
by

Duresso, Samson Wubshet MA, (Psychology)

School of Medicine

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The following people and institutions contributed to the publication of work undertaken as part of this thesis:

- Samson W. Duresso, School of Medicine (Psychology), University of Tasmania
- Allison J. Matthews, School of Medicine (Psychology), University of Tasmania
- Stuart G. Ferguson, School of Medicine (Pharmacy), University of Tasmania
- Raimondo Bruno, School of Medicine (Psychology), University of Tasmania


Samson Wubshet Duresso was the primary author and contributed to the development of the research questions, data collection, result interpretation and manuscript writing. Raimondo Bruno contributed to the research questions, research design, data analysis and interpretation in addition to providing guidance, review and restructuring of the papers. Stuart Ferguson and Allison Matthews provided particular guidance and reviews on structuring, wording, and result interpretation.


Samson Wubshet Duresso was the primary author and contributed to the development of the research questions, data collection, result interpretation and manuscript writing. Raimondo Bruno contributed to the research questions, research design, survey questions and data analysis and interpretation in addition to providing guidance, review and restructuring of the
papers. Stuart Ferguson and Allison Matthews provided particular guidance and reviews on structuring, wording, and result interpretation

**Paper 3 (Chapter 4):** Duresso, S. W., Bruno, R., Matthews, A. J., Ferguson, S. G.,


Samson Wubshet Duresso was the primary author and contributed to the development of the research questions, data collection, data analysis, result interpretation and manuscript writing. Raimondo Bruno and Stuart Ferguson provided guidance, review and restructuring of the papers and contributed to the research questions and data analysis and interpretation. Allison Matthews provided particular guidance reviews on structuring, wording, and interpretation.

**Paper 4 (Chapter 5):** Duresso, S. W., Bruno, R., Matthews, A. J., & Ferguson, S. G.


Samson Wubshet Duresso was the primary author and contributed to the development of the research questions, data collection, result interpretation and manuscript writing. Stuart Ferguson and Raimondo Bruno contributed to the research questions, research design, EMA survey questions and data analysis and interpretation in addition to providing guidance, review and restructuring of the papers. Allison Matthews provided particular guidance and reviews on structuring, wording, and interpretation
We the undersigned agree with the above stated “proportion of work undertaken” for each of the above published/submitted peer-reviewed manuscripts contributing to this thesis:

Signed: ______________________  ______________________

Samson Wubshet DURESSEO  Associate Professor Raimondo Bruno
Candidate  Supervisor
School of Medicine,  School of Medicine
University of Tasmania  University of Tasmania

Signed: ______________________

Professor Juan J. Canales  Professor Ben Canny
Head, Division of Psychology  Head of School
School of Medicine  School of Medicine
University of Tasmania  University of Tasmania

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Khat (a natural stimulant plant) has become a public health concern due to adverse health risks and negative social functioning associated with frequent chewing. Increased frequency of khat use is associated with use disorder, dependence and increased physical and psychological health problems. Despite the prevalence of khat use and increasing consumption and use disorder in Ethiopia, there has been inadequate and insufficient research available to understand its potential psychological and health consequences. In the Ethiopian context, very little is known about the nature of khat dependence, the outcome of khat cessation attempts and the characteristics of withdrawal symptoms and craving during khat abstinence. Hence, the main aims of the studies in this thesis is to validate the existence of a khat use disorder syndrome using DSM-5 criteria and to explore the nature and the time course of any withdrawal syndrome in relation to the cessation of khat use among frequent khat users. In Study 1 of this thesis, the presence of khat use disorder syndrome was validated using DSM-5 criteria and its relationship with increased experience of harms was examined on a sample of 400 current khat-chewers (aged 16 and above recruited from khat markets and cafes from university and general community in Adama, Ethiopia) between September 2014 and January 2015. Accordingly, 10.5% (95% CI=7.9–13.9) were categorized as experiencing mild, 8.8% (95% CI=6.4–12.0) moderate and 54.5% (95% CI=49.6–59.3) severe khat use disorder. Participants demonstrated increased financial, academic and self-reported mental health problems associated with use. Participants with khat use disorder also had higher psychological distress and poorer quality of life. Despite this, there are low levels of help-seeking for these problems. Only one-third (32.9%) of individuals with khat use disorder reported life-time access to help-
seeking largely from friends and relatives. Hence, the construct of a substance use disorder syndrome for khat using DSM-5 criteria appears valid and performs in a manner consistent with other substances of dependence In Study 2, a Cross-sectional data from a sample of 388 past year khat consumers (same participants used in study 1) were collected to determine the efficacy of the Severity of Dependence Scale (SDS) as a screening tool for DSM-5 defined Khat Use Disorder. Participants self-completed survey comprising an SDS scale, current substance use disorder symptoms (modified Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV), and validated measures of health, psychological distress, quality of life and academic functioning. Nearly three-quarters (73%) of the sample experienced DSM-5 Khat Use Disorder. The SDS demonstrated excellent discrimination (AUC=0.92), with an optimal cut-off score of 3 or above. Those screened positive had more frequent and higher dose of khat use; greater financial problems in relation to khat use; more problems related to academic functioning in daily life; greater psychological distress and poorer quality of life than their counter partners. The SDS, as a brief and simple screening tool, appears to validly identify individuals with khat use disorder syndrome and higher rates of adverse consequences. Hence, there is clear evidence that some consumers are both concerned with their use and experience problems in relation to khat use. In Study 3, a naturalistic data collected from 59 daily and near daily khat consumers (from Adama University in Ethiopia) using electronic diary, were used to monitor the outcomes of an unassisted quit attempt and to examine predictors of success of khat abstinence. While 80%, reached at least 7 continuous days of abstinence, 93% lapsed, on the average, after 11 days post-quit (SD=7) and only 7% maintained continuous abstinence for 28 days post-quit. Although regular khat chewers have motivation and desire to quit, they
Abstract

seem to have difficulties maintaining abstinence with unassisted quit attempts. Treatment aids are very likely to assist chewers in their quit attempts. None of the demographic factors were predictive of successful abstinence. In Study 4, the elevation and shape of the growth curves of the major withdrawal symptoms and craving of frequent khat chewers (participants used in study 3) were examined for 3 pre-quit and 14 post-quit days. Electronic Diary (ED) was used to collect real time data of khat withdrawal symptoms and cravings. The development of withdrawal symptoms was evident, and all withdrawal symptoms followed similar overall patterns with salient elevations after the quit day and curvatures around the first week of post quit period, indicating the persistence and severity of these symptoms over time. In addition, craving, irritability and restlessness had significantly reverted to their baseline level during the 2nd week of the post quit period. The need for interventions is necessary to support individuals during the period of increased symptoms of dysphoria and to reduce the risk of relapse. Participants’ anticipation to quit and the initial quitting experience were likely to intensify withdrawal symptoms and provoke lapse in the long run. In conclusion, khat chewing has multiple effects on frequent and chronic consumers. While khat is a mild stimulant, there is clear evidence of khat use disorder and that some khat users are both concerned with their use and experience substantial and clinically significant problems associated with their use. The SDS, being a brief screening tool, appears to validly identify individuals with khat use disorder syndrome and with high rates of adverse consequences. In addition, self-motivated individuals for unassisted quit attempts seem to experience difficulties in maintaining abstinence since expectation of the quit experience by itself is likely to intensify withdrawal symptoms and craving among the chewers and facilitate eventual lapse. Hence, there is considerable scope to intervene at an organizational level to curb and minimize problems in relation to khat.
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Samson Duresso
University of Tasmania
Introduction
Introduction

Khat (*Catha edulis*) is a stimulant plant widely cultivated in East African countries and the Arabian Peninsula (Luqman & Danowski, 1976). Khat is harvested in the early hours of the morning and sold in markets in late morning, often, after being prepared as a bundle of leaves, wrapped in banana leaves to preserve freshness (Luqman & Danowski, 1976). Chewing fresh and young leaves of a khat tree, mostly in a social setting, is the most common mode of consumption and it is an old and widespread habit in the Horn of Africa (e.g. Ethiopia, Kenya and Somalia). Considering its popularity and its being a major source of foreign exchange, khat is deeply engrained in Ethiopian society and culture, and significant for the nation’s economy (Gebissa, 2008). It is a high-cash income crop for the producers, for retailers as well as for the government revenue through taxation (Getahun & Krikoria, 1973; Kennedy, 1987; Lemessa, 2001). In Ethiopia, 85-90% of khat produced is exported (Lemessa, 2001) making a very significant input to the country’s foreign income. For instance, in 1999/2000, khat worth $ 55 million USD was exported to different countries ranking second in export revenue (Lemessa, 2001).

Distribution and Prevalence of khat use

Khat circulates freely in Ethiopia and khat chewing is legal (Elmi, 1983; Gebissa, 2010). Previously, khat was available only near to where it was grown. However, currently, the fact that khat has become a critical commodity for the survival of millions of producers and marketers, plays a vital role in the dramatic expansion of khat production and consumption (Gebissa, 2008)

In Ethiopia, the chewing of khat has a deep rooted socio-cultural tradition (Kalix & Braenden, 1985). In addition to the use of khat for religious purposes, it is consumed for recreational
purposes (Kennedy, 1987). It is most valued for its stimulant effects and usually chewed in company to facilitate social interactions (Kennedy, 1987; Elmi, 1983). Occasionally, khat may be chewed individually, to improve alertness, (Kalix, 1984a) and to enhance work capacity and performance (Kennedy, 1987; Elmi, 1983). Despite the negative attitudes of non-chewers and critical warnings from the medical community, khat consumption has spread from Harar to all parts of Ethiopia in the last three decades (Dachew, Bifftu, & Tiruneh, 2015).

Studies documented that the number of khat chewers in Ethiopia has significantly increased over time and now it has become popular nearly in all segments of the Ethiopian population (Selassie & Gebre, 1996). Khat is used habitually by craftsmen, farmers and labourers during physical work in order to facilitate physical and mental alertness; to prevent sleepiness and overcome physical fatigue (Alem, Kebede, & Kullgren, 1999; Ayana & Mekonen, 2004). More recently, several studies have reported an increased prevalence of khat chewing among various parts of the community (Alem et al., 1999; Ayenew, Tadesse, & Azale, 2012). Adults from different occupations including university instructors (Ihunwo, Kayanja, & Amadi-Ihunwo, 2004) and a fairly large proportion of students of secondary and higher education chew khat regularly (Adugna, Jira, & Molla, 1994; Cox & Rampes, 2003; Ihunwo et al., 2004).

Research reports suggest that 80–90% of male adult and 10–60% of the female adult population in East Africa chew khat on a daily basis (Numan, 2004; Odenwald et al., 2005). Similarly, in Ethiopia, the prevalence of past month khat use was estimated at 27.3% among men and 11.0% among women (Gebrehanna, Berhane, & Worku, 2014b). More people from the age group between 18 and 24 (34.4%) use khat than other age groups (Gelaw & Haile-Amlak, 2004). While the prevalence of past month khat use across Ethiopia is estimated at 15.3%, the life time, current or past month use of khat vary from regions to regions in the
country (Gebrehanna et al., 2014b). In the major towns of Oromia regional state, khat chewing is growing and becoming a common pastime among youths and adults. A survey of secondary school students in some parts of this region (Agaro, Western Oromia), revealed a current khat chewing prevalence of 65% and that two thirds of the most frequent users were students between the ages of 15 and 22 years (Adugna et al., 1994). A cross-sectional survey conducted among university staff, revealed a lifetime and past month prevalence of 46% and 30.8%, respectively (Gelaw & Haile-Amlak, 2004; Y. Gelaw & A. Haile-Amlak, 2004). Similarly, in Butajira, (Oromia) life time and current khat chewing prevalence were 55.7% and 50%, respectively (17.4 % chewing on a daily basis) (Alem et al., 1999). In the Amhara region (Bahirdar and surrounding districts in the north), where once khat had been strongly discouraged by the community, the consumption of khat has recently become a common practice, with a 27% lifetime prevalence rate among college students, of which 46% report the onset of the use during their senior years in secondary school (Kebede, 2002).

Khat chewing has also become a common practice among high school, college, and university students. The purposes of khat chewing among university students were to increase concentration and remain alert and to reduce fatigue while studying (Ayana & Mekonen, 2004). Among Ethiopian university students (n=3268), the estimated life-time and past month khat use are 24.0% and 7.7%, respectively (Gebrehanna, Berhane, & Worku, 2014a). In some parts of Ethiopia the prevalence of lifetime and current chewing of khat among secondary school students are 18.4% and 10.9%, respectively (Nigussie, Gobena, & Mossie, 2013). A national study conducted in 2011 revealed that the estimated prevalence of past month khat use for non-student and student adolescents were 23.0% and 7.5%, respectively (Kebede et al., 2005).
Khat chewing sessions are usually accompanied by simultaneous usage of cigarettes, alcohol and illicit drugs. Heavy chewers tend to report using khat to stay awake, increase productivity or feel ‘high’ and alcohol to reduce tension from these stimulatory effects or to neutralize the stimulating effect and sleeplessness caused by the khat and go to sleep (Griffiths, 1998). Studies revealed that 60% of khat chewers (African diaspora-Somalia) in London also smoked cigarettes; 75% of these were men, smoking 5–45 cigarettes per day (Griffiths, 1998) Few used any other drugs and the most common was cannabis, used by 6% of the sample. Khat has also been linked to the misuse of other drugs. In Ethiopia, unlimited access to khat, cigarettes and alcohol with no age limits might have contributed to poly drug uses among people. The most common poly-drug concurrent uses in the capital city (Addis Ababa) were tobacco and cannabis resin (hashish) 14.9%; khat, alcohol and diazepam (valium) 14.9%; and khat, tobacco and alcohol 14.8% (Selassie & Gebre, 1996).

**Pharmacokinetics and Pharmacology of Khat**

The most common and traditional way of consuming khat is chewing the fresh leaves of a young shoot. A ball of chewed khat, which is often kept in either side of the cheeks (M. Banjaw & Schmidt, 2005), will be masticated slowly and intermittently to release the active ingredients and eventually swallowed, or spit out at the end of the chewing session (Cox & Rampes, 2003b; Nencini, Ahmed, & Elmi, 1986). A small proportion of consumers, especially elderly people, ingest khat in the form of a drink prepared from fresh and shredded or dried khat leaves and very rarely smoke-dried leaves.

In a khat chewing session, initially there is an atmosphere of cheerfulness, optimism and a general sense of well-being. After about two hours, tension, emotional instability and
irritability appears, later leading to feelings of low mood, and sluggishness. Chewers tend to leave the session feeling exhausted (Cox & Rampes, 2003).

In fresh khat leaves, a higher proportion of the more desirable cathinone is normally found; as leaves age or become dry, cathinone breaks down into cathine, and the content of cathine is relatively higher. As a result, the consumption of non-fresh khat leaves leads to the occurrence of more unwanted adverse effects (Kalix, 1981). Hence, khat chewers often prefer to chew fresh leaves since they contain a higher ratio of cathinone to cathine and cause better psychostimulant effects with fewer systemic adverse effects (Cox & Rampes, 2003).

A typical chewing session on average may last five to six hours and on average 100–500 g of khat is chewed (Al-Hebshi & Skaug, 2005; Elmi, 1983; Kalix, 1990; Matloob, 2003; Nencini & Ahmed, 1989). The juice of the chewed leaves is swallowed, but not the residues (Toennes, Harder, Schramm, Niess, & Kauert, 2003). The chewing process effectively liberates 80% of cathinone and cathine, and over 90% of norephedrine (Toennes et al., 2003; Toennes & Kauert, 2002). The euphoric effect of khat ingestion appears shortly after the chewing begins, often after 30 minutes (Widler, Mathys, Brenneisen, Kalix, & Fisch, 1994). This suggests that absorption of alkaloids takes place first in the oral mucosa (Toennes et al., 2003). While the peak plasma levels for cathinone and other ingredients of khat leaves are attained after 1–3.5 h (Brenneisen, Fisch, Koelbing, Geisshusler, & Kalix, 1990; Halket, Karasu, & Murray-Lyon, 1995), maximal plasma concentrations of cathinone and cathine are reached at 2.3 and 2.6, respectively (Toennes et al., 2003). Metabolism of cathinone is rapid, occurring mainly during the first passage through the liver. The terminal half-life for cathinone is short-lived (1.5±0.8 hours) than for cathine (5.2±3.4 hours) (Toennes et al., 2003), which indicates that the longer
the time that chewing sessions takes place, the higher the levels of cathine accumulated than cathinone and the more the unwanted systemic effects may result.

Khat contains more than 40 alkaloids, glycosides, tannins, amino acids, vitamins and minerals (Halbach, 1972). Since khat contains a variety of compounds the chewing of khat may have many different effects. The most common effects include those on the gastro-intestinal system and on the nervous system (Kalix, 1984). Effects on the autonomic (peripheral) nervous system include constipation, urine retention and acute cardiovascular stimulation. In terms of effects on the central nervous system, increased alertness and psychiatric symptoms are common (Kalix & Braenden, 1985). The most active constituents of Catha Edulis are cathinone and cathine and the psychostimulant effect of chewing khat on the nervous system is thought to be the result of these two phenylalkylamines, which are structurally similar to amphetamine (Nencini, Amiconi, Befani, Abdullahi, & Anania, 1984). As a result, much of the research regarding khat use focuses on the pharmacological effects of cathinone and cathine.

Khat has been termed a ‘natural amphetamine’ for its sympathomimetic and central nervous system stimulation analogous to the effects of amphetamine (Brenneisen et al., 1990; Kalix, 1988). Studies argue that khat produces similar clinical effects to amphetamine except for some difference due to slight pharmacodynamic variations, differences in dosage and the mode of consumption (Cox & Rampes, 2003). Acute ingestion of khat induces dopaminergic and serotonergic actions in the central pathways (Kalix, 1981). Cathinone [(-)-alpha-aminopropiophenone], is considered to be the most active ingredient of khat. It has been isolated and synthesised and its effects have been shown to be similar to amphetamine, but with a lower potency - approximately half as potent as (+, dextro) amphetamine (Kalix, 1981).
However, cathinone is estimated to be 7–10 times more potent in terms of psychostimulant effects than the other primary ingredient, cathine (Nencini, Grassi, Botan, Asseyr, & Paroli, 1989). Cathine is both milder and briefer in its psychostimulant action than cathinone and plays only a minor role in the effects of khat. It is believed that cathine is responsible for many of the unwanted adverse effects such as feelings of low mood and sluggishness (Cox & Rampes, 2003).

**Pharmacological and Psychological effects of khat chewing**

Khat use is associated with a variety of psychological and behavioural changes in individuals. Ingestion of khat is acutely self-limiting that most consumers may typically stop chewing in 4 - 6 hours. However, chronic and long-term intake can lead to impairment of mental health, possibly contributing to ‘mental deterioration’ especially when age of initiation is early (Kalix & Braenden, 1985). Khat chewing may have both short term and long-term psychological effects. Short term effects may be positive and negative and are mostly common among those who consume small amounts. They may include a feeling of well-being, tiredness, hyperactivity, mild euphoria, excitement, increased alertness/concentration, restlessness, irritability and increased energy levels (Cox & Rampes, 2003). On the other hand, long term effect may include, insomnia schizophreniform psychotic illness, mania (Yousef, Huq, & Lambert, 1995) and, very rarely, depression (Pantelis, Hindler, & Taylor, 1989b). Some chewers, owing to the strength of the khat variety, also experience unpleasant effects during the chewing process, such as anxiety, tension, and restlessness (Cox & Rampes, 2003). In few cases, chewers may show a range of experiences, from minor reactions to the development of a psychotic illness. Most reports of khat psychosis are of low incidence which may be attributed to two fundamental issues. Firstly, in countries where khat is widely used, there are very limited health facilities and people are managed at home by their family. Secondly, owing
to the mode of consumption, the dose of khat tends to be self-limiting, unlike amphetamines, which are available in a pure form for oral or parenteral administration (Yousef et al., 1995). Therefore, psychotic reactions due to excessive use are much less frequent with khat than with amphetamines. Moreover, some research findings (Alem & Shibre, 1997; Critchlow & Seifert, 1987) confirm that adverse effects of khat are dose-related. For instance, (Dhadphale & Omolo, 1988) found that when khat was chewed in moderate quantities there was little morbidity, but when the amount chewed per day was excess (greater than two bundles), morbidity significantly increased.

