 Study 2 – Associations between sociocultural measures and ST use characteristics

In the case of sociocultural measures, I wanted to cover previously assessed measures relating to peer and familial use of ST products. But in addition, this study took into account ST use in company and household permissibility of ST use – two potentially important measures as suggested by existing literature pertaining to tobacco smoking (Moran et al., 2004, Owusu et al., 2017). More groundwork is needed to help identify or develop other items that might be important measures of sociocultural factors relating to ST use in South Asian settings. Through repeated administrations of these items over time and comparisons, it would be possible to gain further

insights into any changes in social norms surrounding ST use within these populations.

6.2.3.3 Study 3 – Systematic review of CVD risks association with ST use

The steps of the systematic review were based on published guidance from the Centre for Reviews and Dissemination (2009). Only longitudinal observational study designs were considered for inclusion, unlike earlier reviews of South Asian studies on ST-related CVD risks (Rahman et al., 2011). Given the potential for confounding, I was careful to only include studies that adequately controlled for smoking exposure either at the design or the analysis stage. Methodological quality of included studies was assessed using the NOS scale for non-randomised study designs (Wells et al., 2000).

6.3 Limitations of the research

With the exception of the systematic review which focuses on longitudinal data, the rest of the research findings are based on cross-sectional data, much like the majority of existing ST literature. Most of the papers identified in the policy review are also reports of cross-sectional study designs. This represents one of the limitations of the research, given that it prevented the assessment of predictive validity in the case of the dependency scales, and that temporality could not be established for the sociocultural associations assessed.

Another of the key limitations of the overall research relates to the generalisability of findings. The survey used to collect data on ST dependence and sociocultural factors was conducted in an urban area in New Delhi, India. Moreover, study participants were recruited through convenience sampling, further limiting the representativeness of the sample. To address this limitation, similar studies across diverse settings are needed, including rural areas, given that ST consumption patterns have been found to vary across urban and rural settings in South Asian countries (Flora et al., 2009, Gupta, 2013). With regard to the systematic review, despite reports of ST consumption in several countries, most do not have any studies on their associated cardiovascular health risks. As a result, risk estimates from some countries have been extrapolated to wider geographical regions.

Yet another important limitation is that all my analyses have relied exclusively on quantitative data. Although this approach has allowed me to meet the study objectives, qualitative methods dependent on conceptual rather than numerical analysis, could have provided important insights into the different aspects covered by this research. For instance, data gathered through document analysis, interviews or observations could have led to greater understanding of which motives are most relevant to the development of ST dependence in South Asian settings, or the possible

mechanisms linking the sociocultural factors with ST use practices. However, these approaches did not form a part of my doctoral work.

6.4 Reflections and conclusions

At the individual level, psychometric properties of ST dependence scales – based on three different approaches – were assessed among adult ST users in a South Asian setting, and generally found to be valid measures for assessing physical dependence, based on significant associations found with heaviness and consistency of ST use. However, a high internal consistency score was found for only the OSSTD measure, whereas its original multidimensional factor structure was not replicated in this research. Overall, the findings of the validation study suggested that each scale had their own advantages and limitations, but there was room for them to be modified, or newer scales to be developed in order to better measure ST dependence in South Asian settings. In the absence of further research on test-retest reliability and predictive validation of the existing scales, it would be hard to make a recommendation on which of them was best suited for contextual application. At the interpersonal level, sociocultural factors – as explored using measures of descriptive norms (e.g. ST use among close friends and family members, ST use permissibility within households, etc.) – showed distinctive patterns of distribution according to users' sociodemographic characteristics. In addition, the sociocultural measures were found to be significantly associated with ST use practices, including quit rates and intentions. Although exploratory in nature, these findings suggested that interventions and strategies targeting sociocultural factors would be important for achieving effective ST control in South Asian settings. However, the analyses should be replicated using a different sampling method that minimised the risk of bias, and ensured representativeness of the study sample. In terms of consequences associated with ST use, ever use of South Asian ST products was found to significantly increase the risk of incident IHD based on systematically reviewed evidence of longitudinal observational studies. These findings did not extend to other geographical regions, suggesting the need for greater regulation of South Asian ST products.

While the focus of these three studies were to address specific gaps identified in the literature, I additionally wanted to explore the extent of research more directly relevant to the development and implementation of different ST control policies within the SA region. The inclusion of this work meant that there were aspects of the thesis that covered the different levels of the ecological model of health behaviours (Sallis et al., 2015), namely individual, interpersonal, as well as wider environmental factors influencing ST use in South Asian settings. In addition, the decision to research multiple areas using a range of appropriate methodologies and analytical techniques, allowed me the opportunity to build my capacity for research and public health action around ST, particularly within a setting that faced the greatest burden from their use.

On reflection, there are some things I could have done differently. In particular, I could have dedicated more time to the measurement of biological markers, and ways to verify the results. Up to 10% of the samples could have been shipped to the UK for independent validation of cotinine results. These steps might have allowed a better appreciation of where things went wrong, even if it did not change the outcome. But despite the limitations, this research has made a substantial and original contribution to the ST literature and suggested some key directions for future research work to follow. Given the high levels of dependence, the sociocultural contexts that both allow the continued uptake of ST by newer generations of users as well as exert a negative influence on cessation practices, and the large public health burden associated with ST use, it is imperative that future research efforts continue within the directions suggested. In addition, research is also needed to inform stronger policies that reduce both the demand and supply of ST use in South Asian settings. Finally, as responses to tackle ST use are developed and implemented, it will be important to monitor and evaluate their effects using robust methodologies, taking into account the social and economic inequalities that determine patterns of ST use. Effective cooperation between different stakeholders will be key to achieving control of this complex public health issue.

Appendices

Appendix 1.1. Search strategies for ST policy review

For all following searches, MEDLINE was searched using the OVID interface on 24/06/2017 for the period January, 2012 – June, 2017.

Article 6 – Price and tax measures to reduce demand for ST

1	smokeless tobacco.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] or exp Tobacco, Smokeless/	3783
2	chew* tobacco.mp.	552
3	oral tobacco.mp.	65
4	(snus or snuff or dip* tobacco or betel quid or pan masala or gutk*a or khaini).mp.	2301
5	1 or 2 or 3 or 4	5069
6	(price or pricing or price elasticity).mp.	20832
7	(tax* or taxation or excise tax* or tax elasticity).mp.	108218
8	(economy or economics or economic evaluation).mp.	86125
9	6 or 7 or 8	210142
10	5 and 9	110
11	limit 10 to (english language and humans and yr="2012 -Current")	42

Note: Searches 1 – 5 were the same for all Articles

Articles 9 & 10 – Regulation of ST product contents and disclosures

6	(content* or additive* or disclosure*).mp.	693406
7	5 and 6	263
8	limit 7 to (english language and humans and yr="2012 -Current")	67

Article 11 – Packaging and labelling of ST

6	(pack* or label* or warn* or message*).mp.	702318
7	5 and 6	292
8	limit 7 to (english language and humans and yr="2012 -Current")	82

Article 12 – Education, communication, training and public awareness on ST

6	(awareness or public awareness or public awareness campaign).mp.	102290
7	(media or mass media or mass media campaign).mp.	386485
8	6 or 7	485770
9	5 and 8	227
10	limit 9 to (english language and humans and yr="2012 -Current")	99

Article 13 – Ban on ST advertisement, promotion and sponsorship (TAPS)

6	(promote* or promotion or brand promotion).mp.	661518
7	(advert* or point of sale or point of purchase).mp.	21307
8	sponsor*.mp.	17921
9	6 or 7 or 8	695356
10	5 and 9	509
11	limit 10 to (english language and humans and yr="2012 -Current")	145

Article 14 – Demand reduction measures concerning ST dependence and cessation

6	(cessation or intervention or treatment or dependence or addiction).mp.	4166651
7	5 and 6	1550
8	limit 7 to (english language and humans and yr="2012 -Current")	439

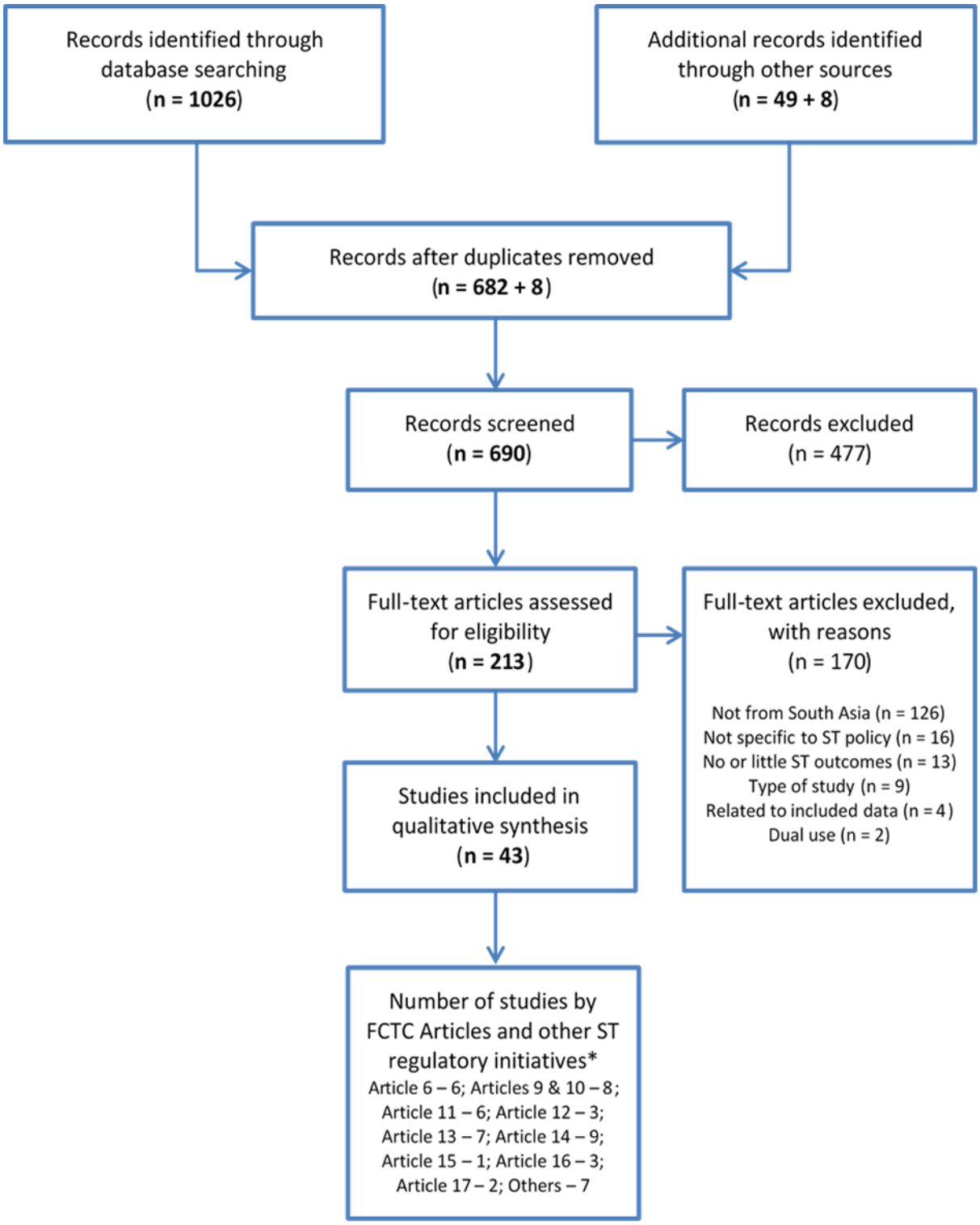
Article 15 – Illicit trade in ST

6	*Tobacco/ or illicit trade.mp. or *Tobacco Products/	18769
7	5 and 6	861
8	limit 7 to (english language and humans and yr="2012 -Current")	147

6.4.1 Article 16 – Access and availability of ST to minors

6	(youth access or sale to minors).mp.	258
7	5 and 6	10
8	limit 7 to (english language and humans and yr="2012 -Current")	5

Appendix 1.2. Flow diagram of study selection process for policy review



* Some studies were relevant to multiple policy areas

Appendix 1.3. Characteristics of included studies in policy review

Reference	Country	Aspect of policy research	Study setting/ Population	Study methods	Summary of findings	Conclusions
FCTC Article 6 – Price and tax measures to reduce demand for ST (6 studies)						
Singh et al. (2012)	India	Impact	Tobacco shopkeepers and ST users ≥18 years in Jaipur City, Rajasthan	Evaluating effect of price rise on ST sale and consumption, using two-stage stratified sampling techniques	ST price increased by 68%; average sale decreased by 38% and consumption by 21% in the same time frame	Increase in price can reduce ST consumption proportional to the magnitude of price rise
Joseph and Chaloupka (2013)	India	Formulation	National survey of youth, aged 13 – 15 years	Estimation of gutkha price elasticity, using Global Youth Tobacco Survey (GYTS) data	Estimated elasticity was -0.58; girls had significantly higher elasticities than boys	Higher prices can be effective deterrents for youth ST use
Nargis et al. (2014)	Bangladesh	Formulation	Nationally representative sample of adult tobacco users and non-users in Bangladesh, aged ≥15 years	Estimation of zarda price elasticity, using International Tobacco Control (ITC) survey data	Estimated price elasticity was -0.64 to -0.39 for different brands of zarda; cross-price elasticity with cigarettes was 0.35	Simultaneous increase in all tobacco taxes can reduce ST use; greater increase in ST tax compared to smoked products needed
Rout and Arora (2014)	India	Implementation	N/A	Examination of tax structure, price and affordability of ST, using secondary data from the Ministry of Finance	In 6 years, tax rates on ST had increased; but overall price rise was less than rise in per capita income, indicating more affordability of ST	ST prices should be raised more than income growth to influence consumption

Kostova and Dave (2015)	India	Formulation	Nationally representative sample of adult tobacco users and non-users in India, aged ≥15 years	Estimation of ST price elasticity, using 2010 GATS data	Estimated price elasticity of ST was -0.21 for adult males; men had higher price elasticities than women	Higher prices can be effective deterrents for adult ST use; men more likely to respond to ST price changes
Selvaraj et al. (2015)	India	Formulation	National sample of households consuming any tobacco or alcohol	Estimation of ST price elasticity by economic groups, using Consumer Expenditure Survey (CES) data	ST price elasticities were highest in the poorest (-0.56) and middle (-0.45) economic groups; cross price elasticities with bidis were positive	Greater responsiveness to price rise in poorer ST consumers; rise in tax rates across all products is critical
FCTC Articles 9 & 10 – Regulation of ST product contents and disclosures (8 studies)						
Saeed et al. (2012)	Pakistan	Formulation	N/A	Testing of 30 brands of naswar for carcinogens and toxic constituents	Levels of all toxins were above recommended limits	Contents of naswar were unregulated, posing a health risk to consumers
Prabhakar et al. (2013)	India	Formulation	N/A	Testing of 10 ST samples for toxic metals	Heavy metal levels were above recommended limits	Contents of ST were unregulated, posing a health risk to consumers
Arain et al. (2015a)	Pakistan	Formulation	Adult oral cancer patients and relatives (30 – 60 years), attending 2 hospitals in Sindh, Pakistan	Case-control study of exposure to Nickel (Ni) in ST among oral cancer patients and healthy relatives	Ni levels significantly higher in patients than controls	Exposure to Ni in ST may be a synergistic risk factors for oral cancer
Arain et al. (2015b)	Pakistan	Formulation	Adult oral cancer patients and relatives	Case-control study of exposure to Arsenic	As levels in biological samples of patients were	Exposure to As in ST may be a synergistic risk

			(30 – 60 years), attending 2 hospitals in Sindh, Pakistan	(As) in ST among oral cancer patients and healthy relatives	significantly higher than controls	factors for oral cancer
Sharma et al. (2015)	India	Formulation	N/A	Testing ST products and packages for nicotine content, warnings, and disclosures	Varying levels of nicotine found, inadequate disclosures on packaging	ST product contents and disclosures not adequately regulated
Stepanov et al. (2015)	India	Formulation	N/A	Testing 12 samples of chaini khaini for TSNAs and nicotine	Very high levels of TSNAs and biologically available nicotine found	Contents of ST were unregulated, posing a health risk to consumers
Siddiqi et al. (2016b)	Nepal, Pakistan, Bangladesh	Implementation	Key actors of ST supply chain	Structured interviews on different ST-related policy areas	Inspections at production sites and retails did not involve product or label testing, or content measurement	Findings indicate several loopholes in regulatory inspection systems
Stepanov et al. (2017)	India	Formulation	N/A	Testing 39 samples of ST products for TSNAs and nicotine	Nicotine varied more than 300-fold and TSNA varied more than 650-fold across products	Contents of ST were unregulated, posing a health risk to consumers
FCTC Article 11 – Packaging and labelling of ST (6 studies)						
Sharma et al. (2015)	India	Implementation	N/A	Testing ST products and packages for nicotine, disclosures and warnings	While some samples had pictorial warnings, many were sold unbranded without health warnings	Policies on ST packaging and labelling not adequately implemented

Gravely et al. (2016)	India	Impact	Adult ST users from 4 states in India, aged > 15 years	Testing the effectiveness of change from symbolic to graphic Health Warning Labels (HWL), using TCP data	27% of participants were unaware of HWLs; graphic HWLs made 20% think about risks of ST/quitting	Implementation of more salient and impactful HWLs to increase awareness of harms and to motivate quitting
Mutti et al. (2016)	India, Bangladesh	Formulation	Adult ST users (≥19 years) and youth users and non-users (16–18 years) from Navi Mumbai, India, and Dhaka, Bangladesh	Assessing effectiveness of four randomly assigned HWLs: (1) text only, (2) symbolic pictorial, (3) graphic pictorial or (4) personal testimonial pictorial	Text-only warnings perceived as less effective than pictorial; Graphic warnings had highest effectiveness ratings among the pictorial styles	Graphic HWLs may have the greatest impact; further research on impact of design and content across levels of education & dependence needed
Siddiqi et al. (2016b)	Nepal, Pakistan, Bangladesh	Implementation	Key actors of ST supply chain	Structured interviews on different ST-related policy areas	Text-only warnings most common, with English-only texts; few pictorial (0 – 13.5%)	Further regulation of HWLs on ST packages needed
Vidhubala et al. (2016)	India	Implementation	N/A	Purchase and testing of 65 varieties of ST in Chennai, India	30.8% had no pictorial warnings; of the text-only warnings, only 2 were in Tamil	Low compliance by ST manufacturers on packaging and labelling regulations
Shekhawat et al. (2017)	India	Implementation	Convenience sample of adult ST users and non-users from 2 villages in Puducherry, India	A cross-sectional study of prevalence and pattern of ST use, with profiling of ST sachets	Of 23 sachets, 18 had no pictorial warning, 54% of participants unaware of HWLs	Pictorial warnings needed on sachets for low SES users
FCTC Article 12 – Education, communication, training and public awareness on ST (3 studies)						

Murukutla et al. (2012)	India	Impact	Nationally representative sample of households with access to mass media	Evaluation of a national television and radio mass media campaign targeting ST users	High campaign recall – 63% ST & 72% dual; campaign awareness associated with better knowledge, cessation intentions & behaviours	Mass media campaigns are feasible & efficacious for ST control in India
Hamill et al. (2015)	India	Impact	N/A	Process outcomes of ChewOnThis.in, an online campaign for advocacy against ST & support for gutkha ban	In 6 weeks, site had had 10949 visits and 1131 registrants; majority learnt of campaign via e-word-of-mouth	ST control advocates can use online media with new indicators (e.g. no. of shares); research on message type needed
Singh et al. (2018)	India	Formulation	Nationally representative sample of adult tobacco users and non-users in India, aged ≥15 years	Study of variations in anti-tobacco campaign awareness by gender, using 2010 GATS data	Greater exposure to anti-smoking than anti-ST information; Males more likely to notice anti-ST messages	Government-sponsored mass media campaigns should target ST users and women
FCTC Article 13 – Ban on TAPS for ST (7 studies)						
Schensul et al. (2013)	India	Implementation	Shops and residents in a low-income neighbourhood in Mumbai, India	A mixed methods study of implementation of ST control legislation	Creative display of ST at point of sale (POS), bulk discounts, offers, & rewards in packets	Promotional activities for ST were widespread
Bansal-Travers et al. (2014)	India	Implementation	Adult tobacco users and non-users from 2 states in India, aged ≥18 years	Study of perceptions and observations of pro-tobacco ads, using TCP India pilot data	74% of ST users exposed to pro-tobacco ads, mostly inside shop or shop windows	Stronger legislation and enforcement of bans on tobacco advertising needed

Sinha et al. (2014)	India	Formulation	Nationally representative sample of adult tobacco users and non-users in India, aged ≥15 years	Study of association between exposure to tobacco ads/promotions and prevalence of use, using 2010 GATS data	Exposure to low levels of ST marketing significantly associated with use (OR=1.24, 1.1-1.4); trend increased with levels of exposure	Exposure to ST marketing (POS, sales, free coupons or samples, surrogate adverts) increased prevalence of use among adults
Kostova and Dave (2015)	India	Formulation	Nationally representative sample of adult tobacco users and non-users in India, aged ≥15 years	Study of association between price & advertising with ST prevalence, using 2010 GATS data	Exposure to ST ads had significant association with higher probability of use; more likely to affect use in women	Advertising restrictions may play a relatively larger role in ST consumption behaviour of women in India
Mistry et al. (2015)	India	Implementation	Shops and students in school-adjacent neighbourhoods in Mumbai, India	Cross-sectional study of compliance with ST legislation; association of vendor and advert densities near schools, with students' use	54% of schools had at least one ad within 100m; ad density within 100m was significantly associated with ST use (OR=2.01, 1.02-3.98)	Greater enforcement of current bans needed
Sardana et al. (2015)	India	Formulation	Sample of youth and young adult tobacco users and non-users in India, aged 15 – 24 years	Study of influence of TAPS on tobacco initiation, using 2010 GATS data	ST used by 14.7% of sample; free samples, sale prices, and coupons significantly associated with ST initiation	Stronger legislative measures should be applied to curb TAPS in the form of free samples, sale prices, etc.
Balappanavar et al. (2017)	India	Implementation	Tobacco outlets within 100m of 15 schools in New Delhi, India	Study to assess compliance with ST legislation	Product-display and signs formed majority of advertising – more for ST than smoked tobacco	Evidence for lack of compliance found in New Delhi, India

FCTC Article 14 – Demand reduction measures concerning ST dependence and cessation (9 studies)						
Pimple et al. (2012)	India	Formulation	224 tobacco users (mostly ST) at a factory worksite in Mumbai, India	A worksite tobacco cessation intervention involving individual and group behaviour therapy	At the end of three interventions, 17% had quit tobacco; presence of oral pre-cancer lesion significantly associated with quitting	Programs built into occupational health and welfare activities are acceptable and feasible to achieve tobacco cessation at worksites
Panda et al. (2013)	India	Formulation	Sample of physicians from 2 high prevalence states in India	A mixed methods study to assess physicians' perception and practice of ST cessation	<30% recorded ST use; low level of knowledge on harmful effects; 23% advised switching to ST for smoking cessation	Need for capacity building on physicians' tobacco cessation skills
Jain et al. (2013)	India	Formulation	Adults daily ST users, mostly male, attending a dental hospital in New Delhi, India	Double-blind placebo-controlled trial of Varenicline (1 mg twice a day, 12 weeks), with behavioural counselling	Abstinence (self-report and biochemically verified) at end of treatment was greater in Varenicline group	Varenicline appears to be safe and effective for treating ST dependence in India
Mishra et al. (2014b)	India	Formulation	Women, current users of tobacco (mostly ST), in a low-income area in Mumbai, India	Community-based intervention, comprising health education, games and counselling sessions, for tobacco cessation	95.2% compliance, 33.5% self-reported abstinence; older women and those consuming tobacco at multiple locations were less likely to quit use	Providing cessation support is an important measure for women users in India
Panda et al. (2015b)	India	Formulation	Sample of Auxiliary Nurse Midwives	A cross-sectional study to assess preparedness	Very low awareness of reproductive effects of	A context-specific capacity building

			(ANMs) in Gujarat and Andhra Pradesh, India	of frontline health workers for tobacco cessation	tobacco; 16% had had on-job training on tobacco control; a small number of ANMs advised switching to ST for smoking cessation	package for ANMs needed on tobacco cessation
Harrell et al. (2016)	India	Formulation	Youth (10 – 19 years), in low-income communities in New Delhi, India	Community-based cluster randomised trial of a 2-year multiple-component intervention engaging youth and community members	No differences in ST use observed in intervention and control conditions	Most disadvantaged youth and ST users may need more intensive interventions
Ruhil (2016)	India	Formulation	Sample of ever ST users in India, aged ≥15 years	Secondary analysis of 2010 GATS data to study influences on the use of counselling as a cessation method	Male and younger (15-24 years) ST users had significantly lower odds of using counselling for ST cessation	Choice of ST cessation method might need to vary according to sociodemographic characteristics of users
Siddiqi et al. (2016a)	Pakistan, UK	Formulation	South-Asian adults who were regular users of ST, in Pakistan and UK	Pilot study of behaviour change intervention (BCI) for ST cessation, along with assessing acceptability & feasibility of delivery	Moderate fidelity scores for adherence to content, and for quality; outcomes showed ST reduction rather than cessation	A newly developed theory-based BCI for ST cessation was found to be acceptable and feasible to deliver; needs further evaluation
Jhanjee et al. (2017)	India	Formulation	100 women tobacco users (mostly ST) in a low-income community in New Delhi, India	Open-labelled randomised study of brief intervention (BI) vs. simple advice	Women in the BI group twice more likely to report abstinence at 3 month follow-up	Results suggestive of a beneficial effect of BI for tobacco cessation in study group

FCTC Article 15 – Illicit trade in ST (1 study)						
Siddiqi et al. (2016b)	Nepal, Pakistan, Bangladesh	Formulation	Key actors of ST supply chain	Structured interviews on different ST-related policy areas	ST products commonly smuggled across the border and openly displayed	A significant amount of smuggled, counterfeit ST products are sold in South Asian markets
FCTC Article 16 – Access and availability of ST to minors (3 studies)						
Lal et al. (2015)	India	Formulation	Nationwide sample of daily tobacco users, aged 15 – 17 years	Estimation of underage expenditure on tobacco, using 2010 GATS data	Underage users spend nearly 271 million USD on ST products	Efforts to reduce sales to underage users need to be strengthened
Mistry et al. (2015)	India	Formulation & Implementation	Shops and students in school-adjacent neighbourhoods in Mumbai, India	Cross-sectional study of compliance with ST legislation; association of vendor and advert densities near schools, with students' use	85% of schools had at least one vendor within 100m; vendor density within 200-500m of schools was associated with current ST use	Greater enforcement of current bans needed; tobacco sales ban near educational institutions could be expanded beyond 100 m
Siddiqi et al. (2016b)	Nepal, Pakistan, Bangladesh	Implementation	Key actors of ST supply chain	Structured interviews on different ST-related policy areas	Limited or no restrictions on ST sale to minors; justification that children were purchasing for adults often provided	There appear to be no restrictions on sale of ST to minors in many South Asian countries
FCTC Article 17 – Economically viable alternatives to ST (2 studies)						
Schensul et al. (2013)	India	Formulation	Shops and residents in a low-income neighbourhood in Mumbai, India	A mixed methods study of implementation of ST control legislation	Selling of ST was an important form of income generation for many households	Multilevel ST control needed, including policies on alternative income generation

Siddiqi et al. (2016b)	Nepal, Pakistan, Bangladesh	Formulation	Key actors of ST supply chain	Structured interviews on different ST-related policy areas	Trade in ST was profitable & provided job security; high demand, good returns, and rapid crop turnover were key incentives for farmers	Evidence of several incentives built-in the supply chain that makes tobacco farming, ST manufacturing, and sale a profitable business
Non-FCTC policy measures for ST control (7 studies)						
Nair et al. (2012)	India	Implementation	8 gutkha users and 13 tobacco vendors in Maharashtra, India	A rapid surveillance using interviews and informal observations, two months after a gutkha ban	Ban had immediate effect on reducing local supply, demand and use; stockpiling and sale for higher prices reported	The ban had reduced, but not eliminated gutkha; long term effects remained to be seen
Dhumal and Gupta (2013)	India	Implementation & Impact	11 current and ex-gutkha users (male, 19-43 years), in Mumbai, India	FGDs to assess implementation and effects of ban on gutkha	All aware of ban, but reported availability at higher costs; most users had switched products	Evidence of poor implementation of gutkha ban found
Mishra et al. (2014a)	India	Implementation & Impact	Tobacco vendors and adult gutkha users in Maharashtra, India	Cross-sectional study of impact of gutkha ban	23.5% quit & 55.8% reduced use, mainly due to non- availability; but available in black market at higher costs	Evidence of non-compliance with gutkha ban found
Pimple et al. (2014)	India	Implementation	ST vendors within 100 yards of 6 schools in Mumbai, India	Study to assess compliance with ST legislation and ban on gutkha	41% of surveyed vendors openly sold gutkha post-ban; some did not display gutkha	Lack of robust enforcement has led to widespread non-compliance with ban

Reddy et al. (2016)	India	Implementation & Impact	Tobacco vendors and adult ST users in Telangana, India	Cross-sectional study of impact of gutkha ban	89.6% vendors & 49.2% users were aware of ban; gutkha sold in different form; 29.9% switched to different product	Evidence of poor implementation of gutkha ban found
Vidhubala et al. (2016)	India	Implementation	N/A	Procurement and testing of gutkha following its ban	26 banned products were procured 3 years after implementation of the ban	Ban on ST is systematically violated in Chennai, India
Deepak et al. (2017)	India	Implementation & Impact	Stratified random sample of ST users and shopkeepers in Chennai, India	Cross-sectional study of impact of gutkha ban	All shopkeepers aware of ban, but continued to buy gutkha; easy to procure, but at higher prices; users reported decrease in consumption	The ban had not had any impact on availability; but some impact on use

Appendix 3.1. Study protocol for ST dependence scale validation

Aim:

The primary aim of the study is to produce validated scales to measure tobacco dependence among ST users in India. The specific objectives are:

- To translate the OSSTD into Hindi using a standard back translation technique and achieve cross-cultural equivalence
- To pre-test the scale in a sample of ST users in India
- To psychometrically evaluate the scale among ST users in India by assessing its internal consistency and validity against a clinical diagnosis of tobacco dependence, the FNTD-ST scale, salivary cotinine measurements, and self-rated ST addiction.

Methodology: Translation of the OSSTD will be carried out according to the steps suggested by Sousa and Rojjanasrirat (2011). These steps are based on a review of other published recommendations for cross-cultural adaptation and validation of scales used in health care research. Forward translation of the scale from English (Source Language) to Hindi (Target Language) will be carried out by two independent translators (Forward Translator 1 & Forward Translator 2), so that two preliminary Hindi versions of the scale are initially produced. The translators will be bilingual, and their backgrounds will also be considered during selection, so that one translator (Forward Translator 1) is familiar with the technical terminology used in the field of ST, while the second translator (Forward Translator 2) will be more familiar with colloquial use of the target language (Hindi). Adequate instructions will be provided to both translators so that conceptual translations rather than literal ones are produced, keeping typical respondents for the scale in mind. The eligibility criteria for both forward translators are summarised in Table 1.