Several authors report that depression is also associated with the cessation of khat chewing. Such behaviour has also been reported following cessation of amphetamine use (Pantelis, Hindler, & Taylor, 1989a). Although there are rare events of self-harm and suicide reported in the literature during both chewing and the subsequent intoxication phase, suicide have been reported in the context of a ‘withdrawal state’ and the distress caused by paranoid symptoms due to overdosing of khat (Giannini & Castellani, 1982). Violent acts, including homicide, are also documented, usually in the context of paranoid or persecutory delusions (Pantelis et al., 1989). A study conducted in Ethiopia by (Alem & Shibre, 1997) and (Alem et al., 1999), described two cases where a patient murdered one of his wives and his daughter and another case of combined homicide and suicide after chewing increased amounts of khat, respectively.

Changes in neurobiological and psychological functions due to chronic drug use are likely to differ as a result of many interrelated factors, such as the class of drugs, the pattern of use, as well as the complex interplay with pre-existing neurodevelopmental factors (Nader et al., 2006). There is some evidence to suggest that primates with pre-existing lowered dopamine (D₂) receptors are more likely to be at increased risk of using cocaine and becoming addicted
Animal studies have also revealed similar results in the rodent model (e.g. (Dalley et al., 2007). Similarly, studies on humans, reported that individuals that become chronic users of cocaine might be more likely to have pre-existing problems in inhibitory control and impulsivity (Verdejo-Garcia, Lawrence, & Clark, 2008). The prefrontal cortex is one of the primary structures that has been implicated in drug-related deficits across multiple studies and accounts for various deficits of cognitive, behavioural, and emotion functioning. Individuals who use multiple drugs, or who are exposed to other high risk environmental conditions may particularly show impairments in these domains (Nader et al., 2006). Therefore, it may be expected that a similar relationship may well exist between pre-existing conditions and behaviour patterns of khat users, which could be considered in future studies.

Studies on neurobiological mechanisms arising from chronic khat use are as rare as those which systematically investigated its long-term impact on the specific cognitive functioning and cognitive and behavioural deficits. Cathinone and cathine, the two compounds of khat, stimulate the central nervous system (CNS) by increasing dopamine (DA), 5-hydroxytryptamine and noradrenaline (Kalix & Braenden, 1985) and release DA in both the substantia nigra and the ventral tegmental area (VTA). The VTA projects to the ventral striatum and the limbic structures and plays a key role in reward-related behaviour. The VTA also projects to the frontal cortex, which plays a role in a variety of cognitive functions including attention and working memory. It is also hypothesized that excessive dopaminergic activity, resulting from chronic consumption of amphetamine-like substances (e.g. khat) may produce negative effects on cognitive functioning (Kalix & Braenden, 1985).

Studies on the residual effect of amphetamine use on cognitive functioning suggest that there is evidence of decreasing cognitive flexibility due to amphetamine use (van der Plas, Crone,
van den Wildenberg, Tranel, & Bechara, 2009). Chronic use of drugs like amphetamine and opiates could result in pronounced neuropsychological impairment in the domains of executive and memory function; and the impairment persists after several years of drug abstinence and may reflect neuropathology in frontal and temporal cortices (Ersche, Clark, London, T., & Sahakian, 2006). Clinically, it appears that some chronic methamphetamine users and dependent subjects seem to be easily distractible and exhibit some difficulties in sustaining attention as well as modest visual-constructional deficits on tasks such as the Rey Complex Figure copy task (Kalechstein, Newton, & Green, 2003). Attentional deficits have also been noted among chronic amphetamine users on some tasks involving attention and/or sustained attention in the Stroop Color Word and Trail making Tests (Kalechstein et al., 2003; Simon et al., 2000). Consistent with these findings, a recent study by London and colleagues (London et al., 2005), depicted that chronic methamphetamine users significantly committed more errors on an auditory version of the Continuous Performance Test (CPT) than drug-free controls, which indicated deficits of sustained attention and vigilance (Borgaro et al., 2003).

Although distractibility and attentional deficits have been reported anecdotally in khat users, these areas of cognitive functioning have not been carefully examined in experimental settings on khat users.

However, given the similarity of khat and amphetamine in terms of chemical structure, pharmacological activity and psychostimulation of the CNS, it is reasonable to assume that prolonged and acute consumption of khat would affect the same neurotransmitters and result in similar neurobiological, physiological and psychological effects (Colzato, Ruiz, van den Wildenberg, Bajo, & Hommel, 2010). This has been demonstrated to some extent by studies that attempted to systematically investigate specific cognitive impairments in abstinent khat users compared to non-chewers (Colzato, Ruiz, van den Wildenberg, & Hommel, 2011,
2012). These studies identified impairments in the inhibition of response conflicts, monitoring of working memory and mental flexibility. Consistent with these findings, a very recent study that examined working memory and information processing speed (Hoffman & al’Absi, 2013), indicated impairments in working memory, specifically, on digit backward measures of short term working memory among chronic khat chewers. However, contrary to the results obtained with chronic methamphetamine users (e.g. (Simon et al., 2000)), the authors found no statistically significant impairment in speed of information processing among chronic khat chewers. In their experimental study on 16 khat users and 16 khat free controls (Colzato et al., 2011) reported that khat users exhibit impairments in the inhibition of response conflicts which may eventually lead to inefficient decision making in everyday life. Inhibition of response is a cognitive ability to hinder unwanted thoughts and actions and is commonly considered as one part of executive control functions (Colzato et al., 2010).

There are significant psychometric relationships between the tests and tasks that are commonly used to assess cognitive control in humans. In this regard, (Miyake et al., 2000) suggested the existence of three major, separable control functions: the ‘‘inhibition’’ of unwanted responses, the ‘‘shifting’’ between tasks and mental sets (also called ‘‘flexibility’’), and the ‘‘updating’’ (and monitoring of) working memory (WM) representations, the model which has been previously used to investigate cognitive impairments among recreational users of cocaine and MDMA (Colzato, Huizinga, & Hommel, 2009; von Geusau, Stalenhoef, Huizinga, Snel, & Ridderinkhof, 2004).

Given the link between khat use and impaired inhibitory control, another study that focused on cognitive flexibility and updating, tested the hypotheses that monitoring of working memory and mental flexibility are impaired in chronic khat users (Colzato et al., 2011) and
compared current (non-intoxicated) khat users (at least over the past 12 months) and matched khat-free controls (with no history of past or current khat use) in a task assessing the efficiency of monitoring information in WM and a task that taps into cognitive flexibility. The result revealed that current khat users performed significantly worse than their counterparts on both tasks. Khat use has long term negative effect on working memory, specifically, on digit backward measures of short-term working memory. However, contrary to the results obtained with chronic methamphetamine users, there was no statistically significant difference in speed of information processing between chronic chat users and their counter partners (Hoffman & al'Absi, 2013).

Overall, although there seem to exist relatively extensive studies and findings on the neurocognitive effects of chronic drug use like amphetamine and cocaine, similar studies on the chronic use of khat are very scarce, particularly in the Ethiopian context, where the substance is widely growing and being consumed by majority of the population including students of secondary and tertiary education (Getahun & Krikoria, 1973; Lemessa, 2001; Selassie & Gebre, 1996). Reasons for chewing include obtaining increased level of alertness, ability to concentrate, improved memory, motivation, flow of ideas, improve mental performance before exams and ultimately good grades (Ayenew et al., 2012; Ihunwo et al., 2004; Zein, 1988). However, interestingly, few studies have reported a significant association between khat chewing and high educational achievement (Al-Hebshi & Skaug, 2005; Alem et al., 1999), though no study has systematically and objectively investigated the interplay among the quantity of khat ingested, cognitive function, memory and the level of academic performance. These mental states would not be long lasting since khat chewing only provides a temporary atmosphere of concentration, mental alertness, cheerfulness, optimism and a
general sense of well-being, which would often disappear after a few hours of chewing or at the end of chewing sessions (Cox & Rampes, 2003)

**Khat Dependence**

Debates exist as to whether khat can actually cause dependence. Some authors describe a ‘psychological’ dependence rather than a physical one (Halbach, 1972). Most argue that cathinone is presumed to be the dependence-producing constituent of khat leaves (Kalix & Khan, 1984). In their experimental studies on animals, cathinone is found to be a reinforcer and maintains very high rates of responding. In studies using pure cathinone extracts, progressive ratio self-administration tests reveal similar break-points for cathinone as for amphetamines (Yanagita, 1986), and cathinone induces conditioned place preference in rodents (Schechter & Meehan, 1993). These findings suggest the existence of a clear dependence potential for cathinone. Tolerance to khat occurs rarely and with the doses often increasing quite slowly. This may be due to the physical limits on the amount of khat that can be consumed at any given time due to the requirement of chewing and the time-limited duration of cathinone vs cathine subjective effects (Kalix, 1988). While the nature of khat dependence remains under active debate, there is accumulating evidence indicating the existence of a mild withdrawal syndrome and some evidence for tolerance (Cox & Rampes, 2003).

However, despite these debates as to whether khat can actually produce dependence (Manghi et al., 2009), physical and psychological dependence of khat were reported by many authors (Griffiths et al., 1997; Kassim & Al'absi, 2016; Kassim & Croucher, 2006; Kassim, Croucher, & al'Absi, 2013; Kassim, Islam, & Croucher, 2010; Nencini et al., 1989). Although limited use may not be related to serious consequences, prolonged exposure could lead to dependence,
psychosis and other psychiatric disorders and physical conditions (Odenwald & al'Absi, 2017). In addition, chronic khat use may cause a significant depletion of dopamine in the nigrostriatal dopamine terminal projections (Banjaw, Miczek, & Schmidt, 2006; Feyissa & Kelly, 2008). Which may result in psychiatric effect which includes depression and psychosis among heavy chewers (Odenwald et al., 2005) Psychological dependence features include chewers urge to fulfil their need of khat on the expenses of their vital needs like food and mood changes during and after chewing (Griffiths et al., 1997; Hassan, Gunaid, El-Khally, & Murray-Lyon, 2002; Kassim & Croucher, 2006). The Severity of Dependence Scale (SDS) developed by Gossop et al. (Gossop et al., 1995) was used to evaluate psychological dependence to many abused drugs through collecting data about the dependence features (Gossop, Best, Marsden, & Strang, 1997; Gossop et al., 1995; Topp & Mattick, 1997).

Chronic drug use is associated with the occurrence of craving and withdrawal symptoms related to the discontinuation of use after long time exposure or habitual and chronic consumption (Giannini & Castellani, 1982). There are conflicting opinions regarding the existence of a withdrawal syndrome due to khat abstinence. However, there are some evidences for the presence of withdrawal manifestations among khat chewers. Depressive moods, drowsiness and hypotension are sometimes seen after khat discontinuation, and khat chewers often continue to use khat in order to avoid the withdrawal symptoms (Alem et al., 1999). Other withdrawal symptoms common among khat quitters were lethargy, feeling sleepy, nightmares, feeling hot in the lower extremities, bad temper, and slight trembling (Al-Habori, 2005; Al-Motarreb, Baker, & Broadley, 2002; Alsanusy & El-Setouhy, 2013). A recent study using the criteria of dependence defined in the American Psychiatric Association Diagnostic Statistic Manual (DSM-IV, 1994) (Kassim et al., 2013) has reported that 31% of khat chewers had khat dependence syndrome, 13% of them reported an increase in khat
chewing, 19% reported cessation attempts, and 17% reported withdrawal symptoms including depression, increased appetite, and interrupted sleep. Some studies have also documented withdrawal symptoms consistent with these, specifically, in relation to khat, including lethargy, anergia, and nightmares, which appear several days after ceasing to chew (Giannini & Castellani, 1982).

Findings on the natural course of withdrawal symptoms of khat are very rare. Although, most symptoms of amphetamine withdrawal may be over in four or five days, some of the symptoms may continue for weeks or months (Watson, Hartmann, & Schildkraut, 1972). Despite the similarity of amphetamine and khat in terms of chemical components and psychopharmacological effect on brain and behaviour, withdrawal symptoms of khat cessation and craving are likely but have yet to be reliably demonstrated.

Craving is viewed as the subjective manifestation of the core motivational processes mediating addictive behavior in drug users (Robinson & Berridge, 2001; Wyvell & Berridge, 2001). The mechanisms of craving are presumed to be both biologically and psychologically oriented reflecting the operation of fundamental brain reward pathways (Baker, Morse, & Sherman, 1986; Robinson & Berridge, 2001; Wyvell & Berridge, 2001). There have been continuing debates among researchers as to the timeframe of craving. While some investigators argued that craving is relatively stable (Anton, Moak, & Latham, 1995; West, Hajek, & Belcher, 1989), others have viewed it as a momentary “pulsatile” state – such a view would suggest that using measures that encompass long time intervals may lack the precision to capture changes in craving (Gawin, 1991; Shiffman et al., 1996). These assumptions have led to advances in assessment methodology which have yielded near real time assessment in the natural environment (Shiffman et al., 1996) supporting the view that craving fluctuates substantially.
even within the course of a day, and that craving reports obtained at different times are different in meanings and predictive power (Shiffman et al., 1996). Findings of addiction studies (Tiffany, 1990) have linked craving to relapse and considered craving as a necessary precondition for relapse (e.g. (Ludwig, Wikler, & Stark, 1974). However, recent accounts of addiction have not considered craving as an inevitable concomitant of relapse (e.g. (Kassel & Shiffman, 1992; Tiffany, 1990).

**Summary**

In summary, khat is a stimulant and highly prevalent drug among youths and adults (Selassie & Gebre, 1996). Several people are estimated to be frequent khat users for its euphoric effects and become dependent to it despite its adverse psychological and mental effects (Kennedy, 1987). Dependence is a chronic disease of brain characterized by disrupting the brain reward pathway mediated by dopamine. It refers to the reward, motivation, memory and related circuitry dysfunctions which have biological, psychological, social and spiritual manifestations and are reflected in an individual pathologically needing reward and/or relief by substance use and other behaviors (Fainsinger, Thai, Frank, & Fergusson, 2006; Wise, 1980; Yoshimura & Yamamoto, 1980). People who are substance dependent are likely to lack the ability to consistently abstain from drugs due to impaired behavioral control, craving and reduced acknowledgment of significant problems with one’s behaviors and interpersonal relationships (Beckson & Tucker, 2014). Long-term effects of drugs on the brain may result in lack of the ability to experience any pleasure out of regular consumptions. This leads to the need for larger amounts of drug (tolerance) to feel the desired effects of consumption. In the worst case scenario, drugs may simply be needed just to feel normal as they no longer make the individual experience pleasurable effects which ultimately leads to substance use disorder (Hasin et al., 2013; O'Brien, 2011). Dependence often involves cycles of craving, relapse and
remission. Without treatment or engagement in recovery activities, dependence is progressive and can result in psychological and mental malfunctioning (Matto, 2005; Wise, 1988). Chronic and dependent drug use is likely to change brain structure and function which could be long lasting and lead to harmful behaviors which are often characterized by compulsive drug seeking and use despite experience of adverse consequences (Lu, Wang, Luo, Zhang, & Shi, 2009; Volkow & Li, 2004).

Findings obtained from previous studies revealed that khat is a potential drug of dependence and that some individuals with chronic use of khat may become severely dependent and face a number of psychological problems, indicating that greater risk of harms as being significantly related to heavier and more frequent khat chewing (Ihunwo et al., 2004; Odenwald, 2007; Odenwald et al., 2007). Dependent khat chewers are more likely to display certain psychological symptoms like stress, anxiety, depression, irritability and emotional instability more frequently than non-chewers (Odenwald, 2007).

Ethiopia, like many other khat growing countries is facing a wide range of problems of high khat use; with the percentage of khat users in the general population increasing (Belew, Kebede, Kassaye, & Enquoselassie, 2000). There have been very limited efforts to minimize the problem. In 1996, Ethiopia showed an overall prevalence of about 30% and that the use of khat has spread among all segments of the population with a house-to-house survey in rural areas of Ethiopia giving a comparable figure of 32% (Belew et al., 2000). The struggle over khat, in Ethiopia, has always been between two camps: those who believe in the economic benefits of khat outweighing the negative social, psychological and health consequences on the one hand, and those who maintain strong position that khat is the cause of so much idleness, violence, and social immorality that any amount of economic benefit cannot justify
its continued use (Gebissa, 2008). Failure to regulate these problems not only threatens the health of youths, students and active parts of the population but also the future economic and social development of the country as a whole (Lemessa, 2001; Selassie & Gebre, 1996).

Prevention of substance abuse in general and khat use disorder in particular for the sake of psychological and mental well-being of the community and the students presents a complex problem to health professionals, law enforcement agencies, and educators in Ethiopia (Lemessa, 2001; Selassie & Gebre, 1996). Although khat is a legal drug, possession and chewing in the work-place and educational institutions are illegal in most khat-growing countries, including Ethiopia (Cox & Rampes, 2003; Elmi, 1983). Hence, people prefer to chew khat away from family members, work-places and other commitments and they are likely to leave early or miss work or classes for this purpose (Gelaw & Haile-Amlak, 2004). The roots of the difficulties in dealing with khat use may be attributed to lack of proper knowledge of its multidimensional consequences on the part of the universities and on the part of law makers at large since there is a scarcity of evidence in regard to virtually all aspects of khat use – such as the nature of khat use disorder syndrome and the related psychological and mental health problems, experience of khat dependence and more importantly abstinence difficulties and associated withdrawal syndromes. In this regard, the current study aims to examine the presence of khat use disorder and the potential psychological and mental health consequences related to chronic khat use and make contributions to public health professionals, policy makers, administrators and educators in understanding the nature of use disorder, the severity of khat dependence and the potential factors that hinder the effectiveness of the approaches in attempting to curb khat abuse. The studies further aim to explore the effectiveness of chewers in their attempts to quit chewing; the extent of chewers’ capability of maintaining abstinence and the type and nature of withdrawal syndromes and the level of
craving that involve during the quitting process. These are considered to be major contributors to relapse and key obstacles to cessation in chronic khat users and vital components of treatment interventions. Understanding these may create opportunities to help design effective intervention and treatment mechanisms which involve the changing of deeply imbedded behaviors often through a combination of medications and behavioral therapies (Matto, 2005).

Objectives of the studies

The prevalence of khat chewing and its potential psychological and health related consequences have been less investigated among the wide range of population in Ethiopia. Very little is known about the presence of khat use disorder and its association with psychological and health related harms.

Since khat produces clinical effects similar to amphetamine (Cox & Rampes, 2003), most chewers are likely to experience both positive and negative feelings during and after chewing sessions (Pantelis et al., 1989b). The core aspects of the psychological and emotional effects of khat use and the level and the severity of khat dependence syndrome have been investigated to some extent (Kassim et al, 2010). Withdrawal-like symptoms and tolerance have been recently reported and some correlates have also been identified as potential liability factors for the spread of khat chewing and for the development of khat dependency (Kassim et al, 2013; Halbach, 1972; Luqman and Danwoski, 1976; Douglas et al., 2011; Alem and Shibre, 1997; Gelaw and HileAmlak, 2004). Previous studies have provided initial support for the use of SDS-khat as a valid research tool for assessing psychological aspects of khat dependence (Elmi, 1983; Kalix & Braenden, 1985; Nakajima et al., 2014) To date, however, no previous study has attempted to determine a cut-off score of the severity of dependence against diagnoses of khat use disorder/dependence, nor to examine the association of the scores on the
SDS-khat with the psychological health and other behaviours known to be correlated with dependence.

Experiences of withdrawal symptoms during periods of abstinence are one of the most significant factors in dependent and chronic drug use. Most theories of dependence have posited that continued drug use is, at least in part, driven by avoidance of withdrawal symptoms. During termination of frequent substance use for a period of time, the dysphonic states experienced or the physiological adaptation to the chronic presence of the drug facilitate the desire to use a certain drug of dependence (Ferguson & Shiffman, 2009). The experience and severity of withdrawal symptoms is a key factor in craving and a significant barrier to cessation/reduction of problem drug use and addressing withdrawal is a key component of many treatments of drug abuse (Shoptaw, Kao, Heinzerling, & Ling, 2009). In this regard, despite some evidence indicating the presence of a withdrawal syndrome, craving and a degree of tolerance related to chronic khat chewing (Cox & Rampes, 2003), very little research works have been conducted, to date, on the nature and outcomes of khat cessation attempts as well as the trend, severity and time course of withdrawal symptoms in relation to khat, particularly in the Ethiopian context.

The general aim of this thesis is to investigate if khat chewing causes problems in individuals and to determine the evidence for clinically meaningful khat use disorder and withdrawal syndromes. The studies in the subsequent chapters have examined unique but highly interrelated subject matters in relation to khat chewing and associated adverse consequences. Overall, the studies in this thesis are novel and provide new insights and knowledge in the areas of khat research and suggest potential intervention strategies that could help public health professionals to effectively identify khat use disorders and to better understand the
multidimensional adverse consequences and syndromes associated with the disorder and to address the khat problems among individuals in the community in Ethiopia.

**Study 1 (Chapter 2): “Is khat use disorder a valid diagnostic entity?”**
This is the first survey study at the community level. It aimed to examine khat use disorder using DSM-5 criteria and to determine its relationship with the typical patterns of khat consumption, the experience of psychological and academic/behavioural problems and quality of life. It addresses the validity of khat use disorder by exploring the structure of this syndrome and the relationship between the syndrome and functional consequences. It examined how participants with khat use disorder differed from those who do not have the disorder in terms of patterns (duration, amount and type) of khat consumption and experience of other harms. The study used a survey comprising current clinical symptoms (using a modified Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV), and validated measures of health, psychological distress, quality of life and academic functioning.

This study has been published as an original research article on *Addiction journal* (2016, IF 5.789) – a monthly peer-reviewed scientific journal by the Society for the Study of Addiction to Alcohol and other Drugs. The journal covers original research relating to alcohol, illicit drugs, tobacco, and behavioral addictions.

**Study 2 (Chapter 3): “Using the Severity of Dependence Scale to Screen for DSM-5 Khat Use Disorder”**.
The main objectives of this study were to determine the efficiency of the Severity of Dependence Scale (SDS) as a screening tool for DSM-5 defined khat use disorder among khat chewers and to examine the validity of the cut-off points in identifying a group of individuals
who use khat at greater frequency and quantity and experience functional problems associated with khat use. The study used a survey comprising of current substance use disorder and a severity of dependence scale (SDS) which assessed the psychological components of dependence over the past year,

This study has been published as an original research article on *Human Psychopharmacology Clinical and Experimental* (2015, IF 2.44) – an international journal for the publication of quality clinical and experimental research on both new and established psychotropic medicines; experimental studies of other centrally active drugs including herbal products in clinical social and psychological contexts as well as clinical/scientific papers on drugs of abuse and drug dependency.

**Study 3 (Chapter 4): “Stopping Khat use: Predictors of success in an unaided quit attempt.”**

The main objective of this study was, using electronic diaries, to monitor the outcomes of an unassisted khat cessation attempts among 59 frequent (daily and near daily) khat users who were self-motivated to quit.

This study has been published as an original research article on *Drug and Alcohol Review* (2014, IF 2.294) – a bimonthly peer-reviewed medical journal covering the health effects of alcohol and other drugs.
Study 4 (Chapter 5): “Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment.”

The main aim of this study was to determine the nature and the time course of any withdrawal symptoms among 59 frequent (daily and near daily) khat chewers in relation to the cessation of khat use over 2 weeks period of quit attempts. This study employed Electronic Diaries issuing random prompts to collect real-time data from participants 4 to 7 times a day, over 3 days assessment of pre-quit ad lib khat consumption and 14 days assessment of post quit khat use.

This study has been published as an original research article on *Psychology of Addictive Behaviors* (2016, IF 2.543) – a peer-reviewed academic journal of the American Psychological Association that publishes original articles related to the psychological aspects of addictive behaviors 8 times a year.
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Chapter 1: Introduction


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Is khat use disorder a valid diagnostic entity?

Samson W. Duresso 1, Allison J. Matthews 1, Stuart G. Ferguson 1 & Raimondo Bruno 1

1 School of Medicine, University of Tasmania, Hobart, Australia

Abstract

Aims: This study aimed to validate the presence of a khat use disorder syndrome using DSM-5 criteria and to examine its relationship with increased experience of harms.

Design: Cross-sectional, purposive sample of current khat chewers, recruited from khat markets and cafes.

Setting: Participants were recruited from the general community and from Adama Science and Technology University in Ethiopia.

Participants: 400 current khat consumers aged 16 and above were recruited between September 2014 and January 2015.

Measures: Survey comprising current clinical symptoms (using a modified Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV), and validated measures of health, psychological distress, quality of life and academic functioning.

Findings: A third (35.5% 95%CI 31.0-40.3) of respondents reported daily khat use and a quarter (25.4% 95%CI 21.4-30.0) using 3 times or more per week. Using DSM-5 criteria, 10.5% (95%CI 7.9-13.9) were categorised as experiencing mild, 8.8% (95%CI 6.4-12.0) moderate and 54.5% (95%CI 49.6-59.3) a severe khat use disorder. Confirmatory factor analysis demonstrated good fit of symptoms to a single underlying construct, consistent with other substance use disorders. Individuals categorised as khat use disordered demonstrated significantly greater frequency (OR=45.29; 95% CI = 10.97-19.01) and quantity of khat use (OR= 2.35; 95% CI = 1.29-4.29). They also demonstrated increased financial problems associated with use, greater problems with academic functioning, and higher rates of self-reported mental health problems, higher psychological distress and poorer quality of life. Treatment access was poor, with only one third (32.9%) of individuals
with khat use disorder reporting lifetime access, near-exclusively related to help-seeking from friends and relatives.

**Conclusion**: The construct of a substance use disorder syndrome for khat using DSM-5 criteria appears valid and performs in a manner consistent with other substances of dependence. Individuals with khat use disorder experience substantial problems in association with khat use. Despite this, there are low levels of help-seeking for these problems.

**Keywords** Catha, central nervous system stimulants, DSM-5, DSM-IV, khat, khat dependence, khat use disorder, stimulant use disorder, substance–related disorders.
Introduction

Khat (catha edulis) is a cathinone-based stimulant which is a controlled substance in most western countries but legal in several African countries, including Ethiopia (Kalix, Geisshusler, Brenneisen, Koelbing, & Fisch, 1990). A 2011 population prevalence study estimated past month use at 15.3% across Ethiopia. Among Ethiopian university students (n=3,268), lifetime prevalence was estimated to be 24.0%, while 7.7% reported past month khat use (E. Gebrehanna, Y. Berhane, & A. Worku, 2014a). Khat chewing has also spread to the UK, Europe and USA (Kassim & Croucher, 2006). Due to the socio-economic and health consequences of khat use without any useful therapeutic outcomes (World Health Organization Expert Committee on Drug, 2003), the need for international control has become a public health concern, with many countries recently banning use (Kassim & Al’absi, 2015).

While fresh khat leaves contain multiple psychoactive constituents, the primary ingredient is cathinone. This rapidly degrades after harvesting and on chewing to cathine and norephedrine. Subjective effects of both khat chewing (Widler, Mathys, Brenneisen, Kalix, & Fisch, 1994) and pure cathinone (Brenneisen, Fisch, Koelbing, Geisshusler, & Kalix, 1990) demonstrate amphetamine-like physiological and subjective effects in humans. Cathinone dose-dependently increases dopamine levels in vivo (Pehek, Schechter, & Yamamoto, 1990), and demonstrates affinities for dopamine (Fleckenstein et al., 1999) and noradrenaline transporters (Cleary & Docherty, 2003), as well as having inhibitory effects on monoamine oxidase (Nencini, Amiconi, Befani, Abdullahi, & Anania, 1984). Cathine has been noted as the primary contributor to peripheral adverse effects from khat (Cox & Rampes, 2003; Yanagita, 1979).

A typical khat chewing session lasts for several hours, during which 100-500g of leaves are chewed thoroughly and stored in the cheek for several minutes before being spat out, with juice from the leaves swallowed (Feyissa & Kelly, 2008). While this efficiently extracts the alkaloid (Toennes &
Kauert, 2002), it is laborious, as typically cathinone concentrations are \(~1\text{mg/g/leaf}\) (Feyissa & Kelly, 2008). Onset is slow, with peak plasma levels of cathinone after 2.3 hours; and the products cathine and norephedrine peaking later at 2.6 and 2.8h respectively (Toennes, Harder, Schramm, Niess, & Kauert, 2003). Terminal half-life for cathinone is much briefer (1.5±0.8h) than for cathine (5.2 ± 3.4h) (Toennes et al., 2003), meaning that as the length of time that chewing sessions extends, cathine levels accumulate to a greater extent than cathinone and more unwanted systemic effects may result (Cox & Rampes, 2003). Anecdotal reports from chewers suggest that negative effects of khat also increase over the course of chewing, which limits the duration of sessions (and hence dose consumed). It is not clear if this relates to any accumulated physiological effects of cathine, although continuous self-administration studies in rodents demonstrate a greater rate of cathinone infusions in early (cathinone dominated) compared to later (cathine dominated) portions of study sessions (Gosnell, Yracheta, Bell, & Lane, 1996), which would be consistent with this hypothesis.

Debates exist as to whether khat can actually produce dependence (Manghi et al., 2009). A recent study has revealed that higher frequency of khat chewing was associated with psychological dependence (Kassim, Islam, & Croucher, 2010); also see (Nakajima, Dokam, Alsameai, et al., 2014). In studies using pure extracts, progressive ratio self-administration tests suggest similar break points for cathinone as for amphetamines (Yanagita, 1986); and cathinone induces conditioned place preference in rodents (Schechter & Meehan, 1993). These and other effects (see (Feyissa & Kelly, 2008) for a review) suggest clear dependence potential for cathinone. However, given the limited cathinone dose available through khat chewing, there may be substantially lower dependence potential from use of the natural plant than from direct administration of cathinone. Similarly, tolerance to khat occurs rarely (Kassim, Croucher, & al'Absi, 2013a), potential due to the physical limits on the amount of khat that can be consumed during sessions (Kalix, 1988). There is accumulating evidence indicating the existence of a mild withdrawal syndrome, consisting of anergia, nightmares, depressed moods, drowsiness and hypotension (Alem, Kebede, & Kullgren,
Chapter 2: Is khat use disorder a valid diagnostic entity?

1999; Giannini & Castellani, 1982; Pantelis, Hindler, & Taylor, 1989) and khat chewers often continue to use khat in order to avoid these withdrawal symptoms (Giannini & Castellani, 1982).

Habitual khat chewers exhibit compulsive behaviours in khat markets and have the tendency to secure daily khat supply at the expense of other vital needs (Kalix & Braenden, 1985; Nencini, 1988). These are described as psychological dependence by some authors (Connor, Rostom, & Makonnen, 2002; Gosnell et al., 1996; Kalix, 1990), and some studies of frequent consumers have estimated that dependence syndromes may indeed be common (Kassim, Hawash, Johnston, & Croucher, 2012).

Despite the prevalence of khat use, and potential psychological and health consequences, there has been inadequate study of the nature of symptoms of substance use disorder relating to khat. As such, this study aimed to examine the presence, structure, and external validity of a khat use disorder (KUD) syndrome using current Diagnostic and Statistical Manual (DSM-5) criteria, as well as the more clinically familiar DSM-IV dependence syndrome. Specifically, the study aimed to answer the following:

1. Are use disorder symptoms experienced in relation to khat? This was addressed by using DSM criteria to identify cases of use disorder in relation to khat.

2. Do these symptoms produce a syndrome that performs in the same manner as other stimulants? To address this aim, confirmatory factor analysis was used to examine symptom structure, to determine if all symptoms relate to a shared latent process.

3. Does the presence of a khat use disorder syndrome perform validly, relating to an increased experience of harms? To address this aim, differences between individuals with KUD and Non-KUD in terms of variables such as patterns of consumption, mental health, financial, occupational and cognitive functioning problems were examined.
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MATERIALS AND METHOD

Design/Study sample size

Planned sample size was 500; 454 responses were collected using purposive sampling. Responses with missing responses on core (DSM) items were excluded, leaving 400 cases. Most of the excluded cases provided no data to these core items (n=48), with the inclusion of individuals with 25% missing data only increasing sample size by 6. As such, we are confident that the risk of bias by the exclusion of these cases is low.

Participants

Four hundred current khat consumers were recruited from the general community (Adama, Ethiopia) and from Adama Science and Technology University between September 2014 and January 2015 (26.4% of adults in the region are estimated to chew khat (Haile & Lakew, 2015)). Recruitment occurred through posters displayed in khat markets, khat cafes, on campus and on social networking sites. Minimum eligibility criteria were ≥16 years and use of khat at least once in the past year.

Participants completed either a self-administered online 40-minute khat use survey (19%; n=86) in English; or an Amharic paper version (81%; n=368) with overall response rate of 83.9% of those receiving the paper survey. The English survey was translated to Amharic and then back translated for verification by language experts from Adama Science and Technology University and cross-checked further with multiple multilingual speakers.

The Tasmania Human Research Ethics Network granted approval for the study (#HO013036), with additional local ethical clearance obtained from Adama Science and Technology University.
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Measures

Items derived from the Ethiopian national census and from the tool kit for Conducting School Surveys on Drug Abuse (Degenhardt et al., 2006) were used to assess age, sex, education level, employment status and parental status. Items assessing frequency, quantity, type and perceived strength of khat; and frequency of alcohol and tobacco use were adapted from the tool kit for Conducting School Surveys on Drug Abuse (Degenhardt et al., 2006). Nicotine dependence among tobacco smokers (33; 95%CI 28–37) was assessed using the Fagerström Test (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991)

Past year khat use disorder (KUD) symptoms were assessed using a modified version of the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV (Ruan et al., 2008; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993), with item content expanded to include craving. The reliability and validity of the AUDADIS in relation to abuse and dependence disorders for a range of substances is well documented in numerous international studies (Grant et al., 2004; Grant, Harford, Dawson, Chou, & Pickering, 1995). To assess withdrawal, 19 symptoms were taken from the Composite International Diagnostic Interview (CIDI) Substance Abuse Module to reflect the possible range of this syndrome following chronic use of similar stimulants. Positive diagnosis of khat withdrawal as operationalized consistently with DSM stimulant withdrawal criteria (dysphoria plus at least two additional symptoms present concurrently, at a level considered distressing, or withdrawal relief).

To validate the khat dependence syndrome, differences on a range of consumption (frequency, duration, and quantity), demographics and problems (mental health, quality of life, financial problems) were examined. Sex and education level have also been associated with khat dependence in prior studies (Nakajima, Dokam, Kasim, et al., 2014).
The Kessler Psychological Distress Scale (Kessler et al., 2002) was used to assess non-specific psychological distress. At a cut-off of 30, the scale has high specificity (0.99), and approximately 86% scoring in this range meet past year criteria for DSM-IV anxiety or affective disorders (Andrews & Slade, 2001).

A subjective multi-domain quality of life measure (The Personal Wellbeing Index (PWI-5th edition), with Australian normative data was used to assess quality of life (Group, 2013). The scale was recently developed by the International Wellbeing Group (IWbG) and comprised seven items that, together, provide a measure of global subjective wellbeing (SWB). Over 150 researchers from more than 50 countries and provinces had engaged in this international collaboration to upgrade the PWI into a valid cross-cultural instrument, so it can be used for international research purposes. This is supported by the large number of international translations of the scale (http://www.acqol.com.au/instruments#measures). However, currently there are normative data available for Ethiopia nor for any African countries, and as such the most comprehensive normative dataset was applied, which originates from Australia. Regardless, the nature of the items is such that higher scores will always reflect higher quality of life, and as such the weighting process applied for the norms of data will not change participants relative scores. In this series of studies, a binary score was created such that people scoring two standard deviations below the population mean for the scale (using Australian norms) were classed as reporting ‘low’ quality of life. While the absolute values of the extremes of the distribution of PWI scores in Ethiopia are not known but it is undoubtable that people scoring in the ranges used in this study to denote ‘low’ perceived quality of life validly reported lower levels of quality of life than other participants. Moreover, less than one quarter of the survey sample reported scores in the ‘low’ range which has face validity and is relatively comparable with levels reported in studies of substance consuming populations in Australia (Dietze et al., 2010).
Typical frequency of cognitive and academic impairment in the past six months was assessed using a 12-item academic functioning questionnaire pilot tested and refined from cognitive and executive function questionnaires used in similar studies (Schwartz, 2007). Initially 40 items were developed, taken from existing scales (cognitive and executive function questionnaires) in the literature. These were examined in a pilot survey at the study site (in Adama Ethiopia). In the main khat study, the scale was examined using Confirmatory Factor Analysis (CFA) to ensure that it formed an appropriate scale: the reported scale had 12 items with acceptable factor loadings and acceptable fit indices (RMSEA=0.086 (0.05); CFI=0.987 and TLI=0.984). In the reported studies, however, single survey items were reported. These have clear face validity as measures of perceived cognitive problems and are consistent with the literature (Schwartz, 2007).

**Statistical Analysis**

Symptom rates were reported using 95% CIs. Chance-corrected concordance between DSM-IV and DSM-5 syndromes were assessed using the kappa statistic (Cohen, 1960). Syndrome structure was assessed by conducting unifactorial confirmatory factor analysis with additional item-response theory (IRT) measures, in Mplus v7.0, using robust estimators to account for skewed data. Model fit indices were examined to assess structural fit, including root mean squared error of approximation (RMSEA); Tucker-Lewis Index (TLI) and comparative fit index (CFI); RMSEA <0.06, TLI >0.95 and CFI >0.95 are considered to indicate good fit (Hu & Bentler, 1999; Mulaik, 2007; Steiger, 2007). Recent simulation studies suggest that N>200 is sufficient for robust estimation of such a structure (Myers, Ahn, & Jin, 2011). To assess whether there were particular patterns of symptoms among participants, latent class models were estimated using DSM-5 items. Three criteria were used to assess model fit (Ramo, Grov, Delucchi, Kelly, & Parsons, 2010). The Lo–Mendell–Rubin adjusted log-likelihood ratio test (LMR-ALRT) statistic (Lo, Mendell, & Rubin, 2001), was used to compare models with different number of classes: a value of p<0.05 suggests that the model with one additional class is a better explanation of the data. Akaike
Information Criterion (AIC) and the Bayesian Information Criterion (sample-size adjusted; BIC) were used to assess model fit (lower values indicate better fit). Entropy (range 0.0–1.0) was also used, with higher values reflecting clearer classification of individuals (Ramo et al., 2010). To assess if khat use disorder relates to increased rates of harms, odds ratios (OR) for experience of problems were calculated from independent logistic regression models using SPSS Statistics v22.

RESULTS

Mean participant age was 30 years [standard deviation (SD) =7, range 17-49], and more than three-quarters were male. Most had not completed secondary education (see Table 1). One-third of the sample was university students (Table 1). Approximately a third of respondents reported daily khat use and a quarter reported using three times or more per week.