Table 1: Eligibility criteria for forward translators

Qualifications	**Forward Translator 1**	**Forward Translator 2**
Required	Native speaker of Hindi/Spoken Hindi since early childhood Proficient in reading and writing Hindi Spoken English since early childhood Proficient in reading and writing English College degree or higher (health related) Work experience in India Knowledge and understanding of tobacco	Native speaker of Hindi/Spoken Hindi since early childhood Proficient in reading and writing Hindi Spoken English since early childhood Proficient in reading and writing English College degree or higher (not health related) Work experience in India Lived at least 5 years in India as an adult

Desirable	Certified as professional Hindi translator Lived at least 2 years in an English-speaking country as an adult	Certified as professional Hindi translator Lived at least 2 years in an English-speaking country as an adult

The two preliminary Hindi versions of the scale will be compared against one another and to the original English version by a third bilingual individual (independent reviewer), with the following qualifications:

Table 2: Eligibility criteria for independent reviewer

Qualifications	**Independent reviewer**
Required	Native speaker of Hindi / Spoken Hindi since early childhood Proficient in reading and writing Hindi Spoken English since early childhood Proficient in reading and writing English College degree or higher Lived at least 5 years in India as an adult Prior participation and experience in health research and translation
Desirable	Certified as professional Hindi translator Lived at least 2 years in an English-speaking country as an adult

The three bilingual individuals (Forward Translators 1 & 2 and Independent Reviewer) will then meet to discuss any discrepancies in the translation, which will be resolved through consensus, and one combined forward-translated version of the scale will be produced in Hindi. Additionally, two native speakers of Hindi, who are also ST users, will be invited to the reconciliation meeting to provide their comments on the quality of the translation. Back translation to the source language (English) will be carried out by another set of two independent bilingual translators (Back Translator 1 & Back Translator 2) from distinct backgrounds, who are either native speakers of English or have spoken English since early childhood. These translators will be blind to the original English version of the scale, having never seen it previously. This step will result in two independently back-translated versions of the scale in English. The qualifications for back translators are summarised in Table 3.

Table 3: Eligibility criteria for back translators

Qualifications	**Forward Translator 1**	**Forward Translator 2**
Required	Native speaker of English/Spoken English since early childhood Proficient in reading and writing English Proficient in reading and writing Hindi No prior knowledge about original	Native speaker of English / Spoken English since early childhood Proficient in reading and writing English Proficient in reading and writing Hindi No prior knowledge about original

	scales College degree or higher (health related) Prior work experience in the field of tobacco control	scales College degree or higher (not health related) Lived at least 5 years in an English-speaking country as an adult
Desirable	Spoken Hindi since early childhood In-depth knowledge of source and target cultures	Spoken Hindi since early childhood In-depth knowledge of source and target cultures

The back-translated versions will be compared to the original English version of the scale by a multi-disciplinary committee, which will comprise of at least one methodologist (investigator or member of research team), one professional who is familiar with content area of the scale, all translators, and the developers of original scale. Any discrepancies that arise during this process will be discussed by the committee and resolved through consensus, and one pre-final version of the scale will be produced in the target language (PF-TL). If discrepancies cannot be resolved for certain items, then the translation and back-translation steps will be repeated for just those items using another set of bilingual translators. Finally, a checklist[1] will be used to monitor and document every step of the translation process.

Pre-testing: The PF-TL version of the scale will be pre-tested in a sample of up to 10 individuals, to ensure equivalence before full psychometric testing. Other purposes served by a pretesting phase may include – (a) assessing the likelihood of success of the planned recruitment approaches, (b) assessing the time taken to collect data, and (c) personal training of the researcher in tool administration. Modifications will be made as required and a final version of the scale will be produced for data collection.

Participant eligibility criteria: The final phase of the study will include a full psychometric evaluation of the translated, culturally-adapted and pretested version of the OSSTD, and this will be carried out in a sample of ST users in India. The psychometric approaches used will include the estimation of the scale's internal consistency and validity to measure ST dependence. Individuals will be considered as eligible if they fit the following inclusion and exclusion criteria:

Inclusion criteria:

- Adults aged 18 years or older
- Fluent in spoken Hindi
- Current use of ST (defined as any use of ST during the past 7 days)
- Used ST for at least one year

[1] Acquadro, C., Conway, K., Hareendran, A., Aaronson, N. and European Regulatory Issues and Quality of Life Assessment (ERIQA) Group, 2008. Literature review of methods to translate health-related quality of life questionnaires for use in multinational clinical trials. *Value in Health*, *11*(3), pp.509-521.

- Used ST at least once a week for the last 6 months
- Able to provide informed consent

Exclusion criteria:

- Current use of smoked tobacco including cigarettes, bidis or water pipes (defined as any use of these products during the past 30 days)
- History of mental illness
- Any acute or serious medical illness requiring urgent care or hospitalisation

Sample size: A sample size of at least 10 individuals per item on the OSSTD will be recruited, requiring a total of at least 230 eligible ST users for the validation study.

Study setting and participant identification: Data may be collected from any of the following settings in New Delhi, India.

- A multispecialty, tertiary care hospital – where study participants may be recruited from among hospital staff, patients and patient attendants
- A community setting – where a local NGO or community based organisation may be approached for assistance in recruiting members from the community
- A workplace setting (such as a factory) – where employees may be approached for participating in the research study

Preliminary visits will be carried out to each of these settings in order to work out a feasible recruitment strategy and all necessary permissions for carrying out the research study will be obtained in advance. Further clarity on recruitment strategies will be obtained following an initial visit to New Delhi, about 3 months prior to data collection. During this visit, efforts will be made to identify a particular hospital/ community centre/ factory, and initial contacts with the administrative authorities at the selected sites will be made.

Hospital-based recruitment: Study participants may be recruited from among hospital staff, patients, and patient attendants. For the purposes of recruiting hospital staff, the administrative department of the hospital will initially be approached and through them, information regarding the study will be communicated to other hospital departments. Smokeless users among the hospital staff who are interested in participation will be asked to contact the chief investigator. Recruitment of patients and accompanying attendants may take place in both out-patient settings and in-patient wards of select hospital departments. In the out-patient setting, patients will normally be registered by a receptionist before consultation. For the purposes of this study, the receptionist will inform each patient about the study at the time of registration, and refer ST users who are willing to participate to the researcher for eligibility screening and participation.

Participants recruited from the in-patient wards will mostly include patient attendants. In this setting, preliminary information regarding the study will be shared with individuals by the researcher and identified ST users will be invited to participate.

Community-based recruitment: Study participants may be recruited from among members of a community. For assistance with recruitment, a local NGO or similar organisation working within the chosen community will be approached. With their help, a pre-recruitment event may be organised. Or if there is already an event planned by the identified community organisation, then permission to be present at such an event will be obtained beforehand. The purpose of this activity will be to provide information regarding the study to members of the community. Information on the collaborating centre's contact details will also be provided to individuals who may be interested in participating. This event will be planned after discussions with the identified organisation. It may include a brief presentation about the research study, as well as any other activity suggested by the community organisation. Care will be taken to ensure that no undue burden is placed on the collaborating organisation as a result of this research study. Community members expressing an interest in the study will be invited to the community centre/ NGO office for eligibility screening and recruitment. Snowballing and word-of-mouth referrals from screened and recruited participants will also be used as a recruitment method.

Workplace-based recruitment: Study participants may be recruited from among employees of a workplace-based setting such as a factory. Depending on the chosen site, preliminary information regarding the research study will be communicated to the employees, using methods decided in collaboration with the administrative staff at the chosen site. Smokeless users among the factory employees who are interested in the study will be asked to approach the researcher for eligibility screening and recruitment.

Eligibility screening and recruitment: Having identified individuals who are interested in the study, the researcher will formally screen each participant for eligibility using a screening questionnaire. All individuals screened for eligibility at the hospital/ community centre/ workplace setting may be offered health awareness measurements such as BMI and blood pressure, as part of the recruitment strategy. The measurements will be carried out either by the researcher or identified trained personnel at each research site. Individuals with adverse medical findings will be referred to a medical centre for follow-up care.

Those who meet all eligibility criteria will be invited to participate in the study and informed written consent will be sought after providing all the details as per the participant information sheet. For individuals who cannot read or write, the participant information sheet will be read out and a thumb impression will be requested in the presence of a literate witness, who will

countersign the consent form. Informed consent will be obtained from all participants for collecting both questionnaire data and saliva samples. While no personally identifiable data such as name, date of birth, address, or telephone number will be collected from study participants, each participant will be given a unique participant identification (ID) number, which will be recorded on the consent form, study questionnaire and salivary sample tube.

All study participants will be recruited on a thoroughly voluntary basis and informed that they are free to withdraw from the research at any time during the interview without facing any untoward consequences as a result of their decision to withdraw. On participation, individuals will be offered a voucher for the value of approximately 1 GBP (100 Indian Rupees) as compensation for time spent in providing the interview data. A period of at least 24 hours will be allowed for potential participants who express any uncertainty about their willingness to participate in the study. Information regarding the study as per the participant information sheet will be provided to these individuals and they will be requested to contact (or) return to the research site should they decide to participate.

Data collection: The following are all the data that will be collected for the purposes of this study:

- Socio-demographic data – including age, gender, education, employment and income
- Tobacco use data – including ST use characteristics and past smoking-related data
- Tobacco dependence data – measured by OSSTD, TDS-ST, FTND-ST, and self-rated ST addiction
- Saliva sample for cotinine measurements

These data will be collected through face-to-face interviews, so that no items are omitted and data may be collected from individuals who cannot read and write Hindi. Participants will also be asked to provide saliva samples, which will be transported to the laboratory for biochemical analysis to measure cotinine levels, using Enzyme-Linked Immuno Sorbent Assay (ELISA) kits from Salimetrics.

Statistical analyses: Demographic and tobacco use data will be explored using descriptive statistical analyses and the association between these data and tobacco dependence scores will be assessed using chi-squared tests for categorical variables and t-tests for continuous variables. The psychometric properties of the dependence scales will also be evaluated by examining their internal consistency reliability and validity measures.

The extent to which the different items within the OSSTD are correlated with one another will be evaluated by computing Cronbach's alpha coefficient; internal consistency will also be evaluated for the OSSTD subscales. The tobacco dependence scores of study participants as measured by

the OSSTD and FTND-ST scales will be compared against each other to establish concurrent validity of the scales. A diagnosis of tobacco dependence as established by the TDS-ST, as well as salivary cotinine measurements will be used to establish criterion validity. Finally, an exploratory factor analysis will also be performed to examine the loading pattern and cross loading of items within the Oklahoma Scale (OSSTD).

Ethics approval: The protocol and all supporting documents, including the study questionnaire, participant information sheet and consent form, will be submitted for ethical approval to the University of York Health Sciences Research Governance Committee. Ethics approval will also be sought from an independent ethics committee in India.

Appendix 3.2. Construct sheet for study questionnaire and Codebook

Screening questionnaire

Construct	# of Items	Survey item
Language	1	1
Age	1	2
ST use in the past week, regular use & length of time	3	3 - 5
ST cessation assistance	1	6
Smoking screener: Use in the last 30 days	2	7 - 8
Frequent alcohol use & drug use in the last 30 days	1	9
History of mental illness	1	10

Main questionnaire

Construct	Instrument	# of Items	Survey item
Socio-demographic			
Age		1	2
Gender, Pregnant, breastfeeding		3	1 – 3
Education, Employment, Assets	GATS - India[2]	3	4 – 6
Religion	Census of India[3]	1	7
ST use history			
Frequency of ST use		2	8, 9
Age of 1st use	OSSTD study[4]	1	10
Daily ST use	Tobacco use supplement, current population survey[5] (modified for ST)	3	11 – 13
Quantifying maximum use	OSSTD study	2	14, 14a
Reducing ST use, reasons	Nondaily Cigarette Smoking Study[6]	2	15, 15a
ST products	Modified from GATS – India	11	16, 17
Social use, household use, use by friends and family members	Created for study + National Youth Tobacco Survey (modified for ST)	5	18 – 22
ST dependence			
TDS-ST	Modified for ST[7]	10	23 – 32
FTND-ST[8]		6	33 – 38

[2] WHO 2010; GATS (Global Adult Tobacco Survey); *India: core questionnaire with optional questions*
[3] Census of India 2011; http://www.censusindia.gov.in/
[4] MUSHTAQ, N., BEEBE, L. A., VESELY, S. K. & NEAS, B. R. 2013; A multiple motive/multi-dimensional approach to measure smokeless tobacco dependence. *Addictive behaviours*
[5] US Department of Commerce, Census Bureau 2012; National Cancer Institute-sponsored Tobacco Use Supplement to the Current Population Survey (2010-11): http://appliedresearch.cancer.gov/tus-cps/info.html
[6] AHLUWALIA 2011; Pfizer GRAND Program - Factors Influencing Nondaily Cigarette Smoking and Cessation Conduct nine focus groups to: (Aim 1) and to (Aim 2) conduct an online survey of 2,400 triethnic smokers.
[7] Mushtaq, N. and Beebe, L.A., 2015. Assessment of the Tobacco Dependence Screener among smokeless tobacco users. *Nicotine & Tobacco Research*, *18*(5), pp.885-891.
[8] Ebbert, J. O., Patten, C. A. & Schroeder, D. R. 2006; The fagerström test for nicotine dependence-smokeless tobacco (FTND-ST); *Addictive behaviours,* 31**,** 1716-1721

OSSTD	OSSTD study	23	39 – 61
Self-rated addiction	1 item from CDS-12[9] (modified for ST)	1	62
ST use behaviours			
Carrying ST	California Tobacco Survey[10] (modified for ST)	1	63
Buying ST	GATS – India + 1 item created for study	4	64 - 67
Urge to use	Mood and Physical Symptoms Scale[11]	2	68, 69
Past year quit attempts	Modified from Nondaily Cigarette Smoking Study	3	70, 70a - b
Planned quit attempts	West & Sohal, 2006[12]	1	70c
Use of assistance to quit ST	Modified from GATS – India	1	71
Quit intention	Prochaska, Diclemente, 1991[13] (modified for ST)	1	72
Physician advise to quit	California Tobacco Survey	5	73 – 77
Smoking history			
Lifetime 100 cigarettes	CDC[14]	1	82
Age of 1st use		1	83
Daily/Quantifying max. use	TUS – CPS	3	84 – 86
Smoked tobacco products		1	87
Quit history, Use of quit assistance	Modified from GATS – India	2	88, 89
Reasons to quit	Ahluwalia et al.[15]	1	90
Health			
Perceived vulnerability	Borrelli et al.[16]	2	78, 79
Harm, Smoking vs. ST	1 item from KIS-II[17]	2	80, 81
Past MI, Angina, HT etc.	Adapted from BRFSS 2011[18]	6	91 - 96
Exercise, diet	BRFSS 2011	4	97 – 99
Health question	1 item from SF-36[19]	1	100

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Codebook

No.	Name	Variable Label	Entry Codes
General information			
ID	P_ID	Participant identification	001, 002, 003…. 233
Date	DATE	Date of registration	dd.mm.yyyy
Socio-demographic Data			
1.	SEX	Gender of participant	Male=1, Female=2
2.	PREG	Pregnancy Status	Yes=1, No=2, N/A=(-999)
3.	BSTF	Breastfeeding status	Yes=1, No=2, N/A=(-999)
4.	EDUC	Education level completed	No formal schooling=1 Less than primary school=2 Primary school completed=3 Less than secondary=4 Secondary school=5 Higher secondary school=6 College/University=7 Post-graduate degree=8
5.	OCCU	Occupation	Government employee=1 Non-government employee=2 Self-employed=3, Student-4 Homemaker=5 Retired=6 Unemployed, able to work=7 Unable to work=8
6a.	ASSET_ELEC	Electricity in household	Yes=1, No=2
6b.	ASSET_TOILE	Toilet in household	Yes=1, No=2
6c.	ASSET_TEL	Fixed telephone in household	Yes=1, No=2
6d.	ASSET_MOBL	Cell phone in household	Yes=1, No=2
6e.	ASSET_TV	Television in household	Yes=1, No=2
6f.	ASSET_RADI	Radio in household	Yes=1, No=2
6g.	ASSET_FRIDG	Refrigerator in household	Yes=1, No=2
6h.	ASSET_CAR	Car in household	Yes=1, No=2
6i.	ASSET_MOTO	Motorcycle in household	Yes=1, No=2
6j.	ASSET_WASH	Washing machine in house	Yes=1, No=2
7.	RELG	Religion	Hindu=1, Muslim=2, Christian=3, Sikh=4, Buddhist=5, Jain=6, Jewish=7, Parsi/Zoroastrian=8, No religion=9, Other=10
ST use history			
8.	N_DAY_ST	Days of ST used in last week	_____ days
9.	N_TIME_ST	Number of times per day ST used in last week	_____ times
10.	AGE_START	Age when started using ST	_____ years
11.	ST_DAILY	ST use history	Yes=1, No=2
12.	ST_DAY_MAX	ST used in days per week when used most	_____ days/week

13.	ST_TIME_MAX	Number of times ST used per day when used most	_____ times/day
14.	ST_CUR_DAIL	Current ST use	Daily=1, Less than daily=2
14a.	DUR_DAILY_ST	Duration of daily ST use in months	_____ months, N/A=(-999); Convert where response is in years or weeks e.g. 2 weeks=0.46 months
15.	REDUC_ST	Trying to cut down ST use	Yes=1 No=2
15a.	REAS_STRED_ILL	Reason for ST use reduction - Diagnosed with illness	Yes=1, No=2, N/A=(-999)
15b.	REAS_STRED_COST	High cost of ST	Yes=1, No=2, N/A=(-999)
15c.	REAS_STRED_NAG	Nagged or judged by people	Yes=1, No=2, N/A=(-999)
15d.	REAS_STRED_HEALTH	Own health	Yes=1, No=2, N/A=(-999)
15e.	REAS_STRED_HEFFCTS	Feel health effects of ST use	Yes=1, No=2, N/A=(-999)
15f.	REAS_STRED_CTRL	Get control of own life	Yes=1, No=2, N/A=(-999)
15g.	REAS_STRED_SMELL	Tired of smell or taste	Yes=1, No=2, N/A=(-999)
15h.	REAS_STRED_JLT	No reason, just want to	Yes=1, No=2, N/A=(-999)
15i.	REAS_STRED_OTHER	Other reason	Yes=1, No=2, N/A=(-999)
16a.	PROD_ZAR	Ever used or not – Zarda	Yes=1, No=2
16b.	PROD_BQUID	Betel quid with tobacco	Yes=1, No=2
16c.	PROD_KHAINI	Khaini	Yes=1, No=2
16d.	PROD_GUTK	Gutka	Yes=1, No=2
16e.	PROD_TPOW	Dry tobacco powder	Yes=1, No=2
16f.	PROD_PASTE	Tobacco paste	Yes=1, No=2
16g.	PROD_SNUS	Snus	Yes=1, No=2
16h.	PROD_OTHER	Other product	Yes=1, No=2
17a.	ZAR_USE	Used Zarda in past 7 days	Yes=1, No=2
17a.i.	N_DAY_ZAR	Days Zarda used in past 7 days	_____ days, N/A=(-999)
17a.ii.	N_TIME_ZAR	Number of times Zarda used	_____times/day, N/A=(-999)
17b.	BQUID_USE	Used betel quid (paan) with tobacco in past 7 days	Yes=1, No=2
17b.i.	N_DAY_BQ	Days betel quid (paan) with tobacco used in past 7 days	_____ days, N/A=(-999)
17b.ii.	N_TIME_BQ	Number of times betel quid (paan) with tobacco used	_____ times/day, N/A=(-999)

17c.	KHAINI_USE	Used Khaini or tobacco & lime mixture in past 7 days	Yes=1, No=2
17c.i.	N_DAY_KHAINI	Days Khaini or tobacco & lime mix used in past 7 days	_____ days, N/A=(-999)
17c.ii.	N_TIME_KHAINI	Number of times Khaini or tobacco & lime mixture used	_____ times/day, N/A=(-999)
17d.	GUTK_USE	Used Gutka or tobacco, betel-nut & catechu in past 7 days	Yes= 1, No=2
17d.i.	N_DAY_GUTK	Days Gutka used in past 7 days	_____days, N/A=(-999)
17d.ii.	N_TIME_GUT	Number of times Gutka used	_____times/day, N/A=(-999)
17e.	TPOW_USE	Used dry tobacco powder (Gul, Mishri) in past 7 days	Yes= 1, No=2
17e.i.	N_DAY_TPOW	Days dry tobacco powder used in past 7 days	_____days, N/A=(-999)
17e.ii.	N_TIME_TPOW	Number of times dry tobacco powder (Gul, Mishri) used	_____times/day, N/A=(-999)
17f.	PASTE_USE	Used tobacco paste (creamy snuff, Gudakhu) in past 7 days	Yes= 1, No=2
17f.i.	N_DAY_PASTE	Days tobacco paste used in past 7 days	_____days, N/A=(-999)
17f.ii.	N_TIME_PASTE	Number of times tobacco paste (creamy snuff, Gudakhu) used	_____times/day, N/A=(-999)
17g.	SN_USE	Used Snus in past 7 days	Yes= 1, No=2
17g.i.	N_DAY_SN	Days Snus used in past 7 days	_____days, N/A=(-999)
17g.ii.	N_TIME_SN	Number of times Snus used	_____times/day, N/A=(-999)
17h.	OTHER_USE	Used _____ in past 7 days	Yes= 1, No=2
17h.i.	N_DAY_OTHE	Days ____ used in past 7 days	_____days, N/A=(-999)
17h.ii.	N_TIME_OTHER	Number of times ____ used	_____times/day, N/A=(-999)
18.	ST_USE_COMP	ST use in company	Mainly with people=1 Mainly when alone=2 As often by yourself as with others=3
19.	N_ST_FRND	ST use among five closest friends	None=0, One=1, Two=2, Three=3, Four=4, All five=5
20.	N_ST_FAMLY	ST use among five closest relatives	None=0, One=1, Two=2, Three=3, Four=4, All five=5
21a.	ST_USE_REL_PARENT	Relation with ST user - Parents, grandparents	Yes=1, No=2, If none of the relatives use ST N/A=(-999)
21b.	ST_USE_REL_SIBL	Relation with ST user - Siblings	Yes=1, No=2, If none of the relatives use ST N/A=(-999)
21c.	ST_USE_REL_PART	Relation with ST user - Partners	Yes=1, No=2, If none of the relatives use ST N/A=(-999)
21d.	ST_USE_REL_	Relation with ST user -	Yes=1, No=2, If none of the

	CHIL	Children	relatives use ST N/A=(-999)
21e.	ST_USE_REL_OTHER	Relation with ST user - Other	Yes=1, No=2, If none of the relatives use ST N/A=(-999)
22.	ST_USE_HH	ST use in household	ST use is never allowed=1 Allowed during special occasions/ with visitors=2 Allowed at all times=3
ST Dependence Scales: Tobacco Dependence Screener			
23.	CD_MORE	Chew/dip more than intended to	Yes=1 No or not applicable=2
24.	FAIL_QUIT	Failure in quit or cut down attempt	Yes=1 No or not applicable=2
25.	CRAVE_ST_QUIT	Crave ST after quit or cut down	Yes=1 No or not applicable=2
26.	PROB_ST_QUIT	Problems/symptoms faced when quit or cut down	Yes=1 No or not applicable=2
27.	RST_ST_USE	Restart ST use because of these withdrawal symptoms	Yes=1 No or not applicable=2
28.	CONT_CD_ILL	Continued to chew/dip while having serious illness	Yes=1 No or not applicable=2
29.	CONT_USE_HP	Continue to use after knowing that it caused health problems	Yes=1 No or not applicable=2
30.	CONT_USE_MP	Continue to use after knowing that it caused mental problems	Yes=1 No or not applicable=2
31.	TOB_DEP	Felt dependent on tobacco	Yes=1, No or not applicable=2
32.	GVUP_WSA	Give up work or social activities to use tobacco	Yes=1 No or not applicable=2
FTND-ST			
33.	ST_RISE	ST use after rising up	After 60 minutes=0 31-60 minutes=1 6-30 minutes=2 Within 5 minutes=3
34.	STJ_SWL	Swallow tobacco juice	Never=0, Sometimes=1 Always=2
35.	DIF_GVUP	Chew hate to give up most	First one in the morning=1 Any other=0
36.	N_CANS	Number of cans used per week	1=0, 2-3=1, More than 3=2
37.	CHEW_FREQ	Chewing more frequently during the first hours after awakening	Yes=1, No=0
38.	CHEW_AIL	Chewing in ailment	Yes=1, No=0
OSSTD			
39.	CD_CONTROL	Controlled by chewing/ dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
40.	CD_MOOD	Mood change by chewing/dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
41.	CD_PLEAS	Importance of chewing/ dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7

42.	CD_URGE	Difficulty to ignore an urge to chew/dip	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
43.	CD_CONC	Chewing/ dipping for concentration	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
44.	CD_HNGCTRL	Chewing/dipping to control hunger	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
45.	CD_COMPANY	Chew/dip gives company like a close friend	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
46.	CD_TRIG	Trigger urges for chew/dip	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
47.	CD_FOCUS	Chewing/dipping helps stay focused	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
48.	CD_CRV_FREQ	Frequency of craving for chew/dip	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
49.	CD_WTCTRL	Chewing/dipping for weight control	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
50.	CD_HOOK	Hooked on chew/dip	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
51.	CD_REACH	Chew/dip without thinking	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
52.	CD_CRV_TIMES	Crave chew/dip at certain times of the day	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
53.	CD_ALONE	Lonely without chewing/dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
54.	CD_HEAVY	Considered heavy chewer/dipper by others	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
55.	CD_DIFF	Difficult to do work without chewing/dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
56.	CD_RISING	Chewing/dipping after rising up	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
57.	CD_ UNAWR	Unaware when chewing/dipping	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
58.	CD_THNK	Chewing/dipping helps thinking	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
59.	CD_BETTER	Chewing/dipping improves feeling	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
60.	CD_FEELGOOD	Chewing/dipping makes feel good	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
61.	CD_OVEREAT	Keeps away from overeating	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
62.	R_ADDICT	Addiction rate	1=1, 2=2, 3=3, 4=4, 5=5, 6=6, 7=7
ST – Buying and Carrying			
63.	ST_CARRY	Carrying ST	Yes=1, No=2
64a.	ST_BUY_PAC	ST bought in packets	_____ packets, N/A=(-999)
64b.	ST_BUY_CAN	ST bought in cans	_____ cans, N/A=(-999)
64c.	ST_BUY_OTHER	ST bought in other units	_____ units, N/A=(-999)

65.	ST_BUY_DUR	Duration this buy was meant to last in days	_____ days; Convert where the response is in hours, weeks or months e.g. 2 weeks=14 days
66.	ST_BUY_PRI	Price of purchase	_____ INR
67.	ST_BUY_PLACE	Place of ST purchase	Kiosk=1, Street vendor=2 Store=3, Internet=4 Outside the country=5 Another person=6, Other=7
ST – Behaviours, Health Risks and Quit Intentions			
68.	URG_ST	Urge to use ST	Not at all=0, Little of the time=1, Some of the time=2 Lot of the time=3, Almost all the time=4, All the time=5
69.	URG_ST_STRENGTH	Strength of the urge	No urges=0, Slight=1, Moderate=2, Strong=3, Very strong=4, Extremely strong=5
70.	Q_ATMP	Quit attempt	Yes=1, No=2
70a.	Q_ATMP_N	Number of quit attempts	_____ number N/A=(-999)
70b.	Q_ATMP_DUR	Quit duration	_____days, N/A=(-999) Convert where the response is in hours, weeks or months e.g. 2 weeks=14 days
70c.	Q_ATMP_PLAN	Plan for quit attempt	I did not plan the quit attempt in advance=1, Planned it for later the same day=2, The day before=3, Few days before=4, Few weeks before=5, Few months before=6, In case of no attempts, N/A=(-999)
71a.	METH_QST_COUNS	Method used to quit ST - Counseling	Yes=1 No=2
71b.	METH_QST_NRT	Method used to quit ST - NRT	Yes=1 No=2
71c.	METH_QST_PRESMED	Method used to quit ST - Prescription medicines	Yes=1 No=2
71d.	METH_QST_TRADMED	Method used to quit ST - Traditional medicines	Yes=1 No=2
71e.	METH_QST_QLINE	Method used to quit ST - Quit line	Yes=1 No=2
71f.	METH_QST_SELF	Method used to quit ST - Self	Yes=1 No=2
71g.	METH_QST_NA	Method used to quit ST - Never tried	Yes=1 No=2
71h.	METH_QST_OTHER	Method used to quit ST - Other	Yes=1 No=2
72.	INT_Q_ST	Intention to quit ST use	Never expect to quit=1 May quit in future, but not

			within 6 months=2 Will quit in the next 6 months=3 Will quit in the next 30 days=4
73.	N_VISIT_DOC	Number of time visit a doctor	_____Number
74.	Q_ST_USE	ST use during any visit to a doctor in past 12 months	Yes=1, No=2 N/A=(-999)
75.	ADV_Q_ST	Advice to stop ST during any visit to a doctor or health care provider in past 12 months	Yes=1 No=2 N/A=(-999)
76.	ASST_Q_ST	Assistance to quit ST during any visit to doctor/health care provider in past 12 months	Yes=1 No=2 N/A=(-999)
77.	REF_Q_ST	Reference by doctor to quit ST during any visit in past 12 months	Yes=1 No=2 N/A=(-999)
78.	ST_OC	How likely to develop oral cancer if continued ST use	No chance=1, Very unlikely=2, Unlikely=3 Moderate chance=4, Likely=5, Very likely=6, Certain to happen=7, Missing=Blank
79.	ST_HD	How likely to develop Heart disease if continued ST use	No chance=1, Very unlikely=2, Unlikely=3, Moderate chance=4, Likely=5, Very likely=6, Certain to happen=7, Missing=Blank
80.	ST_ SMK	ST compared to smoking	More health risks=1 Less=2, Same=3, Don't know=4, Missing=Blank
81.	RED_HRISK	Limiting ST use in last year	Never=1, Rarely=2, Sometimes=3, Often=4 Always=5, Missing=Blank
Past Smoking History			
82.	SMK_CIG	Smoked at least 100 cigarettes in lifetime	Yes=1 No=2
83.	AGE_SMK	Age when started smoking	_____years; If does not smoke at all N/A=(-999)
84.	DUR_SMK	Duration of smoking	Yes=1, No=2, If does not smoke at all N/A=(-999)
85.	SMK_DAYS	Days per week smoked during the time in life when smoked the most	_____days; If does not smoke at all N/A=(-999)
86.	N_CIG_SMK	Number of cigarettes smoked per day	_____times/cigarettes per day If does not smoke at all N/A=(-999)
87a.	SMK_PROD_CIG	Product commonly used for smoking - Cigarettes	Yes=1, No=2 If does not smoke at all N/A=(-999)

87b.	SMK_PROD_ROLLED	Product commonly used for smoking - Hand-rolled tobacco	Yes=1, No=2 If does not smoke at all N/A=(-999)
87c.	SMK_PROD_BIDI	Product commonly used for smoking - Bidi	Yes=1, No=2 If does not smoke at all N/A=(-999)
87d.	SMK_PROD_CIGAR	Product commonly used for smoking - Cigar	Yes=1, No=2 If does not smoke at all N/A=(-999)
87e.	SMK_PROD_CHER	Product commonly used for smoking - Cheroot	Yes=1, No=2 If does not smoke at all N/A=(-999)
87f.	SMK_PROD_CGRILLO	Product commonly used for smoking - Cigarillo	Yes=1, No=2 If does not smoke at all N/A=(-999)
87g.	SMK_PROD_PIPE	Product commonly used for smoking - Pipe	Yes=1, No=2 If does not smoke at all N/A=(-999)
87h.	SMK_PROD_WPIPE	Product commonly used for smoking - Water pipe	Yes=1, No=2 If does not smoke at all N/A=(-999)
87i.	SMK_PROD_OTHER	Product commonly used for smoking - Other	Yes=1, No=2 If does not smoke at all N/A=(-999)
88.	DUR_QSMK	Duration of quit smoking in years	_____years; Convert months to years where needed; Not quit=999, If does not smoke at all N/A=(-999)
89a.	METH_QSMK_COUNS	Method used to quit smoking - Counseling	Yes=1, No=2, Not quit=999, If does not smoke at all N/A=(-999)
89b.	METH_QSMK_NRT	Method used to quit smoking - NRT	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
89c.	METH_QSMK_PRESMED	Method used to quit smoking - Prescription medicines	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
89d.	METH_QSMK_TRADMED	Method used to quit smoking - Traditional medicines	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
89e.	METH_QSMK_QLINE	Method used to quit smoking - Quit line	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
89f.	METH_QSMK_SWITCH	Method used to quit smoking - Switching to ST	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
89g.	METH_QSMK_SELF	Method used to quit smoking - Self	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)

89h.	METH_QSMK_ OTHER	Method used to quit smoking - Other	Yes=1, No=2, Not quit=999 If does not smoke at all N/A=(-999)
90a.	REAS_QSMK_ ILL	Reason for quitting smoking - Diagnosed with illness	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90b.	REAS_QSMK_ COST	Reason for quitting smoking - High cost of smoking	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90c.	REAS_QSMK_ NAG	Reason for quitting smoking - Nagged or judged by people	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90d.	REAS_QSMK_ HEFFECTS	Reason for quitting smoking - Feel health effects of smoking	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90e.	REAS_QSMK_ HEALTH	Reason for quitting smoking - Own health	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90f.	REAS_QSMK_ BREATH	Reason for quitting smoking - Tired of feeling out of breath	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90g.	REAS_QSMK_ CTRL	Reason for quitting smoking - Get control of own life	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90h.	REAS_QSMK_ SMELL	Reason for quitting smoking - Tired of smell or taste	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90i.	REAS_QSMK_ JLT	Reason for quitting smoking - No reason, just did	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90i.	REAS_QSMK_ BANS	Reason for quitting smoking - Bans, restrictions	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
90i.	REAS_QSMK_ OTHER	Reason for quitting smoking - Other	Yes=1, No=2, Not quit=99 If does not smoke at all N/A=(-999)
Health Behaviours			
91.	MI	Had heart attack	Yes=1, No=2, Don't know=3 Missing=Blank
92.	CHD	Had angina or coronary heart disease	Yes=1, No=2, Don't know=3 Missing=Blank
93.	HT	Had hypertension or raised blood pressure	Yes=1, No=2, Don't know=3 Missing=Blank
94.	CAN	Had cancer	Yes=1, No=2, Don't know=3 Missing=Blank
95.	ASTH	Had asthma	Yes=1, No=2, Don't know=3 Missing=Blank
96.	TGP	Had teeth or gum problems	Yes=1, No=2, Don't know=3 Missing=Blank

97.	P_ACTIVITY	Participation in physical exercises	_____days per month Missing=Blank
97a.	DUR_ACTIVITY	Duration of physical exercises in minutes	_____minutes, Missing=Blank, N/A=(-999); Convert hours to minutes where needed
98.	ALCOHOL	Number of alcoholic drinks in past month	_____drinks Missing=Blank
99.	S_FRUIT	Servings of fruit per day	_____servings Missing=Blank
100.	S_VEG	Servings of vegetables per day	_____servings Missing=Blank
101.	HLTH_COND	Health condition	Poor=1, Fair=2, Good=3 Very good=4, Excellent=5 Missing=Blank

Appendix 3.3. Approved versions of survey documents

Participant information sheet, Version: 2, Date: 17/06/2014

Translation, Cultural Adaptation and Validation of a Smokeless Tobacco (ST) Dependence Scale in a South Asian Setting

Name of Researcher: Aishwarya Vidyasagaran, PhD Student, University of York

I would like to invite you to take part in the above named study. But first, I want to provide you with the following information to help you decide if you would like to take part.

What is the purpose of this study?

In India, the use of ST is very widespread and researchers have found that its use is associated with health problems like cancer, heart disease and oral disease. Many ST users find it difficult to give up the habit and become dependent or addicted to ST products.

Researchers find it useful to measure this ST dependence or addiction, and some measurement scales (set of questions) have been developed for this purpose. One such scale is the Oklahoma Scale for Smokeless Tobacco Dependence (OSSTD).

This scale has recently been developed and applied to measure tobacco dependence among ST users in the US. The purpose of this study is to assess whether a Hindi version of the OSSTD can be applied to measure tobacco dependence among ST users in India.

Who is doing the study?

This study is being carried out as part of the researcher's PhD training at the Department of Health Sciences, University of York.

Who is being asked to participate?

I will be asking many ST users in India - who are 18 years or older, and fluent in spoken Hindi to take part in the study.

What will be involved if I take part in this study?

If you decide to take part, you will be asked to:

- Sign a consent form (or) provide your thumbprint on the consent form in the presence of a literate witness
- Participate in a face-to-face interview with the researcher
- Provide a saliva sample (this is done by chewing on a cotton stick for two minutes)

The interview will last about 40 minutes. The questions in the interview will not be difficult to answer. They are just to find out some details about your tobacco use habit. The saliva test will not harm you in any way.

Why do I need to provide a saliva sample?

Your saliva will be sent to some scientists who will test the sample to assess the amount of tobacco use by measuring cotinine levels, a metabolite of nicotine present in tobacco. These scientists will not have your name or any information you provide during the interview.

What are the advantages and disadvantages of taking part?

There are no direct advantages or disadvantages of taking part in the study. However, your participation in the study will help researchers explore and understand tobacco dependence associated with ST use in India. This understanding may be applied to the development of more effective ST cessation treatments. On completing the interview, you will be offered a voucher for the value of approximately 100 Indian Rupees as compensation for time spent in providing the interview data.

Do I have to take part?

Your participation in the study is entirely voluntary – You do not have to take part if you don't want to, you do not have to give a reason, and there will be no consequences based on your decision.

Can I withdraw from the study at any time?

You are free to withdraw from the study any time during the interview without giving any reasons for withdrawing. Just let me know that you don't want to take part any more. However, should you choose to withdraw, please note that the data you have already provided will still be used by the researcher as detailed below.

Will the information I give be kept confidential?

Provided no evidence of criminal activities emerges during the interview, all the information you provide, along with the results of the saliva test will be kept private and secret. This means that the answers you give and the saliva results will only be viewed by researchers at the University of York and not be shown to anyone else.

What will happen to the information I provide?

All the information you give will be put into a computer and subsequently used by researchers at the University of York to see if the OSSTD scale can be used to measure tobacco dependence among ST users in India.

Who has reviewed this study?

Health Sciences Research Governance Committee, University of York and Institutional Ethics Committee, Indian Institute of Public Health – Delhi. Please remember you do not have to take part if you do not want to, but we hope you will find it interesting if you do.

Contact information:

If you would like more information, or have any questions about the study, please contact:

Aishwarya Vidyasagaran

Email: av661@york.ac.uk

Phone: (Telephone numbers of research sites in India will be provided)

Thank you for reading this information.

Consent form

Version: 2, Date: 17/06/2014

Please confirm agreement to the statements below by putting your initials (or) thumbprints in the boxes provided.

I have understood all the information contained in the participant information sheet	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	
I understand my participation in the study is entirely voluntary and that I am free to withdraw from the study: At any time during the interview Without having to give a reason for withdrawing Without my medical care or legal rights being affected	
I understand that the information I provide during the study may be looked at by researchers at the University of York. I give permission for these individuals to have access to my data for analysis.	
If I choose to withdraw from the study, the data that I have already provided will still be used by researchers for analysis	
I understand that any information I provide, including personal details, will be kept confidential, stored securely and only accessed by those researchers carrying out the study, unless evidence of any criminal activities emerge during the interview	
I understand that any information I give may be included in published documents but all information will be anonymised	
I agree to provide a saliva sample for cotinine level measurements	
I agree to take part in this study	

Thank you for agreeing to take part in this study

Participant Signature (or) Thumbprint …… Date ……

Name of Participant ……...

Signature of Literate Witness ….…… Date ……

Name of Literate Witness ……...

Researcher Signature ….……. Date ……

Name of Researcher …….....

Survey Questionnaire

Version: 1.4, Date: 31/01/2015

S.No. |__|__|__| Site ID |__|__|

Socio-demographic Data

1. Please indicate your gender

[ ] Male (पुरुष)

[ ] Female (महिला)

2. Are you currently pregnant? (क्या आप इस समय गर्भवती हैं /क्या आप पेट से हैं?)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Not Applicable (लागू नहीं होता है)

3. Are you currently breastfeeding? (क्या आप इस समय स्तनपान कर रही हैं / क्या आप अभी बच्चे को अपना दूध पिला रहीं हैं?)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Not Applicable (लागू नहीं होता है)

4. What is the highest level of education you have completed? (आपने अपनी पढ़ाई कहाँ तक पूरी की है?)

[ ] No formal schooling

[ ] Less than primary school completed

[ ] Primary school completed

[ ] Less than secondary school completed

[ ] Secondary school completed

[ ] Higher secondary school completed

[ ] College/University completed

[ ] Post-graduate degree completed

5. Which of the following best describes your main work status? (निम्न में से कौन सा कार्य, आपके मुख्य कार्य को अच्छी तरह बताता है)

[ ] Government employee (सरकारी कर्मचारी)

[ ] Non-government employee (गैर - सरकारी कर्मचारी /प्राइवेट कंपनी के कर्मचारी)

[ ] Self-employed (स्वरोजगार / कोई अपना काम)

[ ] Student (छात्र / छात्रा)

[ ] Homemaker (गृहिणी / गृहस्थ)

[ ] Retired (सेवानिवृत्त)

[ ] Unemployed, able to work (बेरोजगार, काम करने योग्य)

[ ] Unemployed, unable to work (बेरोजगार, काम न करने योग्य)

6. Please tell me whether you / your household have the following items (कृपया बताएँ, आपके पास या आपके घर में निम्न आइटम है या नहीं):

[ ] Electricity (बिजली)

[ ] Flush Toilet (फ्लश शौचालय)

[ ] Fixed Telephone (टेलीफोन)

[ ] Cell Telephone (सेल फोन / मोबाइल फ़ोन)

[ ] Television (टेलीविज़न)

[ ] Radio (रेडियो)

[ ] Refrigerator (फ्रिज)

[ ] Car (कार)

[ ] Moped/Scooter/Motorcycle (मोपेड / स्कूटर / मोटर साइकिल)

[ ] Washing machine (वाशिंग मशीन)

7. What is your Religion? (आपका धर्म क्या है?)

[ ] Hindu (हिंदू)

[ ] Muslim (मुस्लिम)

[ ] Christian (ईसाई)

[ ] Sikh (सिख)

[ ] Buddhist (बौद्ध धर्म)

[ ] Jain (जैन)

[ ] Jewish (यहूदी धर्म)

[ ] Parsi / Zoroastrian (पारसी)

[ ] No religion (कोई धर्म नहीं)

[ ] Other, please state (अन्य, कहने कृपया) …….

Smokeless Tobacco Use History

The following questions are about using Smokeless Tobacco (ST) products, such as Tobacco leaf mixture, Betel quid with tobacco, Khaini or tobacco-lime mixture, Gutkha or tobacco-betel nut-catechu mixture, Gul, Mishri, Tobacco paste, Snus, etc. (अगले कुछ प्रश्न धूम्ररहित तंबाकू के

इस्तेमाल से संबंधित हैं, जैसे तंबाकू की पत्ती, तंबाकू वाला पान, खैनी, गुटखा, गुल, तम्बाकू पेस्ट, आदि)

8. In the past 7 days, on how many days did you use ST? (पिछले 7 दिनों में, आपने कितने दिनों धूम्ररहित तंबाकू का उपयोग किया था?)

|__| Days (दिन)

9. In the past 7 days, on the days that you used ST, how many times per day did you use ST? (पिछले 7 दिनों में जब भी आपने धूम्ररहित तंबाकू का इस्तेमाल किया तो एक दिन में कितनी बार इसका उपयोग किया?)

|__||__| Times (समय)

10. How old were you when you first used ST? (जब आपने पहली बार धूम्ररहित तंबाकू का सेवन किया तो उस समय आपकी उम्र क्या थी?)

|__||__| Years (साल)

11. Have you ever used ST daily for 6 months or more? (क्या आपने धूम्र रहित तम्बाकू का उपयोग कभी प्रतिदिन लगातार छः महीनों या उससे ज्यादा के लिए किया है?)

[ ] Yes (हाँ)

[ ] No (नहीं)

12. Think of the time in your life when you used THE MOST amount of ST. During that time, on how many days per week did you use ST? (अपने जीवन के ऐसे समय का विचार करिये जब आपने धूम्ररहित तंबाकू का सबसे अधिक मात्रा में उपयोग किया. उस दौरान आपने धूम्ररहित तंबाकू का उपयोग हर हफ्ते में कितने दिन किया?)

|__| Days per week

13. Think of the time in your life when you used THE MOST amount of ST. During that time, on the days that you used ST, how many times per day did you use ST? (अपने जीवन के ऐसे समय का विचार करिये जब आपने धूम्ररहित तंबाकू का सबसे अधिक मात्रा में उपयोग किया. उन दिनों, आपने एक दिन में कितनी बार धूम्ररहित तंबाकू का उपयोग किया?)

|__||__| Times per day

14. Do you currently use ST on a daily (or) less than daily basis? (क्या आप अभी प्रतिदिन या उससे कम समय बार धूम्ररहित तंबाकू उपयोग करते हैं?)

[ ] Daily

[ ] Less than daily

a. [IF DAILY:] How long have you been using ST daily? [यदि प्रतिदिन], कितने समय से आप प्रतिदिन धूम्ररहित तंबाकू का उपयोग कर रहे हैं?)

|__||__| Weeks (हफ्तों)

|__||__| Months (महीनों)

|__||__| Years (वर्षों)

15. Are you currently trying to cut down on your ST use? (क्या आप अभी धूम्ररहित तम्बाकू के उपयोग को कम करने का प्रयास कर रहे हैं?)

[ ] Yes (हाँ)

[ ] No (नहीं)

a. [IF YES:] Why are you currently trying to cut down on your ST use? Check all that applies [यदि हाँ] तो आप अभी धूम्ररहित तम्बाकू के उपयोग को कम करने का प्रयास क्यों कर रहे हैं? जो भी लागू होता हैं उन्हें चिन्हित करे

[ ] I have been diagnosed with an illness (मुझे एक बीमारी हो गयी है)

[ ] The cost of ST use is too high (धूम्ररहित तम्बाकू का उपयोग बहुत खर्चीला है)

[ ] I got nagged or people are judging me (लोग मुझे ताना मारते हैं)

[ ] My health (मेरा स्वास्थ्य)

[ ] I have started to feel health effects of ST use (मैंने धूम्ररहित तम्बाकू के प्रभावों को महसूस करना सुरु कर दिया है)

[ ] I want to get control of my life (मुझे अपनी जिंदगी पर नियंत्रण पाना चाहता हूँ)

[ ] I am tired of the smell or taste (मैं इसकी महक और स्वाद से तंग आ चूका हूँ)

[ ] I don't know, I just want to (मुझे पाता नहीं लेकिन मैं ऐसा करना चाहता हूँ)

[ ] Other reason (कोई और कारण) ……

16. Which of these ST products have you ever used? Check all that applies (इनमें से कौन सा धूम्ररहित तम्बाकू उत्पाद अपने उपयोग किया है? जो भी लागू होता हैं उन्हें चिन्हित करे)

[ ] Tobacco leaf or leaf mixture (Zarda) (तम्बाकू की पत्ती या तम्बाकू की पत्ती का मिश्रण (ज़र्दा)

[ ] Betel quid (Pan) with tobacco (पान के साथ तम्बाकू)

[ ] Khaini or tobacco, lime mixture (खैनी या तम्बाकू, चूने का मिश्रण)

[ ] Gutka or tobacco, betel-nut & catechu mixture (गुटखा या तम्बाकू, पान-सुपारी और कत्थे का मिश्रण)

[ ] Dry tobacco powder (Gul, Mishri) (तम्बाकू का सूखा पावडर (गुल, मिश्री)

[ ] Tobacco paste (Creamy snuff, Gudakhu) (तम्बाकू की लेई (क्रीम जैसी सुंघनी, गुडाखू)

[ ] Snus

[ ] Any other form of ST, specify type (और किसी प्रकार का धूम्ररहित तम्बाकू, उसका प्रकार बताएं)

17. Which of the following ST products have you used in the past 7 days? For each product,

please answer YES (or) NO (इनमे से कौन सा धूम्ररहित तम्बाकू उत्पाद आपने पिछले सात दिनों में उपयोग किया है? प्रत्येक उत्पाद के लिए हाँ या ना में उत्तर दें)

a. Tobacco leaf or tobacco leaf mixture (Zarda) तम्बाकू की पत्ती या तम्बाकू की पत्ती का मिश्रण (ज़र्दा)

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use tobacco leaf or tobacco leaf mixture (Zarda)? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन तम्बाकू की पत्ती या तम्बाकू की पत्ती का मिश्रण (ज़र्दा) का उपयोग किया?

|__| Days (Range: 1 - 7)

ii. On the days that you used tobacco leaf or tobacco leaf mixture, how many times on average did you use the product each day? जिन दिनों आपने तम्बाकू की पत्ती या तम्बाकू की पत्ती के मिश्रण का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99)

b. Betel quid (Pan) with tobacco पान के साथ तम्बाकू

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use betel quid (Pan) with tobacco? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन पान के साथ तम्बाकू का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used betel quid (Pan) with tobacco, how many times on average did you use the product each day? जिन दिनों आपने पान के साथ तम्बाकू का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99)

c. Khaini or tobacco & lime mixture खैनी या तम्बाकू, चूने का मिश्रण

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use Khaini or tobacco & lime mixture? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन खैनी या तम्बाकू, चूने के मिश्रण का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used Khaini or tobacco & lime mixture, how many times on average did you use the product each day? जिन दिनों आपने खैनी या तम्बाकू, चूने के मिश्रण का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99)

d. Gutka or tobacco, betel-nut & catechu mixture (गुटखा या तम्बाकू, पान-सुपारी और कत्थे का मिश्रण)

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use Gutka or tobacco, betel-nut & catechu mixture? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन गुटखा या तम्बाकू, पान-सुपारी और कत्थे का मिश्रण का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used Gutka or tobacco, betel-nut & catechu mixture, how many times on average did you use the product each day? (जिन दिनों आपने गुटखा या तम्बाकू, पान-सुपारी और कत्थे के मिश्रण का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99)

e. Dry tobacco powder (Gul, Mishri) तम्बाकू का सूखा पावडर (गुल, मिश्री)

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use dry tobacco powder (Gul, Mishri)? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन तम्बाकू के सूखे पावडर (गुल, मिश्री) का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used dry tobacco powder (Gul, Mishri), how many times on average did you use the product each day? जिन दिनों आपने तम्बाकू के सूखे पावडर (गुल, मिश्री) का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99)

f. Tobacco paste (Creamy snuff, Gudakhu) तम्बाकू की लेई (क्रीम जैसी सुंघनी, गुडाखु)

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use tobacco paste (Creamy snuff, Gudakhu)? [यदि हाँ] पिछले सात दिनों में आपने कितने दिन तम्बाकू की लेई (क्रीम जैसी सुंघनी, गुडाखु) का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used tobacco paste (Creamy snuff, Gudakhu), how many times on average did you use the product each day? जिन दिनों आपने तम्बाकू की लेई (क्रीम जैसी सुंघनी, गुडाखु) का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99) प्रतिदिन (1-99) बार

g. Snus (तम्बाकू चूर्ण)

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use Snus?
[यदि हाँ] पिछले सात दिनों में आपने कितने दिन तम्बाकू चूर्ण का उपयोग किया है?

|__| Days (Range: 1 - 7)

ii. On the days that you used Snus, how many times on average did you use the product each day? जिन दिनों आपने तम्बाकू तम्बाकू चूर्ण का उपयोग किया, प्रतिदिन औसतन कितनी बार आपने इस उत्पाद का उपयोग किया?

|__||__| Times per day (Range: 1 - 99) प्रतिदिन (1-99) बार

h. ……...

[ ] Yes (हाँ)

[ ] No (नहीं)

i. [IF YES] In the past 7 days, on how many days did you use ……?

|__| Days (Range: 1 - 7) (1-7) दिन

ii. On the days that you used this product, how many times on average did you use it each day?

|__||__| Times per day (Range: 1 - 99) प्रतिदिन (1-99) बार

Sociocultural measures

18. In the past 7 days, did you use ST? पिछले सात दिनों में क्या आपने ने धूम्र-रहित तम्बाकू का उपयोग किया है?

[ ] Mainly when you were with people (मुख्यतः जब मैं और लोगों के साथ थे)

[ ] Mainly when you were alone (मुख्यतः जब मैं अकेला था)

[ ] As often by yourself as with others (दूसरों के साथ या अकेले एक बराबर)

19. How many of your five closest friends use ST? आपके पांच सबसे नजदीकी दोस्तों में से कितने धूम्र-रहित तम्बाकू का उपयोग करते हैं?

[ ] None (कोई नहीं)

[ ] One (एक)

[ ] Two (दो)

[ ] Three (तीन)

[ ] Four (चार)

[ ] All five (सभी पांच)

20. How many of your five closest relatives use ST? आपके पांच सबसे नजदीकी रिश्तेदारों में से कितने धूम्र-रहित तम्बाकू का उपयोग करते हैं?

[ ] None (कोई नहीं)

[ ] One (एक)

[ ] Two (दो)

[ ] Three (तीन)

[ ] Four (चार)

[ ] All five (सभी पांच)

21. Among your closest relatives, who all use ST? Check all that applies आपके सबसे नजदीकी रिश्तेदारों में से कौन कौन धूम्र-रहित तम्बाकू का उपयोग करता हैं? (जो सब सही हो उन्हें चिन्हित करें)

[ ] Parents, Grandparents, Parents-in-law (माता-पिता, दादा-दादी, सास-ससुर)

[ ] Siblings (including sister- or brother-in-law) भाई-बहन (भाभी या जीजा भी)

[ ] Partners (including wife or husband) साझेदार (पति या पत्नी भी)

[ ] Children (including son- or daughter-in-law) बच्चे (बेटा या बहु भी)

[ ] Any other relatives living in the same household (उसी घर में रहने वाला कोई और रिश्तेदार)

22. Which statement best describes ST use in your household? इनमे से कौन सा धूम्र-रहित तम्बाकू के आपके घर में उपयोग की सबसे सटीक व्याख्या करता है?

[ ] ST use is never allowed (धूम्ररहित तम्बाकू के उपयोग की आज्ञा कभी भी नहीं दी जायेगी)

[ ] ST use is allowed during special occasions or when there are visitors (धूम्ररहित तम्बाकू के उपयोग की आज्ञा केवल ख़ास अवसर या जब मेहमान होंगे तब होगी)

[ ] ST use is allowed at all times (धूम्ररहित तम्बाकू के उपयोग की आज्ञा हमेशा रहेगी)

Smokeless Tobacco Dependence Scales

Tobacco Dependence Screener

23. Have you often had periods of days when you chew/dip a lot more than you intended to? (क्या अक्सर ऐसा होता है कि आप अपनी इच्छा से ज्यादा तम्बाकू खाते है?)

☐ Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

24. Have you ever tried to quit or cut down on tobacco and found you could not? (क्या आपने कभी तम्बाकू छोड़ने या कम करने की कोशिश की है और पाया है की आप इसे छोड़ नहीं सकते?)

☐ Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

25. Did you crave tobacco after you quit or cut down on it? (क्या आपको तम्बाकू सेवन छोड़ने या कम करने के बाद दोबारा तम्बाकू खाने की इच्छा हुई?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

26. Did you have any of the following problems when you quit or cut down on tobacco: irritation, nervousness, restlessness, trouble concentrating, headache, drowsiness, upset stomach, heart slow down, increased appetite or body weight, hand-shakes, depression? (क्या आपको तम्बाकू छोड़ने या कम करने के बाद इनमें से किसी तकलीफ़ का सामना करना पड़ा: चिडचिडापन, घबराहट, अशांति, ध्यान लगाने में मुश्किल, सिरदर्द, सुस्ती, पेट ख़राब रहना, ह्रदय गति धीमी होना, ज्यादा भूख लगना या वजन का बढ़ना, हाँथ कांपना या उदासी?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

27. Did you ever start using tobacco again to keep from having such problems? (क्या इन मुसीबतों से दूर रहने के लिए आपने फिर से तम्बाकू का इस्तेमाल कभी शुरू किया?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

28. Have you ever continued to chew/dip when you had a serious illness that you knew made it unwise to use tobacco? (क्या आपने कभी किसी बीमारी के दौरान तम्बाकू सेवन किया, ये जानने के बाद भी कि ऐसा करना आपकी सेहत के लिये हानिकारक है)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

29. Did you continue to use tobacco after you knew that it caused you health problems? (तम्बाकू खाने से आपको स्वास्थ्य सम्बन्धी मुसीबतें होती हैं, क्या यह जानने के बाद भी आपने उसका इस्तेमाल जारी रखा?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

30. Did you continue to use tobacco after you knew that it caused you mental problems? (तम्बाकू से आपको मानसिक मुसीबतें होती हैं, क्या ये जानते हुए भी आपने तम्बाकू का इस्तेमाल जारी रखा?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

31. Have you ever felt like you were dependent on tobacco? (क्या आपने कभी ऐसा महसूस किया की आप तम्बाकू पर निर्भर हैं?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

32. Have you ever given up work or social activities so you could use tobacco? (क्या आपने कभी तम्बाकू सेवन के लिए अपने काम या किसी सामाजिक कार्य (दोस्तों से मिलना, कहीं घुमने जाना,

इत्यादि) का त्याग किया?)

☐Yes (हाँ) ☐ No or Not Applicable (नहीं या लागू नहीं होता है)

Fagerström Test for Nicotine Dependence - Smokeless Tobacco (FTND-ST)

33. How soon after you wake up do you place your first dip? (सुबह उठने के कितनी देर बाद आप पहला तम्बाकू सेवन करते हैं)

☐5 मिनट के भीतर ☐6 - 30 मिनट में ☐31 - 60 मिनट में ☐ 60 मिनट के बाद

34. How often do you intentionally swallow tobacco juice? (आप कितनी बार जान-बूझ कर तम्बाकू का रस निगल जाते हैं)

☐Always (हमेशा) ☐Sometimes (कभी कभी) ☐Never (कभी नहीं)

35. Which chew would you hate to give up most? (आप किस समय के तंबाकू सेवन को छोडना सबसे ज्यादा नापसन्द करेंगे)

☐The first one in the morning (सुबह का पहला वाला) ☐Any other (कोई और)

36. How many cans/pouches per week do you use? (आप एक हफ्ते में कितने डब्बे / थैलियां इस्तेमाल करते हैं)

☐More than 3 (तीन से ज्यादा) ☐2 से 3 ☐1

37. Do you chew more frequently during the first hours after awakening than during the rest of the day? (क्या आप बाकी दिन के मुकाबले में सुबह के पहले तंबाकू सेवन को ज्यादा चबाते हैं)

☐Yes (हाँ) ☐No (नहीं)

38. Do you chew if you are so ill that you are in bed most of the day? (जब आप बीमारी के कारण बिस्तर पर पड़े हुए हैं क्या तब भी आप तंबाकू सेवन करते हैं?)