Khat Use Disorder Symptoms

‘Continuing to use despite knowledge of physical or psychological harm’ was the most commonly endorsed dependence criterion (Table 3). ‘Interference with role obligations’, ‘continued use despite interpersonal problems’ and ‘use in larger amounts or for longer than intended’ (50%) were also commonly reported. Endorsement of withdrawal symptoms following 24 hours of abstinence was prevalent (Table 2). However, symptoms that persisted beyond the acute ‘come-down’ period following use and were distressing were less common. Among these, depressed mood (38%), hypersomnia (34%), and irritability (31%) were predominant. While only one-quarter (28%) had experienced two or more of these symptoms lasting for more than 48 hours, use of khat for withdrawal relief was more common (>50%).
Table 1: Demographic characteristics of the sample (n=400)

<table>
<thead>
<tr>
<th>Item</th>
<th>n</th>
<th>% (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>308</td>
<td>77 (72.6-80.9)</td>
</tr>
<tr>
<td>Student</td>
<td>135</td>
<td>343.8 (29.3-38.5)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤24</td>
<td>113</td>
<td>28.2 (24.1-32.9)</td>
</tr>
<tr>
<td>25-34</td>
<td>176</td>
<td>44 (39.2-48.9)</td>
</tr>
<tr>
<td>35-44</td>
<td>98</td>
<td>24.5 (20.5-28.9)</td>
</tr>
<tr>
<td>≥45</td>
<td>13</td>
<td>3.3 (1.9-5.5)</td>
</tr>
<tr>
<td><strong>Frequency of khat use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>141</td>
<td>35.5 (31.0-40.3)</td>
</tr>
<tr>
<td>3 times or more a week</td>
<td>101</td>
<td>25.4 (21.4-30.0)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amhara</td>
<td>112</td>
<td>28 (23.8-32.6)</td>
</tr>
<tr>
<td>Harari</td>
<td>12</td>
<td>3 (1.7-5.2)</td>
</tr>
<tr>
<td>Oromo</td>
<td>148</td>
<td>37.2 (32.4-41.3)</td>
</tr>
<tr>
<td>SNNP</td>
<td>70</td>
<td>17.6 (14.1-21.5)</td>
</tr>
<tr>
<td>Tigré</td>
<td>32</td>
<td>8 (5.7-11.1)</td>
</tr>
<tr>
<td>Others</td>
<td>26</td>
<td>6.5 (0.1-1.8)</td>
</tr>
<tr>
<td><strong>Educational Level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed Grade 11 or less</td>
<td>222</td>
<td>64 (58-68)</td>
</tr>
<tr>
<td>Completed Grade 12</td>
<td>57</td>
<td>16 (13-20)</td>
</tr>
<tr>
<td>Diploma</td>
<td>66</td>
<td>18.5 (15-23)</td>
</tr>
<tr>
<td>Bachelor’s degree or higher</td>
<td>11</td>
<td>2.8 (1.5-4.9)</td>
</tr>
<tr>
<td>Other</td>
<td>44</td>
<td>11 (8.3-14.4)</td>
</tr>
<tr>
<td><strong>Employment Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>17</td>
<td>6.3 (4.0-9.9)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>145</td>
<td>53.9 (48.0-59.8)</td>
</tr>
<tr>
<td>Employed for wages</td>
<td>68</td>
<td>25.3 (20.4-30.8)</td>
</tr>
<tr>
<td>Looking for work</td>
<td>34</td>
<td>12.6 (9.2-17.1)</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
<td>1.8 (0.8-4.3)</td>
</tr>
</tbody>
</table>

* n= 269. *b* Unable to work, retired, home duty. *c* No school. *d* Other ethnic groups. SNNP = Southern Nations and Nationalities People; CI = confidence interval.

Khat use disorder diagnostic crosswalk

Using DSM-IV, 15.3% (95%CI 12.1-19.1) met criteria for abuse and 60.5% (95%CI 55.6-65.2) for dependence. Using DSM-5, 10.5% (95%CI 7.9-13.9) were categorised as experiencing mild, 8.8% (95%CI 6.4-12.0) moderate and 54.5% (95%CI 49.6-59.3) as a severe khat use disorder. Appendix, Table S1 illustrates the degree of diagnostic agreement between DSM-IV and DSM-5 diagnoses. As would be expected, DSM-5 use disorder captures a broader group than DSM-IV dependence, however, agreement between DSM-IV dependence and moderate (or greater) DSM-5 khat use disorder was good (Kappa=0.90). Similarly, agreement between DSM-IV abuse and receiving any DSM-5 Khat use disorder (Kappa=0.84) was acceptable.
Structure of Khat use disorder

Confirmatory factor analyses demonstrated a good fit of a unifactorial model to both DSM-IV dependence and DSM-5 substance use disorder items, consistent with patterns for other drugs of dependence (Saha et al., 2012) (Table 3). In order to determine whether there were particular common patterns of symptoms (or ‘types’), latent class analyses of DSM-5 khat use disorder symptoms were conducted. Model fit indices for 1-6 class solutions are displayed in supplementary materials (Table A2). While these do not explicitly support a single solution, on inspection of BIC, LMR-ART and structures of each solution, a 3-class model provided the most parsimonious and meaningful structure, with higher order solutions largely representing a fragmentation of these classes. This model identified consumer classes that differed primarily on severity of dependence, in keeping with a unifactorial, dimensional symptom structure. One class, categorised as ‘low dependent’ consumers (35%), had a low probability any symptom (all probabilities ≤0.188). A second group (33%) had >50% probability of endorsement of abuse, physiological dependence, larger/longer and continued use despite physical/psychological harm (Supporting information Figure S1). A final group (32%) had high probability of endorsement of all symptoms.

Correlates of DSM-5 Khat Use Disorder

As a means of external validation of the DSM-5 KUD syndrome, independent logistic regression models (Table 4) demonstrated that those classified with KUD were significantly more likely than other participants to use khat more frequently and in larger amounts. However, there was no difference in duration of khat chewing sessions; age of onset or years of use of khat. Individuals with KUD were more likely to have participated in lifetime ‘help seeking’ for khat use, however, this related to only one-third of the group with KUD, and almost exclusively related to help from family members or friends. Those with KUD were also significantly more likely to be male, daily alcohol consumers and dependent or daily tobacco smokers (Table 4). Half of the group with KUD
had also recently smoked shisha; and while other drug use was uncommon, rates were elevated in this group.

Harms attributed to khat use among the sample were frequent, and were consistently greater among respondents with KUD, even after controlling for gender, tobacco use and other drug use (Table 4). Those with KUD had systematically increased financial problems associated with use, higher rates of self-reported mental health problems and one-quarter screened positive to high levels of psychological distress. Similarly, this group reported poorer quality of life.

Table 2: Past-year endorsement of withdrawal symptoms (n=400)

<table>
<thead>
<tr>
<th>Definition</th>
<th>Symptom present % (95%CI)</th>
<th>Symptom present &gt;24h and problematic % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Core symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed mood</td>
<td>58.5 (53.6-63.2)</td>
<td>37.5 (32.9–42.3)</td>
</tr>
<tr>
<td>Irritable</td>
<td>45.0 (40.2-49.9)</td>
<td>30.5 (26.2–35.2)</td>
</tr>
<tr>
<td>Anxious/nervous</td>
<td>45.5 (40.7-50.4)</td>
<td>23.7 (19.8–28.2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>53.0 (48.1-57.8)</td>
<td>23.3 (19.4–27.6)</td>
</tr>
<tr>
<td>Vivid/unpleasant dreams</td>
<td>55.0 (50.1-59.8)</td>
<td>16.8 (13.4–20.7)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>56.0 (51.1-60.8)</td>
<td>17.8 (14.3–21.8)</td>
</tr>
<tr>
<td>Hypersomnia</td>
<td>57.3 (52.4-62.0)</td>
<td>33.8 (29.3–38.5)</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>42.8 (38.0-47.6)</td>
<td>27.3 (23.1–31.8)</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>42.0 (37.3-46.9)</td>
<td>18.5 (15.0–22.6)</td>
</tr>
<tr>
<td>Restless</td>
<td>52.0 (47.1-56.9)</td>
<td>29.3 (25.0–33.8)</td>
</tr>
<tr>
<td><strong>Additional symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hallucinations</td>
<td>21.5 (17.8-25.8)</td>
<td>8.0 (5.7–11.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>26.5 (22.4-31.0)</td>
<td>14.5 (11.4–18.3)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>24.3 (20.3-28.7)</td>
<td>13.8 (10.7–17.5)</td>
</tr>
<tr>
<td>Concentration problems</td>
<td>48.0 (43.1-52.9)</td>
<td>27.5 (23.4–32.1)</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysphoria and two or more concurrent symptoms, lasting ≥48 hours</td>
<td>28.0 (23.8–32.6)</td>
<td></td>
</tr>
<tr>
<td>Withdrawal relief</td>
<td>43.8 (39.0–48.6)</td>
<td></td>
</tr>
<tr>
<td>Withdrawal present (either concurrent dysphoria + 2 or withdrawal relief)</td>
<td>50.3 (45.4-55.1)</td>
<td></td>
</tr>
</tbody>
</table>

*a Problematic: uncomfortable, upsetting, and caused problems (at work, school, with family or friends).

CI = Confidence interval.
DISCUSSION

The aim of this study was to validate DSM criteria for khat. Use disorder was identified in almost three quarters of this general community sample of frequent chewers. Although there has been limited prior research, these rates are comparable with a smaller study identifying DSM-IV dependence among 63% of participants recruited through khat cafes in UK (Kassim et al., 2012). The khat use disorder syndrome fit well to a unifactorial model, and latent symptom classes were consistent with a dimensional process, consistent with findings for amphetamines (Saha et al., 2012) and other drugs (Compton, Saha, Conway, & Grant, 2009; Kerridge et al., 2011).

Symptom item base rates (IRT ‘difficulties’), however, followed a pattern for khat that contrasts strongly with that identified for other substances, likely reflective of the unique mode of khat consumption when compared to other stimulants. ‘Continuing to use despite knowledge of physical/psychological problems’ was the most frequently reported symptom, despite this being a DSM-IV dependence item rather than the conceptually less severe abuse criteria set. This pattern has also been identified caffeine use disorder (Striley, Griffiths, & Cottler, 2011). The other most commonly reported symptoms were part of the DSM-IV abuse syndrome: ‘failure to fulfil major role obligations’ and ‘continued use despite interpersonal problems’. A khat chewing session typically lasts 5-6 hours (Cox & Rampes, 2003) and is a social process, albeit typically occurring away from home or in khat cafes. While a legal drug, khat possession and chewing in the workplace is illegal in most khat growing countries (Cox & Rampes, 2003; Elmi, 1983). As a result, chewing is most likely to be conducted away from family members, work places and other commitments. Indeed, in a methodologically strong study of university and hospital staff in Ethiopia, half the khat consumers reported leaving work early or missing work entirely to chew khat (Yeshigeta Gelaw, 2004).
### Table 3: Past year symptom base rate, confirmatory factor analysis (CFA) model fit and item response theory parameters for DSM-IV khat dependence and DSM-5 khat use disorder (n=400)

<table>
<thead>
<tr>
<th>DSM-IV Khat dependence</th>
<th>DSM-5 Khat use disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms present</strong></td>
<td><strong>Loadings $^a$</strong></td>
</tr>
<tr>
<td><strong>% (95% CI)</strong></td>
<td><strong>$\alpha$ (SE)</strong></td>
</tr>
<tr>
<td><strong>Loadings $^a$</strong></td>
<td><strong>(discrimination)</strong></td>
</tr>
<tr>
<td><strong>Drug-related legal problems</strong></td>
<td>14.8 (11.6-18.6)</td>
</tr>
<tr>
<td><strong>Recurrent use resulting in failure to fulfil major role obligations</strong></td>
<td>61.5 (56.6-66.1)</td>
</tr>
<tr>
<td><strong>Continued use despite recurrent social/interpersonal problems due to use</strong></td>
<td>56.0 (51.1-60.7)</td>
</tr>
<tr>
<td><strong>Recurrent use in hazardous situations</strong></td>
<td>50.3 (45.4-55.1)</td>
</tr>
<tr>
<td><strong>Craving or a strong desire for khat</strong></td>
<td>45.7 (40.9-50.6)</td>
</tr>
<tr>
<td><strong>Tolerance</strong></td>
<td>40.3 (35.6-45.1)</td>
</tr>
<tr>
<td><strong>Withdrawal</strong></td>
<td>50.3 (45.4-55.1)</td>
</tr>
<tr>
<td><strong>Used in larger amounts or longer than intended</strong></td>
<td>52.0 (47.1-56.8)</td>
</tr>
<tr>
<td><strong>Persistent desire or unsuccessful efforts to reduce use</strong></td>
<td>46.0 (41.1-50.9)</td>
</tr>
<tr>
<td><strong>Social, occupational, other activities reduced due to use</strong></td>
<td>41.5 (36.8-46.4)</td>
</tr>
<tr>
<td><strong>Great deal of time spent using and recovering from use</strong></td>
<td>23.5 (19.6-27.9)</td>
</tr>
<tr>
<td><strong>Continued use despite recurrent physical or psychological problems</strong></td>
<td>63.3 (58.4-67.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CFA model fit indices</strong></th>
<th><strong>Chi-square $^a$</strong></th>
<th><strong>AIC $^a$</strong></th>
<th><strong>BIC $^a$</strong></th>
<th><strong>SSA-BIC $^a$</strong></th>
<th><strong>CFI $^b$</strong></th>
<th><strong>TLI $^b$</strong></th>
<th><strong>RMSEA $^b$</strong></th>
<th><strong>WRMR $^b$</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSM-IV Khat dependence</strong></td>
<td>240.135**</td>
<td>2808.518</td>
<td>2864.398</td>
<td>2819.975</td>
<td>0.979</td>
<td>0.969</td>
<td>0.109</td>
<td>1.417</td>
</tr>
<tr>
<td><strong>DSM-5 Khat use disorder</strong></td>
<td>858.257**</td>
<td>4292.447</td>
<td>4380.260</td>
<td>4310.452</td>
<td>0.979</td>
<td>0.973</td>
<td>0.090</td>
<td>1.390</td>
</tr>
</tbody>
</table>

| **% Met Disorder criteria** | **60.5 (55.6-65.2)** | **73.7 (69.2-77.8)** |

---

**P < 0.01; $^a$ Using the robust MLR estimator (maximum likelihood estimation with robust standard errors), AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; SSA-BIC = sample size-adjusted Bayesian information criterion. With WLSMV the absolute $\chi^2$ value cannot be interpreted or compared. Only the $P$-value can be interpreted. $^b$ Using the WLSMV (weighted least squares estimator with degrees of freedom adjusted for means and variances) estimator, CFI = comparative fit index; CFA=Confirmatory Factor Analysis; RMSEA = root mean square error of approximation; WRMR = weighted root mean residual. TLI = Tucker–Lewis Index; SE = standard error; CI = confidence interval.**
Physical withdrawal symptoms and craving were apparent in half the participants, as were indications of lack of control over use. Unusually, despite regular khat use in the sample, tolerance was the second least commonly reported symptom, and, while those classified with KUD typically chewed larger amounts, session duration (on average 5 hours or more) did not differ according to KUD presence. The infrequency of tolerance has been identified previously (Kalix, 1988) and may relate to the physical limits on the amount of khat that can be ingested at any one time. Additionally, the accumulation of cathine during a chewing session leads to adverse experiences the longer a chewing session continues, placing a limit on the duration of a session.

Despite the extended duration of a typical khat chewing session, the symptom ‘great deal of time spent using’ was uncommon. This is an important reminder of cultural factors in symptom identification, as, while participants viewed this as largely an expected behaviour, practitioners may be quick to consider the duration of even a typical session for non-problematic khat consumers as evidence for the presence of this symptom. The low endorsement of ‘drug-related legal problems’ is a reflection of the legality of khat use in the country.

Although there are no controlled studies on khat withdrawal, changes in mood and sleeping problems, loss of appetite, fatigue, depression and low mood have been commonly associated with khat use (Alem et al., 1999; Cox & Rampes, 2003; Elmi, 1983), consistent with the withdrawal syndrome for related psychostimulants. While almost all had experienced at least one clinically significant withdrawal symptom, only 28% met core requirements for stimulant withdrawal (concurrent dysphoria plus two other symptoms, severe enough to cause distress). Of these symptoms, dysphoria was the most common, supporting its centrality within the syndrome. Insomnia/hypersomnia and psychomotor agitation/retardation were also common. Notably, the inclusion of withdrawal relief (reported by 43.8%) substantially inflates the rates of withdrawal symptoms. Care needs to be taken in the consideration of the presence of this symptom from survey studies.
In this sample, male participants were more likely than female users to have KUD. Cultural norms contribute to this: a recent Ethiopian epidemiological study demonstrated substantially greater prevalence of past-month Khat chewing among males than females (Haile & Lakew, 2015), likely due to cultural acceptability (E. Gebrehanna, Y. Berhane, & A. Worku, 2014b). This provides more opportunities for men than women to use khat freely (Brady & Randall, 1999; Kulis, Marsiglia, Ayers, Booth, & Nuno-Gutierrez, 2012), putting them at higher risk of developing dependence (Baer, Kivlahan, Blume, McKnight, & Marlatt, 2001).

Those categorised as experiencing KUD were using both in larger amounts and more frequently (with half using daily), consistent with the notion of loss of control over use. Similarly, those with KUD had substantially greater levels of financial problems associated with use. In several surveys of khat using communities it was reported that spending excessive time and money on khat were major contributors to family conflict (Dhaifalah & Santavy, 2004; Kassim & Croucher, 2012; Omar et al., 2015).

Individuals with KUD had systematically elevated rates of self-reported problems with concentration, memory, and sustaining motivation. While expectations of higher academic performance are common predictors of khat chewing among university students (Ihunwo, Kayanja, & Amadi-Ihunwo, 2004; Zein, 1988), studies have identified typically poorer academic performance among khat-chewers (Al-Sanosy, 2009; Ayana & Mekonen, 2004). In support of our findings, impairments in the inhibition of response conflicts, monitoring of working memory, and mental flexibility have been identified in abstinent khat consumers (Colzato, Ruiz, van den Wildenberg, Bajo, & Hommel, 2011; Colzato, Sellaro, Ruiz, Sikora, & Hommel, 2013; Hoffman & Al'absi, 2013).
Individuals with KUD also had higher rates of other substance use than non-problematic consumers. However, it is unlikely that these substances were central to the behavioural problems reported: only 29% drank alcohol more than weekly, and only very small minorities reported any cannabis (10%) use. Smoking of tobacco and/or shisha was substantially more common among problematic khat-chewers and are common activities in places where khat is consumed.