☐Yes (हाँ) ☐No (नहीं)

Oklahoma Scale for Smokeless Tobacco Dependence (OSSTD)

Please rate your level of agreement for each of the statement using the following scale (हर वाक्य पर अपनी सहमती के उत्तर पर निशान लगाए):

1	2	3	4	5	6	7
Not true of me at all (मेरे लिए बिलकुल असत्य)						Extremely true of me (मेरे लिए अत्यधिक सही)

CIRCLE ONE NUMBER FOR EACH ITEM (प्रत्येक विषय / अंश के लिए किसी एक संख्या पर गोला बनायें)

39.	Chew/dip controls me (तंबाकू सेवन मुझे नियंत्रित करता है)	1	2	3	4	5	6	7
40.	Chewing improves my mood (तंबाकू सेवन से मेरी मनोदशा में सुधार होता है)	1	2	3	4	5	6	7
41.	Very few things give me pleasure each day like chewing (बहुत कम ऐसी चीजें हैं जो मुझे प्रतिदिन तम्बाकू जैसी ख़ुशी देती हैं)	1	2	3	4	5	6	7
42.	It's hard to ignore an urge to chew/dip (तंबाकू सेवन की तीव्र इच्छा को अनदेखा करना मुश्किल है)	1	2	3	4	5	6	7
43.	I chew/dip when I really need to concentrate (जब मुझे ध्यान लगाने की अधिक जरूरत होती है तो मैं तम्बाकू सेवन करता हूँ)	1	2	3	4	5	6	7
44.	I rely upon chewing/dipping to control my hunger and eating (मैं अपनी भूख को मिटाने के लिये तंबाकू सेवन का सहारा लेता हूँ)	1	2	3	4	5	6	7
45.	Chew/dip keep me company, like a close friend (तम्बाकू, एक नजदीकी दोस्त की तरह मेरा साथ देता है)	1	2	3	4	5	6	7
46.	There are particular sights, smells that trigger strong urges to chew (कुछ देखने से और कुछ सुगन्ध से मुझे तंबाकू सेवन के लिए प्रेरित करती हैं)	1	2	3	4	5	6	7
47.	Chewing/dipping helps me stay focused (तंबाकू सेवन से मुझे ध्यान लगाने में सहायता मिलती है)	1	2	3	4	5	6	7
48.	I frequently crave chew/dip (मुझे अक्सर तंबाकू सेवन की अधिक इच्छा होती है)	1	2	3	4	5	6	7
49.	Weight control is a major reason that I chew/dip (मेरे तंबाकू सेवन का एक प्रमुख कारण है वजन पर नियंत्रण रखना)	1	2	3	4	5	6	7
50.	I'm really hooked on chew/dip (मुझे तंबाकू सेवन की लत है)	1	2	3	4	5	6	7
51.	I find myself reaching for chew/dip without thinking about it (कई बार ध्यान दिए बिना अथवा सोचे बिना ही मैंने अपने आप को तम्बाकू का प्रयोग करते हुए पाया है)	1	2	3	4	5	6	7
52.	I crave chew/dip at certain times of the day (मुझे दिन के कुछ समय में तंबाकू सेवन कि अधिक इच्छा होती है)	1	2	3	4	5	6	7
53.	I would feel alone without my chew/dip (मुझे तंबाकू सेवन के बिना अकेला पन महसूस होगा)	1	2	3	4	5	6	7
54.	Other chewers/ dippers would consider me a heavy chewer/dipper (अन्य तंबाकू सेवकों का मानना है कि मैं काफ़ी	1	2	3	4	5	6	7

	ज्यादा तंबाकू सेवन करता हूँ)							
55.	Some things are very hard to do without chewing/dipping (तंबाकू सेवन के बिना कुछ कार्य करना बहुत कठिन है)	1	2	3	4	5	6	7
56.	I chew/dip within the first 30 minutes of awakening in the morning (मैं सुबह उठने के तीस मिनट के भीतर तंबाकू सेवन करता हूँ)	1	2	3	4	5	6	7
57.	Sometimes I am not aware that I am chewing/dipping (कभी-कभी मुझे पता भी नहीं चलता की मैं तम्बाकू चबा रहा हूँ)	1	2	3	4	5	6	7
58.	Chewing/dipping helps think better (तम्बाकू मुझे बेहतर सोचने में सहायता प्रदान करता है)	1	2	3	4	5	6	7
59.	Chewing/dipping really helps me feel better if I've been feeling down (जब मैं उदास होता हूँ, तब तंबाकू सेवन मुझे बेहतर महसूस करने में मदद करता है)	1	2	3	4	5	6	7
60.	Chewing/dipping makes me feel good (तंबाकू सेवन करने से मुझे अच्छा महसूस होता है)	1	2	3	4	5	6	7
61.	Chewing/dipping keeps me from over eating (तंबाकू मुझे ज्यादा खाना खाने से बचाता है)	1	2	3	4	5	6	7

62. Please rate your addiction to ST using the following scale (कृपया अपनी तम्बाकू खाने की आदत को नीचे दिए गए स्तर पर मापें)

1	2	3	4	5	6	7
I am not addicted to ST at all (मुझे तम्बाकू खाने की आदत बिलकुल नहीं है)					I am extremely addicted to ST (मुझे तम्बाकू खाने की बहुत ही लत है)	

Smokeless Tobacco - Buying and Carrying

63. Do you usually carry ST with you? (आम तौर पर, क्या आप खाने का तम्बाकू अपने साथ रखते हैं?)

[ ] Yes (हाँ)

[ ] No (नहीं)

64. The last time you bought ST for yourself, how many of those did you buy? (पिछली बार जब आपने अपने लिए खाने का तम्बाकू खरीदा, तो कितना खरीदा) [RECORD NUMBER AND CHECK UNIT BELOW]

|__||__||__|

[ ] Packets (थैलियां)

[ ] Cans (डब्बे)

[ ] Other, specify (कोई और मात्रा) ….……...

65. For how long was this buy meant to last? (उतना तम्बाकू कितने देर तक चलाने के लिए खरीदा?)

|__||__| Hours (घंटे)

|__||__| Days (दिन)

|__||__| Weeks (हफ्तों)

|__||__| Months (महीने)

66. In total, how much money did you pay for this purchase? (इस खरीदारी में अपने कुल कितने रुपए खर्च किए) [IF DON'T KNOW, ENTER 999]

|__||__||__| Rupees (रुपए)

67. The last time you purchased ST products for yourself, where did you buy them? (पिछली बार जब आपने अपने लिए कोई खाने का तम्बाकू खरीदा, उसे कहाँ से खरीदा / खरीदीं?)

[ ] Kiosk (किओस्क मशीन)

[ ] Street vendor (गुमटी, सड़क की दूकान)

[ ] Store (दुकान)

[ ] Internet (इंटरनेट)

[ ] Outside the country (विदेश)

[ ] From another person (किसी दुसरे इंसान से)

[ ] Other, specify (कोई और तरीका) ……..

Smokeless Tobacco - Behaviours, Health Risks & Quit Intentions

68. How much of the time have you felt the urge to use ST in the past 24 hours? (पिछले चौबीस घंटे में कितनी बार आपको तम्बाकू खाने की इच्छा हुई?)

Not at all (बिलकुल भी नहीं)	A little of the time (थोड़े कम समय)	Some of the time (थोड़े समय)	A lot of the time (काफी समय)	Almost all the time (लगभग हर समय)	All the time (सारे समय)
0	1	2	3	4	5

69. How strong have the urges been? (तम्बाकू खाने की इच्छा कितनी ज़ोर से हुई?)

No urges (बिलकुल नहीं)	Slight (हल्की)	Moderate (थोड़ी बहुत)	Strong (ज़ोर से)	Very strong (काफी ज़ोर से)	Extremely strong (बहुत ही ज़ोर से)
0	1	2	3	4	5

70. During the past 12 months, have you tried to quit using ST completely? (पिछले 12 महीने में, आपने कभी तम्बाकू खाना पूरी तरह छोड़ने की कोशिश की है?

[ ] Yes (हाँ)

[ ] No (नहीं)

a. [IF YES:] During the past 12 months, how many times have you stopped using ST for one day or longer because you were trying to quit? (पिछले 12 महीने में, जब भी आपने तम्बाकू खाना छोड़ने की कोशिश की, उस कारण कितनी बार एक दिन या एक दिन से ज़्यादा देर तक छोड़ पाये?)

|__||__||__| Number of times (बार)

b. During the past 12 months what is the longest length of time you stopped using ST because you were trying to quit? (पिछले 12 महीने में, जब भी आपने तम्बाकू खाना छोड़ने की कोशिश की, सबसे ज्यादा कितनी देर तक छोड़ पाये?)

|__||__| Hours (घंटे)

|__||__| Days (दिन)

|__||__| Weeks (हफ्तों)

|__||__| Months (महीने)

c. Which of these statements best describes how your most recent quit attempt started? (सबसे हाल में जब आपने छोड़ने की कोशिश की, उसकी शुरुआत के बारे में इनमें से कौन सी बातें सही हैं?)

[ ] I did not plan the quit attempt in advance, I just did it (मैने पेहले से छोड़ने की योजना नहीं बनायी, बस ऐसे ही छोड़ दिया)

[ ] I planned the attempt for later theday (उसी दिन छोड़ने की योजना बना कर उसी दिन छोड़ दिया)

[ ] I planned the attempt the day beforehand (एक दिन पहले ही छोड़ने की योजना बना ली थी)

[ ] I planned the attempt a few days before (कुछ दिन पहले ही छोड़ने की योजना बना ली थी)

[ ] I planned the attempt a few weeks before (कुछ हफ़्ते पहले ही छोड़ने की योजना बना ली थी)

[ ] I planned the attempt a few months before (कुछ महीने पहले ही छोड़ने की योजना बना ली थी)

71. Have you ever used any of the following methods to help you stop ST use? Check all that applies (धूम्ररहित तम्बाकू छोड़ने के लिये आपने क्या इनमें से किसी तरीके की मदद ली है?)

[ ] Counseling, including at a tobacco cessation clinic (परामर्श, तम्बाकू विमुक्ति / तम्बाकू छुड़वाने के चिकित्सालय में)

[ ] Nicotine replacement therapy, such as the patch or gum (निकोटीन के बदले में उपचार, जैसा कि पैच या गम)

[ ] Other prescription medications, for example Bupropion (अन्य निर्धारित उपचार, जैसे कि बूप्रोपियन की गोली)

[ ] Traditional medicines for e.g. Ayurvedic, Homeopathic, Unani (पारंपरिक उपचार, जैसे कि आयुर्वेदिक, होम्योपैथिक, यूनानी)

[ ] A quit line or a telephone support line (धूम्रपान छोड़ने से संबंधित, टेलीफोन पर विमर्श)

[ ] I quit on my own, did not use anything (मैंने खुद ही छोड़ दिया, किसी तरीके की मदद के बिना)

[ ] I have never tried to quit using ST (मैंने कभी छोड़ने की कोशिश नहीं की)

[ ] Other, please describe (कोई और तरीका) ……

72. What best describes your intentions to stop using ST completely? Would you say you…? तम्बाकू छोड़ने के बारे में आपका क्या लक्ष्य है?

[ ] Never expect to quit (मैं कभी छोड़ने की नहीं सोच सकता)

[ ] May quit in the future, but not in the next 6 months (मैं छोड़ सकता हूँ भविष्य में, मगर अगले 6 महीने में नहीं)

[ ] Will quit in the next 6 months (मैं अगले छह महीने में छोड़ दूंगा)

[ ] Will quit in the next 30 days (मैं अगले एक महीने में छोड़ दूंगा)

73. During the past 12 months, how many times did you visit a doctor or health care provider to be seen for a routine examination or an illness or injury? (पिछले 12 महने में आप कितनी बार एक डॉक्टर, या हस्पताल, या स्वास्थ केन्द्र गये हैं, अपना नियमित चेक-अप करवाने या किसी बीमारी या चोट की वज़ह से?)

|__||__||__| Number of times (बार)

74. During any visit to a doctor or health care provider in the past 12 months, were you asked if you use ST? (पिछले 12 महीनों के दौरान जब भी आप किसी डाक्टर या स्वास्थ्य सेवक के पास गए / गईं, तो क्या आपसे यह पूछा गया कि आप धूम्ररहित तंबाकू का सेवन करते हैं?)

[ ] Yes (हाँ)

[ ] No (नहीं)

75. During any visit to a doctor or health care provider in the past 12 months, were you advised to stop using ST? (पिछले 12 महीनों के दौरान जब भी आप किसी डाक्टर या स्वास्थ्य सेवक के पास गए / गईं, तो क्या आपको धूम्ररहित तंबाकू - सेवन छोड़ने की सलाह दी गई?)

[ ] Yes (हाँ)

[ ] No (नहीं)

76. During any visit to a doctor or health care provider in the past 12 months, were you given assistance to stop using ST, such as specific advice on how to quit ST or prescribed medication? (पिछले 12 महीनों के दौरान जब भी आप किसी डाक्टर या स्वास्थ्य सेवक के पास गए, क्या आपको तम्बाकू छोड़ने की मदद दी गयी.. जैसे कि कोई तम्बाकू छोड़ने का तरीका, सलाह या कोई दवाई?)

[ ] Yes (हाँ)

[ ] No (नहीं)

77. During any visit to a doctor or health care provider in the past 12 months, did the doctor or health care provider arrange follow-up with their office about quitting ST or refer you to a tobacco cessation program? (पिछले 12 महीनों के दौरान जब भी आप किसी डाक्टर या स्वास्थ्य सेवक के पास गए, क्या आपको तम्बाकू छोड़ने के लिये दुबारा आने को बोला गया, या कोई योजना में भाग लेने को बताया गया या भेजा गया?)

[ ] Yes (हाँ)

[ ] No (नहीं)

78. Please choose the number of the response that best describes your opinion: If you continue to use ST, how likely do you think it is that you will develop oral cancer? (आपको क्या लगता है - अगर आप तम्बाकू खाना ज़ारी रखेंगे, तो कितनी संभावना है कि आपको मुख का कैंसर हो जायेगा?)

No chance (कोई संभावना नहीं है)	Very unlikely (बहुत कम संभावना है)	Unlikely (कम संभावना है)	Moderate chance (थोड़ी-बहुत संभावना है)	Likely (होने की संभावना है)	Very likely (बहुत ज़्यादा संभावना है)	Certain to happen (ज़रूर होने वाली है)
1	2	3	4	5	6	7

79. Please choose the number of the response that best describes your opinion: If you continue to use ST, how likely do you think it is that you will develop heart disease? (आपको क्या लगता है - अगर आप तम्बाकू खाना ज़ारी रखेंगे, तो कितनी संभावना है कि आपको दिल की बिमारी हो जायेगी?)

No chance (कोई संभावना नहीं है)	Very unlikely (बहुत कम संभावना है)	Unlikely (कम संभावना है)	Moderate chance (थोड़ी-बहुत संभावना है)	Likely (होने की संभावना है)	Very likely (बहुत ज़्यादा संभावना है)	Certain to happen (ज़रूर होने वाली है)
1	2	3	4	5	6	7

80. In your opinion, compared to smoking, using ST has… (बीड़ी-सिगरेट पीने (धूम्रपान) की तुलना में, आपके हिसाब से, तम्बाकू खाना….)

[ ] More health risks (स्वास्थय के लिए ज़्यादा खतरनाक है)

[ ] Less health risks (स्वास्थय के लिए कम खतरनाक है)

[ ] Same health risks (स्वास्थय के लिए दोनों बराबर खतरनाक हैं)

81. In the last year, how often did you try to limit your ST use to decrease your health risks? (अपने स्वास्थय के लिए, पिछले साल आपने कितनी बार तम्बाकू खाना कम करने की कोशिश की?)

[ ] Never (कभी नहीं)

[ ] Rarely (शायद ही कभी)

[ ] Sometimes (कभी कभी)

[ ] Often (अक्सर)

[ ] Always (हमेशा)

Past Smoking History

I would now like to ask you some questions about your past smoking tobacco, including *bidis*, cigarettes, cigars, cheroots, rolled cigarettes, tobacco rolled in maize leaf and newspaper, water pipe, pipes, chillum, chutta. *Please do not answer about ST at this time*.

अब मैं आपसे धूम्रपान से संबंधित कुछ प्रश्न करना चाहूँगा / चाहूँगी, जिसमें बीड़ी, सिगरेट, सिगार, चुरूट, लपेटा हुआ सिगरेट, मक्के की पत्ती या कागज में लपेटी हुई तम्बाकू, हुक्का, पाइप, चिलम, चुट्टा, आदि सम्मिलित है. कृपया इस समय धूम्ररहित तंबाकू के बारे में जवाब न दें

82. Have you smoked at least 100 cigarettes in your entire life time? (क्या आपने अपने पूरे जीवन काल में कम से कम100 सिगरेट का धूम्रपान किया है?)

[ ] Yes

[ ] No

[IF NO, Skip section] (अगर नहीं तो इस भाग को छोड़ दें)

83. How old were you when you first started smoking tobacco? (उस समय आपकी उम्र क्या थी, जब आपने धूम्रपान करना शुरू किया था)

|__||__| Years (साल)

84. Have you ever smoked daily for 6 months or more? (क्या आपने कभी 6 महीने या अधिक के लिए दैनिक/ रोज़ धूम्रपान किया है)

[ ] Yes (हाँ)

[ ] No (नहीं)

85. Think of the time in your life when you SMOKED THE MOST. During that time, on how many days per week did you smoke? (अपने जीवन के उस समय के बारे में सोचें जब आप सबसे ज्यादा धूम्रपान करते थे: उस समय आप एक हफ्ते में कितने दिन धूम्रपान करते थे?

|__| Days (दिन)

86. Think of the time in your life when you SMOKED THE MOST. During that time, on the days that you smoked, how many times /cigarettes did you smoke per day? अपने जीवन के उस समय के बारे में सोचें जब आप सबसे ज्यादा धूम्रपान करते थे: उस समय, जिन दिनों आप धूम्रपान करते थे, आप एक दिन मे कितनी बार/ कितनी सिगरेट पीते थे?

|__||__| Times /Cigarettes per day बार/ सिगरेट एक दिन मे

87. Think of the time in your life when you SMOKED THE MOST. During that time, which of these products did you commonly use? Check all that apply (अपने जीवन के उस समय के बारे में सोचें जब आप सबसे ज्यादा धूम्रपान करते थे। उस समय, आप कौन से उत्पाद अधिकतर इस्तेमाल करते थे? उन सब पर निशान लगाइये जो सही हैं)

[ ] Manufactured cigarette (उत्पादित सिगरेट)

[ ] Hand-rolled tobacco in paper or leaf (पत्ती या कागज में लपेटी हुई तम्बाकू, धूम्रपान के लिए)

[ ] Bidi (बीड़ी)

[ ] Cigar (सिगार)

[ ] Cheroot (चुरूट)

[ ] Cigarillo (छोटी सिगार)

[ ] Pipe (पाइप)

[ ] Water pipe (हुक्का)

[ ] Any other type, specify (कोई और प्रकार, नाम दें) ……

88. How long has it been since you stopped smoking? (आपको धूम्रपान छोड़े हुये कितना समय

हो गया)

|__||__| Months (महीने)

|__||__| Years (साल)

89. Did you use any of the following methods to help you quit smoking? Check all that apply (क्या आपने धूम्रपान छोड़ने के लिये किसी निम्नलिखित तरीके का इस्तेमाल किया? उन सब पर निशान लगाइये जो सही हैं)

[ ] Counselling, including at a cessation clinic (परामर्श, तम्बाकू विमुक्ति चिकित्सालय में)

[ ] Nicotine replacement therapy, such as the patch or gum (निकोटीन के बदले में उपचार, जैसा कि पैच या गम)

[ ] Other prescription medications, for example Bupropion (अन्य निर्धारित उपचार, जैसे कि बूप्रोपियन की गोली)

[ ] Traditional medicines, for example Ayurvedic, Homeopathic, Unani (पारंपरिक उपचार, जैसे कि आयुर्वेदिक, होम्योपैथिक, यूनानी)

[ ] A quit line or a smoking telephone support line (धूम्रपान छोड़ने से संबंधित टेलीफोन पर विमर्श)

[ ] Switching to smokeless tobacco (धूम्ररहित तंबाकू का प्रयोग)

[ ] I quit on my own, did not use anything (अपने आप छोड़ा । किसी तरीके का इस्तेमाल नहीं किया।)

[ ] Other, please describe (कोई और, कृपया विवरण दें)……

90. Why did you stop smoking? (आपने धूम्रपान क्यों बंद किया)

[ ] I was diagnosed with an illness (मैं बीमारी के साथ का निदान हो गया /मुझे कोई बीमारी बताई गई थी)

[ ] The cost of smoking was too high (धूम्रपान की लागत बहुत ज्यादा थी)

[ ] I got nagged or people were judging me (मुझसे लोग कहने लगे थे या मेरे बारे में खराब सोचने लगे थे)

[ ] I started to feel health effects of smoking (मुझे धूम्रपान के स्वास्थ सम्बंधी असर महसूस होने लगे थे)

[ ] My health (मेरा स्वास्थ्य)

[ ] I was tired of feeling out of breath (मुझे सांस लेने में तकलीफ हो रही थी)

[ ] I wanted to get control of my life (मुझे अपने जीवन पर नियंत्रण चाहिये था)

[ ] I was tired of the smell or taste (मैं गंध या स्वाद से थक गया था)

[ ] I don’t know, I just did (मुझे नहीं पता, मैने बस बंद कर दिया)

[ ] Smoking bans or restrictions at home/public places (घर या बाहर धूम्रपान पर मनाही)

[ ] Other reasons (अन्य कारणों से) …….

Health Behaviours

Now I would like to ask you some questions about your general health condition. Has a doctor or health care provider ever told you that you had any of the following? (अब मैं आपसे आपके स्वास्थ के बारे मे सवाल पूछूंगा। क्या कभी डॉक्टर या अन्य स्वास्थकर्मी ने आपको ये बताया है की आपको निम्न में से कोई बीमारी है?)

91. Heart attack, also called myocardial infarction? (दिल का दौरा)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

92. Angina or coronary heart disease? (आंजाइना या दिल की बीमारी)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

93. Hypertension or raised blood pressure? (उच्च रक्तचाप या बढ़ा हुआ ब्लड प्रेशर)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

94. Cancer? (कैंसर)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

95. Asthma? (अस्थमा /दमा)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

96. Teeth and gum problems? (दांतों और मसूड़ों की समस्या)

[ ] Yes (हाँ)

[ ] No (नहीं)

[ ] Don't know (पता नहीं है)

97. During the past month, other than your regular job, on how many days did you participate in any physical activities or exercises? (पिछले महीने में, अपनी नौकरी के अलावा आपने कितने दिन शारीरिक गतिविधि या व्यायाम किया?)

|__||__|Days per month (दिन, महीने में)

a. [IF > 0:] When you took part in this activity, for how many minutes or hours did you usually keep at it? (जब आपने ये गतिविधि की तो आमतौर पर कितने मिनट या घंटे के लिये करी?)

|__||__| Minutes (मिनट)

|__||__| Hours (घंटे)

98. During the past month, how many times have you had a drink containing alcohol (such as Beer, Wine, Rum, or Whiskey)? (पिछले 30 दिनों में आपने कितनी बार किसी भी प्रकार के मादक पेय पदार्थों का सेवन किया - जैसे बीयर, वाइन, रम अथवा व्हिस्की)

|__||__|

99. Over the past 7 days, on average how many servings of fruit did you eat per day (पिछले सात दिन में औसतन कितने फल प्रत्येक दिन आपने खाये हैं?)

|__||__| Servings (फल)

100. Over the past 7 days, on average how many servings of vegetables did you eat per day (पिछले सात दिन में औसतन कितनी कटोरी सब्जियाँ आपने प्रत्येक दिन खाईं हैं?)

|__||__| Servings (कटोरी)

101. In general, would you say your health is…? (आमतौर पर क्या आप ये कहेंगे कि आपका स्वास्थ….?)

[ ] Excellent (उत्कृष्ट है)

[ ] Very Good (बहुत अच्छा)

[ ] Good (अच्छा)

[ ] Fair (ठीक है)

[ ] Poor (खराब है)

Appendix 3.4. Descriptive statistics and figures for ST dependency scale items

Descriptive statistics for TDS-ST

Item	Yes, n (%)
Have you often had periods of days when you chew/dip a lot more than you intended to?	136 (58.4)
Have you ever tried to quit or cut down on tobacco and found you could not?	180 (77.3)
Did you crave tobacco after you quit or cut down on it?	180 (77.3)
Did you have any of the following problems when you quit or cut down on tobacco: irritation, nervousness, restlessness, trouble concentrating, headache, drowsiness, upset stomach, heart slow down, increased appetite or body weight, handshakes, depression?	149 (63.9)
Did you ever start using tobacco again to keep from having such problems?	146 (62.7)
Have you ever continued to chew/dip when you had a serious illness that you knew made it unwise to use tobacco?	133 (57.1)
Did you continue to use tobacco after you knew that it caused you health problems?	218 (93.6)
Did you continue to use tobacco after you knew that it caused you mental problems?	181 (77.7)
Have you ever felt like you were dependent on tobacco?	129 (55.4)
Have you ever given up work or social activities so you could use tobacco?	54 (23.2)

Item no.	1	2	3	4	5	6	7	8	9	10
1	1									
2	0.206 **	1								
3	0.165 *	0.853 **	1							
4	0.363 **	0.275 **	0.339 **	1						
5	0.374 **	0.322 **	0.364 **	0.973 **	1					
6	0.094	-0.036	-0.036	0.125	0.155 *	1				
7	0.027	0.025	0.025	0.094	0.159 *	0.161 *	1			
8	0.070	-0.094	-0.045	0.070	0.119	0.202 **	0.405 **	1		
9	0.328 **	0.110	0.131 *	0.261 **	0.253 **	0.233 **	0.046	-0.025	1	
10	0.051	0.031	-0.042	0.116	0.130 *	0.250 **	-0.022	0.075	0.289 **	1
Item-total	0.556 **	0.518 **	0.531 **	0.735 **	0.774 **	0.434 **	0.291 **	0.307 **	0.545 **	0.374 **

* Correlations are significant at the 0.05 level (2-tailed)

** Correlations are significant at the 0.01 level (2-tailed)

Item no.	**Scale Mean if Item Deleted**	**Scale Variance if Item Deleted**	**Cronbach's Alpha if Item Deleted**
1	5.88	4.227	.665
2	5.69	4.421	.668
3	5.69	4.395	.666
4	5.82	3.853	.617
5	5.84	3.758	.605
6	5.89	4.501	.694
7	5.53	4.974	.693
8	5.69	4.828	.706
9	5.91	4.246	.669
10	6.23	4.696	.696

Descriptive statistics for FTND-ST

Item with responses (scores allocated)	**n (%)**
How soon after you wake up to do you place your first dip?	
Within 5 min (3)	89 (38.2)
6–30 min (2)	86 (36.9)
31–60 minutes (1)	17 (7.3)
After 60 minutes (0)	41 (17.6)
How often do you intentionally swallow tobacco juice?	
Always (2)	18 (7.7)
Sometimes (1)	47 (20.2)
Never (0)	168 (72.1)
Which chew would you hate to give up most?	
The first one in the morning (1)	175 (75.1)
Any other (0)	58 (24.9)
How many cans/pouches per week do you use?	
More than 3 (2)	182 (78.1)
2–3 (1)	40 (17.2)
1 (0)	11 (4.7)
Do you chew more frequently during the first hours after awakening than during the rest of the day?	
Yes (1)	114 (48.9)
No (0)	119 (51.1)
Do you chew if you are so ill that you are in bed most of the day?	
Yes (1)	104 (44.6)
No (0)	129 (55.4)

Item No.	**1**	**2**	**3**	**4**	**5**	**6**
1	1					
2	0.055	1				
3	0.438**	0.075	1			
4	0.203**	0.001	0.029	1		
5	0.271**	-0.022	0.444**	0.037	1	
6	0.357**	0.055	0.237**	0.123	0.192**	1
Item-total	0.816**	0.345**	0.619**	0.402**	0.514**	0.559**

* Correlations are significant at the 0.05 level (2-tailed)

** Correlations are significant at the 0.01 level (2-tailed)

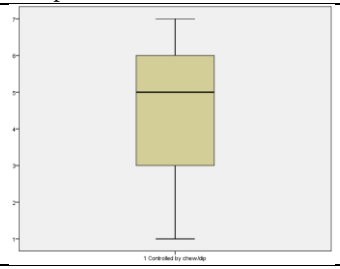
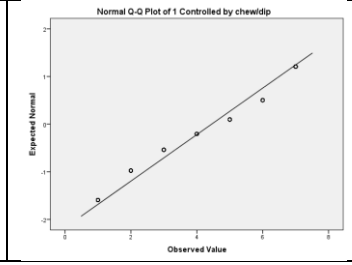
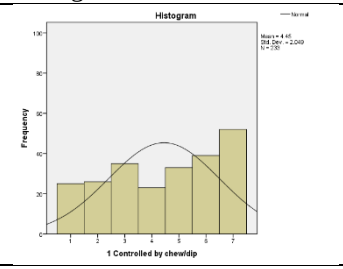
Item no.	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Cronbach's Alpha if Item Deleted
1	3.78	1.915	.360
2	5.38	3.952	.573
3	4.98	3.526	.421
4	4.00	3.845	.524
5	5.24	3.634	.468
6	5.29	3.542	.446

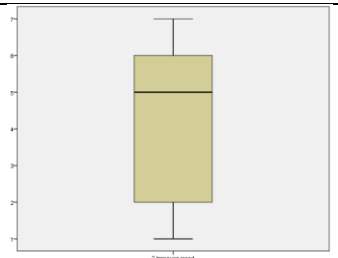
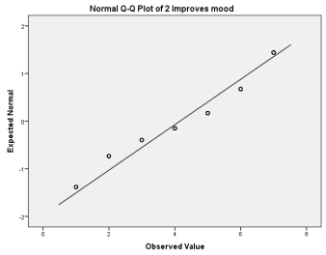
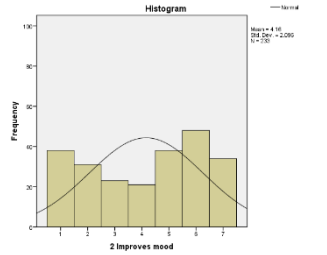
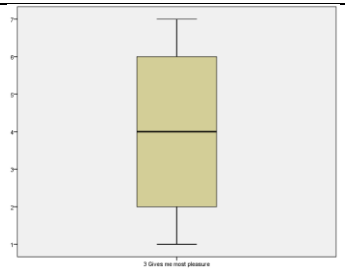
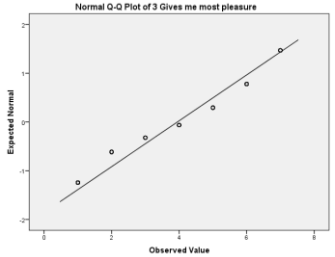
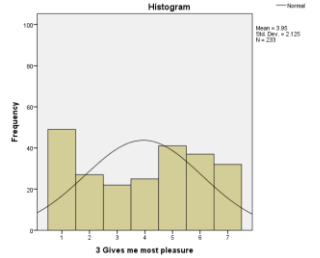
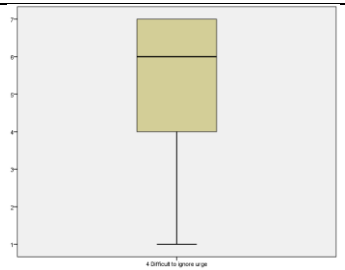
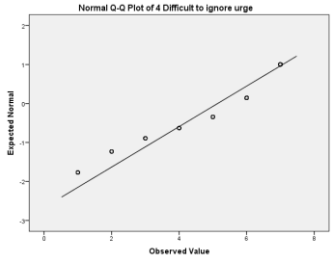
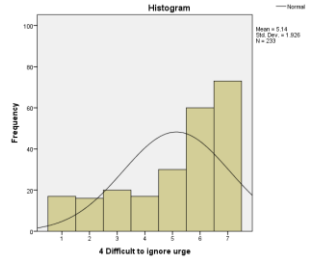
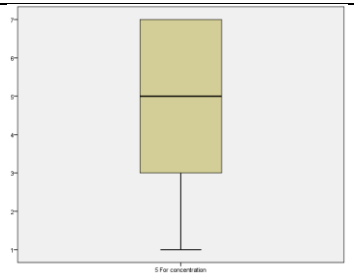
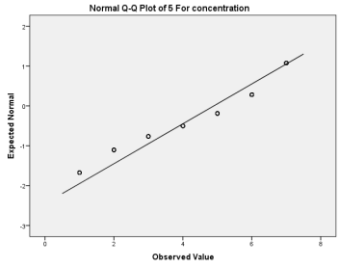
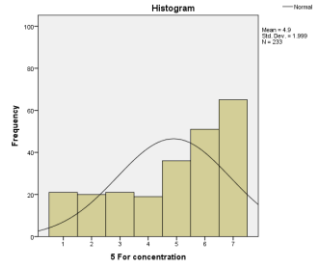
Descriptive statistics for OSSTD