Table 4: Correlates of DSM-5 khat use disorder (n=400)

<table>
<thead>
<tr>
<th>Items</th>
<th>DSM-5 khat use disorder†</th>
<th></th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n=105; 26.3%)</td>
<td>Yes (n=295; 73.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61.9</td>
<td>82.4</td>
<td>2.88** (1.75-4.71)</td>
</tr>
<tr>
<td>Age (≤24)†</td>
<td>32.4</td>
<td>26.8</td>
<td>0.76 (0.47-1.24)</td>
</tr>
<tr>
<td>Full time student</td>
<td>41.9</td>
<td>30.8</td>
<td>0.62 (0.39-0.98)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>3.5</td>
<td>10.5</td>
<td>0.94 (0.48-1.87)</td>
</tr>
<tr>
<td>Employed</td>
<td>12.8</td>
<td>40.5</td>
<td>1.06 (0.54-2.09)</td>
</tr>
<tr>
<td><strong>Patterns of Khat use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First used khat ≤16 years</td>
<td>9.5</td>
<td>16.3</td>
<td>1.85 (0.90-3.80)</td>
</tr>
<tr>
<td>Used khat for ≥5 years</td>
<td>77.1</td>
<td>83.1</td>
<td>1.45 (0.84-2.51)</td>
</tr>
<tr>
<td>Used khat daily in past 12 months</td>
<td>1.9</td>
<td>47.3</td>
<td>45.29** (10.97-19.01)</td>
</tr>
<tr>
<td>Used khat more than once per week</td>
<td>68.9</td>
<td>93.2</td>
<td>6.18** (3.33-11.85)</td>
</tr>
<tr>
<td><strong>Amount chewed per session</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used ≥1.5 bundles of khat daily in past 12 months</td>
<td>14.3</td>
<td>28.1</td>
<td>2.35** (1.29-4.29)</td>
</tr>
<tr>
<td><strong>Chewing session duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 hours or more</td>
<td>69.5</td>
<td>62.6</td>
<td>0.74 (0.46-1.19)</td>
</tr>
<tr>
<td><strong>Other drug use in last six months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily alcohol</td>
<td>0.3</td>
<td>7.8</td>
<td>12.79** (1.72-94.95)</td>
</tr>
<tr>
<td>Daily tobacco</td>
<td>1.5</td>
<td>21.0</td>
<td>3.19* (1.21-8.45)</td>
</tr>
<tr>
<td>High Fagerstrom test for nicotine dependence b‡</td>
<td>0.3</td>
<td>4.8</td>
<td>2.62** (0.33-20.89)</td>
</tr>
<tr>
<td>Any cannabis use</td>
<td>2.1</td>
<td>10.2</td>
<td>5.25** (1.55-17.75)</td>
</tr>
<tr>
<td>Any benzodiazepine use</td>
<td>0.3</td>
<td>5.0</td>
<td>8.08* (1.07-60.96)</td>
</tr>
<tr>
<td>Any shisha use</td>
<td>15.4</td>
<td>48.6</td>
<td>5.20** (2.91-9.30)</td>
</tr>
<tr>
<td><strong>Financial problems in last twelve months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spent money on khat meant for other things</td>
<td>50.5</td>
<td>82.4</td>
<td>4.93** (3.02-8.04)</td>
</tr>
<tr>
<td>Sold belongings to buy khat</td>
<td>7.6</td>
<td>52.2</td>
<td>13.24** (6.22-28.21)</td>
</tr>
<tr>
<td>Worried about the amount of money spent on khat</td>
<td>11.4</td>
<td>62.7</td>
<td>13.03** (6.83-24.86)</td>
</tr>
<tr>
<td>Had khat related debts</td>
<td>11.4</td>
<td>53.6</td>
<td>8.94** (4.70-17.01)</td>
</tr>
<tr>
<td>Made excuses about money spent on khat</td>
<td>13.3</td>
<td>67.1</td>
<td>13.27** (7.19-24.49)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Help seeking</td>
<td>3.8</td>
<td>32.9</td>
<td>12.37** (4.42-34.59)</td>
</tr>
<tr>
<td><strong>Mental health</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kessler 10 ≥ 30‡</td>
<td>0.3</td>
<td>25.4</td>
<td>56.15** (7.72-41.40)</td>
</tr>
<tr>
<td>Self-reported mental health problem</td>
<td>2.9</td>
<td>40.4</td>
<td>22.78** (7.05-73.56)</td>
</tr>
<tr>
<td><strong>Quality of life (n=386)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal wellbeing (PWI 2SD below mean) d</td>
<td>85.4</td>
<td>34.6</td>
<td>0.09** (0.05-0.17)</td>
</tr>
<tr>
<td>Satisfaction with life (PWI 2SD below mean) e</td>
<td>75.7</td>
<td>28.6</td>
<td>0.13** (0.08-0.22)</td>
</tr>
<tr>
<td><strong>Academic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble keeping attention on activity for too long</td>
<td>19.6</td>
<td>81.9</td>
<td>18.57** (10.44-33.01)</td>
</tr>
<tr>
<td>Difficulty in organizing/scheduling routine tasks</td>
<td>40.2</td>
<td>84.4</td>
<td>8.05** (4.83-13.40)</td>
</tr>
<tr>
<td>Trouble listening in lectures</td>
<td>10.8</td>
<td>54.6</td>
<td>9.95** (5.10-19.41)</td>
</tr>
<tr>
<td>Trouble making study plans</td>
<td>44.1</td>
<td>77.0</td>
<td>4.23** (2.62-6.83)</td>
</tr>
</tbody>
</table>
Table 4: continued

<table>
<thead>
<tr>
<th>Items</th>
<th>DSM-5 khat use disorder*</th>
<th>No (n=105; 26.3%)</th>
<th>%</th>
<th>No (n=105; 26.3%)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spent lot of time doing nothing</td>
<td></td>
<td>46.1</td>
<td>79.1</td>
<td>4.42** (2.73-7.17)</td>
<td></td>
</tr>
<tr>
<td>Unable to do two or three tasks in a row</td>
<td></td>
<td>54.9</td>
<td>82.6</td>
<td>3.91** (2.38-6.42)</td>
<td></td>
</tr>
<tr>
<td>Trouble remembering things to do</td>
<td></td>
<td>8.8</td>
<td>74.1</td>
<td>28.97** (14.85-56.49)</td>
<td></td>
</tr>
<tr>
<td>Don’t stick to tasks to completion</td>
<td></td>
<td>25.5</td>
<td>79.8</td>
<td>11.54** (6.78-19.64)</td>
<td></td>
</tr>
<tr>
<td>Lack of attention</td>
<td></td>
<td>11.8</td>
<td>79.4</td>
<td>29.74** (15.26-57.99)</td>
<td></td>
</tr>
<tr>
<td>Trouble with short term memory</td>
<td></td>
<td>7.8</td>
<td>70.6</td>
<td>28.17** (13.10-60.60)</td>
<td></td>
</tr>
<tr>
<td>Difficulty sustaining concentration</td>
<td></td>
<td>15.7</td>
<td>79.4</td>
<td>20.76** (11.32-38.08)</td>
<td></td>
</tr>
<tr>
<td>Lack of concentration on studies</td>
<td></td>
<td>9.8</td>
<td>73.8</td>
<td>25.86** (12.78-52.31)</td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.01; * Based on median split for the sample; $^1$ score of ≥ 6 on Fagerström Test for Nicotine Dependence (FTND) scale; $^2$ Scores on K10 30–50 indicating very high psychological distress derived from the K10 cut-offs that were used in the Australian National Mental Health and Wellbeing Survey (Australian Bureau of Statistics, 2008); $^3$ Personal Wellbeing Index (PWI) cut-off is mean – 2 standard deviations (SD) (73.83) based on the generic normal ranges calculated by using the survey mean scores as data from 30 surveys conducted between April 2001 and August 2001. $^4$LAW (Life as a Whole) cut-off is mean – 2 SD (76.01) based on the generic normal ranges calculated by using the survey mean scores as data from 30 surveys conducted April 2001 and August 2001. $^5$ These effects do not remain statistically significant after controlling for gender differences. $^6$ These effects remain statistically significant after controlling for gender differences. $^7$ These effects remain statistically significant after controlling for any use of tobacco and other drugs (shisha, benzodiazepine, cannabis). OR = odds ratio; CI = confidence interval.

Khat chewing has previously been associated with increased rates of consumption of other drugs, mainly tobacco, alcohol and psychotropic agents (Kassim, Islam, & Croucher, 2011; D. Kebede et al., 2005; Y. Kebede, 2002; Malaju & Asale, 2013; Reda, Moges, Biadgilign, & Wondmagegn, 2012; Tesfaye, Byass, Wall, Berhane, & Bonita, 2008); and severity of khat dependence was also significantly related to nicotine dependence (Kassim, Croucher, & al'Absi, 2013b). Cigarettes are believed to enhance the stimulatory effect obtained during chewing and to reduce its bitter taste.

This study had several limitations; first the diagnostic data was based on survey self-report, rather than the gold standard of clinical diagnosis; and survey responses may also be susceptible to social desirability and recall bias. However, in multiple studies, the AUDADIS-IV has demonstrated good to excellent reliability and validity (Chatterji et al., 1997; Cottler et al., 1997; Grant et al., 1995; D. Hasin, Carpenter, McCloud, Smith, & Grant, 1997; D. S. Hasin, Van Rossem, McCloud, & Endicott, 1997; Pull et al., 1997) for the identification of illicit drug use disorders. We also believe that our use of anonymous self-administered survey provided anonymity, and hence minimized response bias. Secondly, participants were drawn from a defined geographical region.
(Adama, Ethiopia) and recruited using convenience sampling, primarily through khat cafes. This clearly increased the likelihood of involvement of frequent chewers, hence at elevated risk of khat use disorder. As such, the base rates of symptoms identified here will necessarily be greater than a population-representative sample. However, this sampling framework was appropriate for the aims of this study. Thirdly, there could be some potential interpretive problems arising from the presence of polysubstance use. Given the social context of khat use, polysubstance use, especially of cigarettes and shisha, is likely unavoidable. While poly-substance use had the potential to contribute to symptoms, this is unlikely to have a substantial inflating effect, given the low proportion reporting frequent use, low levels of dependence, and the finding that increased rates of adverse effects remained after controlling for polysubstance use.

In conclusion, despite the fact that khat chewing is legal, deep-rooted and a culturally acceptable habit in Ethiopia, some people clearly experience substantial and clinically significant problems related to khat use. There are a range of interventions possible in order to minimize harm in relation to khat. Primary prevention activities, such as community-based interventions focusing on improving understanding about positive and negative impacts of khat, and strategies to reduce negative impacts, may delay initiation or problematic consumption of khat. In this study, among those experiencing problems with khat, help-seeking was so poor that this was near universally from untrained family/friends rather than from medical centers. While khat plays a substantial role in Ethiopia’s economy (Feyisa & Aune, 2003) (for rural producers, regional economies and source of foreign exchange), it is associated with health and public safety problems which are addressed with weak legislative responses. Recent khat bans have also lead to the criminalization of users and sellers and illegal drug markets (Klein, Beckerleg, & Hailu, 2009). Therefore, promoting evidence-based approaches to khat regulation that accounts for positive aspects of the khat economy and the needs of rural producers is useful (Klein et al., 2009). One option for improving individual and community well-being may be the introduction of a regulatory system that levies...
the product, whereby the funds raised can be directed toward treatment and harm minimization programs, as is the case in many countries in relation to proceeds from gambling. This could also be applied to support training of primary care practitioners to improve awareness of the health implications of khat and how to provide targeted assessment and intervention.

Finally, according to Ministry of Education policy, khat chewing is banned at schools and higher learning institutions (Gebrehanna, Berhane, & Worku, 2014). However, it is reported that students are the second largest consumers of khat next to drivers (Kandari, Yadav, Thakur, & Kandari, 2014); and that even university staff report missing work hours in order to chew khat. As such there is substantial scope to intervene at an organizational level in relation to khat use to reduce its impact on productivity, as well as negative impacts on academic function and more general wellbeing.
**SUPPORTING INFORMATION**

**Table S1:** Diagnostic crosswalk between DSM-IV and DSM-5 diagnostic categories (N=400)

<table>
<thead>
<tr>
<th>DSM-5 substance use disorder</th>
<th>DSM-IV abuse</th>
<th>DSM-IV dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Kappa = 0.838**</td>
<td></td>
<td>Kappa = 0.706**</td>
</tr>
<tr>
<td>23.0 (92)</td>
<td>3.3 (13)</td>
<td>26.3 (105)</td>
</tr>
<tr>
<td>3.0 (12)</td>
<td>70.8 (283)</td>
<td>13.3 (53)</td>
</tr>
<tr>
<td>Kappa = 0.592**</td>
<td></td>
<td>Kappa = 0.867**</td>
</tr>
<tr>
<td>26.0 (104)</td>
<td>19.5 (78)</td>
<td>39.3 (157)</td>
</tr>
<tr>
<td>0(0)</td>
<td>54.5 (218)</td>
<td>0.3 (1)</td>
</tr>
<tr>
<td>Kappa = 0.719**</td>
<td></td>
<td>Kappa = 0.899**</td>
</tr>
<tr>
<td>25.3 (101)</td>
<td>11.5 (46)</td>
<td>35.8 (143)</td>
</tr>
<tr>
<td>0.8 (3)</td>
<td>62.5 (250)</td>
<td>3.8 (15)</td>
</tr>
</tbody>
</table>

*p<.05; ** p<.01; *** p<.001

**Table S2:** Latent class fit statistics for DSM-5 Khat use disorder symptom items, with 1 to 6 classes (N=400)

<table>
<thead>
<tr>
<th>Model</th>
<th>AIC</th>
<th>BIC</th>
<th>ssaBIC</th>
<th>LMR-ALRT</th>
<th>LMR-ALRT p-value</th>
<th>Entropy</th>
<th>Percentage in each class</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Class 1</td>
</tr>
<tr>
<td>1 class</td>
<td>5862</td>
<td>5906</td>
<td>5871</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>2 class</td>
<td>4386</td>
<td>4477</td>
<td>4404</td>
<td>1531.856</td>
<td>0.001</td>
<td>0.957</td>
<td>61</td>
</tr>
<tr>
<td>3 class</td>
<td>4227</td>
<td>4366</td>
<td>4255</td>
<td>180.518</td>
<td>&lt;0.001</td>
<td>0.859</td>
<td>32</td>
</tr>
<tr>
<td>4 class</td>
<td>4196</td>
<td>4383</td>
<td>4234</td>
<td>54.167</td>
<td>0.383</td>
<td>0.837</td>
<td>26</td>
</tr>
<tr>
<td>5 class</td>
<td>4175</td>
<td>4411</td>
<td>4224</td>
<td>43.254</td>
<td>0.483</td>
<td>0.872</td>
<td>18</td>
</tr>
<tr>
<td>6 class</td>
<td>4154</td>
<td>4438</td>
<td>4212</td>
<td>44.547</td>
<td>0.274</td>
<td>0.887</td>
<td>14</td>
</tr>
</tbody>
</table>
Figure S1: Response probabilities according to group for the three-class solution
REFERENCES


Chapter 2: Is khat use disorder a valid diagnostic entity?


Chapter 2: Is khat use disorder a valid diagnostic entity?


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Using the Severity of Dependence Scale to Screen for DSM-5 Khat Use Disorder

Samson Duresso, Allison Matthews, Stuart G. Ferguson, Raimondo Bruno

School of Medicine, University of Tasmania, Hobart, Australia

Abstract

Objective: This study aimed to determine the efficacy of the Severity of Dependence Scale (SDS) as a screening tool for DSM-5 defined Khat Use Disorder.

Methods: Cross-sectional, purposive sample of past year khat consumers aged 16 and above recruited from khat markets and cafes from university and general community in Adama, Ethiopia. Participants self-completed a survey comprising current substance use disorder.

Results: The SDS formed a unifactorial structure, consistent with the dependence construct. Almost three-quarters (73%) of the sample were identified as experiencing DSM-5 Khat Use Disorder. The SDS demonstrated excellent discrimination (AUC=0.92), and an optimal cut-off as a score of 3 or greater, with sensitivity of 81% and specificity of 96%. This classification validly identified a group with more frequent and higher dose khat use than participants that did not screen positive.

Conclusion: While khat is a mild stimulant, there is clear evidence that some consumers are both concerned with their use and experience problems associated with their use. Consistent with its application for other drugs, the SDS is a brief and simple screening tool that appears to validly identify individuals experiencing a khat use disorder syndrome and experiencing high rates of adverse consequences in association with use.

Keywords: Drug Dependence; Drug Use Disorders; Drug Overdose; Substance Abuse
INTRODUCTION

Khat (*Catha edulis Forsk*) contains multiple alkaloids that produce psychostimulant effects similar to that of amphetamines (Feyissa & Kelly, 2008; Graziani, Milella, & Nencini, 2008). The main constituents—cathinone and cathine—increase dopamine, serotonin and noradrenaline release in the central nervous system (Kalix, 1980, 1990; Kalix & Braenden, 1985). Previously, due largely to cultural norms, khat use in Ethiopia was largely restricted to males in certain social strata (Odenwald, Klein, & Warfa, 2010). Likely reflecting social change and easy access to khat, chewing is now more widely spread across social class, age and gender (Alem, Kebede, & Kullgren, 1999). Khat is habitually consumed by craftsmen, farmers, and labourers, and also academics and students (Adugna, Jira, & Molla, 1994; Alem et al., 1999; Ayana & Mekonen, 2004; Ayenew, Tadesse, & Azale, 2012; Ihunwo, Kayanja, & Amadi-Ihunwo, 2004). These consumers report subjective factors such as increased alertness and concentration (Ayana & Mekonen, 2004; Zein, 1988) and relief of physical and mental stress as motivating factors for their use (Wedegaertner et al., 2010). A 2011 population prevalence study estimated past month use at 15.3% across Ethiopia (22.6% among males; 9.1% among females). Among Ethiopian university students, lifetime prevalence was estimated at 24.0%, while 7.7% reported past month khat use (Gebrehanna, Berhane, & Worku, 2014). Global spread of khat use is largely attributed to easy air transportation for khat export and migration of people from East Africa and Yemen to the UK and other Western countries (Griffiths et al., 2010; Stevenson, Fitzgerald, & Banwell, 1996).

Khat has become a public health concern due to adverse health risks and negative social functioning associated with frequent chewing. Multiple studies have demonstrated that chewing is associated with increased strain in family relationships and poorer Productivity (Omar et al., 2015). It has also been associated with cardiovascular disease such as hypertension, and oral cancer (Aden, Dimba, Ndolo, & Chindia, 2006; El-Wajeh & Thornhill, 2009). Several studies have identified khat use
disorder at high rates among samples of frequent chewers, including adverse physical and mental health effects (Duresso, Matthews, Ferguson, & Bruno, 2016; Omar et al., 2015), but only small proportions of these seeking help for their problems associated with use (Duresso et al., 2016).

Core physiological aspects of dependence, such as withdrawal symptoms and tolerance, have been recently reported among regular users (Duresso et al., 2016) and identified as potential liability factors for the spread of khat chewing (Douglas, Boyle, & Lintzeris, 2011; Halbach, 1972; Kassim, Croucher, & al'Absi, 2013; Luqman & Danowski, 1976). Studies which have used the Severity of Dependence Scale (SDS) (Gossop et al., 1995) to assess for psychological aspects of khat dependence (Griffiths et al., 1997; Kassim & Croucher, 2006; Kassim, Islam, & Croucher, 2010) identified that increased khat use frequency is associated with higher SDS scores and that greater SDS scores are associated with more physical (e.g. insomnia) and psychological health problems (e.g. anxiety, agitation, restlessness) after using khat (Elmi, 1983; Kalix & Braenden, 1985; Nakajima et al., 2014) Elmi, 1983; Kalix & Braenden, 1985; Nakajima, Dokam, Alsameai, et al., 201. Such findings support the potential utility of the SDS in relation to khat for healthcare providers to efficiently identify those experiencing khat related harms (Young, Butt, Hersi, Tohow, & Mohamed, 2016). Recent studies have provided initial support for the use of SDS-khat as a valid research tool for assessing psychological aspects of khat dependence (Elmi, 1983; Kalix & Braenden, 1985; Nakajima et al., 2014). To date, however, no work has sought to determine a cut-off point for screening against khat diagnoses of use disorder/dependence, nor to examine whether scores on the SDS for khat are also associated with physical and psychological health and other behaviours known to be correlated with dependence. This is particularly important as previous studies have revealed low rates of treatment-seeking among those experiencing problems with khat use (e.g. Duresso et al., 2016).
Chapter 3: Using the Severity of Dependence Scale to Screen for DSM-5 Khat Use Disorder.

The goal of the current study was to examine whether the SDS can be applied as a valid screening tool to efficiently identify potential cases of khat dependence. The SDS is particularly beneficial as a screening tool for use disorder as it is in the public domain, brief, suitable for a range of substances, and easily administered. The measure has been demonstrated to be reliable, valid and culturally adaptable in measuring problems related to drug use in the past 12 months (Ferri, Marsden, M, Laranjeira, & Gossop, 2000; Gossop, Best, Marsden, & Strang, 1997; Topp & Mattick, 1997a). The SDS has been demonstrated to sensitively identify - within a short time frame and without specific clinical training - individuals with substance dependence in relation to a range of drug types including amphetamines, cannabis and opioids (Gossop, Griffiths, et al., 1997; Topp & Mattick, 1997b) Although the scale has been used in similar ways for khat research (Kassim et al., 2010), the cut-off values applied for identification of ‘cases’ have been estimates derived from prior work with stimulant drugs. As such, empirical evaluation of cut-off points for their sensitivity in identifying individuals experiencing khat use disorder is important, as is validating these thresholds against multiple measures of problems associated with use of the drug.