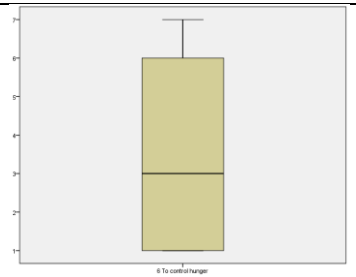
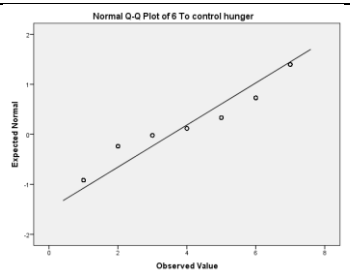
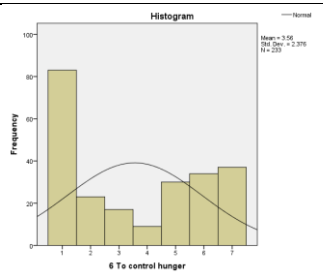
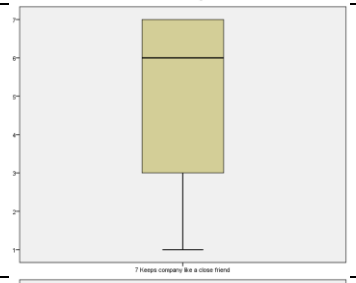
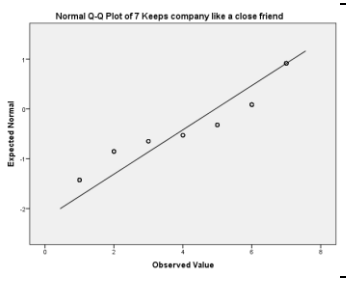
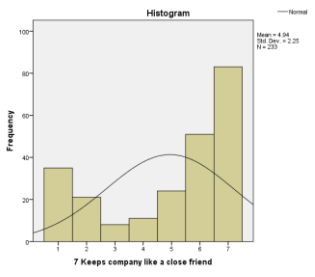
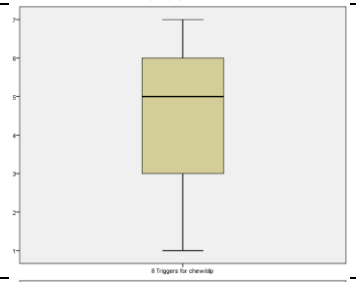
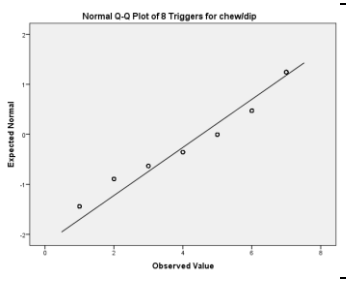
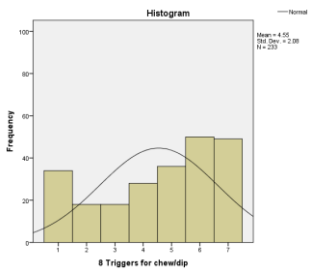
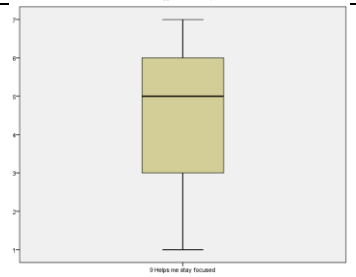
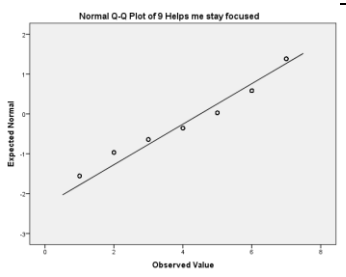
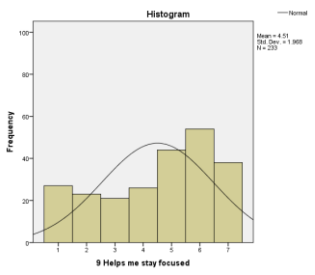
Item no.	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Cronbach's Alpha if Item Deleted
1 Controlled by chew/dip	100.15	732.364	.921
2 Improves mood	100.45	730.041	.921
3 Gives me most pleasure	100.66	734.675	.922
4 Difficult to ignore urge	99.46	735.405	.921
5 For concentration	99.71	728.983	.920
6 To control hunger	101.05	726.864	.922
7 Keeps company like close friend	99.66	712.079	.918
8 Triggers for chew/dip	100.06	741.479	.922
9 Helps me stay focused	100.10	729.779	.920
10 Frequent craving	99.32	730.114	.919
11 For weight control	102.79	776.374	.925
12 Hooked	99.03	727.641	.918
13 Reach without thinking	100.28	741.797	.923
14 Crave at certain times of day	99.01	741.056	.920
15 Feel alone without	99.78	722.295	.919
16 Considered as heavy user by other users	99.87	723.512	.919
17 Difficult to do some things without	99.73	709.431	.918
18 Within 30 minutes of rising	99.00	732.875	.921
19 Unaware when using	100.86	726.636	.921
20 Helps me think better	100.24	714.509	.917
21 Feel better when down	99.44	738.170	.920
22 Feel good	99.33	734.729	.920
23 Keeps from overeating	101.35	731.634	.922

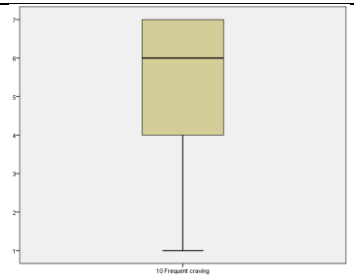
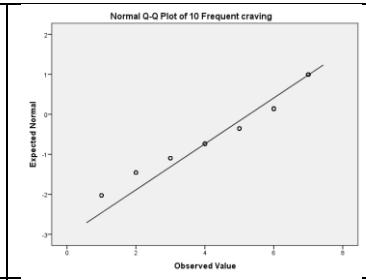
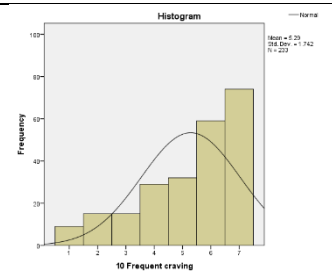
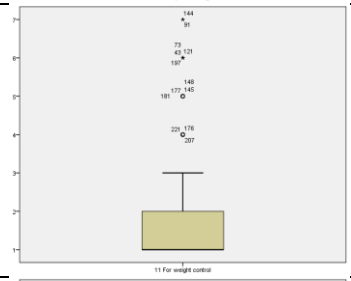
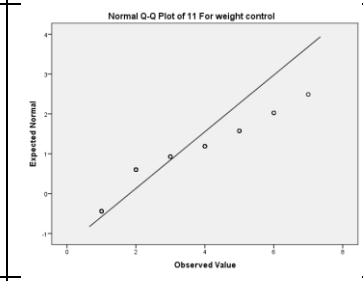
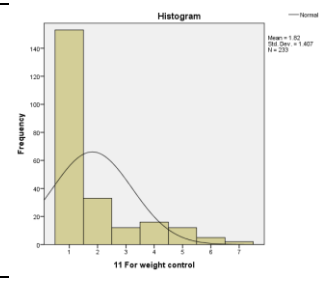
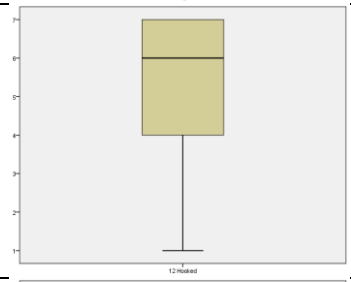
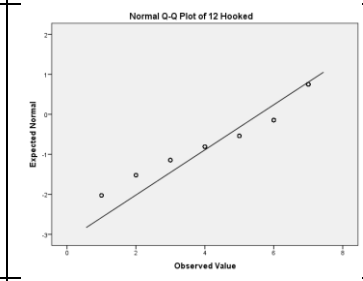
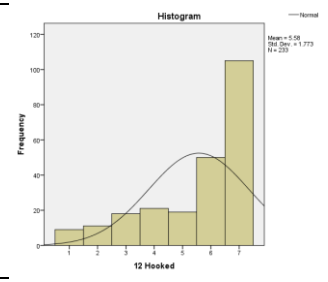
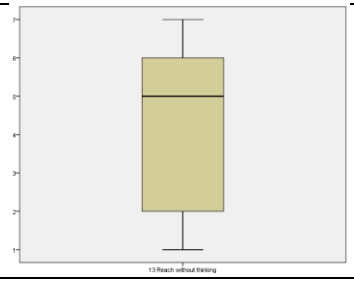
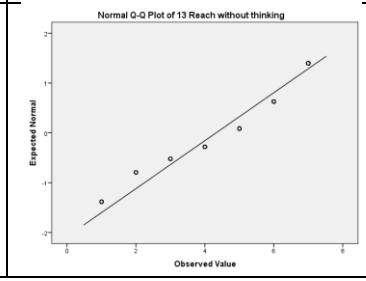
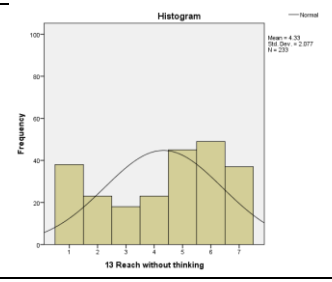
Item No.	Items	N	Central tendency measures			Measures of dispersion			Distribution of scores	
		Valid (Missing)	Mean	5% trimmed mean	Median	SD	Min	Max	Skew	Kurtosis
Primary dependence motives (PDM)										
Subscale 1: Loss of control & Craving										
1	Chew/dip controls me	233 (0)	4.45	4.50	5	2.05	1	7	-0.26	-1.27
12	I'm really hooked on chew/dip	233 (0)	5.58	5.74	6	1.77	1	7	-1.13	0.14
4	It's hard to ignore an urge to chew/dip	233 (0)	5.14	5.27	6	1.93	1	7	-0.86	-0.49
10	I frequently crave chew/dip	233 (0)	5.29	5.42	6	1.74	1	7	-0.90	-0.19
Subscale 2: Tolerance & Automaticity										
16	Other chewers/dippers consider me a heavy chewer/dipper	233 (0)	4.74	4.82	5	2.01	1	7	-0.48	-1.02
18	I chew/dip within the first 30 min of awakening in the morning	233 (0)	5.61	5.79	7	2.02	1	7	-1.34	0.36
13	I find myself reaching for chew/dip without thinking about it	233 (0)	4.33	4.36	5	2.08	1	7	-0.38	-1.22
19	Sometimes I am not aware that I am chewing/dipping	233 (0)	3.74	3.71	4	2.18	1	7	0.03	-1.49
Secondary dependence motives (SDM)										
Subscale 3: Affective enhancement										
2	Chewing/dipping improves my mood	233 (0)	4.16	4.18	5	2.10	1	7	-0.21	-1.37
21	Chewing/dipping really helps me feel better if I've been feeling down	233 (0)	5.16	5.29	6	1.81	1	7	-0.93	-0.17
22	Chewing/dipping makes me feel good	233 (0)	5.28	5.42	6	1.83	1	7	-1.00	-0.16
Subscale 4: Affiliative attachment										
7	Chew/dip keeps me company, like a close friend	233 (0)	4.94	5.05	6	2.25	1	7	-0.75	-1.02
15	I would feel alone without my chew/dip	233 (0)	4.83	4.92	5	2.08	1	7	-0.70	-0.87
3	Very few things give me pleasure each day like chewing/dipping	233 (0)	3.95	3.94	4	2.12	1	7	-0.09	-1.39

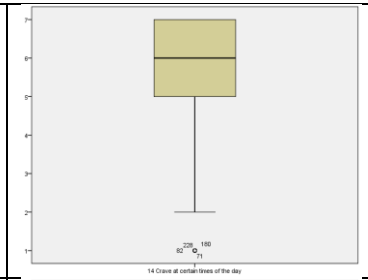
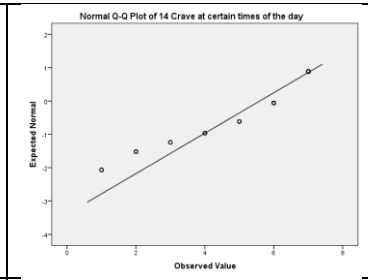
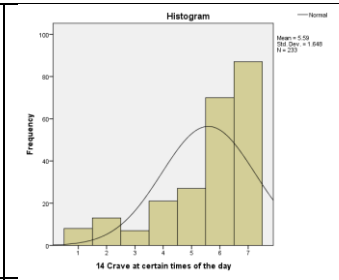
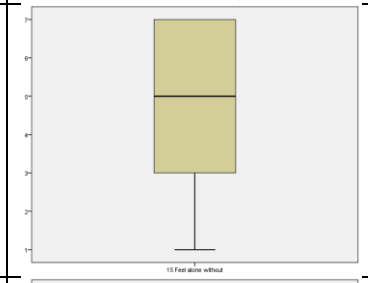
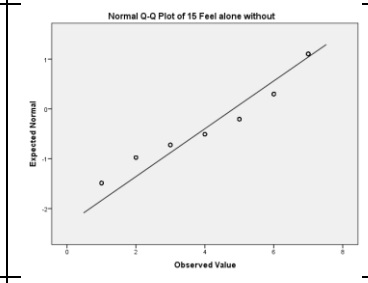
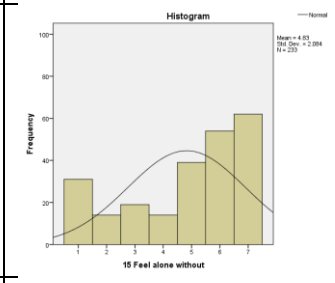
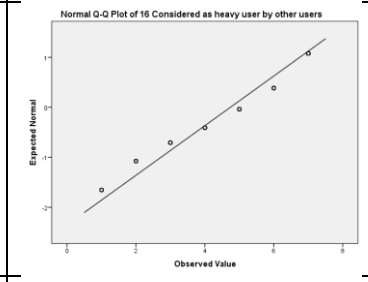
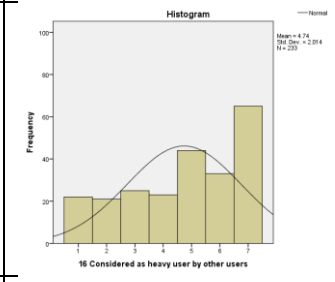
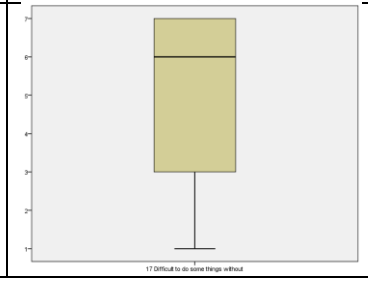
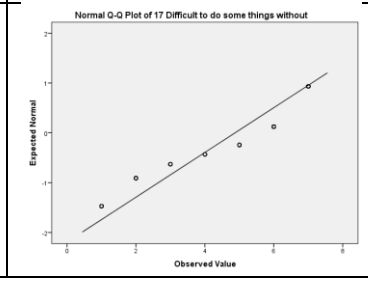
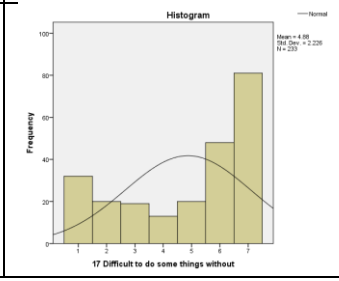
Subscale 5: Cognitive enhancement										
5	I chew/dip when I really need to concentrate	233 (0)	4.90	5.00	5	1.99	1	7	-0.66	-0.86
9	Chewing/dipping helps me stay focused	233 (0)	4.51	4.56	5	1.97	1	7	-0.47	-1.02
20	Chewing/dipping helps think better	233 (0)	4.37	4.41	5	2.02	1	7	-0.54	-1.06
Subscale 6: Weight control										
6	I rely upon chewing/dipping to control my hunger and eating	233 (0)	3.56	3.51	3	2.38	1	7	0.20	-1.62
11	Weight control is a major reason that I chew/dip	233 (0)	1.82	1.64	1	1.41	1	7	1.77	2.23
23	Chewing/dipping keeps me from over eating	233 (0)	3.25	3.17	2	2.25	1	7	0.35	-1.52
Subscale 7: Cue exposure										
8	There are particular sights and smells that trigger strong urges to chew/dip	233 (0)	4.55	4.61	5	2.08	1	7	-0.48	-1.09
14	I crave chew/dip at certain times of the day	233 (0)	5.59	5.75	6	1.65	1	7	-1.30	0.87
17	Some things are very hard to do without chewing/dipping	233 (0)	4.88	4.97	6	2.23	1	7	-0.64	-1.14

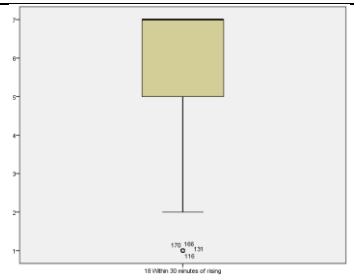
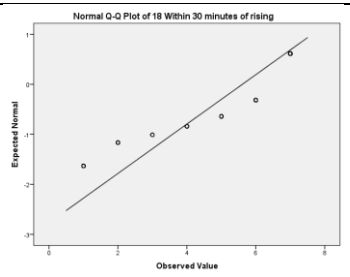
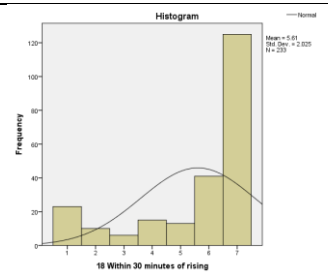
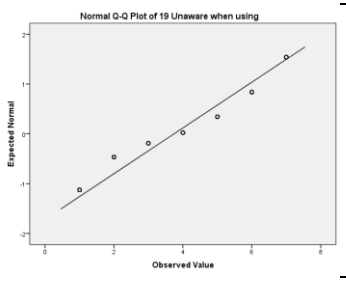
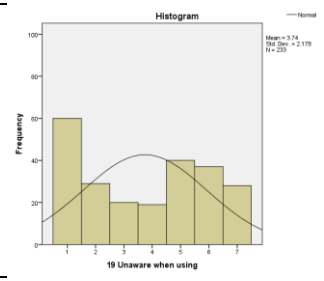
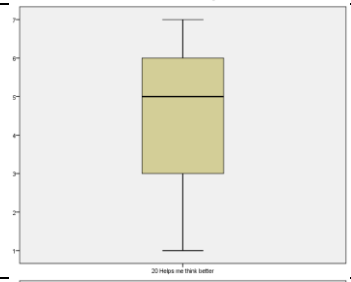
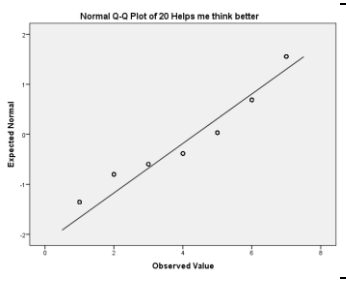
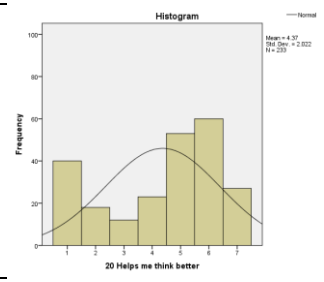
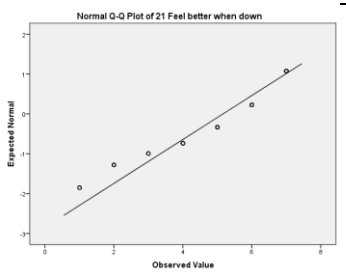
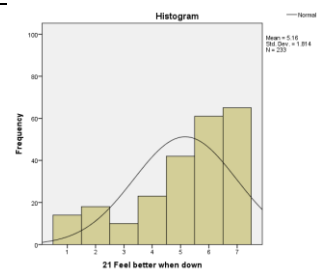
Item	Boxplot	Normal Q-Q Plot	Histogram
1			

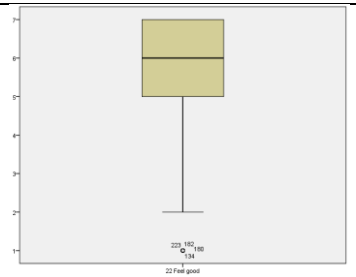
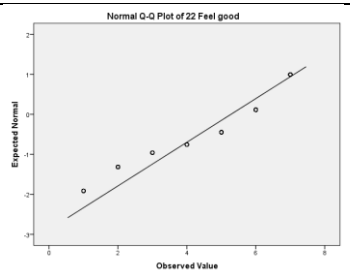
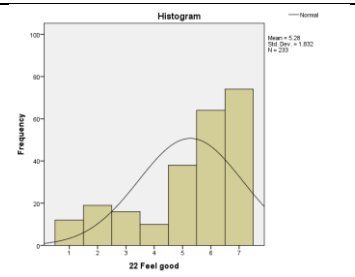
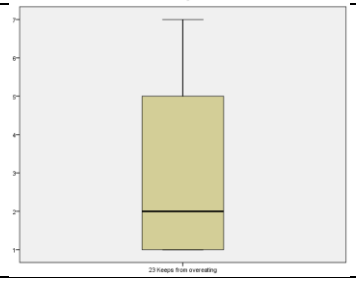
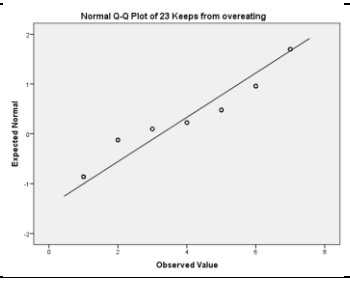
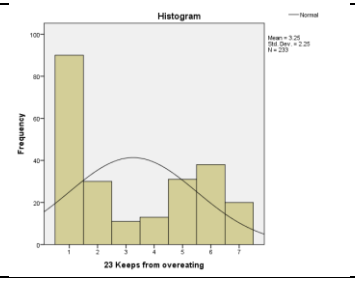
2		 Normal Q-Q Plot of 2 Improves mood Expected Normal Observed Value	 Histogram Frequency 2 Improves mood
3		 Normal Q-Q Plot of 3 Gives me most pleasure Expected Normal Observed Value	 Histogram Frequency 3 Gives me most pleasure
4		 Normal Q-Q Plot of 4 Difficult to ignore urge Expected Normal Observed Value	 Histogram Frequency 4 Difficult to ignore urge
5		 Normal Q-Q Plot of 5 For concentration Expected Normal Observed Value	 Histogram Frequency 5 For concentration

6	 6 To control hunger	 Normal Q-Q Plot of 6 To control hunger Expected Normal Observed Value	 Histogram Normal Mean = 3.56 Std. Dev. = 2.376 N = 233 Frequency 6 To control hunger
7	 7 Keeps company like a close friend	 Normal Q-Q Plot of 7 Keeps company like a close friend Expected Normal Observed Value	 Histogram Normal Mean = 4.94 Std. Dev. = 2.25 N = 233 Frequency 7 Keeps company like a close friend
8	 8 Triggers for chew/dip	 Normal Q-Q Plot of 8 Triggers for chew/dip Expected Normal Observed Value	 Histogram Normal Mean = 4.55 Std. Dev. = 2.08 N = 233 Frequency 8 Triggers for chew/dip
9	 9 Helps me stay focused	 Normal Q-Q Plot of 9 Helps me stay focused Expected Normal Observed Value	 Histogram Normal Mean = 4.51 Std. Dev. = 1.968 N = 233 Frequency 9 Helps me stay focused

10			
11**			
12*			
13			

14	 14 Crave at certain times of the day	 Normal Q-Q Plot of 14 Crave at certain times of the day Expected Normal Observed Value	 Histogram Frequency 14 Crave at certain times of the day
15	 15 Feel alone without	 Normal Q-Q Plot of 15 Feel alone without Expected Normal Observed Value	 Histogram Frequency 15 Feel alone without
16	 16 Considered as heavy user by other users	 Normal Q-Q Plot of 16 Considered as heavy user by other users Expected Normal Observed Value	 Histogram Frequency 16 Considered as heavy user by other users
17	 17 Difficult to do some things without	 Normal Q-Q Plot of 17 Difficult to do some things without Expected Normal Observed Value	 Histogram Frequency 17 Difficult to do some things without

18*	 18 Within 30 minutes of rising	 Normal Q-Q Plot of 18 Within 30 minutes of rising Expected Normal Observed Value	 Histogram Frequency 18 Within 30 minutes of rising
19	 19 Unaware when using	 Normal Q-Q Plot of 19 Unaware when using Expected Normal Observed Value	 Histogram Frequency 19 Unaware when using
20	 20 Helps me think better	 Normal Q-Q Plot of 20 Helps me think better Expected Normal Observed Value	 Histogram Frequency 20 Helps me think better
21	 21 Feel better when down	 Normal Q-Q Plot of 21 Feel better when down Expected Normal Observed Value	 Histogram Frequency 21 Feel better when down

22			
23			

* Y-axis on Histogram = 0 – 120

** Y-axis on Histogram = 0 – 140

Appendix 3.5. Sociodemographic variations in ST dependence measures

Age

Scale and subscales	Age groups	N	Mean (SD)	β (SE)	p-value
TDS-ST	18-29 years	133	6.26 (2.30)	0.467	0.124
	30+ years	100	6.73 (2.26)	(0.302)	
FTND-ST	18-29 years	133	5.79 (2.21)	-0.129	0.645
	30+ years	100	5.66 (1.99)	(0.280)	
OSSTD	18-29 years	133	32.34 (8.31)	-1.655	0.146
	30+ years	100	30.68 (8.92)	(1.135)	
Loss of control & Craving	18-29 years	133	5.18 (1.42)	-0.164	0.393
	30+ years	100	5.02 (1.49)	(0.192)	
Tolerance & Automaticity	18-29 years	133	4.71 (1.49)	-0.239	0.228
	30+ years	100	4.47 (1.49)	(0.198)	
Affective enhancement	18-29 years	133	4.95 (1.39)	-0.193	0.323
	30+ years	100	4.76 (1.58)	(0.195)	
Affiliative attachment	18-29 years	133	4.73 (1.60)	-0.363	0.105
	30+ years	100	4.37 (1.79)	(0.223)	
Cognitive enhancement	18-29 years	133	4.67 (1.65)	-0.177	0.434
	30+ years	100	4.49 (1.77)	(0.225)	
Weight control	18-29 years	133	3.07 (1.47)	-0.448	0.021
	30+ years	100	2.62 (1.44)	(0.193)	
Cue exposure	18-29 years	133	5.03 (1.50)	-0.072	0.724
	30+ years	100	4.96 (1.58)	(0.203)	

Gender

Scale and subscales	Gender	N	Mean (SD)	β (SE)	p-value
TDS-ST	Male	118	6.45 (2.37)	0.029	0.923
	Female	115	6.48 (2.21)	(0.301)	
FTND-ST	Male	118	5.25 (2.17)	0.989	< 0.001
	Female	115	6.23 (1.94)	(0.270)	
OSSTD	Male	118	29.61 (9.00)	4.083	< 0.001
	Female	115	33.70 (7.66)	(1.096)	
Loss of control & Craving	Male	118	4.84 (1.54)	0.544	0.004
	Female	115	5.39 (1.30)	(0.187)	
Tolerance & Automaticity	Male	118	4.27 (1.55)	0.674	0.001
	Female	115	4.94 (1.35)	(0.191)	
Affective enhancement	Male	118	4.68 (1.50)	0.377	0.051
	Female	115	5.06 (1.42)	(0.192)	
Affiliative attachment	Male	118	4.15 (1.69)	0.848	< 0.001
	Female	115	5.00 (1.58)	(0.215)	
Cognitive enhancement	Male	118	4.35 (1.94)	0.493	0.027
	Female	115	4.84 (1.37)	(0.221)	
Weight control	Male	118	2.64 (1.48)	0.475	0.013
	Female	115	3.11 (1.43)	(0.191)	
Cue exposure	Male	118	4.67 (1.58)	0.673	0.001
	Female	115	5.34 (1.41)	(0.196)	

Education

Scale and subscales	Education	N	Mean (SD)	β (SE)	p-value
TDS-ST	No formal school	119	6.74 (2.25)	-0.689	0.003
	Up to secondary	96	6.45 (2.18)	(0.233)	
	> secondary	18	4.72 (2.47)		
FTND-ST	No formal school	119	6.25 (1.83)	-1.028	< 0.001
	Up to secondary	96	5.45 (2.17)	(0.209)	
	> secondary	18	3.83 (2.33)		
OSSTD	No formal school	119	33.58 (7.52)	-3.826	< 0.001
	Up to secondary	96	30.51 (9.21)	(0.856)	
	> secondary	18	24.72 (7.62)		
Loss of control & Craving	No formal school	119	5.42 (1.31)	-0.598	< 0.001
	Up to secondary	96	4.93 (1.47)	(0.145)	
	> secondary	18	4.04 (1.59)		
Tolerance & Automaticity	No formal school	119	4.86 (1.29)	-0.571	< 0.001
	Up to secondary	96	4.51 (1.64)	(0.151)	
	> secondary	18	3.36 (1.32)		
Affective enhancement	No formal school	119	5.08 (1.38)	-0.362	0.017
	Up to secondary	96	4.69 (1.55)	(0.151)	
	> secondary	18	4.39 (1.52)		
Affiliative attachment	No formal school	119	4.94 (1.51)	-0.691	< 0.001
	Up to secondary	96	4.34 (1.80)	(0.169)	
	> secondary	18	3.41 (1.53)		
Cognitive enhancement	No formal school	119	4.90 (1.42)	-0.651	< 0.001
	Up to secondary	96	4.44 (1.83)	(0.171)	
	> secondary	18	3.30 (2.09)		
Weight control	No formal school	119	2.96 (1.39)	-0.267	0.080
	Up to secondary	96	2.92 (1.57)	(0.152)	
	> secondary	18	2.07 (1.25)		
Cue exposure	No formal school	119	5.41 (1.35)	-0.685	< 0.001
	Up to secondary	96	4.66 (1.59)	(0.152)	
	> secondary	18	4.15 (1.59)		

Asset ownership

Scale and subscales	Assets	N	Mean (SD)	β (SE)	p-value
TDS-ST	Up to 3 assets	139	6.69 (2.24)	-0.483	0.047
	4 – 7 assets	79	6.20 (2.34)	(0.242)	
	> 7 assets	15	5.73 (2.37)		
FTND-ST	Up to 3 assets	139	6.03 (1.96)	-0.636	0.005
	4 – 7 assets	79	5.41 (2.18)	(0.222)	
	> 7 assets	15	4.73 (2.68)		
OSSTD	Up to 3 assets	139	33.13 (8.05)	-2.903	0.001
	4 – 7 assets	79	29.56 (9.21)	(0.898)	
	> 7 assets	15	28.55 (7.45)		
Loss of control & Craving	Up to 3 assets	139	5.35 (1.36)	-0.499	0.001
	4 – 7 assets	79	4.82 (1.56)	(0.151)	
	> 7 assets	15	4.42 (1.16)		