In order to address this question, a large sample of frequent khat consumers were assessed with the SDS and the modified version of the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) to determine Diagnostic and Statistical Manual of Mental Disorders-IV and -5 cases of khat dependence and khat use disorder, respectively. The AUDADIS is a validated standardized instrument against which the cut-off values were determined. Using a representative sample of the general population, the test-retest reliability of AUDADIS has shown good to excellent reliability and validity for the identification of range of illicit drug dependence and use disorders (Grant, Harford, Dawson, Chou, & Pickering, 1995; Hasin, Carpenter, McCloud, Smith, & Grant, 1997; Ruan et al., 2008) Moreover, a recent study (Duresso et al., 2016) which examined khat use disorder (KUD) symptoms among frequent khat users using AUDADIS-IV,
demonstrated that the scale performed validly, with the psychometric properties of the scale consistent with that identified for other substances, and that those categorised as experiencing khat use disorder using at greater quantity, frequency and experiencing more associated problems than non-disordered participants.

The core aim of the current study was to evaluate the use of the SDS as it relates to screening for cases of khat use disorder under the DSM-5 system. Specifically, the study aims at answering two core research questions:

1. *Does the SDS for khat use perform in a similar way to existing diagnostic measures of khat use disorders? If so, what is an adequate cut-off score for case identification for screening purposes?* To address this, scores on SDS and AUDADIS-IV were used to identify DSM-IV cases of khat dependence and DSM-5 cases of khat use disorder.

2. *Are these cut-off scores valid in terms of identifying a group of individuals using khat at greater frequency and quantity, and experiencing functional problems?* To address this, the validity of the SDS cut-off scores were evaluated against the frequency and quantity of khat use, levels of psychological distress as measured by Kessler Psychological Distress Scale (K-10), quality of life as measured by Personal Wellbeing Index (PWI –Australian Normative Data) and level of impairments in academic functioning.

**MATERIALS AND METHODS**

**Participants**

Participants were recruited through a purposive sampling strategy in Adama, Ethiopia in 2013 and 2014. Inclusion criteria required that participants be at least 16 years old and had used khat at least
once in the preceding year (Duresso et al., 2016). Initially, 454 participants were recruited however after excluding 76 cases missing dependence data, 388 participants were retained for the analyses.

**Measures**

Khat use disorder (KUD) and khat dependence were assessed using a modified version of the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) (Ruan et al., 2008; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993), with item content expanded to include craving and withdrawal items (Duresso et al., 2016). This was used to derive past 12-month DSM-IV dependence and DSM-5 use disorder diagnoses in relation to khat use. The AUDADIS is a fully structured diagnostic interview designed to assess alcohol and drug use/disorders in clinical samples and the general population (Grant et al., 1995). Reliability was good to excellent. The observed reliability of the DSM-IV diagnosis and dimensional scales for the substance use psychiatric disorders indicates that the AUDADIS-IV can be usefully applied in various research settings, particularly in studies of the general population and community samples with alcohol and drug diagnosis.

**Severity of Dependence Scale (SDS)**

The SDS is a commonly used 5-item screening tool, with demonstrated sensitivity for the identification of dependence in relation to amphetamines, cannabis and other drugs (Gossop, Best, et al., 1997). The scale assesses psychological components of dependence over the past year, namely, compulsion to use a drug (the impaired loss of control over drug use), and preoccupation and anxiety about drug use (Gossop et al., 1995). While the SDS has been found to be a valid and reliable single factor uni-dimensional scale for measuring alcohol dependence (Lawrinson, Copeland, Gerber, & Gilmour, 2007) cocaine dependence (Kaye & Darke, 2002) and for amphetamine dependence (Topp & Mattick, 1997a), uni-dimensionality has not been universally
identified using exploratory factor analysis (Ferri et al., 2000; Tsai et al., 2012). In relation to khat specifically, a bilingual adaptation of the scale (Arabic and English) identified two factors (Nakajima et al., 2014). These provide some demonstrations that the scale should work in the context of khat use. However, there is no clear information as to where to place a cut-off on the scores to practically identify individuals that may be experiencing such a level of problems, so they can benefit from further assessment or an intervention. The SDS items are (all in relation to the past year):

1. Did you ever think your use of khat was out of control?
2. Did the prospect of missing khat make you very anxious or worried?
3. Did you worry about your khat use?
4. Did you wish you could stop using khat?
5. How difficult would you find it to stop or go without?

Items are scored on a 4-item Likert scale (items 1-4: 0=never; 1=sometimes; 2=often; 3=always; item 5: 0=not difficult; 1=quite difficult; 2=very difficult; 3=impossible), with a possible total score of 15.

Construct validity of the SDS was assessed through relationships between cut-off points and measures of quantity and frequency of consumption. To test the predictive validity of the SDS cut-off points, health (mental health) and socio economic (quality of life and financial) factors were assessed. Non-specific psychological distress was assessed using Kessler Psychological Distress Scale (K-10) (Kessler et al., 2002), using a cut-off score of 30 to indicate ‘very high’ levels of psychological distress. A subjective multi-domain quality of life measure, with Australian normative data was used to assess quality of life (Group, 2013). Frequency of cognitive and academic impairment in the past six months was assessed using a 12-item academic functioning
scale that was refined by the current researchers from cognitive and executive function questionnaires used in similar studies (Schwartz, 2007).

**Statistical Analysis**

Receiver operating characteristic (ROC) analyses were conducted to identify the point that best strikes a balance between the sensitivity (proportion of true-positives) and specificity (proportion of true-negatives) of the SDS as a screening tool for DSM-IV khat dependence or DSM-5 Khat Use Disorder. While application-agnostic procedures, such as the Youden Index (Youden, 1950) were reported (the SDS value that maximises sensitivity and specificity), because the aim of the study was to identify a screening cut-off, these were selected as the lowest SDS score that was a) within the 95%CI of the maximum Youden Index value that also b) maximised specificity above 90% and maintained sensitivity at approximately 80% or greater. Other diagnostic efficiency measures were calculated using Diagnostic and Agreement Statistics (DAGstat) (Mackinnon, 2000).

The structure of SDS khat items were assessed using unifactorial confirmatory factor analysis with additional item-response theory (IRT) measures, in Mplus v7.0, using robust estimators to account for skewed data. Model fit indices were examined to assess structural fit, including root mean squared error of approximation (RMSEA); Tucker-Lewis Index (TLI) and comparative fit index (CFI); RMSEA <0.06, TLI >0.95 and CFI >0.95 are considered to indicate good fit (Hu & Bentler, 1999; Mulaik, 2007; Steiger, 2007). Recent simulation studies suggest that N>200 is sufficient for robust estimation of such a structure (Myers, Ahn, & Jin, 2011). To provide some construct and predictive validation of these cut-off points on the SDS, using IBM SPSS Statistics v22, odds ratios with 95% confidence intervals (95%CI) derived from independent logistic regression models were used to examine if having an SDS score above the identified cut-point relates to increased rates of
harms in terms of variables such as patterns of consumption, mental health, and financial and occupational problems. In other words, if the cut-off points are valid then they should discriminate between people that are and are not experiencing problems associated with khat use. These were conducted for the identified cut-points for DSM-IV dependence and for DSM-5 khat use disorder.

RESULTS

The mean participant age was 30 years (SD=7, range 17-49); and approximately three-quarters (76.5%) were male. The majority were currently employed (80%) with nearly one-quarter (22%) having a diploma or higher university qualifications. One third (35%) had used khat on a daily basis; the remainder (60%) typically used three or more times a week (Table 1).

SDS for Khat

Table 2 shows the distribution of responses of the SDS items. Thirty percent of the sample (95% CI = 26–35) did not endorse any of the SDS items (total score = 0), a further 5% (95% CI = 3.2–7.5) only nominated the lowest level of concern (‘sometimes’) for one of the five SDS items (total score = 1).
Table 1: Demographic characteristics of the sample (N=388)

<table>
<thead>
<tr>
<th>Gender</th>
<th>n</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>297</td>
<td>76.5 [72.1, 80.5]</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤24</td>
<td>112</td>
<td>28.9 [24.6, 33.6]</td>
</tr>
<tr>
<td>25-34</td>
<td>171</td>
<td>44.1 [39.2, 48.0]</td>
</tr>
<tr>
<td>35-44</td>
<td>93</td>
<td>24.0 [20.0, 28.5]</td>
</tr>
<tr>
<td>≥45</td>
<td>12</td>
<td>3.1 [1.8, 5.3]</td>
</tr>
</tbody>
</table>

Frequency of khat use (n=385)

| Daily  | 136 | 35.1 [30.5-40.0] |
| 3 times or more a week | 233 | 60.5 [55.6-65.3] |

Ethnicity (n=386)

| Amhara | 109 | 28.2 [23.9-32.9] |
| Harari  | 12  | 3.1 [1.8-5.4]    |
| Oromo   | 143 | 37.0 [32.4-41.9] |
| SNNP    | 68  | 17.6 [14.1-21.7] |
| Tigré   | 30  | 7.8 [5.5-10.9]   |
| Others  | 24  | 6.2 [4.2-9.1]    |

Educational Level

| Completed Grade 11 or less | 213 | 54.9 [50.0-59.8] |
| Completed Grade 12 (secondary education) | 55  | 14.2 [11.1-18.0] |
| Diploma                     | 66  | 17.0 [13.6-21.1] |
| Bachelor’s degree or higher | 7   | 1.8 [0.9-4.7]   |
| No formal school            | 47  | 12.1 [9.2-15.7] |

Employment Status (n=258)

| Current Student | 133 | 34.3 [29.7-39.1] |
| Unemployed      | 15  | 5.83 [3.6-9.4]   |
| Self-employed   | 141 | 54.7 [48.6-60.6] |
| Employed for wages | 65  | 25.2 [20.3-30.8] |
| Looking for work | 32  | 12.4 [8.9-17.0]  |
| Others *         | 5   | 1.9 [0.8-4.5]    |

Notes: CI = confidence interval; SNNP = Southern Nations and Nationalities People
*Unable to work, retired, home duty ♣ other Ethnic groups

Structure of the SDS for Khat

Table 3 presents CFA results for a unifactorial model of SDS for khat items. Fit indices were satisfactory (both CFI and TLI > 0.95 (Hu & Bentler, 1999) although the RMSEA value suggested that there remained notable model misfit. The correlation between scores on the SDS and the DSM-5 symptom count were highly correlated (r=0.81, p<0.001).
Table 2: Distribution of responses to items of the SDS for Khat (N=388)

<table>
<thead>
<tr>
<th>SDS Items</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you ever think your use of khat was out of control?</td>
<td>43.8</td>
<td>170</td>
<td>35.1</td>
<td>136</td>
<td>16.0</td>
<td>62</td>
<td>5.2</td>
<td>20</td>
</tr>
<tr>
<td>Did the prospect of missing khat make you very anxious or worried?</td>
<td>48.2</td>
<td>187</td>
<td>28.1</td>
<td>109</td>
<td>17.0</td>
<td>66</td>
<td>6.7</td>
<td>26</td>
</tr>
<tr>
<td>Did you worry about your khat use?</td>
<td>43.8</td>
<td>170</td>
<td>34.0</td>
<td>132</td>
<td>16.5</td>
<td>64</td>
<td>5.7</td>
<td>22</td>
</tr>
<tr>
<td>Did you wish you could stop using khat?</td>
<td>39.9</td>
<td>155</td>
<td>29.6</td>
<td>115</td>
<td>18.0</td>
<td>70</td>
<td>12.4</td>
<td>48</td>
</tr>
<tr>
<td>How difficult would you find it to stop or go without khat?</td>
<td>53.1</td>
<td>206</td>
<td>28.9</td>
<td>112</td>
<td>14.9</td>
<td>58</td>
<td>3.1</td>
<td>12</td>
</tr>
</tbody>
</table>

Note: SDS = Severity of Dependence Scale.

ROC analysis was applied to examine the performance of the SDS khat in identifying the presence of DSM-5 khat use disorder (KUD) and DSM-IV khat dependence. Figure 1 presents the graphical plot that illustrates the diagnostic ability of SDS-Khat for DSM-5 KUD with its varying discrimination thresholds. For both criterion, area under the curve (AUC) values were >0.92, suggesting that the scale has an excellent ability to discriminate between those with and without KUD (Table 4). Given the distribution of scale total scores (Table 4), cut points were determined emphasising specificity; selected on the basis of the dual criteria of a) identifying the cut-point within the 95% of the scale score that maximised the Youden Index and b) maintained specificity above 90% and maintained sensitivity approximately at 80% or greater. This identified that SDS scores of 4 or above were appropriate for identification of cases of likely DSM-IV khat dependence; and SDS scores of 3 or greater were appropriate for cases of likely DSM-5 khat use disorder (with values of SDS ≥ 4 for moderate and ≥ 5 for severe use disorder respectively).
Table 3: Unifactorial confirmatory factor analysis and Item Response Theory parameter estimates for SDS for khat items (N=388)

<table>
<thead>
<tr>
<th>SDS Items</th>
<th>CFA Loadings</th>
<th>α (SE) (discrimination)</th>
<th>β₁ (SE) (difficulty)</th>
<th>β₂ (SE) (difficulty)</th>
<th>β₃ (SE) (difficulty)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How difficult would you find it to stop or go without khat?</td>
<td>0.724</td>
<td>1.368 (0.096)</td>
<td>-0.585 (0.101)</td>
<td>1.007 (0.106)</td>
<td>2.725 (0.208)</td>
</tr>
<tr>
<td>Did you ever think your use of khat was out of control?</td>
<td>0.908</td>
<td>2.514 (0.178)</td>
<td>-1.007 (0.078)</td>
<td>0.561 (0.071)</td>
<td>1.785 (0.116)</td>
</tr>
<tr>
<td>Did the prospect of missing khat make you very anxious or</td>
<td>0.844</td>
<td>1.890 (0.130)</td>
<td>-0.825 (0.085)</td>
<td>0.525 (0.079)</td>
<td>1.791 (0.125)</td>
</tr>
<tr>
<td>worried?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you worry about your khat use?</td>
<td>0.914</td>
<td>2.153 (0.148)</td>
<td>-1.031 (0.085)</td>
<td>0.510 (0.075)</td>
<td>1.811 (0.122)</td>
</tr>
<tr>
<td>Do you wish you could stop using khat?</td>
<td>0.815</td>
<td>1.537 (0.104)</td>
<td>-1.245 (0.107)</td>
<td>0.287 (0.084)</td>
<td>1.395 (0.110)</td>
</tr>
<tr>
<td>CFA model fit indices</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFI</td>
<td>0.989</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLI</td>
<td>0.978</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMSEA</td>
<td>0.161</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WRMR</td>
<td>0.938</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. CFA = confirmatory factor analysis; CFI = Comparative Fit Index; RMSEA = root mean square error of approximation; SDS = Severity of Dependence Scale; TLI = Tucker–Lewis Index; WLSMV = weighted least squares estimator with degrees of freedom adjusted for means and variances estimator; WRMR = weighted root mean residual.

FIGURE 1 Receiver operating characteristic (ROC) for the Severity of Dependence Scale using Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition khat use disorder diagnosis as criterion
Variables Associated with Khat Use Disorder

In Table 5, groups above and below these two cut-off values were compared using independent logistic regression models. These demonstrate that both of these cut-off points (SDS ≥ 3 for likely khat use disorder and SDS ≥ 5 for likely severe khat use disorder) are valid as they identify groups with substantially greater rates of behaviours suggesting heavier khat use (more frequent and greater volumes of use) as well as higher rates of experience of harms associated with their use (more financial problems, more cognitive problems, poorer quality of life, higher rates of mental health problems) and greater rates of help-seeking for khat use. While those classified above these cut-off points for likely caseness also had significantly higher rates of other substance use, this was typically still only a minority of the group (e.g. 10% reporting past six-month cannabis use) or of more common substances typically co-consumed in places where khat is also consumed (e.g. shisha). As such, as has been demonstrated previously (Duresso et al., 2016), it is not likely that this greater rate of polysubstance use has been the driving factor in group membership.

DISCUSSION

The purpose of the current study was to determine the efficacy of the SDS as a screening tool for khat use disorder. The Severity of Dependence Scale is a short, easily administered instrument for measuring psychological components of dependence, and is recognised as a robust screening tool across a variety of substances in diverse populations (Gossop, Best, et al., 1997; Gossop et al., 1995). In keeping with studies of similar substances (Ferri et al., 2000; Gonzalez-Saiz et al., 2008; Gossop et al., 1995; Kaye & Darke, 2002; Lawrinson et al., 2007), this study clearly supports the use of the SDS to screen for problems related to khat use.
Confirmatory factor analyses supported a unifactorial structure for the scale. This supports the use of a total scale score for the SDS, and is consistent with findings for the SDS in relation to methamphetamine (Topp & Mattick, 1997a) and khat (Kassim et al., 2010). There has been one recent study that identified two factors within the SDS items for khat, with two items (3 and 4 – worry about use and wish to stop) separating from the remainder (Nakajima et al., 2014). However, this was identified via exploratory techniques, and the fit indices identified here provide no good empirical rationale for the more complex model. Similarly, the DSM dependence/use disorder syndrome symptoms for both methamphetamine (Topp & Mattick, 1997a) and khat (Duresso et al., 2016) are unifactorial.

The ROC analysis suggests that a score on the SDS of 3 or more provides good sensitivity and specificity for possible cases of khat use disorder; this cut-off has demonstrated construct validity identifying a group with behaviours indicative of use disorder and greater rates of adverse consequences associated with use. While this value appears on the surface to be low, requiring only the most moderate of responses to three items, or a strong response to a single item, it is consistent with scores identified using the SDS to screen for cases of DSM-IV ecstasy dependence (Bruno, Gomez, & Matthews, 2011). Moreover, the optimal cut-off values for DSM-IV khat dependence are consistent with those identified for cannabis in adolescents (Martin, Copeland, Gates, & Gilmour, 2006).
Table 4: Diagnostic Efficiency of the SDS scores for DSM-IV and DSM-5 Khat use disorders. (Using DSM-IV and DSM-5 diagnosis as criteria)

<table>
<thead>
<tr>
<th>SDS Score</th>
<th>Sample Proportion Scoring (%)</th>
<th>DSM-IV Dependence</th>
<th>DSM-5 any KUD</th>
<th>DSM-5 Moderate KUD</th>
<th>DSM-5 Severe KUD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC=0.946 (95% CI=0.918 to 0.966)</td>
<td>AUC=0.924 (95% CI=0.894 to 0.949)</td>
<td>AUC= 0.958 (95% CI=0.934 to 0.976)</td>
<td>AUC= 0.942 (95% CI=0.915 to 0.964)</td>
<td></td>
</tr>
<tr>
<td>≥0</td>
<td>100.0</td>
<td>100.00</td>
<td>0.00</td>
<td>100.00</td>
<td>0.00</td>
</tr>
<tr>
<td>≥1</td>
<td>69.6</td>
<td>97.85</td>
<td>72.90</td>
<td>90.49</td>
<td>87.50</td>
</tr>
<tr>
<td>≥2</td>
<td>64.4</td>
<td>94.85</td>
<td>81.29</td>
<td>85.56</td>
<td>93.27^</td>
</tr>
<tr>
<td>≥3</td>
<td>60.3</td>
<td>92.27</td>
<td>87.74^</td>
<td>80.99</td>
<td>96.15</td>
</tr>
<tr>
<td>≥4</td>
<td>55.9</td>
<td>87.55</td>
<td>91.61</td>
<td>75.35</td>
<td>97.12</td>
</tr>
<tr>
<td>≥5</td>
<td>47.2</td>
<td>74.68</td>
<td>94.19</td>
<td>63.38</td>
<td>97.12</td>
</tr>
<tr>
<td>≥6</td>
<td>35.6</td>
<td>57.51</td>
<td>97.42</td>
<td>47.89</td>
<td>98.08</td>
</tr>
<tr>
<td>≥7</td>
<td>28.6</td>
<td>45.92</td>
<td>97.42</td>
<td>38.38</td>
<td>98.08</td>
</tr>
<tr>
<td>≥8</td>
<td>20.1</td>
<td>32.19</td>
<td>98.06</td>
<td>26.76</td>
<td>98.08</td>
</tr>
<tr>
<td>≥9</td>
<td>15.7</td>
<td>24.89</td>
<td>98.06</td>
<td>20.77</td>
<td>98.08</td>
</tr>
<tr>
<td>≥10</td>
<td>10.1</td>
<td>16.74</td>
<td>100.00</td>
<td>13.73</td>
<td>100.00</td>
</tr>
<tr>
<td>≥11</td>
<td>5.7</td>
<td>9.44</td>
<td>100.00</td>
<td>7.75</td>
<td>100.00</td>
</tr>
<tr>
<td>≥12</td>
<td>3.1</td>
<td>5.15</td>
<td>100.00</td>
<td>4.23</td>
<td>100.00</td>
</tr>
<tr>
<td>≥13</td>
<td>1.8</td>
<td>3.00</td>
<td>100.00</td>
<td>2.46</td>
<td>100.00</td>
</tr>
<tr>
<td>≥14</td>
<td>1.0</td>
<td>1.72</td>
<td>100.00</td>
<td>1.41</td>
<td>100.00</td>
</tr>
<tr>
<td>≥15</td>
<td>0.5</td>
<td>0.86</td>
<td>100.00</td>
<td>0.70</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Note. Sensitivity = % true positive; specificity = % true negative. The cut-off values in bold are for clinical screening and represent the lowest score within the 95% CI of maximum Youden that maximised specificity above 90% while maintaining sensitivity at approximately 80% or greater. Area under the ROC curve reflects the ability of the scale to discriminate between case and non-case; all values >0.8 = excellent discrimination. AUC = area under the curve; CI = confidence interval; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; KUD = khat use disorder; ROC = receiver operating characteristic; SDS = Severity of Dependence Scale. ^ Point at which Youden Index [(sensitivity + specificity) − 1] is maximised.
Consistent with the strong linear relationship between SDS items and DSM-5 symptom count, optimal cut-offs on the SDS increased steadily at each of the defined DSM severity levels (3 or more for any khat use disorder; 4 of more for moderate; 5 or more for severe). This SDS value for likely cases of severe DSM khat use disorder is consistent with that validated for screening for DSM(-III-R) amphetamine dependence (Topp & Mattick, 1997a). This spread of cut points on the scale may be useful for stepped level assessments and interventions, with, for example, individuals scoring 3 possibly optimally serviced by brief motivational interviewing interventions (Kaye & Darke, 2002); and those scoring 5 or above referred to more formal assessment and support interventions (Kassim et al., 2010).