Tolerance & Automaticity	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	4.69 (1.43) 4.51 (1.59) 4.27 (1.59)	-0.200 (0.159)	0.211
Affective enhancement	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	5.01 (1.45) 4.64 (1.55) 4.75 (1.14)	-0.244 (0.157)	0.120
Affiliative attachment	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	4.87 (1.58) 4.20 (1.82) 3.82 (1.38)	-0.593 (0.176)	0.001
Cognitive enhancement	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	4.83 (1.53) 4.37 (1.86) 3.47 (1.85)	-0.576 (0.178)	0.001
Weight control	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	3.01 (1.44) 2.60 (1.43) 3.02 (1.80)	-0.194 (0.157)	0.216
Cue exposure	Up to 3 assets 4 – 7 assets > 7 assets	139 79 15	5.36 (1.34) 4.42 (1.66) 4.80 (1.54)	-0.596 (0.159)	< 0.001

Appendix 3.6. Sensitivity analyses of salivary cotinine measurements

For entire sample (n = 233)

Variable	Cotinine < 0.8 ng/ml	Cotinine >= 0.8 ng/ml	Statistical test	p-value	Adj p-value
Continuous variables, mean (SD)					
Age	31.89 (12.24)	29.79 (10.87)	t-test	0.179	-
Duration of ST use in years	14.78 (11.56)	11.48 (9.06)	t-test	0.027	0.405
Weekly ST use in grams	87.54 (70.14)	86.05 (58.36)	t-test	0.862	-
Times of ST use per day	17.88 (14.70)	16.56 (13.89)	t-test	0.498	-
Categorical variables, n (%)					
Gender					
Male	40 (48.8)	78 (51.6)	Pearson	0.675	-
Female	42 (51.2)	73 (48.4)			
Number of ST products currently used					
1 product	64 (78.0)	110 (72.8)	Pearson	0.383	-
> 1 product	18 (22.0)	41 (27.2)			
Zarda in past 7 days					
No	81 (98.8)	150 (99.3)	Fisher	1.000	-
Yes	1 (1.2)	1 (0.7)			
Paan in past 7 days					
No	68 (82.9)	141 (93.4)	Pearson	0.012	0.180
Yes	14 (17.1)	10 (6.6)			
Gutkha in past 7 days					
No	41 (50.0)	55 (36.4)	Pearson	0.044	0.660
Yes	41 (50.0)	96 (63.6)			
Khaini in past 7 days					
No	45 (54.9)	73 (48.3)	Pearson	0.341	-
Yes	37 (45.1)	78 (51.7)			
Snus in past 7 days					
No	81 (98.8)	145 (96.0)	Fisher	0.426	-
Yes	1 (1.2)	6 (4.0)			
Gul in past 7 days					
No	76 (92.7)	148 (98.0)	Fisher	0.070	-
Yes	6 (7.3)	3 (2.0)			
Had teeth or gum problems*					
No	45 (54.9)	87 (41.6)	Pearson	0.606	-
Yes	37 (45.1)	62 (58.4)			
Former or current smoker					
No	73 (89.0)	124 (82.1)	Pearson	0.164	-
Yes	9 (11.0)	27 (17.9)			
Alcohol in past 30 days*					
No	65 (79.3)	114 (76.5)	Pearson	0.631	-
Yes	17 (20.7)	35 (23.5)			

* Missing values = 2

By batch of analysis

Variable	Batches 1 & 2 (n = 161)	Batch 3 (n = 72)	Statistical test	p-value	Adj p-value
Continuous variables, mean (SD)					
Age	30.24 (11.18)	31.18 (11.90)	t-test	0.560	-
Duration of ST use in years	12.71 (10.41)	12.50 (9.49)	t-test	0.885	-
Weekly ST use in grams	78.40 (61.19)	104.85 (62.30)	t-test	0.003	0.045**
Times of ST use per day	14.76 (12.39)	22.08 (16.50)	t-test	0.001	0.015**
Categorical variables, n (%)					
Gender					
Male	91 (56.5)	27 (37.5)	Pearson	0.007	0.105
Female	70 (43.5)	45 (62.5)			
Number of ST products currently used					
1 product	126 (78.3)	48 (66.7)	Pearson	0.060	-
> 1 product	35 (21.7)	24 (33.3)			
Zarda in past 7 days					
No	159 (98.8)	72 (100.0)	Fisher	1.000	-
Yes	2 (1.2)	0 (0.0)			
Paan in past 7 days					
No	139 (86.3)	70 (97.2)	Fisher	0.010	0.015
Yes	22 (13.7)	2 (2.8)			
Gutkha in past 7 days					
No	72 (44.7)	24 (33.3)	Pearson	0.103	
Yes	89 (55.3)	48 (66.7)			
Khaini in past 7 days					
No	86 (53.4)	32 (44.4)	Pearson	0.206	-
Yes	75 (46.6)	40 (55.6)			
Snus in past 7 days					
No	158 (98.1)	68 (94.4)	Fisher	0.207	-
Yes	3 (1.9)	4 (5.6)			
Gul in past 7 days					
No	154 (95.7)	70 (97.2)	Fisher	0.725	-
Yes	7 (4.3)	2 (2.8)			
Had teeth or gum problems*					
No	94 (59.1)	38 (52.8)	Pearson	0.367	-
Yes	65 (40.9)	34 (47.2)			
Former or current smoker					
No	138 (85.7)	59 (81.9)	Pearson	0.462	-
Yes	23 (14.3)	13 (18.1)			
Alcohol in past 30 days*					
No	122 (76.7)	57 (79.2)	Pearson	0.681	-
Yes	37 (23.3)	15 (20.8)			

* Missing values = 2

** Significant adjusted p-value

Batches 1 & 2 (n = 161)

Variable	**Cotinine < 0.8 ng/ml**	**Cotinine >= 0.8 ng/ml**	**Statistical test**	**p-value**	**Adj p-value**
Continuous variables, mean (SD)					
Age	31.89 (12.24)	28.52 (9.75)	t-test	0.056	-
Duration of ST use in years	14.78 (11.56)	10.56 (8.62)	t-test	0.009	0.135
Weekly ST use in grams	87.54 (70.14)	68.91 (48.91)	t-test	0.052	-
Times of ST use per day	17.88 (14.70)	11.52 (8.34)	t-test	0.001	0.015**
Categorical variables, n (%)					
Gender					
Male	40 (42.8)	51 (64.6)	Pearson	0.044	0.660
Female	42 (51.2)	28 (35.4)			
Number of ST products currently used					
1 product	64 (78.0)	62 (78.5)	Pearson	0.947	-
> 1 product	18 (22.0)	17 (21.5)			
Zarda in past 7 days					
No	81 (98.8)	78 (98.7)	Fisher	1.000	-
Yes	1 (1.2)	1 (1.3)			
Paan in past 7 days					
No	68 (82.9)	71 (89.9)	Pearson	0.200	-
Yes	14 (17.1)	8 (10.1)			
Gutkha in past 7 days					
No	41 (50)	31 (39.2)	Pearson	0.170	-
Yes	41 (50)	48 (60.8)			
Khaini in past 7 days					
No	45 (54.9)	41 (51.9)	Pearson	0.705	-
Yes	37 (45.1)	38 (48.1)			
Snus in past 7 days					
No	81 (98.8)	77 (97.5)	Fisher	0.616	-
Yes	1 (1.2)	2 (2.5)			
Gul in past 7 days					
No	76 (92.7)	78 (98.7)	Fisher	0.117	-
Yes	6 (7.3)	1 (1.3)			
Had teeth or gum problems*					
No	45 (54.9)	49 (63.6)	Pearson	0.262	-
Yes	37 (45.1)	28 (36.4)			
Former or current smoker					
No	73 (89.0)	65 (82.3)	Pearson	0.221	-
Yes	9 (11.0)	14 (17.7)			
Alcohol in past 30 days*					
No	65 (79.3)	57 (74.0)	Pearson	0.434	-
Yes	17 (20.7)	20 (26.0)			

* Missing values = 2

** Significant adjusted p-value

Appendix 3.7. Additional validation results of ST dependency scales

Duration of ST use

Measures	Univariate model				Multivariate model*			
	β	SE	t-value	p-value	β	SE	t-value	p-value
TDS-ST	0.128	0.038	3.366	0.001	0.107	0.022	4.952	<0.001
Dependence diagnosis	0.357	0.188	1.901	0.059	0.379	0.107	3.534	<0.001
FTND-ST	0.108	0.042	2.597	0.010	0.121	0.024	5.028	<0.001
OSSTD	0.017	0.010	1.618	0.107	0.026	0.006	4.247	<0.001
Loss of control & Craving	0.109	0.061	1.772	0.078	0.116	0.036	3.241	0.001
Tolerance & Automaticity	-0.005	0.060	-0.083	0.934	0.067	0.036	1.873	0.062
Affective enhancement	0.070	0.061	1.162	0.246	0.110	0.035	3.154	0.002
Affiliative attachment	0.072	0.053	1.358	0.176	0.103	0.031	3.291	0.001
Cognitive enhancement	0.055	0.052	1.043	0.298	0.107	0.030	3.529	0.001
Weight control	0.051	0.061	0.846	0.398	0.131	0.035	3.746	<0.001
Cue exposure	0.168	0.057	2.924	0.004	0.141	0.034	4.215	<0.001
Self-rated ST addiction	0.109	0.057	1.925	0.055	0.095	0.033	2.904	0.004

Note: Square root transformation of ST use duration applied

*Model adjusts for age and gender of study participants

Duration of daily ST use

Measures	Univariate model				Multivariate model*			
	β	SE	t-value	p-value	β	SE	t-value	p-value
TDS-ST	0.126	0.037	3.442	0.001	0.119	0.024	4.947	<0.001
Dependence diagnosis	0.288	0.180	1.596	0.112	0.358	0.121	2.970	0.003
FTND-ST	0.115	0.040	2.850	0.005	0.136	0.027	5.021	<0.001
OSSTD	0.025	0.010	2.573	0.011	0.035	0.007	5.386	<0.001
Loss of control & Craving	0.164	0.057	2.862	0.005	0.176	0.038	4.585	<0.001
Tolerance & Automaticity	0.037	0.058	0.640	0.523	0.115	0.040	2.892	0.004
Affective enhancement	0.119	0.058	2.051	0.041	0.164	0.038	4.277	<0.001
Affiliative attachment	0.114	0.050	2.281	0.024	0.148	0.034	4.365	<0.001

Cognitive enhancement	0.084	0.050	1.663	0.098	0.142	0.033	4.233	<0.001
Weight control	0.075	0.058	1.296	0.196	0.148	0.039	3.837	<0.001
Cue exposure	0.187	0.055	3.420	0.001	0.171	0.037	4.635	<0.001
Self-rated ST addiction	0.135	0.053	2.535	0.012	0.132	0.036	3.701	0.138

Note: Square root transformation of daily ST use duration applied

*Model adjusts for age and gender of study participants

Quantity of ST use

Measures	**Univariate model**				**Multivariate model***			
	β	SE	t-value	p-value	β	SE	t-value	p-value
TDS-ST	0.715	0.083	8.619	<0.001	0.666	0.079	8.443	<0.001
Dependence diagnosis	2.768	0.424	6.528	<0.001	2.565	0.402	6.378	<0.001
FTND-ST	0.640	0.094	6.791	<0.001	0.566	0.094	6.017	<0.001
OSSTD	0.151	0.023	6.467	<0.001	0.135	0.023	5.774	<0.001
Loss of control & Craving	0.841	0.140	6.006	<0.001	0.702	0.139	5.037	<0.001
Tolerance & Automaticity	0.868	0.134	6.468	<0.001	0.792	0.133	5.936	<0.001
Affective enhancement	0.594	0.143	4.156	<0.001	0.467	0.139	3.352	<0.001
Affiliative attachment	0.537	0.124	4.325	<0.001	0.476	0.122	3.894	<0.001
Cognitive enhancement	0.715	0.119	5.994	<0.001	0.630	0.117	5.408	<0.001
Weight control	0.539	0.144	3.738	<0.001	0.595	0.139	5.345	<0.001
Cue exposure	0.595	0.137	4.343	<0.001	0.499	0.134	3.717	<0.001
Self-rated ST addiction	0.749	0.131	5.735	<0.001	0.695	0.123	5.626	<0.001

Note: Square root transformation of ST use quantity applied

*Model adjusts for age, gender, and number of products currently consumed

Frequency of ST use

Measures	**Univariate model**				**Multivariate model***			
	β	SE	t-value	p-value	β	SE	t-value	p-value
TDS-ST	0.323	0.039	8.251	<0.001	0.296	0.036	8.170	<0.001
Dependence diagnosis	1.241	0.200	6.218	<0.001	1.131	0.184	6.131	<0.001
FTND-ST	0.332	0.043	7.723	<0.001	0.295	0.042	7.063	<0.001
OSSTD	0.080	0.011	7.479	<0.001	0.071	0.010	6.881	<0.001

Loss of control & Craving	0.463	0.063	7.291	<0.001	0.392	0.062	6.352	<0.001
Tolerance & Automaticity	0.478	0.061	7.905	<0.001	0.440	0.059	7.516	<0.001
Affective enhancement	0.264	0.067	3.941	<0.001	0.192	0.064	3.012	0.003
Affiliative attachment	0.291	0.057	5.087	<0.001	0.264	0.055	4.825	<0.001
Cognitive enhancement	0.330	0.056	5.909	<0.001	0.281	0.053	5.267	<0.001
Weight control	0.332	0.066	4.881	<0.001	0.306	0.062	4.955	<0.001
Cue exposure	0.334	0.063	5.318	<0.001	0.293	0.060	4.879	<0.001
Self-rated ST addiction	0.360	0.061	5.910	<0.001	0.332	0.056	5.918	<0.001

Note: Square root transformation of ST use frequency applied

*Model adjusts for age, gender, and number of products currently consumed

Quit intentions in following 6 months

Dependence scale	**Intend to quit ST**	**N**	**Mean (SD)**
TDS-ST	Yes	164	6.24 (2.33)
	No	69	6.99 (2.11)
FTND-ST	Yes	164	5.41 (2.12)
	No	69	6.51 (1.89)
OSSTD	Yes	164	30.51 (8.82)
	No	69	34.28 (7.44)
Loss of control & Craving	Yes	164	4.85 (1.49)
	No	69	5.73 (1.12)
Tolerance & Automaticity	Yes	164	4.51 (1.55)
	No	69	4.83 (1.33)
Affective enhancement	Yes	164	4.70 (1.53)
	No	69	5.25 (1.25)
Affiliative attachment	Yes	164	4.39 (1.67)
	No	69	5.00 (1.67)
Cognitive enhancement	Yes	164	4.38 (1.76)
	No	69	5.10 (1.45)
Weight control	Yes	164	2.85 (1.51)
	No	69	2.94 (1.37)
Cue exposure	Yes	164	4.83 (1.56)
	No	69	5.42 (1.37)
Self-rated ST addiction	Yes	163	4.92 (1.68)
	No	68	5.57 (1.15)

Appendix 4.1. Crosstabs analyses of sociocultural factors

ST use among closest friends – by age

Categorised age	**No ST users among closest friends, n (%)**	**At least 1 ST user among closest friends, n (%)**	**Total, n (%)**
18 – 29 years	12 (37.5)	121 (60.2)	133 (57.1)
30+ years	20 (62.5)	80 (39.8)	100 (42.9)
Total	32 (100.0)	201 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.806[a]	1	.016		
Continuity Correction[b]	4.916	1	.027		
Likelihood Ratio	5.754	1	.016		
Fisher's Exact Test				.021	.014
Linear-by-Linear Association	5.781	1	.016		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 13.73.					
b. Computed only for a 2x2 table					

ST use among closest friends – by gender

Gender	**No ST users among closest friends, n (%)**	**At least 1 ST user among closest friends, n (%)**	**Total, n (%)**
Male	12 (37.5)	106 (52.7)	118 (50.6)
Female	20 (62.5)	95 (47.3)	115 (49.4)
Total	32 (100.0)	201 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.564[a]	1	.109		
Continuity Correction[b]	1.990	1	.158		
Likelihood Ratio	2.585	1	.108		
Fisher's Exact Test				.129	.079
Linear-by-Linear Association	2.553	1	.110		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 15.79.					
b. Computed only for a 2x2 table					

ST use among closest friends – by education

Education level completed	**No ST users among closest friends, n (%)**	**At least 1 ST user among closest friends, n (%)**	**Total, n (%)**
No school	16 (50.0)	103 (51.2)	119 (51.1)
Up to secondary	15 (46.9)	81 (40.3)	96 (41.2)
> secondary	1 (3.1)	17 (8.5)	18 (7.7)
Total	32 (100.0)	201 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	1.314[a]	2	.518
Likelihood Ratio	1.557	2	.459
Linear-by-Linear Association	.115	1	.735
N of Valid Cases	233		
a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 2.47.			

ST use among closest friends – by asset ownership

Number of assets owned	**No ST users among closest friends, n (%)**	**At least 1 ST user among closest friends, n (%)**	**Total, n (%)**
0-3 assets	21 (65.6)	118 (58.7)	139 (59.7)
4-7 assets	11 (34.4)	68 (33.8)	79 (33.9)
> 7 assets	0 (0.0)	15 (7.5)	15 (6.4)
Total	32 (100.0)	201 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	2.612[a]	2	.271
Likelihood Ratio	4.650	2	.098
Linear-by-Linear Association	1.505	1	.220
N of Valid Cases	233		
a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 2.06.			

ST use among closest family members – by age

Categorised age	**No ST users among closest family, n (%)**	**At least 1 ST user among closest family, n (%)**	**Total, n (%)**
18 – 29 years	51 (62.2)	82 (54.3)	133 (57.1)
30+ years	31 (37.8)	69 (45.7)	100 (42.9)
Total	82 (100.0)	151 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.351[a]	1	.245		
Continuity Correction[b]	1.048	1	.306		
Likelihood Ratio	1.359	1	.244		
Fisher's Exact Test				.269	.153

Linear-by-Linear Association	1.345	1	.246		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 35.19.					
b. Computed only for a 2x2 table					

ST use among closest family members – by gender

Gender	**No ST users among closest family, n (%)**	**At least 1 ST user among closest family, n (%)**	**Total, n (%)**
Male	58 (70.0)	60 (39.7)	118 (50.6)
Female	24 (29.3)	91 (60.3)	115 (49.4)
Total	82 (100.0)	151 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	20.427[a]	1	.000		
Continuity Correction[b]	19.205	1	.000		
Likelihood Ratio	20.903	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	20.339	1	.000		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 40.47.					
b. Computed only for a 2x2 table					

ST use among closest family members – by education

Education level completed	**No ST users among closest family, n (%)**	**At least 1 ST user among closest family, n (%)**	**Total, n (%)**
No school	27 (32.9)	92 (60.9)	119 (51.1)
Up to secondary	41 (50.0)	55 (36.4)	96 (41.2)
> secondary	14 (17.1)	4 (2.6)	18 (7.7)
Total	82 (100.0)	151 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	24.847[a]	2	.000
Likelihood Ratio	24.712	2	.000
Linear-by-Linear Association	23.804	1	.000
N of Valid Cases	233		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.33.			

ST use among closest family members – by asset ownership

Number of assets owned	**No ST users among closest family, n (%)**	**At least 1 ST user among closest family, n (%)**	**Total, n (%)**
0-3 assets	36 (43.9)	103 (68.2)	139 (59.7)
4-7 assets	36 (43.9)	43 (28.5)	79 (33.9)

> 7 assets	10 (12.2)	5 (3.3)	15 (6.4)
Total	82 (100.0)	151 (100.0)	201 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	15.508[a]	2	.000
Likelihood Ratio	15.256	2	.000
Linear-by-Linear Association	15.435	1	.000
N of Valid Cases	233		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.28.			

ST use in company – by age

Categorised age	**Mainly in company, n (%)**	**Other, n (%)**	**Total, n (%)**
18 – 29 years	28 (70.0)	105 (54.4)	133 (57.1)
30+ years	12 (30.0)	88 (45.6)	100 (42.9)
Total	40 (100.0)	193 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.290[a]	1	.070		
Continuity Correction[b]	2.684	1	.101		
Likelihood Ratio	3.392	1	.065		
Fisher's Exact Test				.080	.049
Linear-by-Linear Association	3.275	1	.070		
N of Valid Cases	233				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 17.17.					
b. Computed only for a 2x2 table					

ST use in company – by gender

Gender	**Mainly in company, n (%)**	**Other, n (%)**	**Total, n (%)**
Male	31 (77.5)	87 (45.1)	118 (50.6)
Female	9 (22.5)	106 (54.9)	115 (49.4)
Total	40 (100.0)	193 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Sig.(2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	13.934[a]	1	.000		
Continuity Correction[b]	12.667	1	.000		
Likelihood Ratio	14.634	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	13.874	1	.000		
N of Valid Cases	233				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 19.74.					
b. Computed only for a 2x2 table					

ST use in company – by education

Education level completed	Mainly in company, n (%)	Other, n (%)	Total, n (%)
No school	14 (35.0)	105 (54.4)	119 (51.1)
Up to secondary	13 (32.5)	83 (43.0)	96 (41.2)
> secondary	13 (32.5)	5 (2.6)	18 (7.7)
Total	40 (100.0)	193 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	41.697[a]	2	.000
Likelihood Ratio	30.060	2	.000
Linear-by-Linear Association	20.053	1	.000
N of Valid Cases	233		
a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 3.09.			

ST use in company – by asset ownership

Number of assets owned	Mainly in company, n (%)	Other, n (%)	Total, n (%)
0-3 assets	14 (35.0)	125 (64.8)	139 (59.7)
4-7 assets	19 (47.5)	60 (31.1)	79 (33.9)
> 7 assets	7 (17.5)	8 (4.1)	15 (6.4)
Total	40 (100.0)	193 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	16.733[a]	2	.000
Likelihood Ratio	14.973	2	.001
Linear-by-Linear Association	16.241	1	.000
N of Valid Cases	233		
a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 2.58.			

ST use within households – by age

Categorised age	No ST use within households, n (%)	ST use allowed within households, n (%)	Total, n (%)
18 – 29 years	71 (64.5)	62 (50.4)	133 (57.1)
30+ years	39 (35.5)	61 (49.6)	100 (42.9)
Total	110 (100.0)	123 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.738[a]	1	.029		
Continuity Correction[b]	4.179	1	.041		
Likelihood Ratio	4.764	1	.029		
Fisher's Exact Test				.034	.020

Linear-by-Linear Association	4.718	1	.030		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 47.21.					
b. Computed only for a 2x2 table					

ST use within households – by gender

Gender	**No ST use within households, n (%)**	**ST use allowed within households, n (%)**	**Total, n (%)**
Male	76 (69.1)	42 (34.1)	118 (50.6)
Female	34 (30.9)	81 (65.9)	115 (49.4)
Total	110 (100.0)	123 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	28.368[a]	1	.000		
Continuity Correction[b]	26.988	1	.000		
Likelihood Ratio	28.994	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	28.247	1	.000		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 54.29.					
b. Computed only for a 2x2 table					

ST use within households – by education

Education level completed	**No ST use within households, n (%)**	**ST use allowed within households, n (%)**	**Total, n (%)**
No school	38 (34.5)	81 (65.9)	119 (51.1)
Up to secondary	54 (49.1)	42 (34.1)	96 (41.2)
> secondary	18 (16.4)	0 (0.0)	18 (7.7)
Total	110 (100.0)	123 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	34.420[a]	2	.000
Likelihood Ratio	41.626	2	.000
Linear-by-Linear Association	32.844	1	.000
N of Valid Cases	233		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.50.			

ST use within households – by asset ownership

Number of assets owned	**No ST use within households, n (%)**	**ST use allowed within households, n (%)**	**Total, n (%)**
0-3 assets	49 (44.5)	90 (73.2)	139 (59.7)
4-7 assets	50 (45.5)	29 (23.6)	79 (33.9)

> 7 assets	11 (10.0)	4 (3.3)	15 (6.4)
Total	110 (100.0)	123 (100.0)	233 (100.0)

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	20.280[a]	2	.000
Likelihood Ratio	20.597	2	.000
Linear-by-Linear Association	19.154	1	.000
N of Valid Cases	233		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.08.			

ST use among closest friends – by ST use among closest family members

Sociocultural measure	No ST users among closest family	At least 1 ST user among closest family	Total
No ST users among closest friends	12	20	32
At least 1 user among closest friends	70	131	201
Total	82	151	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.087[a]	1	.769		
Continuity Correction[b]	.009	1	.924		
Likelihood Ratio	.086	1	.770		
Fisher's Exact Test				.843	.457
Linear-by-Linear Association	.086	1	.769		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 11.26.					
b. Computed only for a 2x2 table					

ST use among closest friends – by ST use in company

Sociocultural measure	Mainly in company	Other	Total
No ST users among closest friends	1	31	32
At least 1 ST user among closest friends	39	162	201
Total	40	193	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.144[a]	1	.023		
Continuity Correction[b]	4.063	1	.044		
Likelihood Ratio	6.986	1	.008		
Fisher's Exact Test				.022	.013
Linear-by-Linear Association	5.122	1	.024		
N of Valid Cases	233				

0 cells (.0%) have expected count less than 5. The minimum expected count is 5.49.
Computed only for a 2x2 table

ST use among closest friends – by ST use within households

Sociocultural measure	No ST use within households	ST use allowed within households	Total
No ST users among closest friends	16	16	32
At least 1 user among closest friends	94	107	201
Total	110	123	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.116[a]	1	.734		
Continuity Correction[b]	.022	1	.881		
Likelihood Ratio	.116	1	.734		
Fisher's Exact Test				.849	.440
Linear-by-Linear Association	.115	1	.734		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 15.11.					
b. Computed only for a 2x2 table					

ST use among closest family members – by ST use in company

Sociocultural measure	Mainly in company	Other	Total
No ST users among closest family	15	67	82
At least 1 ST user among closest family	25	126	151
Total	40	193	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.113[a]	1	.737		
Continuity Correction[b]	.024	1	.878		
Likelihood Ratio	.112	1	.738		
Fisher's Exact Test				.720	.434
Linear-by-Linear Association	.112	1	.738		
N of Valid Cases	233				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 14.08.					
b. Computed only for a 2x2 table					

ST use among closest family members – by ST use within households

Sociocultural measure	No ST use within households	ST use allowed within households	Total
No ST users among closest family	65	17	82

At least 1 user among closest family	45	106	151
Total	110	123	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	52.177[a]	1	.000		
Continuity Correction[b]	50.211	1	.000		
Likelihood Ratio	54.609	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	51.953	1	.000		
N of Valid Cases	233				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 38.71.					
b. Computed only for a 2x2 table					

ST use in company – by ST use within households

Sociocultural measure	No ST use within households	ST use allowed within households	Total
Mainly in company	26	14	40
Other	84	109	193
Total	110	123	233

Chi-square tests

Test	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.132[a]	1	.013		
Continuity Correction[b]	5.301	1	.021		
Likelihood Ratio	6.178	1	.013		
Fisher's Exact Test				.015	.011
Linear-by-Linear Association	6.106	1	.013		
N of Valid Cases	233				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 18.88.					
b. Computed only for a 2x2 table					

Appendix 4.2. Adjusted linear regression models of associations between sociocultural measures and ST use practices

Age of first ST use

Variables	β	SE	t-value	p-value
(Constant)	3.202	.229	13.958	.000
Age of participant	.030	.004	7.333	.000
Gender	.176	.108	1.636	.103
Up to secondary	.160	.109	1.466	.144
> secondary	.002	.207	.009	.993
4-7 assets owned	.030	.109	.279	.781
>7 assets owned	.112	.198	.563	.574
Smoked at least 100 cigarettes in lifetime	.201	.125	1.601	.111
Closest friends using ST or not	-.129	.127	-1.010	.313
Closest relatives using ST or not	-.048	.102	-.468	.640
ST use mainly in company	.265	.127	2.086	.038
ST use allowed at home or not	-.100	.101	-.988	.324

Duration of ST use

Variables	β	SE	t-value	p-value
(Constant)	.516	.280	1.841	.067
Age of participant	.093	.005	18.557	.000
Gender	-.229	.132	-1.742	.083
Up to secondary	-.216	.133	-1.619	.107
> secondary	-.043	.253	-.169	.866
4-7 assets owned	-.026	.133	-.195	.846
>7 assets owned	-.219	.242	-.907	.365
Smoked at least 100 cigarettes in lifetime	-.131	.153	-.856	.393
Closest friends using ST or not	.172	.156	1.103	.271
Closest relatives using ST or not	.118	.125	.946	.345
ST use mainly in company	-.464	.155	-2.995	.003
ST use allowed at home or not	.089	.124	.717	.474

Quantity of ST use

Variables	β	SE	t-value	p-value
(Constant)	8.715	1.185	7.353	.000
Age of participant	.002	.021	.104	.918
Gender	-.114	.556	-.205	.838
Up to secondary	-1.200	.564	-2.127	.035
> secondary	-2.040	1.072	-1.903	.058
4-7 assets owned	.192	.561	.343	.732
>7 assets owned	.937	1.023	.916	.360
Smoked at least 100 cigarettes in lifetime	-.228	.648	-.353	.725
Closest friends using ST or not	.617	.658	.936	.350
Closest relatives using ST or not	.031	.528	.059	.953
ST use mainly in company	-1.088	.656	-1.660	.098
ST use allowed at home or not	.317	.524	.604	.546

Frequency of ST use

Variables	**β**	**SE**	**t-value**	**p-value**
(Constant)	3.807	.543	7.018	.000
Age of participant	-.005	.010	-.511	.610
Gender	-.243	.255	-.953	.341
Up to secondary	-.636	.258	-2.462	.015
> secondary	-1.345	.491	-2.742	.007
4-7 assets owned	.380	.257	1.479	.140
>7 assets owned	.769	.468	1.643	.102
Smoked at least 100 cigarettes in lifetime	-.353	.296	-1.192	.235
Closest friends using ST or not	.341	.301	1.131	.259
Closest relatives using ST or not	.199	.242	.823	.411
ST use mainly in company	-.474	.300	-1.579	.116
ST use allowed at home or not	.357	.240	1.487	.138

Appendix 4.3. Adjusted logistic regression models of associations between sociocultural measures and ST use practices

Logistic regression models adjust for age (continuous variable), gender (Ref=Male), highest level of education completed (Ref=no formal schooling), household asset ownership (Ref=0 – 3 assets), ever-smoking (Ref=never-smoking), ST use among closest friends (Ref=No), ST use among closest relatives (Ref=No), ST use mainly in company (Ref=No), and ST use permissibility within households (Ref=No). The fully adjusted models additionally control for ST dependence diagnosis (Ref=not dependent), perceptions of ST-related health risks (Ref=not likely to develop oral cancer/heart disease), and doctor's advice to quit ST use (Ref=no advice received).