Table 5: Correlates of DSM-5 khat use disorder according to SDS groupings (N=388)

<table>
<thead>
<tr>
<th>Items</th>
<th>DSM-5 khat use disorder</th>
<th></th>
<th>DSM-5 Severe khat use disorder</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screened negative</td>
<td>Screened positive</td>
<td>Screened negative</td>
<td>Screened positive</td>
</tr>
<tr>
<td></td>
<td>(SDS&lt;3)</td>
<td>(SDS≥3) n=234</td>
<td>(SDS&lt;5) n=205</td>
<td>(SDS≥5) n=183</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>OR (95%CI)</td>
<td>%</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>63.0</td>
<td>85.5</td>
<td>3.46 (2.12-5.63) ***</td>
<td>65.9</td>
</tr>
<tr>
<td>Age (≤24)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36.4</td>
<td>23.9</td>
<td>0.55 (0.35-0.86) **</td>
<td>35.1</td>
<td>21.9</td>
</tr>
<tr>
<td>Full time student</td>
<td>42.2</td>
<td>29.1</td>
<td>0.56 (0.37-0.86) **</td>
<td>42.4</td>
</tr>
<tr>
<td>Unemployed</td>
<td>10.4</td>
<td>12.8</td>
<td>1.27 (0.67-2.42)</td>
<td>10.7</td>
</tr>
<tr>
<td>Patterns of khat use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First used khat ≤16 years</td>
<td>10.4</td>
<td>16.7</td>
<td>1.73 (0.93-3.21)</td>
<td>11.2</td>
</tr>
<tr>
<td>Used khat for ≥5 years</td>
<td>77.3</td>
<td>83.8</td>
<td>1.52 (0.91-2.53)</td>
<td>78.5</td>
</tr>
<tr>
<td>Used khat daily in past 12 months (n=385)</td>
<td>7.2</td>
<td>53.6</td>
<td>14.84 (7.63-28.86) ***</td>
<td>14.9</td>
</tr>
<tr>
<td>Amount chewed per session</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used ≥1.5 bundles of khat per session in past 12 months</td>
<td>14.3</td>
<td>31.6</td>
<td>2.78 (1.64-4.71) ***</td>
<td>15.6</td>
</tr>
<tr>
<td>Chewing session duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 hours or more (n=382)</td>
<td>70.4</td>
<td>61.3</td>
<td>0.67 (0.43-1.03)</td>
<td>65.0</td>
</tr>
<tr>
<td>Other drug use in last six months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily alcohol (n=384)</td>
<td>0.7</td>
<td>12.4</td>
<td>21.32 (2.87-158.29) **</td>
<td>3.5</td>
</tr>
<tr>
<td>Daily tobacco (n=383)</td>
<td>5.9</td>
<td>35.2</td>
<td>8.70 (4.21-17.97) ***</td>
<td>10.8</td>
</tr>
<tr>
<td>High FTND b (n=385)</td>
<td>0.0</td>
<td>8.2</td>
<td>-</td>
<td>1.0</td>
</tr>
<tr>
<td>Any cannabis use (n=378)</td>
<td>2.6</td>
<td>10.2</td>
<td>4.19 (1.42-12.38) **</td>
<td>4.5</td>
</tr>
<tr>
<td>Any benzodiazepine use (n=382)</td>
<td>1.3</td>
<td>7.4</td>
<td>5.99 (1.36-26.30) *</td>
<td>3.0</td>
</tr>
<tr>
<td>Any shisha use (n=386)</td>
<td>21.4</td>
<td>51.7</td>
<td>3.93 (2.47-6.24) ***</td>
<td>25.5</td>
</tr>
<tr>
<td>Financial problems in last twelve months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spent money on khat meant for other things</td>
<td>59.1</td>
<td>85.9</td>
<td>4.22 (2.59-6.87) ***</td>
<td>61.5</td>
</tr>
<tr>
<td>Sold belongings to buy khat</td>
<td>13.6</td>
<td>58.1</td>
<td>8.79 (5.18-14.91) ***</td>
<td>18.5</td>
</tr>
</tbody>
</table>
Table 5: continued

<table>
<thead>
<tr>
<th>Items</th>
<th>Screened negative (SDS&lt;3)</th>
<th>Screened positive (SDS≥3)</th>
<th>Screened negative (SDS&lt;5)</th>
<th>Screened positive (SDS≥5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=154</td>
<td>n=234</td>
<td>n=205</td>
<td>n=183</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Worried about the amount of money spent on khat</td>
<td>20.1</td>
<td>67.9</td>
<td>8.41 (5.20-13.60) ***</td>
<td>26.3</td>
</tr>
<tr>
<td>Had khat related debts</td>
<td>14.3</td>
<td>60.7</td>
<td>9.26 (5.50-15.61) ***</td>
<td>21.5</td>
</tr>
<tr>
<td>Made excuses about money spent on khat</td>
<td>16.9</td>
<td>75.6</td>
<td>15.29 (9.12-25.63) ***</td>
<td>27.8</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access to treatment for khat</td>
<td>9.7</td>
<td>35.5</td>
<td>5.09 (2.81-9.25) ***</td>
<td>16.1</td>
</tr>
<tr>
<td>Mental health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K-10 ≥ 30</td>
<td>0.0</td>
<td>42.3</td>
<td>-</td>
<td>2.9</td>
</tr>
<tr>
<td>Self-reported mental health problem</td>
<td>2.6</td>
<td>48.7</td>
<td>35.63 (12.78-99.34) ***</td>
<td>10.2</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal wellbeing (PWI 2SD below mean)</td>
<td>20.9</td>
<td>72.1</td>
<td>9.77 (6.03-15.85) ***</td>
<td>30.5</td>
</tr>
<tr>
<td>Satisfaction with life (PWI 2SD below mean)</td>
<td>30.7</td>
<td>77.3</td>
<td>7.66 (4.84-12.14) ***</td>
<td>40.4</td>
</tr>
<tr>
<td>Academic function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble keeping attention on activity for too long (n=384)</td>
<td>29.6</td>
<td>88.8</td>
<td>18.84 (11.02-32.21) ***</td>
<td>43.1</td>
</tr>
<tr>
<td>Difficulty in organizing/scheduling routine tasks (n=384)</td>
<td>48.0</td>
<td>88.8</td>
<td>8.57 (5.11-14.38) ***</td>
<td>56.9</td>
</tr>
<tr>
<td>Trouble listening in lectures (n=384)</td>
<td>15.8</td>
<td>60.8</td>
<td>8.26 (4.97-13.75) ***</td>
<td>22.3</td>
</tr>
<tr>
<td>Trouble making study plans (n=384)</td>
<td>49.3</td>
<td>80.6</td>
<td>4.27 (2.71-6.72) ***</td>
<td>52.5</td>
</tr>
<tr>
<td>Spent lot of time doing nothing (n=384)</td>
<td>44.1</td>
<td>87.5</td>
<td>8.88 (5.37-14.70) ***</td>
<td>51.0</td>
</tr>
<tr>
<td>Unable to do two or three tasks in a row (n=384)</td>
<td>57.2</td>
<td>87.1</td>
<td>5.03 (3.05-8.30) ***</td>
<td>63.4</td>
</tr>
<tr>
<td>Trouble remembering things to do (n=384)</td>
<td>17.1</td>
<td>82.8</td>
<td>23.26 (13.52-40.02) ***</td>
<td>31.2</td>
</tr>
<tr>
<td>Don’t stick to tasks to completion (n=384)</td>
<td>33.6</td>
<td>86.2</td>
<td>12.38 (7.49-20.46) ***</td>
<td>45.5</td>
</tr>
<tr>
<td>Lack of attention (n=384)</td>
<td>23.0</td>
<td>86.6</td>
<td>21.68 (12.70-36.99) ***</td>
<td>39.1</td>
</tr>
<tr>
<td>Trouble with short term memory (n=384)</td>
<td>18.4</td>
<td>77.2</td>
<td>14.96 (8.96-24.96) ***</td>
<td>31.7</td>
</tr>
<tr>
<td>Difficulty sustaining concentration (n=384)</td>
<td>27.6</td>
<td>85.3</td>
<td>15.25 (9.17-25.37) ***</td>
<td>41.1</td>
</tr>
<tr>
<td>Lack of concentration on studies (n=384)</td>
<td>19.1</td>
<td>81.5</td>
<td>18.64 (11.05-31.45) ***</td>
<td>33.2</td>
</tr>
</tbody>
</table>

Note. CI = confidence interval; DSM - 5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; FTND = Fagerström Test for Nicotine Dependence; K - 10 = Kessler Psychological Distress Scale; OR = odds ratio; PWI = Personal Wellbeing Index; SDS = Severity of Dependence Scale. a Based on median split for the sample. b A score of 26 on FTND scale. c Scores on K - 10 30–50 indicating very high psychological distress derived from the K - 10 cut - offs that were used in the Australian National Mental Health and Wellbeing Survey (Australian Bureau of Statistics, 2008). d PWI cut - off is mean – 2SD (73.83) based on the generic normal ranges calculated by using the survey mean scores as data from 30 surveys conducted between April 2001 and August 2013. e Satisfaction with life cut - off is mean – 2SD (76.01) based on the generic normal ranges calculated by using the survey mean scores as data from 30 surveys conducted April 2001 and August 2013.

*p < .05. **p < .01. ***p < .001.
We consider the following as limitations of the present study. Firstly, participants were recruited using purposive sampling which necessarily increased the probability of involvement of frequent khat chewers with higher risk of khat use disorders. However, given that the purpose of the study was to determine the utility of the SDS in screening for khat use disorder, this bias away from representativeness to a more heavily consuming sample actually facilitated achieving the aims of this work. Secondly, as the results were completely based on self-reported data, there may be some degree of recall bias and susceptibility to social desirability of responses. However, since we maintained anonymity through the use of self-administered questionnaire, we believe that response bias was significantly minimized. Finally, AUDADIS-IV used in this study might have not validly identified cases of khat use disorders. However, recent results of a related study have revealed that the modified AUDADIS-IV does validly identify cases of Khat Use Disorders and individuals experiencing problems (e.g. Duresso et al., 2016).

CONCLUSION

Considering the findings for the SDS in relation to similar drugs, it is apparent that, while the scale appears universally applicable as a brief screening tool, cut-off values differ across substance types and require independent identification. A cut-off value of 3 or greater on the SDS provides high sensitivity and specificity for the presence of DSM-5 khat use disorder and identifies a group of consumers with higher quantity and frequency of use and experiencing substantially greater harms in association with their use of khat. Hence, consistent with earlier studies (Kassim, Islam, & Croucher, 2011), the simple, one minute screen provided by the SDS can provide a useful tool in research for identifying individuals with probable use disorders; and in primary care as a means of identification of most appropriate interventions in a stepped care context and that such services still need to be developed and delivered.
REFERENCES


Chapter 3: Using the Severity of Dependence Scale to Screen for DSM-5 Khat Use Disorder.


Chapter 3: Using the Severity of Dependence Scale to Screen for DSM-5 Khat Use Disorder.


4

Stopping Khat use: Predictors of Success in an Unaided Quit Attempt

Samson W. Duresso, Raimondo Bruno, Allison J. Matthews, Stuart G. Ferguson
School of Medicine, University of Tasmania, Hobart, Australia

Abstract

Introduction and Aims. Despite the adverse effects of khat use and chewers interest in cessation, there are few studies that have reported on the outcome of khat cessation attempts, and limited resources available for potential quitters. We used electronic diaries to monitor the outcomes of an unassisted quit attempt among daily and near daily khat consumers and examine predictors of success.

Design and Methods. Sixty participants between the ages of 18 and 35 years who regularly chewed khat and who were attempting to quit were purposively recruited from an Ethiopian University campus. Real-time prospective daily recording of khat use was obtained for an average of 10 days prior to quit day (range 6–13) and 28 post-quit days (range 9–31), using an electronic diary.

Results. Almost all (95%) achieved initial abstinence. Of these, 80% reached at least seven continuous days of abstinence; 7% maintained continuous abstinence for 28 days post-quit. While 93% lapsed (average 11 days post-quit, SD = 7), only a smaller proportion relapsed (41%: chewed for at least three consecutive days after at least 5 days of abstinence). Among the three variables considered, only quantity of khat use predicted continuous abstinence.

Discussion and Conclusions. Regular khat chewers have difficulties in maintaining abstinence despite having motivation and desire to quit. This implies that treatment aids may be needed to assist chewers’ in their quit attempts. Controlled experimental trial through the use of available low cost quit aids and behavioural resources is crucial in order to increase success rates for those seeking to desist from khat use.
Key words: khat abstinence, lapse, relapse, unassisted quit attempt.

INTRODUCTION:

Khat (Catha edulis) is a plant whose leaves contain cathinone and cathine, which produces stimulant effects analogous to amphetamine (Nencini & Ahmed, 1989). In Ethiopia, the chewing of khat for religious and recreational purposes is a deep rooted socio-cultural tradition (Kalix & Braenden, 1985). It is valued for stimulant effects and usually chewed in company to facilitate social interaction (Kalix & Khan, 1984) and to enhance work performance (Elmi, 1983). A 2011 population prevalence study estimated use at 15.3% across Ethiopia (Males: 22.6%; Females: 9.1%).

Khat use is associated with a variety of psychological and behavioural changes. The most common subjective effects of the initial stage of khat chewing include increased motor stimulation, euphoria, and a sense of excitement and energy (Nencini, Fraioli, Pascucci, & Nucerito, 1998; Widler, Mathys, Brenneisen, Kalix, & Fisch, 1994). Chewers also report improvement in the ability to communicate and subjective excellence in work performance (Cox & Rampes, 2003). Conversely, later after chewing ceases, unpleasant after-effects such as insomnia, numbness, poor concentration and low mood tend to dominate the experience. Higher potency khat consumption may also induce unpleasant acute effects, such as anxiety, tension, and restlessness (Cox & Rampes, 2003).

Importantly, khat users experience symptoms of dependence (Duresso, Matthews, Ferguson, & Bruno, 2016). Ingestion of khat is self-limiting, but chronic use seems to be associated with poorer mental health (Kalix & Braenden, 1985). Chewers may experience a range of symptoms from minor unpleasant after-effects such as low mood and poor concentration to more significant problems like insomnia, anxiety, irritability, depression, aggression, and restlessness (Duresso et al., 2016; Odenwald et al., 2007; Pantelis, Hindler, & Taylor, 1989).
It is not surprising, therefore, that many users express a desire to quit, or at least reduce, their khat consumption (Alsanusy & El-Setouhy, 2013).

Despite the negative consequences of khat use and consumer interest in cessation, there are a dearth of studies reporting on the outcome of khat cessation attempts, and few cessation resources available for potential quitters (Alsanusy & El-Setouhy, 2013). Most consumers describe easy access to khat and social pressure as major factors for continued khat use, and others acknowledged long leisure times with little to do as an interfering issue in their attempts to remain abstinent (Alsanusy & El-Setouhy, 2013). While there is a small literature examining pharmacological aids for ceasing khat use (Giannini, Miller, & Turner, 1992; Giannini & Nakoneczie, 1995), there are reports of successful quitting without medical interventions. As little is known about the nature of khat dependence, here we describe the outcomes of unassisted khat cessation among 60 khat users who were motivated to quit.

METHODS

Participants

Sixty participants (3 recent graduates and 57 under graduate students) who were attempting to quit khat were recruited through advertisement and fliers in and around Adama Science and Technology University campus (Ethiopia). While the inclusion criteria included regular habit of khat chewing, at minimum of 3 days per week, for 2 years by self-report and high motivation and overall interest to quit chewing during the study quit periods, the exclusion criteria, on the other hand, included current significant medical condition, current diagnosis of a significant psychiatric disorder, as indicated on the MINI International Neuropsychiatric Interview, history of alcohol or drug abuse or dependence disorder or use of alcohol at hazardous or harmful levels, evident via a score of 16 or higher on the AUDIT, current regular
tobacco use (self-reported), and current use of a contraindicated prescription or psychotropic medications (self-reported). The Tasmania Human Research Ethics Network granted approval for the study (#HO013347), with additional local ethical clearance obtained from Ministry of Education via Adama Science and Technology University in Ethiopia.

**Procedure**

After obtaining informed consent, participants were trained on the use of the Electronic Dairy (ED). The EDs were 10 Android-based smartphones (LG© P500) running customisable software (HBART; http://www.utas.edu.au/health/research/groups/behavioural-and-situational-research-group-bsrg/hbart), which were provided by University of Tasmania. These devices were provided to participants for the duration of the study. At the completion of the study, participants returned their device, the participant data removed, and the device was then used for subsequent participants; in this way, the 10 individual units were used across the entire cohort of participants. This software was specifically developed for real-time data capture and has been used in numerous previous studies across a range of behaviours (Peacock, Cash, Bruno, & Ferguson, 2015; B. Schuz, Schuz, & Ferguson, 2015; N. Schuz, Walters, Frandsen, Bower, & Ferguson, 2014). Subjects were trained to use the ED to report every instance of khat chewing during the monitoring period. Similar to previous smoking studies using the methods of ecological momentary assessment (EMA) (Shiffman et al., 1997; Shiffman & Ferguson, 2008; Shiffman et al., 2006), the ED was designed to issue random prompts for assessments 4-7 times a day. During both chewing and random assessments, participants reported their current mood and social context. Participants monitored their chewing on the ED for 10 (M=10.8; SD=1.2) days prior to cessation and met with the researcher in three study visits, scheduled on the second, fifth and tenth days after the initial screening visit. During study visit 1, the information sheet was read, consent forms were
signed, participants were enrolled in database, baseline surveys were conducted, EMA booklets were handed out, the phones (EMA devices) were set up, phones chargers were provided, and the next appointments were booked. During visit 2, EMA data was downloaded, compliance was checked, additional training if needed was provided, participants were instructed to monitor chewing for 10 consecutive days and the next appointment was booked. During the third visit, the day before quit day, subjects were instructed to quit chewing the next day (target quit day, TQD). The first actual full day of abstinence (i.e. no chewing for 24 hours) was labelled the quit day.