Reduction in ST use

Variables	**aOR**	**95% CI**	**p-value**
Age	0.99	0.97 – 1.02	0.603
Gender	0.55	0.28 – 1.11	0.097
Education level completed			0.338
Up to secondary school	0.72	0.18 – 2.94	0.652
> secondary school	0.49	0.13 – 1.78	0.279
Household asset ownership			0.061
4-7 assets	13.06	1.47 – 116.22	0.021
> 7 assets	12.94	1.54 – 108.70	0.018
Smoked at least 100 cigarettes in lifetime	0.67	0.29 – 1.52	0.336
ST use among closest friends	0.51	0.22 – 1.17	0.113
ST use among closest family	0.83	0.42 – 1.64	0.598
ST use mainly in company	0.80	0.34 – 1.87	0.612
ST use within household	0.96	0.49 – 1.87	0.908
Constant	0.39		0.467

Reduction in ST use – fully adjusted model

Variables	**aOR**	**95% CI**	**p-value**
Age	0.99	0.97 – 1.02	0.640
Gender	0.55	0.27 – 1.12	0.100
Education level completed			0.261
Up to secondary school	0.64	0.15 – 2.67	0.542
> secondary school	0.42	0.11 – 1.58	0.202
Household asset ownership			0.062
4-7 assets	13.14	1.47 – 117.26	0.021
> 7 assets	12.69	1.51 – 106.80	0.019
Smoked at least 100 cigarettes in lifetime	0.67	0.29 – 1.53	0.340
ST use among closest friends	0.56	0.24 – 1.32	0.186
ST use among closest family	0.91	0.45 – 1.84	0.796
ST use mainly in company	0.85	0.35 – 2.03	0.709

ST use within household	0.97	0.48 – 1.94	0.930
ST dependence	0.54	0.29 – 0.99	0.050
ST-related health risk	1.18	0.60 – 2.31	0.640
Received doctor's advice	0.91	0.40 – 2.06	0.823
Constant	0.51		0.618

Quit attempts

Variables	**aOR**	**95% CI**	**p-value**
Age	0.99	0.97 – 1.02	0.761
Gender	1.65	0.78 – 3.49	0.191
Education level completed			0.096
Up to secondary school	3.38	0.82 – 13.88	0.092
> secondary school	1.56	0.45 – 5.32	0.481
Household asset ownership			0.651
4-7 assets	1.82	0.50 – 6.59	0.362
> 7 assets	1.50	0.45 – 4.93	0.507
Smoked at least 100 cigarettes in lifetime	0.69	0.29 – 1.64	0.403
ST use among closest friends	0.43	0.19 – 0.99	0.048
ST use among closest family	1.30	0.65 – 2.60	0.451
ST use mainly in company	0.48	0.19 – 1.23	0.126
ST use within household	0.55	0.28 – 1.10	0.091
Constant	1.52		0.661

Quit attempts – fully adjusted model

Variables	**aOR**	**95% CI**	**p-value**
Age	0.99	0.97 – 1.03	0.914
Gender	1.44	0.67 – 3.10	0.356
Education level completed			0.093
Up to secondary school	3.39	0.81 – 14.20	0.095
> secondary school	1.52	0.43 – 5.42	0.515
Household asset ownership			0.819
4-7 assets	1.52	0.40 – 5.80	0.541
> 7 assets	1.31	0.38 – 4.52	0.674
Smoked at least 100 cigarettes in lifetime	0.63	0.26 – 1.54	0.310
ST use among closest friends	0.35	0.14 – 0.85	0.021
ST use among closest family	1.06	0.51 – 2.21	0.866
ST use mainly in company	0.51	0.20 – 1.33	0.168
ST use within household	0.62	0.30 – 1.27	0.193
ST dependence	1.43	0.74 – 2.75	0.286
ST-related health risk	1.40	0.68 – 2.86	0.359
Received doctor's advice	3.24	1.39 – 7.56	0.006
Constant	0.56		0.586

Quit intentions

Variables	aOR	95% CI	p-value
Age	0.99	0.97 – 1.03	0.853
Gender	0.84	0.40 – 1.75	0.636
Education level completed			0.090
Up to secondary school	4.72	1.15 – 19.28	0.031
> secondary school	2.77	0.80 – 9.61	0.108
Household asset ownership			0.758
4-7 assets	1.22	0.33 – 4.48	0.768
> 7 assets	0.92	0.27 – 3.08	0.893
Smoked at least 100 cigarettes in lifetime	0.78	0.33 – 1.83	0.565
ST use among closest friends	0.49	0.21 – 1.15	0.102
ST use among closest family	1.36	0.68 – 2.75	0.383
ST use mainly in company	0.78	0.32 – 1.89	0.578
ST use within household	0.48	0.24 – 0.97	.040
Constant	1.43		.713

Quit intentions – fully adjusted model

Variables	aOR	95% CI	p-value
Age	0.99	0.97 – 1.03	0.803
Gender	0.77	0.36 – 1.64	0.496
Education level completed			0.097
Up to secondary school	4.46	1.07 – 18.57	0.040
> secondary school	2.44	0.69 – 8.64	0.168
Household asset ownership			0.849
4-7 assets	1.06	0.27 – 4.07	0.935
> 7 assets	0.85	0.25 – 2.97	0.805
Smoked at least 100 cigarettes in lifetime	0.78	0.33 – 1.89	0.590
ST use among closest friends	0.54	0.23 – 1.30	0.170
ST use among closest family	1.33	0.64 – 2.77	0.438
ST use mainly in company	0.76	0.30 – 1.89	0.551
ST use within household	0.49	0.23 – 1.01	0.054
ST dependence	0.63	0.33 – 1.20	0.163
ST-related health risk	0.92	0.45 – 1.90	0.831
Received doctor's advice	2.54	1.11 – 5.80	0.028
Constant	1.01		0.996

Appendix 5.1. Systematic review search strategies in included databases

MEDLINE was searched using the OVID interface on 21/07/2014 for the period 1946 – July, 2014

1	smokeless tobacco*.mp. or Tobacco, Smokeless/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	3209
2	(oral* adj3 tobacco*).mp.	526
3	(chew* adj3 tobacco*).mp.	929
4	(spit* adj3 tobacco*).mp.	48
5	(dip* adj3 tobacco*).mp.	62
6	gutk?a.mp.	79
7	kiwam.mp.	1
8	zarda.mp.	20
9	mawa.mp.	9
10	tuibur.mp.	3
11	shamma.mp.	15
12	gul.mp.	40
13	snuf*.mp.	1161
14	snus.mp.	271
15	chimo.mp.	13
16	iqmik.mp.	12
17	toombak.mp.	28
18	tumbaku.mp.	1
19	mishri.mp.	7
20	m?sheri.mp.	24
21	n?swar.mp.	19
22	(p?an adj3 (masala or quid)).mp.	85
23	gudak?u.mp.	4
24	k?aini.mp.	26
25	(maras adj3 (powder or tobacco*)).mp.	24
26	(quid adj3 (betel or tobacco*)).mp.	665
27	((twist* or plug*) adj3 tobacco*).mp.	11
28	((loose leaf or toothpaste*) adj3 tobacco*).mp.	13
29	((pouch* or mix* or powder*) adj3 tobacco*).mp.	223
30	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	5144
31	exp Cardiovascular Diseases/ or cardiovascular disease*.mp.	1909655
32	exp Myocardial Infarction/ or myocardial infarc*.mp.	191342
33	heart attack*.mp.	3783
34	exp Heart Arrest/ or heart arrest*.mp.	40876
35	exp Coronary Disease/ or exp Coronary Artery Disease/ or coronary disease*.mp.	187076
36	coronary event*.mp.	5067
37	cardio?vascular mortalit*.mp.	7538
38	cardiac mortalit*.mp.	1807
39	cardio?vascular death*.mp.	3791
40	exp Death, Sudden, Cardiac/ or cardiac death*.mp.	21449
41	exp Cerebrovascular Disorders/ or cerebrovascular disorder*.mp.	279788
42	cerebro?vascular accident*.mp.	4911
43	cerebro?vascular event*.mp.	2762
44	cerebro?vascular disease*.mp.	13619
45	exp Stroke/ or stroke*.mp.	193317
46	brain isch?emia.mp. or exp Brain Ischemia/	83487
47	exp Intracranial Hemorrhages/ or exp Cerebral Hemorrhage/ or intracranial h?emorrhag*.mp.	58630
48	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44	1962081

	or 45 or 46 or 47	
49	30 and 48	291

EMBASE was searched using the OVID interface on 21/07/2014 for the period 1974 – July, 2014

1	smokeless tobacco*.mp. or Tobacco, Smokeless/	3570
2	(oral* adj3 tobacco*).mp.	1686
3	(chew* adj3 tobacco*).mp.	1342
4	(spit* adj3 tobacco*).mp.	58
5	(dip* adj3 tobacco*).mp.	496
6	gutk?a.mp.	143
7	kiwam.mp.	1
8	zarda.mp.	23
9	mawa.mp.	12
10	tuibur.mp.	3
11	shamma.mp.	19
12	gul.mp.	94
13	snuf*.mp.	1367
14	snus.mp.	332
15	chimo.mp.	17
16	iqmik.mp.	8
17	toombak.mp.	33
18	tumbaku.mp.	2
19	mishri.mp.	14
20	m?sheri.mp.	25
21	n?swar.mp.	35
22	(p?an adj3 (masala or quid)).mp.	119
23	gudak?u.mp.	5
24	k?aini.mp.	37
25	(maras adj3 (powder or tobacco*)).mp.	39
26	(quid adj3 (betel or tobacco*)).mp.	806
27	((twist* or plug*) adj3 tobacco*).mp.	10
28	((loose leaf or toothpaste*) adj3 tobacco*).mp.	36
29	((pouch* or mix* or powder*) adj3 tobacco*).mp.	467
30	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	7965
31	exp Cardiovascular Diseases/ or cardiovascular disease*.mp.	3009471
32	exp Myocardial Infarction/ or myocardial infarc*.mp.	305621
33	heart attack*.mp.	5318
34	exp Heart Arrest/ or heart arrest*.mp.	50954
35	exp Coronary Disease/ or exp Coronary Artery Disease/ or coronary disease*.mp.	229960
36	coronary event*.mp.	7211
37	cardio?vascular mortalit*.mp.	18420
38	cardiac mortalit*.mp.	2844
39	cardio?vascular death*.mp.	6199
40	exp Death, Sudden, Cardiac/ or cardiac death*.mp.	27068
41	exp Cerebrovascular Disorders/ or cerebrovascular disorder*.mp.	381459
42	cerebro?vascular accident*.mp.	84695
43	cerebro?vascular event*.mp.	4682
44	cerebro?vascular disease*.mp.	62096
45	exp Stroke/ or stroke*.mp.	290422
46	brain isch?emia.mp. or exp Brain Ischemia/	107180
47	exp Intracranial Hemorrhages/ or exp Cerebral Hemorrhage/ or intracranial h?emorrhag*.mp.	90060
48	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	3089072
49	30 and 48	1123

PsycINFO was searched using the OVID interface on 21/07/2014 for the period 1967 – July. 2014

1	smokeless tobacco*.mp. or Tobacco, Smokeless/	847
2	(oral* adj3 tobacco*).mp.	58
3	(chew* adj3 tobacco*).mp.	155
4	(spit* adj3 tobacco*).mp.	23
5	(dip* adj3 tobacco*).mp.	12
6	gutk?a.mp.	14
7	kiwam.mp.	0
8	zarda.mp.	1
9	mawa.mp.	0
10	tuibur.mp.	0
11	shamma.mp.	7
12	gul.mp.	15
13	snuf*.mp.	191
14	snus.mp.	140
15	chimo.mp.	0
16	iqmik.mp.	4
17	toombak.mp.	0
18	tumbaku.mp.	3
19	mishri.mp.	0
20	m?sheri.mp.	0
21	n?swar.mp.	1
22	(p?an adj3 (masala or quid)).mp.	5
23	gudak?u.mp.	0
24	k?aini.mp.	3
25	(maras adj3 (powder or tobacco*)).mp.	1
26	(quid adj3 (betel or tobacco*)).mp.	40
27	((twist* or plug*) adj3 tobacco*).mp.	0
28	((loose leaf or toothpaste*) adj3 tobacco*).mp.	3
29	((pouch* or mix* or powder*) adj3 tobacco*).mp.	34
30	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	1107
31	exp Cardiovascular Diseases/ or cardiovascular disease*.mp.	6933
32	exp Myocardial Infarction/ or myocardial infarc*.mp.	3768
33	heart attack*.mp.	807
34	exp Heart Arrest/ or heart arrest*.mp.	5
35	exp Coronary Disease/ or exp Coronary Artery Disease/ or coronary disease*.mp.	367
36	coronary event*.mp.	183
37	cardio?vascular mortalit*.mp.	323
38	cardiac mortalit*.mp.	109
39	cardio?vascular death*.mp.	114
40	exp Death, Sudden, Cardiac/ or cardiac death*.mp.	412
41	exp Cerebrovascular Disorders/ or cerebrovascular disorder*.mp.	18202
42	cerebro?vascular accident*.mp.	13697
43	cerebro?vascular event*.mp.	234
44	cerebro?vascular disease*.mp.	1793
45	exp Stroke/ or stroke*.mp.	22856
46	brain isch?emia.mp. or exp Brain Ischemia/	396
47	exp Intracranial Hemorrhages/ or exp Cerebral Hemorrhage/ or intracranial h?emorrhag*.mp.	1489
48	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	37063
49	30 and 48	20

CINAHL Plus was searched using EBSCOhost interface on 21/07/2014 for the period 1937 – July, 2014

S1	(MH "Tobacco, Smokeless") OR "smokeless tobacco"	1,147
S2	dip* N3 tobacco*	9
S3	spit* N3 tobacco*	15
S4	chew* N3 tobacco*	147
S5	oral* N3 tobacco*	145
S6	gutk#a	25
S7	chimo	0
S8	Snus	150
S9	snuf*	222
S10	gul	10
S11	shamma	1
S12	tuibur	0
S13	mawa	0
S14	zarda	4
S15	Kiwam	0
S16	Iqmik	1
S17	k#aini	1
S18	gudak#u	0
S19	p#an N3 (masala or quid)	8
S20	n#swar	3
S21	m#sheri	0
S22	mishri	1
S23	Tumbaku	1
S24	Toombak	4
S25	maras N3 (powder or tobacco*)	5
S26	quid N3 (betel or tobacco*)	149
S27	(twist* or plug*) N3 tobacco*	2
S28	(loose leaf or toothpaste*) N3 tobacco*	3
S29	(pouch* or mix* or powder*) N3 tobacco*	35
S30	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29	1,581
S31	(MH "Cardiovascular Diseases+") OR "cardiovascular disease*"	345,941
S32	(MH "Myocardial Infarction+") OR "myocardial infarc*"	34,725
S33	"heart attack*"	2,045
S34	(MH "Heart Arrest+") OR "heart arrest*"	11,963
S35	(MH "Coronary Disease+") OR "coronary disease*"	34,912
S36	"coronary event*"	920
S37	cardio#vascular mortalit*	7488
S38	cardiac mortalit*	1504
S39	cardio#vascular death*	2002
S40	(MH "Death, Sudden, Cardiac") OR "cardiac death*"	5343
S41	(MH "Cerebrovascular Disorders+") OR "cerebrovascular disorder*"	61,714
S42	cerebro#vascular accident*	902
S43	cerebro#vascular event*	656
S44	cerebro#vascular disease*	2299
S45	(MH "Stroke+") OR "stroke*" OR (MH "Stroke Patients")	59,025
S46	(MH "Cerebral Ischemia+") OR "brain isch#emia"	9,278
S47	(MH "Intracranial Hemorrhage+") OR "intracranial h#emorrhag*"	10,397
S48	S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47	360,234
S49	S30 AND S48	84

Web of Science was searched on 21/07/2014 for the period 1898 – July, 2014

1	TOPIC: ("smokeless tobacco")	6,193
2	TOPIC: (oral* Near/3 tobacco*)	1410

3	TOPIC: (chew* Near/3 tobacco*)	1631
4	TOPIC: (spit* Near/3 tobacco*)	106
5	TOPIC: (dip* Near/3 tobacco*)	251
6	TOPIC: (gutk$a)	152
7	TOPIC: (kiwam)	1
8	TOPIC: (zarda)	32
9	TOPIC: (mawa)	41
10	TOPIC: (tuibur)	5
11	TOPIC: (shamma)	44
12	TOPIC: (gul)	267
13	TOPIC: (snuf*)	2283
14	TOPIC: (snus)	425
15	TOPIC: (tumbaku)	2
16	TOPIC: (toombak)	54
17	TOPIC: (iqmik)	14
18	TOPIC: (chimo)	56
19	TOPIC: (n$swar)	29
20	TOPIC: (m$sheri)	35
21	TOPIC: (mishri)	15
22	TOPIC: (quid Near/3 betel) OR TOPIC: (quid Near/3 tobacco*)	1126
23	TOPIC: (maras Near/3 powder) OR TOPIC: (maras Near/3 tobacco*)	36
24	TOPIC: (k$aini)	37
25	TOPIC: (gudak$u)	10
26	TOPIC: (p$an Near/3 masala) OR TOPIC: (p$an Near/3 quid)	165
27	TOPIC: (pouch* Near/3 tobacco*) OR TOPIC: (mix* Near/3 tobacco*) OR TOPIC: (powder* Near/3 tobacco*)	667
28	TOPIC: ("loose leaf" Near/3 tobacco*) OR TOPIC: (toothpaste* Near/3 tobacco*)	26
29	TOPIC: (twist* Near/3 tobacco*) OR TOPIC: (plug* Near/3 tobacco*)	24
30	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	1107
31	TOPIC: ("cardiovascular disease*")	452,038
32	TOPIC: ("myocardial infarc*")	671,962
33	TOPIC: ("coronary event*")	17,881
34	TOPIC: ("coronary disease*")	278,309
35	TOPIC: ("heart arrest*")	40,152
36	TOPIC: ("heart attack*")	12,487
37	TOPIC: ("cardiac death*") OR TOPIC: ("sudden cardiac death*")	62.136
38	TOPIC: (“cardiovascular death*”)	13,157
39	TOPIC: (“cardiac mortalit*”)	6604
40	TOPIC: (“cardiovascular mortalit*”)	28,049
41	TOPIC: ("cerebrovascular disease*")	52,084
42	TOPIC: ("cerebrovascular event*")	9,427
43	TOPIC: ("cerebrovascular accident*")	16,152
44	TOPIC: ("cerebrovascular disorder*")	129,226
45	TOPIC: (stroke*)	600,620
46	TOPIC: ("brain ischemia") OR TOPIC: ("brain ischaemia")	92, 638
47	TOPIC: ("intracranial hemorrhag*") OR TOPIC: ("intracranial haemorrhag*")	26,722
48	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	1,981,661
49	30 and 48	378

The Cochrane Library was searched on 21/07/2014 for the period 1898 – July, 2014

#1	"smokeless tobacco":ti,ab,kw (Word variations have been searched)	147
#2	MeSH descriptor: [Tobacco, Smokeless] explode all trees	106
#3	oral* near/3 tobacco*:ti,ab,kw (Word variations have been searched)	43
#4	chew* near/3 tobacco*:ti,ab,kw (Word variations have been searched)	33
#5	spit* near/3 tobacco*:ti,ab,kw (Word variations have been searched)	15
#6	dip* near/3 tobacco*:ti,ab,kw (Word variations have been searched)	0
#7	"gutkha":ti,ab,kw (Word variations have been searched)	1

#8	kiwam:ti,ab,kw (Word variations have been searched)	0
#9	zarda:ti,ab,kw (Word variations have been searched)	0
#10	mawa:ti,ab,kw (Word variations have been searched)	0
#11	tuibur:ti,ab,kw (Word variations have been searched)	0
#12	shamma:ti,ab,kw (Word variations have been searched)	0
#13	gul:ti,ab,kw (Word variations have been searched)	4
#14	snuf*:ti,ab,kw (Word variations have been searched)	51
#15	snus:ti,ab,kw (Word variations have been searched)	23
#16	chimo:ti,ab,kw (Word variations have been searched)	0
#17	iqmik:ti,ab,kw (Word variations have been searched)	0
#18	toombak:ti,ab,kw (Word variations have been searched)	0
#19	tumbaku:ti,ab,kw (Word variations have been searched)	0
#20	mishri:ti,ab,kw (Word variations have been searched)	0
#21	m*sheri:ti,ab,kw (Word variations have been searched)	0
#22	n*swar:ti,ab,kw (Word variations have been searched)	0
#23	p*an near/3 (masala or quid):ti,ab,kw (Word variations have been searched)	19
#24	gudak*u:ti,ab,kw (Word variations have been searched)	0
#25	k*aini:ti,ab,kw (Word variations have been searched)	0
#26	maras near/3 (powder or tobacco*):ti,ab,kw (Word variations have been searched)	0
#27	quid near/3 (betel or tobacco*):ti,ab,kw (Word variations have been searched)	12
#28	(twist* or plug*) near/3 tobacco*:ti,ab,kw (Word variations have been searched)	0
#29	("loose leaf" or toothpaste*) near/3 tobacco*:ti,ab,kw (Word variations have been searched)	0
#30	(pouch* or mix* or powder*) near/3 tobacco*:ti,ab,kw (Word variations have been searched)	10
#31	#30 or #29 or #28 or #27 or #26 or #25 or #24 or #23 or #22 or #21 or #20 or #19 or #18 or #17 or #16 or #15 or #14 or #13 or #12 or #11 or #10 or #9 or #8 or #7 or #6 or #5 or #4 or #3 or #2 or #1	289
#32	cardiovascular disease*:ti,ab,kw (Word variations have been searched)	14514
#33	MeSH descriptor: [Cardiovascular Diseases] explode all trees	75121
#34	myocardial infarct*:ti,ab,kw (Word variations have been searched)	15891
#35	MeSH descriptor: [Myocardial Infarction] explode all trees	8731
#36	"heart attack":ti,ab,kw (Word variations have been searched)	435
#37	"heart arrest":ti,ab,kw (Word variations have been searched)	1338
#38	coronary disease*:ti,ab,kw (Word variations have been searched)	17473
#39	coronary event*:ti,ab,kw (Word variations have been searched)	5924
#40	cardiovascular mortalit*:ti,ab,kw (Word variations have been searched)	3869
#41	cardiac mortalit*:ti,ab,kw (Word variations have been searched)	3576
#42	cardiovascular death*:ti,ab,kw (Word variations have been searched)	3458
#43	cardiac death*:ti,ab,kw (Word variations have been searched)	4213
#44	MeSH descriptor: [Death, Sudden, Cardiac] this term only	530
#45	"cerebrovascular disorder":ti,ab,kw (Word variations have been searched)	1577
#46	"cerebrovascular accident":ti,ab,kw (Word variations have been searched)	1076
#47	cerebrovascular event*:ti,ab,kw (Word variations have been searched)	1110
#48	"cerebrovascular disease":ti,ab,kw (Word variations have been searched)	956
#49	stroke*:ti,ab,kw (Word variations have been searched)	23739
#50	MeSH descriptor: [Stroke] explode all trees	5302
#51	brain isch*emia:ti,ab,kw (Word variations have been searched)	1890
#52	intracranial haemorrhag*:ti,ab,kw (Word variations have been searched)	234
#53	#52 or #51 or #50 or #49 or #48 or #47 or #46 or #45 or #44 or #43 or #42 or #41 or #40 or #39 or #38 or #37 or #36 or #35 or #34 or #33 or #32	103981
#54	#53 and #31	15

SCOPUS was searched on 21/07/2014 (Article Titles, Abstracts, and Keywords)

1. (TITLE-ABS-KEY(smokeless tobacco*)) OR (TITLE-ABS-KEY(oral* W/3 tobacco*)) OR (TITLE-ABS-KEY(chew* W/3 tobacco*)) OR (TITLE-ABS-KEY(spit* W/3 tobacco*)) OR (TITLE-ABS-KEY(dip* W/3 tobacco*)) OR (TITLE-ABS-

KEY(gutk*a)) OR (TITLE-ABS-KEY(kiwam)) OR (TITLE-ABS-KEY(zarda)) OR (TITLE-ABS-KEY(mawa)) OR (TITLE-ABS-KEY(tuibur)) OR (TITLE-ABS-KEY(shamma)) OR (TITLE-ABS-KEY(gul)) OR (TITLE-ABS-KEY(snuf*)) OR (TITLE-ABS-KEY(snus)) OR (TITLE-ABS-KEY(chimo)) OR (TITLE-ABS-KEY(iqmik)) OR (TITLE-ABS-KEY(toombak)) OR (TITLE-ABS-KEY(tumbaku)) OR (TITLE-ABS-KEY(mishri)) OR (TITLE-ABS-KEY(m*sheri)) OR (TITLE-ABS-KEY(n*swar)) OR ((TITLE-ABS-KEY(p*an W/3 masala) OR TITLE-ABS-KEY(p*an W/3 quid))) OR (TITLE-ABS-KEY(gudak*u)) OR (TITLE-ABS-KEY(k*aini)) OR ((TITLE-ABS-KEY(maras W/3 powder) OR TITLE-ABS-KEY(maras W/3 tobacco*))) OR ((TITLE-ABS-KEY(quid W/3 betel) OR TITLE-ABS-KEY(quid W/3 tobacco*))) OR ((TITLE-ABS-KEY(twist* W/3 tobacco*) OR TITLE-ABS-KEY(plug* W/3 tobacco*))) OR ((TITLE-ABS-KEY("loose leaf" W/3 tobacco*) OR TITLE-ABS-KEY(toothpaste* W/3 tobacco*))) OR ((TITLE-ABS-KEY(pouch* W/3 tobacco*) OR TITLE-ABS-KEY(mix* W/3 tobacco*) OR TITLE-ABS-KEY(powder* W/3 tobacco*))) – **7921**

2. (TITLE-ABS-KEY("cardiovascular disease*")) OR (TITLE-ABS-KEY("myocardial infarct*")) OR (TITLE-ABS-KEY("heart attack*")) OR (TITLE-ABS-KEY("heart arrest*")) OR (TITLE-ABS-KEY("coronary disease*")) OR (TITLE-ABS-KEY("coronary event*")) OR (TITLE-ABS-KEY("cardiovascular mortalit*")) OR (TITLE-ABS-KEY("cardiac mortalit*")) OR (TITLE-ABS-KEY("cardiovascular death*")) OR ((TITLE-ABS-KEY("cardiac death*") OR TITLE-ABS-KEY("sudden cardiac death*"))) OR (TITLE-ABS-KEY("cerebrovascular disorder*")) OR (TITLE-ABS-KEY("cerebrovascular accident*")) OR (TITLE-ABS-KEY("cerebrovascular event*")) OR (TITLE-ABS-KEY("cerebrovascular disease*")) OR (TITLE-ABS-KEY(stroke*)) OR ((TITLE-ABS-KEY("brain ischemia") OR TITLE-ABS-KEY("brain ischaemia"))) OR ((TITLE-ABS-KEY("intracranial hemorrhag*") OR TITLE-ABS-KEY("intracranial haemorrhag*"))) – **939,074**
3. Combining 1 AND 2 = 384 documents

Other databases:

- African Journals Online (AJOL) – searched on 21/07/2014

(smokeless tobacco*) OR (oral* tobacco*) OR (chew* tobacco*) OR (snuf*) OR (quid) – 42; (cardiovascular disease*) OR (cardiovascular mortalit*) OR (myocardial infarct*) OR (stroke*) – 500
Combining both searches = 1 reference

- Latin American and Caribbean Health Sciences Literature (LILACS) – searched on 21/07/2014

("SMOKELESS TOBACCO/") or ("CHEWING TOBACCO/") or ("GUTKHA") or ("SNUFF") or ("SNUS") or ("CHIMO") or ("PAAN") or ("KHAINI") or ("MARAS") or ("QUID") – 93; ("CARDIOVASCULAR DISEASES/") or ("MYOCARDIAL INFARCTION/") or ("HEART ARREST") or ("CORONARY DISEASE/") or ("CORONARY HEART DISEASE/") or ("CEREBROVASCULAR DISORDERS/") or ("CEREBROVASCULAR ACCIDENT/") or ("STROKE”") or ("BRAIN ISCHEMIA") or ("INTRACRANIAL HEMORRHAGES/") – 3628
Combining both searches = 0 references

- WHO Index Medicus of the Eastern Mediterranean Region (IMEMR) – searched on 21/07/2014

("TOBACCOBETEL") or ("GUTKHA") or ("SHAMMA") or ("SNUFF") or ("SNUS") or ("CHIMO") or ("TOOMBAK") or ("MISHRI") or ("NISWAR") or ("PAAN") or ("MARAS") or ("QUID") – 100; ("CARDIOVASCULARDISEASE") or ("MYOCARDIALINFARCTION/") or ("CORONARYDISEASE") or ("CEREBROVASCULAR/") or ("STROKE") – 984
Combining both searches = 0 references

- WHO Index Medicus of the South-East Asian Region (IMSEAR) – searched on 21/07/2014

(smokeless tobacco) OR (chewing tobacco) OR (gutkha) OR (snuff) OR (paan) OR (khaini) OR (quid) – 439; (cardiovascular disease) OR (myocardial infarction) OR (cardiovascular mortality) OR (stroke) – 5504
Combining both searches = 101 references

- PakMediNet (17/07/2014) – No references

- IndMed (17/07/2014) – No references

- ProQuest Dissertations & Theses Global™ - searched on 17/07/2014

"smokeless tobacco*" OR (oral* NEAR/3 tobacco*) OR (chew* NEAR/3 tobacco*) OR (spit* NEAR/3 tobacco*) OR (dip* NEAR/3 tobacco*) OR gutk*a OR kiwam OR zarda OR mawa OR tuibur OR shamma OR gul OR snuf* OR snus OR chimo OR iqmik OR toombak OR tumbaku OR mishri OR m*sheri Or n*swar OR p*an NEAR/3 (masala OR quid) OR gudak*u OR k*aini OR quid NEAR/3 (betel OR tobacco*) OR maras NEAR/3 (powder OR tobacco*) – 502; "cardiovascular disease*" OR "myocardial infarct*" OR (heart AND (attack* OR arrest*)) OR (coronary AND (disease* OR event*)) OR (cardiovascular AND (mortalit* OR death*)) OR (cardiac AND (mortalit* OR death*)) OR (cerebrovascular AND (disorder*OR event* OR accident* OR disease*)) OR stroke* OR "brain isch*emia" OR "intracranial h*emorrhag*" – 16594
Combining both searches = 9 references

- Open Grey (17/07/2014) – No references

- EThOS (17/07/2014) – 1 reference

Appendix 5.2. Screening form for full-text articles

Study details (citation):

General Information

Date form completed	
Initials of reviewer	
Study author contact details	

Study eligibility

Study Characteristic	**Eligibility criteria**	**Criteria met? (Yes/No/Unclear)**
Type of study	Longitudinal observational study design	
Exposure	Ever use of ST	
	Subsample of exclusive ST users if smokers included (or) controlled for smoking	
Comparison	Control group of no tobacco users	
Outcome	Clearly defined according to ICD criteria	
	IHD (fatal or non-fatal)	
	Stroke (fatal or non-fatal)	

Decision

Include /Exclude	
Reasons if excluded	

Appendix 5.3. Data extraction form

Study details (citation):

General information and study characteristics

		Comments
Date form completed		
Type of publication		
Contact details of authors		
Country, Region		
Study design		
Study setting		
Duration of study		

Participants, exposure and outcome

		Comments
Sample size		
Age		
Gender		
Current/past ST users		
Type of ST used		
How was exposure assessed?		
Did the sample include smokers?		
Use of alcohol assessed?		
Outcome (IHD/stroke)		
How was outcome assessed?		

Data used in analysis

		Comments
Exposed group (n)		
Control group (n)		
Cases in exposed (n)		
Cases in unexposed (n)		
Statistical method used		
Confounders controlled for		

Appendix 5.4. Newcastle-Ottawa quality assessment scale templates and assessment

Cohort studies: A study can be awarded a maximum of one star for each numbered item within the 'Selection' and 'Outcome' categories. A maximum of two stars can be given for 'Comparability'.

Selection

1. Representativeness of the exposed cohort
    a. Truly representative of the average _____ (describe) in the community ✵
    b. Somewhat representative of the average _____ in the community ✵
    c. Selected group of users, e.g. nurses, volunteers
    d. No description of the derivation of the cohort
2. Selection of the non-exposed cohort
    a. Drawn from the same community as the exposed cohort ✵
    b. Drawn from a different source
    c. No description of the derivation of the non-exposed cohort
3. Ascertainment of exposure
    a. Secure record (e.g. surgical records) ✵
    b. Structured interview ✵
    c. Written self-report
    d. No description
4. Demonstration that outcome of interest was not present at start of study
    a. Yes ✵
    b. No

Comparability

1. Comparability of cohorts on the basis of the design or analysis
    a. Study controls for _____ (select the most important factor) ✵
    b. Study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1. Assessment of outcome
    a. Independent blind assessment ✵
    b. Record linkage ✵
    c. Self-report
    d. No description
2. Was follow-up long enough for outcomes to occur
    a. Yes ✵ (select an adequate follow up period for outcome of interest)
    b. No
3. Adequacy of follow up of cohorts
    a. Complete follow up - all subjects accounted for ✵
    b. Subjects lost to follow up unlikely to introduce bias ✵ (small number lost: < ____ % (select an adequate %), or description provided of those lost)
    c. Follow up rate < ____% (select an adequate %) and no description of those lost
    d. No statement

Case-control studies: A study can be awarded a maximum of one star for each numbered item within the 'Selection' and 'Exposure' categories. A maximum of two stars can be given for 'Comparability'.

Selection

1. Is the case definition adequate?
    a. Yes, with independent validation ✵
    b. Yes, e.g. record linkage or based on self-reports
    c. No description
2. Representativeness of the cases
    a. Consecutive or obviously representative series of cases ✵
    b. Potential for selection biases or not stated
3. Selection of Controls
    a. Community controls ✵
    b. Hospital controls
    c. No description
4. Definition of Controls
    a. No history of disease (endpoint) ✵
    b. No description of source

Comparability

1. Comparability of cases and controls on the basis of the design or analysis
    a. Study controls for _____ (Select the most important factor.) ✵
    b. Study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor)

Exposure

1. Ascertainment of exposure
    a. Secure record (e.g. surgical records) ✵
    b. Structured interview where blind to case/control status ✵
    c. Interview not blinded to case/control status
    d. Written self-report or medical record only
    e. No description
2. Same method of ascertainment for cases and controls
    a. Yes ✵
    b. No
3. Non-response rate
    a. Same rate for both groups ✵
    b. Non respondents described
    c. Rate different and no designation

Methodological quality of included studies – NOS ratings

Reference	Study design	NOS categories of study quality assessment		
		Selection	Comparability	Exposure/Outcome
INTERHEART study – 52 countries				
Teo et al. (2006)	Case-control	AMI cases defined and identified by clinical and ECG findings***** All eligible cases over a defined time period***** Community and hospital controls***** Controls had no history of outcome*****	Controlled for smoking and additional factors******	Structured interviews, not blinded to case/control status (not explicitly stated) Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
ASIA				
Gupta et al. (2005)	Cohort	Cohort representative of ST users in the community***** Non-exposed cohort drawn from same community as exposed***** Ascertainment of exposure through structured interviews***** Outcomes (IHD and stroke deaths) not present at start of study*****	ST-only users; controlled for additional factors******	Outcomes assessed through record linkage***** Follow-up conducted after 5-6 years Minimal lost to follow-up (<3%); unlikely to introduce bias*****
Rahman and Zaman (2008)	Case-control	AMI and angina pectoris cases defined and identified by clinical and ECG findings***** Representative series of cases***** Hospital controls Controls defined as non-IHD patients attending the hospital*****	ST-only users; controlled for additional factors******	Structured interviews, not blinded to case/control status Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
Rahman et al. (2012b)	Case-control	AMI and angina pectoris cases defined and identified by clinical and investigative findings***** Representative series of cases***** Community and hospital controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Structured interviews, not blinded to case/control status Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
Mateen et al. (2012)	Case-control	Stroke deaths defined and identified through verbal autopsy, independently validated***** All eligible cases over a defined time period***** Community controls***** Adult injury deaths as controls, history of outcome not stated	Controlled for smoking and additional factors******	Structured interviews, not blinded to case/control status Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
Alexander (2013)	Case-control	AMI cases defined and identified by clinical and investigative findings***** All eligible cases over a defined time period***** Community or hospital controls*****	ST-only users; controlled for additional factors******	Structured interviews, not blinded to case/control status (not explicitly stated) Same methods of exposure ascertainment used for cases and controls*****

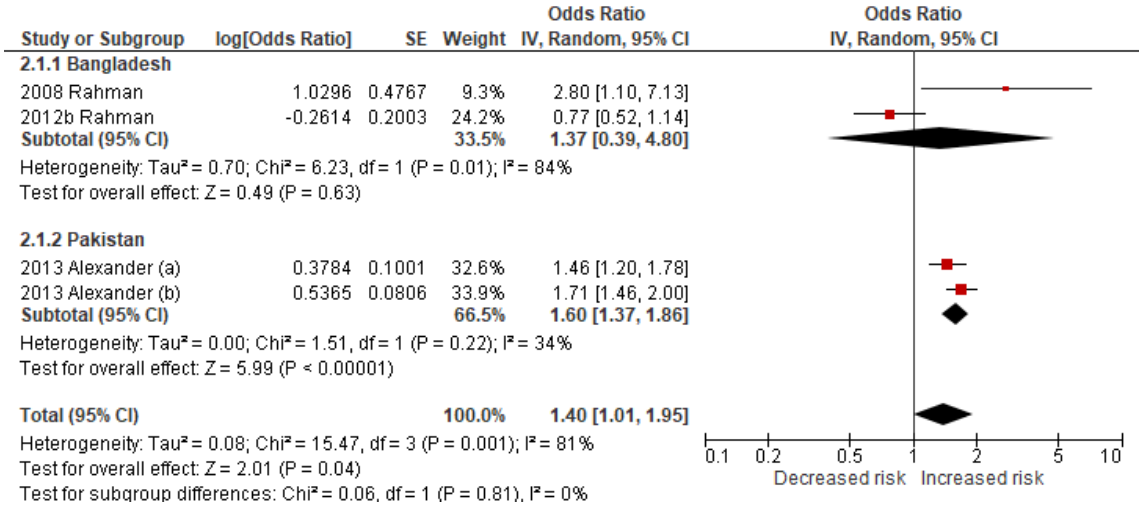
		Controls had no history of outcome*****		Non-response rates comparable in groups*****
Gajalakshmi and Kanimozhi (2015)	Case-control	Stroke deaths defined and identified through verbal autopsy, sample of reports independently validated***** Representative series of cases in urban area; additional efforts made to minimise selection bias in rural cases***** Community controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Structured interviews, not blinded to case/control status (not explicitly stated); quality control of interviews described***** Same methods of exposure ascertainment used for cases and controls***** Low rates of non-response in cases (< 5%)*****
EUROPE				
Huhtasaari et al. (1992)	Case-control	AMI cases defined and identified using WHO criteria* All eligible cases over a defined time period***** Community controls***** Controls had no history of outcome*****	Controlled for smoking and additional factors******	Exposure ascertainment by self-report Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
Bolinder et al. (1994)	Cohort	Selected group of users – construction workers Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report Outcomes (IHD and stroke deaths) not present at start of study*****	ST-only users; controlled for additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after 12 years***** Nearly complete follow-up*****
Huhtasaari et al. (1999)	Case-control	AMI deaths (including sudden cardiac deaths) defined and identified using WHO criteria* All eligible cases over a defined time period***** Community controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Exposure ascertainment by self-report Same methods of exposure ascertainment used for cases and controls***** Non-response rates comparable in groups*****
Asplund et al. (2003)	Case-control	Stroke cases defined and independently validated***** All eligible cases over a defined time period***** Community controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Exposure ascertainment by self-report Same methods of exposure ascertainment used for cases and controls***** Non-response rates comparable in groups*****
Hergens et al. (2005)	Case-control	AMI cases and deaths identified through record linkage All eligible cases over a defined time period***** Community controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Exposure ascertainment by self-report Same methods of exposure ascertainment used for cases and controls***** Similar non-response rates in both groups*****
Johansson et al. (2005)	Cohort	Cohort representative of ST users in the community***** Non-exposed cohort drawn from same community as exposed***** Ascertainment of exposure through structured interviews***** Outcome (IHD) not present at the start of study*****	ST-only users; controlled for additional factors******	Outcome defined and assessed through record linkage***** Follow-up conducted after 12 years***** Nearly complete follow-up*****
Hergens et al. (2007)	Cohort	Selected group of users – construction workers Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report	ST-only users; controlled for additional	Outcome defined and assessed through record linkage***** Follow-up conducted after 19 years (mean)*****

		Outcome (AMI) not present at the start of study*****	factors******	Complete follow-up*****
Wennberg et al. (2007)	Case-control	AMI deaths defined and identified through record linkage; independently validated***** All eligible cases over a defined time period***** Community controls***** Controls had no history of outcome*****	ST-only users; controlled for additional factors******	Exposure ascertainment by self-report Same methods of exposure ascertainment used for cases and controls***** Non-response rates not adequately described
Hergens et al. (2008)	Cohort	Selected group of users – construction workers Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report Outcome (stroke cases and deaths) not present at start of study*****	ST-only users; controlled for additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after 18 years (mean)***** Nearly complete follow-up*****
Hansson et al. (2009)	Cohort	Selected group of users – Swedish Twin Registry Non-exposed cohort drawn from same community as exposed***** Ascertainment of exposure through structured interviews***** Outcomes (IHD and stroke) not present at start of study*****	Controlled for smoking and additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after 4.9 years (mean) No statement about adequacy of follow-up
NORTH AMERICA				
Accortt et al. (2002)	Cohort	Representative cohort***** Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report Outcomes (IHD and stroke) not present at start of study*****	ST-only users; controlled for additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after about 20 years ***** Nearly complete follow-up*****
Henley et al. (2005)	Cohort CPS I	Representative cohort***** Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report Outcomes (IHD and stroke) not present at start of study*****	ST-only users; controlled for additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after 12 years ***** Nearly complete follow-up*****
Henley et al. (2005)	Cohort CPS II	Representative cohort***** Non-exposed cohort drawn from same community as exposed***** Exposure ascertainment through self-report Outcomes (IHD and stroke) not present at the start of study*****	ST-only users; controlled for additional factors******	Outcomes defined and assessed through record linkage***** Follow-up conducted after 18 years ***** Nearly complete follow-up*****

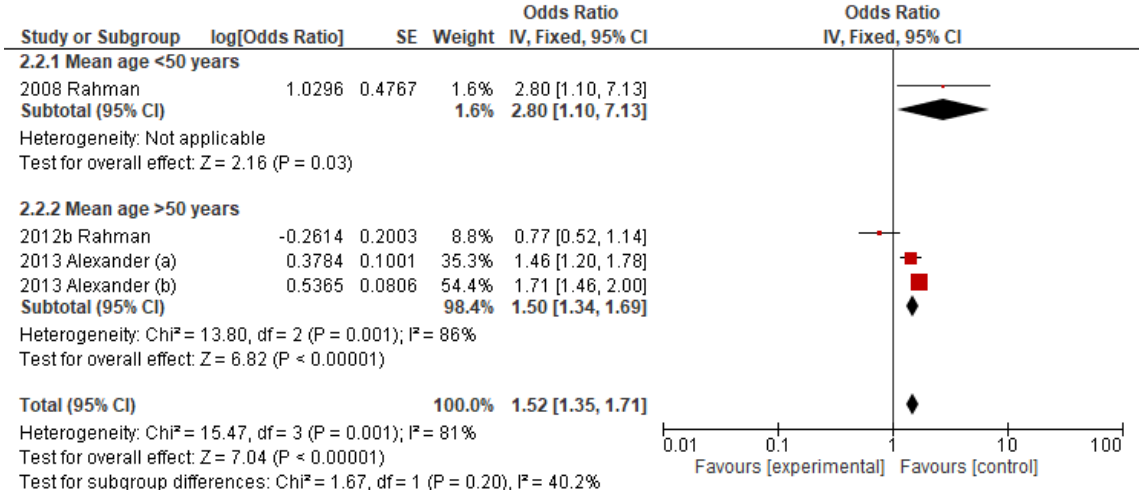
Abbreviations: NOS – Newcastle-Ottawa Scale, EGC – Electrocardiogram, ST – Smokeless Tobacco, IHD – Ischaemic Heart Disease, AMI – Acute Myocardial Infarction, WHO – World Health Organization, CPS – Cancer Prevention Study

Appendix 5.5. Sources of heterogeneity

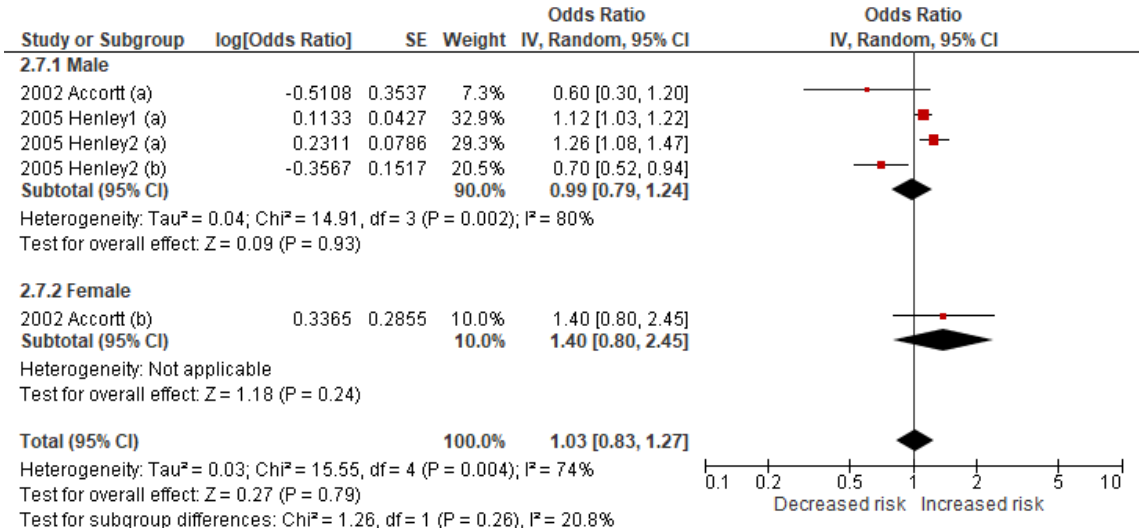
Asian studies reporting risk of IHD – Country



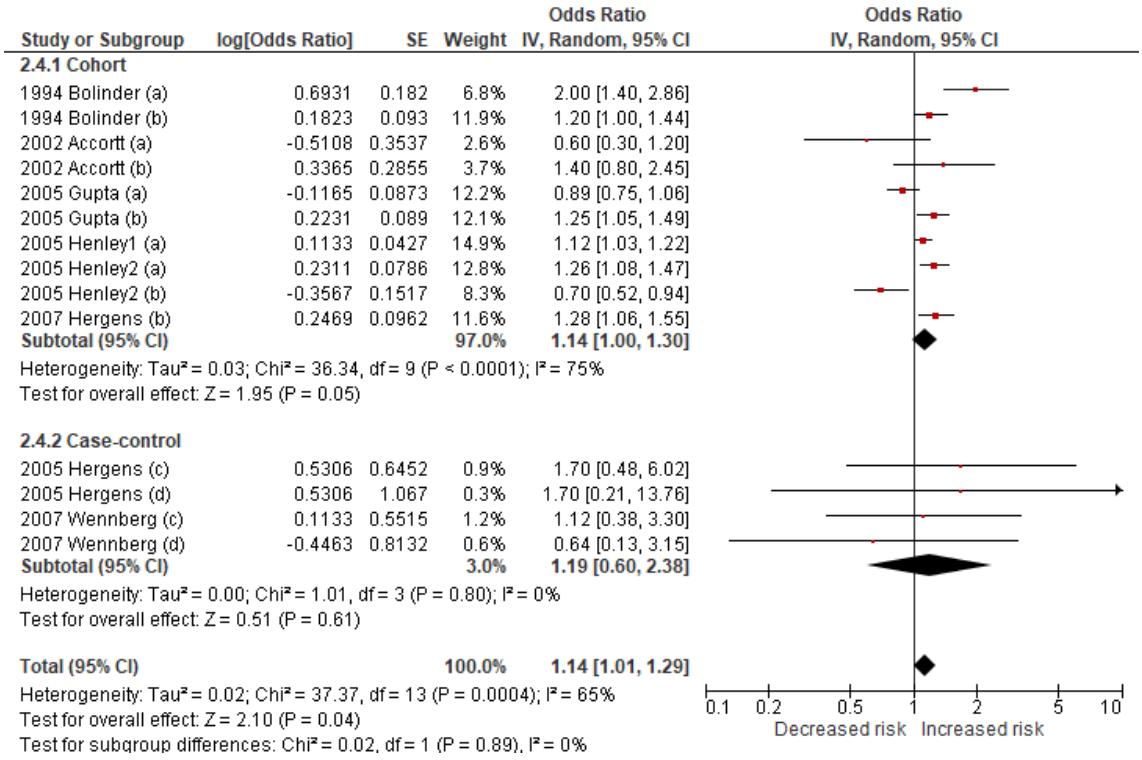
Asian studies reporting risk of IHD – Mean age of participants



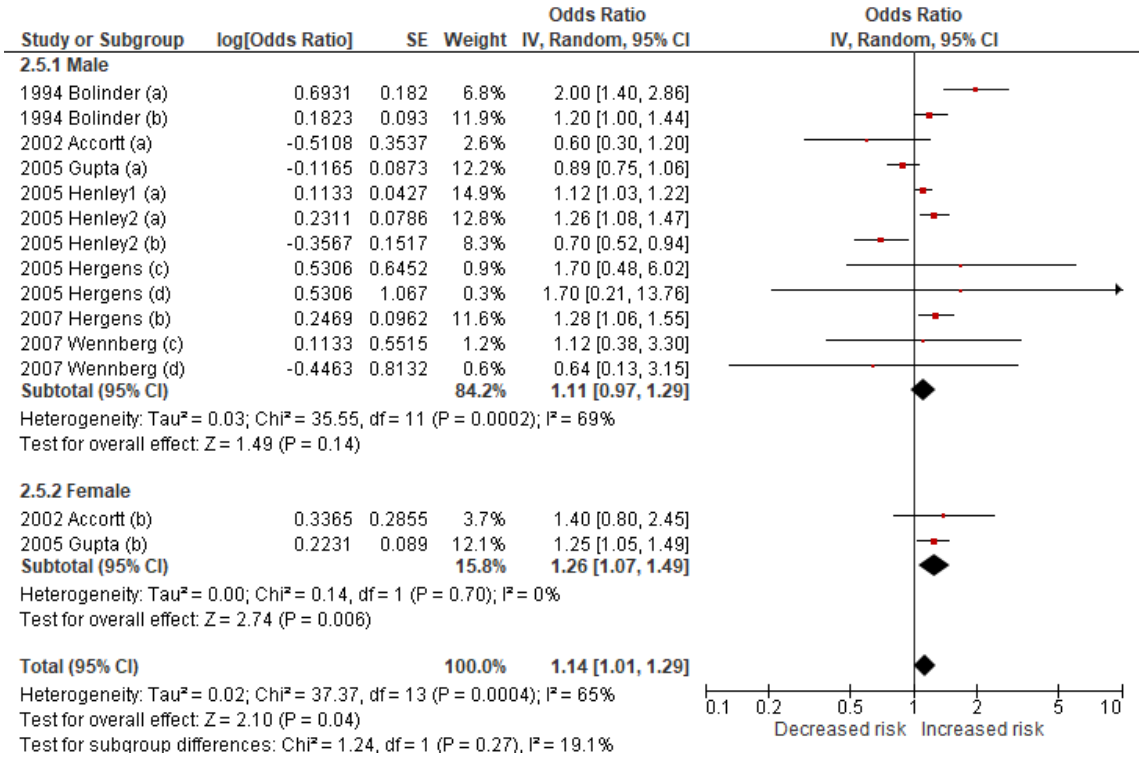
American studies reporting risk of fatal IHD – Gender of participants



All studies reporting risk of fatal IHD – Study design

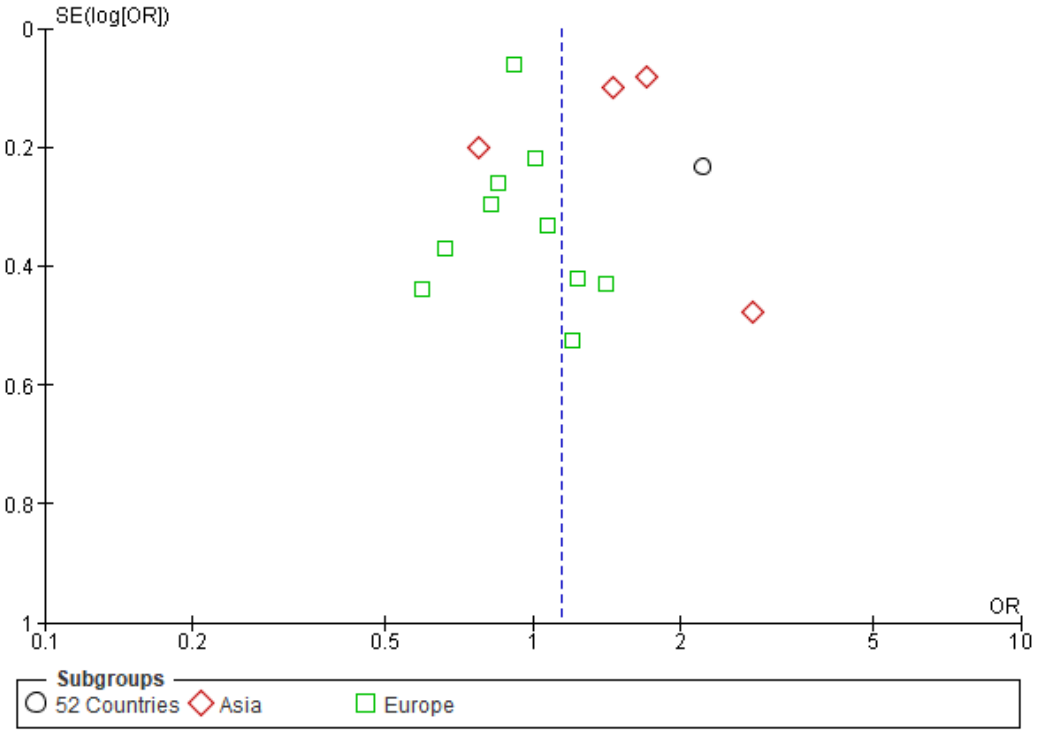


All studies reporting risk of fatal IHD – Gender of participants

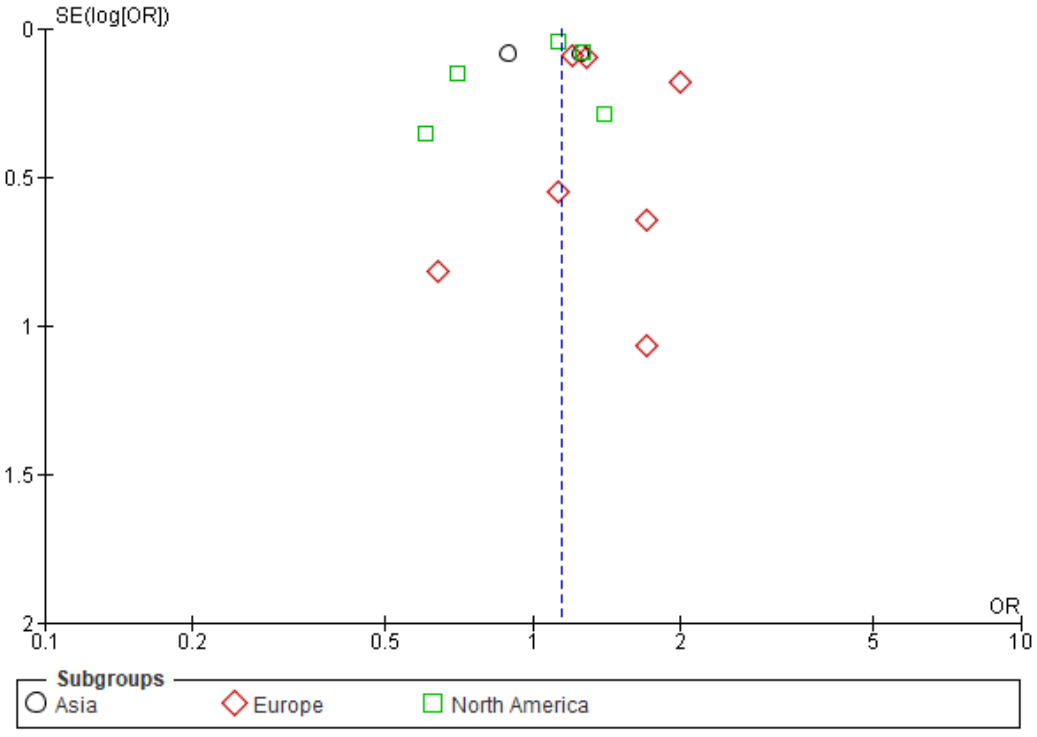


Appendix 5.6. Funnel plots to assess risk of publication bias

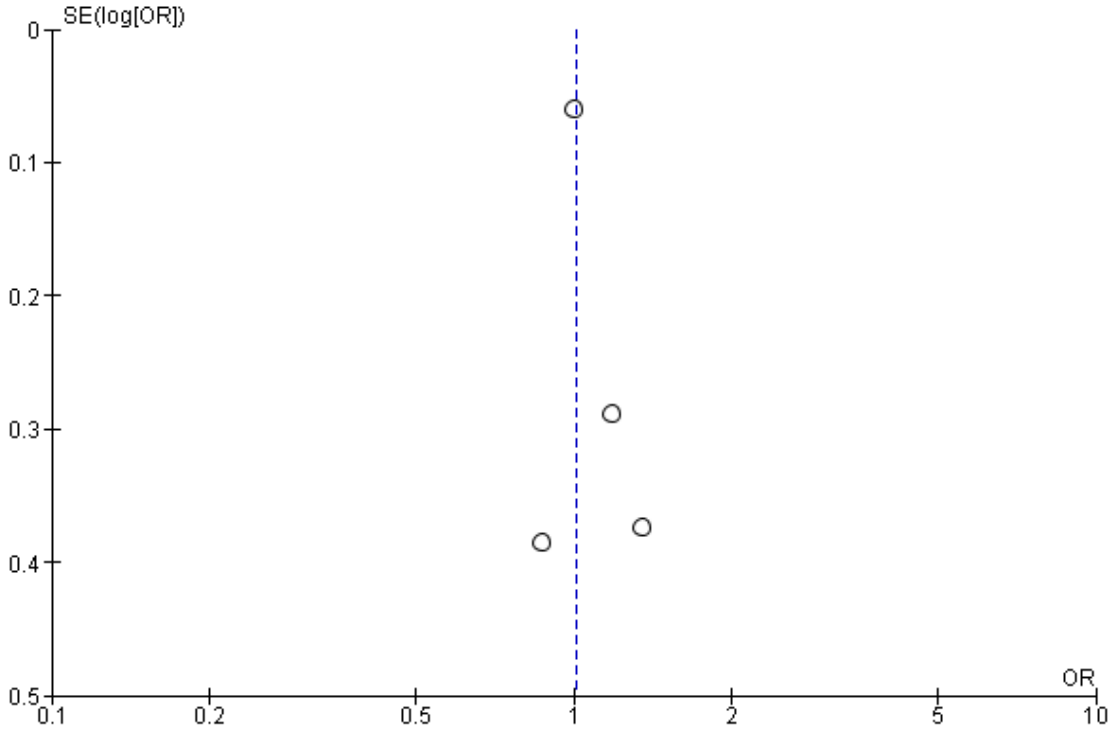
Incident IHD



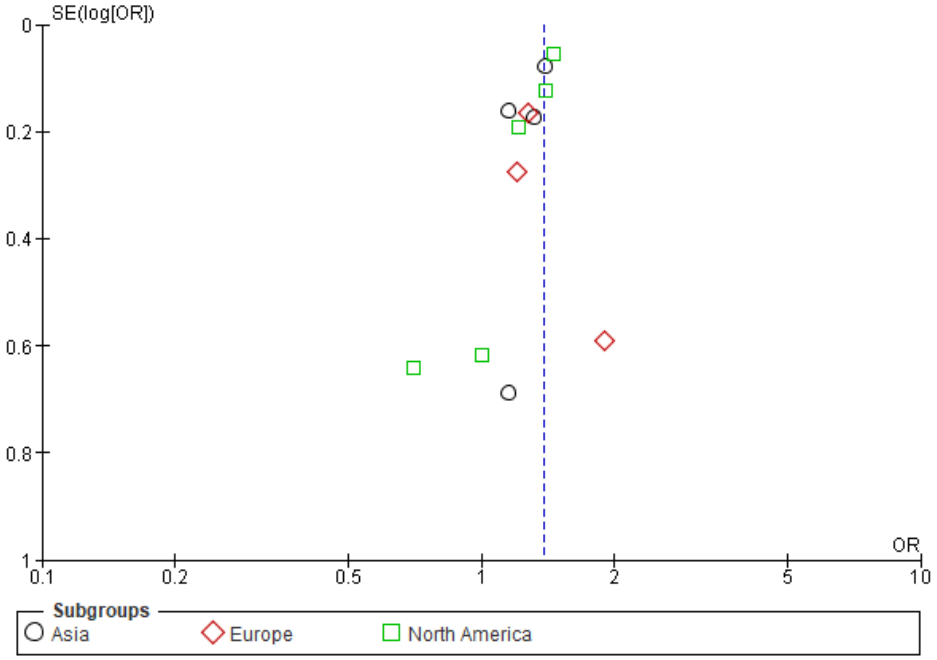
Fatal IHD



Incident stroke



Fatal stroke



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