Total monitoring ranged from 20 to 44 days, with an average of 34.7 (SD=6.7) days, close to the intended 38 days. Post-quit monitoring continued for up to 4 weeks after cessation (M=24.0, SD=6.5) with an additional four visits scheduled approximately weekly. During visits 4 - 6, EMA data was downloaded, compliance was checked, participants were instructed to quit chewing for the next four weeks and the next appointment was booked. During the last visit, EMA data was downloaded, phone and charger were collected, participants were debriefed, and experiences were shared. All participants were reimbursed AUD 63.00 which is equivalent to ETB 950.00 for seven study visits.

**Outcome measures**

The focus of this study was primarily descriptive, examining the outcomes of an unassisted quit attempt by regular users with a desire to discontinue use. Correlates of success were solely a secondary aim and the numbers of variables examined were constrained given the substantial burden of participation already placed on participants through use of the prospective data collection approach.
Regardless, the three predictors of success (gender, amount of khat and psychological distress) examined as secondary aims were based from an examination of what little is known about dependent khat use. In Ethiopia, the use of Khat (current and lifetime) is significantly higher among males than female and males are more likely to continue chewing in their life time than females (Wedegaertner et al., 2010; Zein, 1988). It has been indicated that chewers who either use a larger amount of khat per chewing session or consume additional stimulants like caffeine and nicotine might find it difficult to minimize use or succeed in quit attempts (Mihretu, Teferra, & Fekadu, 2017). Some findings have also suggested that some individuals engage in khat chewing in order to get relief from symptoms of mental distress such as depression and anxiety which may indicate an association between mental distress and continued khat chewing (Wedegaertner et al, 2010).

Outcome analyses were based on participants’ reports of khat chewing on the ED and the Time Line Follow Back (TLFB) survey. All participants had calendar like note books for the full period of assessment to record their daily khat chewing activity in addition to the ED. All interviews and surveys, including the EMA surveys, were conducted in English. Three different outcome milestones as adapted from previous studies on cigarette use were used in the analysis (Shiffman et al., 2006). Since no definitions of abstinence currently exist for khat use, we adapted established outcomes from the smoking cessation literature. Initial abstinence was defined as 24 hours without khat chewing based on ED diary entries. Khat abstinence was defined as no use of khat in the last 7 days and continuous abstinence was defined as no chewing since TQD. Individual monitoring days were considered abstinence days only if both EMA and TLFB data both indicated no chewing. This occurred for 34 out of 59 cases. When dates of no chewing varied between EMA and TLFB data (for 25 out of 59 cases), we selected the EMA quit date if EMA compliance was acceptable (15 of 25 cases). Conversely, if
compliance was poor, we selected the TLFB quit date (10 of 25 cases). The same procedure was used for deciding the lapse and the relapse dates. Initial lapse was the first episode of any amount of khat chewing after initial cessation or during post quit period. Relapse was a resumption of regular chewing at least for three consecutive days after five days without khat. Lapse date variations between TLFB and EMA data, with 4 (7%) participants not lapsing was 5/55 (8%). For 3 participants compliance was acceptable and the EMA date was considered as actual lapse date. For the remaining 2 participants the lapse date was based on TLFB data. With regard to dates of relapse, there were 10 variations out of 25 (17%) instances of relapse, with 34 (57%) participants not relapsing. Four out of ten had acceptable compliance; hence EMA data was set as actual relapse date. For the remaining 6 participants, EMA data compliance was poor and TLFB data was taken as actual relapse date.

RESULTS

Demographic Characteristics:

At baseline, participants reported a variety of demographic measures, including gender, age, years of education completed, typical khat consumption quantity and frequency, prior quit attempts, and psychological distress (K-10) (Andrews & Slade, 2001). Out of 59 eligible participants, 5% (n=2) were recent University graduates and the remaining 95% (n=57) were all university under graduate student (year I–Year III). Participant mean age was 24.8 years (range 20-32; SD=2.8), and predominantly male (n=45, 75%). One-quarter were chewing daily and 38% were chewing near daily (six days per week); when participants used khat, the majority consumed 1 bundle (approximately 100-200gm of leaves; n=44, 73.3%), with the remainder using 1.5 bundles (n=16, 27%). The majority had made prior quit attempts (n=42, 70%), maintaining abstinence on average for 10 weeks (SD=4.0). None of the chewers had current significant medical disorders or history of severe mental illnesses. Scores on the
Alcohol Use Disorders Identification Test (AUDIT) (Babor, 2001) suggested the absence of significant alcohol-related problems (mean=13.3, SD=1.2, range 11-15). All participants reported episodic tobacco smoking, but scores on the Fagstrom Test for Nicotine Dependence (FTND) (T. F. Heatherton, L. T. Kozlowski, R. C. Frecker, & K. O. Fagerstrom, 1991) suggested low dependence (mean=0.90; SD=0.72, range 0-2). No participants screened positively for high psychological distress (≥ 30) on the Kessler Psychological Distress Scale (K-10), with the majority in the well (35%) or mild (58%) range.

**Outcomes**

Table 1 presents the proportion of participants reaching each endpoint. Nearly all reached the target quit date and achieved initial abstinence. Only one participant did not achieve abstinence and dropped out after 6 days of monitoring. One half of chewers quit on the Target Quit Date (TQD) (33, 56%), and the remainder achieved abstinence after (20%) or prior (24%) to TQD. By implication those who failed to achieve abstinence on the TQD were assumed to have chewed on that day. Seven-day abstinence was achieved by 80% of participants.
Table 1: Proportion of participant reaching each endpoint (N=60) \(^a\).

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>% (n)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reached Target Quit Day</td>
<td>98.3% (59)</td>
<td>91.1-99.7</td>
</tr>
<tr>
<td>Achieved Initial Abstinence</td>
<td>96.6 % (57)</td>
<td>88.4-99.0</td>
</tr>
<tr>
<td>Lapsed</td>
<td>93.2% (55)</td>
<td>83.8-97.3</td>
</tr>
</tbody>
</table>

28-day outcomes (n=59)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>% (n)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-day PP Abstinence</td>
<td>79.7% (47)</td>
<td>67.7-88.0</td>
</tr>
<tr>
<td>Continuous Abstinence</td>
<td>6.8% (4)</td>
<td>2.7-16.2</td>
</tr>
<tr>
<td>Relapsed</td>
<td>40.7% (24)</td>
<td>29.1-53.4</td>
</tr>
</tbody>
</table>

\(^a\) Initial abstinence, 24 h time without chewing; lapse, chewed after initial abstinence based on the denominator of subjects who quit (n = 59); 7-day abstinence, abstinence for the preceding 7 days based on the denominator of subjects who quit (n = 59); continuous abstinence, no chewing since TQD based on the denominator of subjects who quit (n = 59); relapse, resumption of regular chewing at least for three consecutive days after 5 days without khat based on the denominator of subjects who quit (n = 59). CI, confidence interval.

Among the 59 participants who achieved initial Abstinence 93% lapsed. Days to lapse ranged from 2 to 25 days (M=11.0, SD=6.9). With regard to relapsing, 41% of those who quit chewing relapsed and only 7% of the participants maintained continuous abstinence throughout the study period. We examined sex, quantity of use and psychological distress (K-10) as predictors of successful quit attempts. As age did not vary substantially it was not considered as a predictor variable. Among the three variables considered, only quantity of khat use predicted continuous abstinence (Table 2).
Table 2: Demographic correlates of khat abstinence

<table>
<thead>
<tr>
<th></th>
<th>Initial Abstinence a</th>
<th></th>
<th>Yes (n=57; 96.7%)</th>
<th></th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>%</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Male b</td>
<td></td>
<td>50.0</td>
<td>75.4</td>
<td>3.26</td>
<td>(0.19-5.55)</td>
</tr>
<tr>
<td>Khat in bundle (1.5) c</td>
<td></td>
<td>25.0</td>
<td>28.1</td>
<td>0.82</td>
<td>(0.08-8.48)</td>
</tr>
<tr>
<td>K10 d</td>
<td></td>
<td>75.0</td>
<td>63.2</td>
<td>1.74</td>
<td>(0.17-17.73)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Seven Days Abstinence</th>
<th></th>
<th>Yes (n=47; 79.7%)</th>
<th></th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n=12; 20.3%)</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td></td>
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<tr>
<td>Male b</td>
<td></td>
<td>58.3</td>
<td>78.7</td>
<td>0.39</td>
<td>(0.10-1.45)</td>
</tr>
<tr>
<td>Khat in bundle (1.5) c</td>
<td></td>
<td>7.1</td>
<td>34.7</td>
<td>0.14</td>
<td>(0.02-1.20)</td>
</tr>
<tr>
<td>K-10 d</td>
<td></td>
<td>75.0</td>
<td>61.7</td>
<td>0.54</td>
<td>(0.13-2.25)</td>
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<table>
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<tr>
<th></th>
<th>Continuous Abstinence a</th>
<th></th>
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<th></th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n=55; 93.2%)</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Male b</td>
<td></td>
<td>72.0</td>
<td>83.3</td>
<td>1.95</td>
<td>(0.21-18.03)</td>
</tr>
<tr>
<td>Khat in bundle (1.5) c</td>
<td></td>
<td>22.8</td>
<td>83.3</td>
<td>0.06*</td>
<td>(0.01-0.55)</td>
</tr>
<tr>
<td>K10 d</td>
<td></td>
<td>63.6</td>
<td>75.0</td>
<td>1.71</td>
<td>(0.17-17.6)</td>
</tr>
</tbody>
</table>

*P < 0.05. None of these are statistically significant other than those for the continuous abstinence – and that analysis should be interpreted with caution given the relatively small n. aNeither the initial or continuous columns have enough power to be able to identify relationships. bMales in each outcome. cRate of people that used large amounts of khat (1.5 bundles or greater per session). dPeople with psychological distress (K-10 scores >=30). CI, confidence interval; OR, odds ratio.

DISCUSSION

In our study, we describe unassisted chewing cessation outcome data in terms of three outcome endpoints. Although a majority of the participants maintained initial and 7-day abstinence, most relapsed within 11 days post quit and very few were able to maintain abstinence throughout the study period. Those who maintained continuous abstinence were not assessed after the study period and could have resumed chewing. In addition, with the exception of quantity of khat consumed, none of the demographic variables examined predicted successful abstinence. Quantity of khat consumed in bundles was statistically significant only for the continuous abstinence group (participants who did not chew throughout the study post-quit period), indicating that those in the continuous abstinence group, who usually consumed one and half bundle or more of khat per session, were likely to maintain abstinence (compared to those who are in the continuous abstinence group but consumed one bundle or less of khat leaves). This finding is somewhat puzzling, as the direction of the association is opposite to

Chapter 4: Stopping Khat use: Predictors of success in Unaided Quit Attempt.
what we would expect based on work in other substances of addiction. It is possible that the heavier users in our study were more committed to quitting, or that other factors explain this discrepancy. However, given the small sample size, we feel that is important to replicate this finding before speculating on the cause of the association; it is entirely possible that this pattern will not be observed in a larger study. Although this may partially reflect low power that potentially limits the ability to identify particular predictors of quit success, this may imply that irrespective of their demographic and situational backgrounds, chewers may need assistance in their attempt to quit chewing, through the provision of behavioural resources and drug treatment. A 12-step self-help group approach has demonstrated a reduced substance use and improved outcomes among stimulant consumers (Donovan & Wells, 2007). Considering this approach as a treatment process for khat abuse could be effective since it may provide low-cost options and may be easy to organize as khat chewing is social by its nature.

This study has some limitations. First, due to the pilot nature of the study this was conducted on only a small sample of university students who used khat regularly, and results may not be generalizable to a larger population. Secondly, the lack of urine screening for verification of abstinence and relying merely on self-reported abstinence was also a limitation; but given that this is the very first study of quit attempts, it is a strength that this was done using prospective recording with ED. Thirdly, outcome variables selected from related smoking cessation literature—especially the criteria of 24 h of cessation for initial abstinence—may not be perfect fit for this specific drug. Similarly, while short-term cessation has been found to predict long-term success (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991), our follow-up duration was relatively brief; further studies are required to determine whether the observed outcomes are maintained over time. And finally, although it is very unlikely that the act of having the study participants set their quit provided assistance in terms of aiding their quit
attempts, we cannot absolutely rule out the possibility that our EMA monitoring procedures could have influenced the outcomes observed. However, considering the scarcity of research findings in this area the current findings undeniably shed light on this matter of substantial concern.

CONCLUSION

Despite khat being a culturally acceptable and legal substance in the country, it is noted that some people do develop problems from use (Duresso et al., 2016) and that even motivated individuals have difficulties maintaining abstinence. It is vital therefore that there is clinical attention made to identifying applicable supports for people to quit chewing. The findings of the present study examining unaided quit attempts may also inform the design of controlled experimental trials to examine the effectiveness of low cost quit aids and behavioural resources for khat that would work in the Ethiopian context in helping quitters successfully maintain abstinence.
REFERENCES

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Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Samson W. Duresso, Raimondo Bruno, Allison J. Matthews, Stuart G. Ferguson

School of Medicine, University of Tasmania, Hobart, Australia

Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Abstract

Research reports show increased prevalence of habitual khat chewing among various parts of the community in Ethiopia. Some users experience problems controlling their use; withdrawal symptoms may be adding to difficulties with reducing or ceasing use. We aimed to describe the nature and the time course of any withdrawal syndrome in relation to the cessation of khat use over the first 2 weeks of a quit attempt.

Fifty-nine participants between the ages of 18 and 35 and who have already chewed ≥1 bundle of khat in their life with a chewing frequency of ≥3 days per week were recruited from Adama Science and Technology University campus. Participants were predominantly male (n = 45, 75%) and had the mean age of 24.8 years (range = 20–32; SD = 2.8).

Participants used smart phones to monitor withdrawal symptoms and cravings. The total assessments were divided in to 3 pre-quit and 14 post-quit days. The development of withdrawal symptoms was evident, and all withdrawal symptoms followed similar overall patterns, with salient elevations after the quit day and curvatures around the first week of post-quit period.

Depression, craving, nervousness, tiredness, restlessness, poor motivation, irritability, and negative affect substantially increased and reached peak on the first week around Day 7 and remained higher compared with the level at baseline indicating the persistence and severity of these symptoms over time. In addition, craving, irritability, and restlessness had significantly reverted to their baseline level during the second week of the post quit duration. We have demonstrated low rates of success during unaided quite attempts from khat and that the withdrawal
syndrome is not trivial. Interventions are necessary to support individuals during the period of increased symptoms of dysphoria and to reduce the risk of relapse.

Keywords: khat withdrawal, khat abstinence, negative affect, craving, positive affect
Research indicated that world-wide, tens of millions of people are estimated to consume khat on a daily basis (Stefan & Mathew, 2005). Global spread of khat use is largely attributed to easy air transportation for khat export and migration of people from East African countries (such as Somalia, Ethiopia, Kenya, etc.) and Yemen to the UK and other Western countries (Griffiths et al., 2010; Stevenson, Fitzgerald, & Banwell, 1996). In Ethiopia, Khat is habitually consumed by craftsmen, farmers, and laborers, and also academics and students (Adugna, Jira, & Molla, 1994; Alem, Kebede, & Kullgren, 1999; Ayana & Mekonen, 2004; Ayenew, Tadesse, & Azale, 2012; Cox & Rampes, 2003; Ihunwo, Kayanja, & Amadi-Ihunwo, 2004). A 2011 population prevalence study estimated past month use at 15.3% across Ethiopia (22.6% among males; 9.1% among females). Among Ethiopian university students, lifetime prevalence was estimated at 24.0%, while 7.7% reported past month khat use (Gebrehanna, Berhane, & Worku, 2014).

Khat (Catha edulis) is a plant with psychostimulant effects from its most active constituents, cathinone and cathine, which are structurally similar to amphetamine (Nencini, Ahmed, Amiconi, & Elmi, 1984). While cathinone is the most active ingredient of khat, cathine has a milder and short-lasting psychostimulant action and plays only a minor role in the effects of khat. It is believed that cathine is responsible for unwanted adverse effects of the drug, such as feelings of low mood and sluggishness (Cox & Rampes, 2003). Symptoms of increased alertness, dependence and adverse psychiatric events can arise due to the effects of khat on the central nervous system (Kalix & Braenden, 1985).
Consumers report that khat is chewed to increase mental alertness; to prevent sleepiness and overcome physical fatigue (Alem et al., 1999; Ayana & Mekonen, 2004). Reports show increased prevalence of khat chewing among various parts of the community in Ethiopia (Alem et al., 1999; Ayenew et al., 2012). Khat is used habitually by craftsmen, farmers and laborers during physical work. University instructors (Ihunwo et al., 2004) and large proportions (64.9% current prevalence) of secondary and higher education students also regularly chew khat (Adugna et al., 1994; Cox & Rampes, 2003; Ihunwo et al., 2004). Students report chewing khat with the aim of gaining concentration and focus and to reduce fatigue (Ayana & Mekonen, 2004).

One of the major issues with regard to chronic drug use is the occurrence of withdrawal symptoms and craving related to the discontinuation of use after long time exposure or habitual and prolonged consumption. In Ethiopia, while few khat chewers (0.6%) reported having continued to chew to prevent withdrawal symptoms (Alem & Shibre, 1997), most chewers (46%) wanted to stop khat chewing and have tried to give up chewing, with nearly half of them (21%) resuming chewing because of dependence and the social interaction associated with khat chewing (Yussuf, Asquith & Ali, 2007). Diagnostic and Statistical Manual (DSM) criteria suggest that the withdrawal syndrome for psychostimulant drugs encompasses dysphoric mood and symptoms such as fatigue, vivid or unpleasant dreams, insomnia or hypersomnja, increased appetite and psychomotor retardation or agitation (American Psychiatric Association, 2000).

Despite conflicting opinions regarding the existence of dependence in relation to khat use, there is accumulating evidence indicating the presence of a withdrawal syndrome, craving, and a degree of tolerance related to chronic khat chewing (Cox & Rampes, 2003). Physical withdrawal
symptoms and craving have been documented, including lethargy, anergia, and nightmares, which appear several days after ceasing to chew (Giannini & Castellani, 1982). Depressive moods, psychotic symptoms, drowsiness and hypotension are sometimes seen after discontinuation of khat, and khat chewers often continue to use the drug in order to avoid the withdrawal symptoms (Alem et al., 1999; Widmann et al., 2017). In support of this, a recent finding (Duresso, Matthews, Ferguson, & Bruno, 2016) indicates the presence of withdrawal symptoms and craving and suggests that many regular khat chewers experience at least one clinically significant withdrawal symptom and 28% meet core requirements for stimulant withdrawal (concurrent dysphoria plus two other symptoms, severe enough to cause distress). Among the common symptoms were dysphoria, insomnia/hypersomnia and psychomotor agitation/retardation.

In summary, chronic khat chewers often experience problems controlling their use and report withdrawal symptoms during periods of abstinence, and the experience and severity of withdrawal symptoms may be a significant barrier to cessation/reduction of problem drug use (Shoptaw, Kao, Heinzerling, & Ling, 2009). Most theories of dependence have posited that continued drug use is, at least in part, driven by withdrawal symptom avoidance and addressing withdrawal is a key component of many treatments (Shoptaw et al., 2009). There is substantial evidence that negative affect interacts with arousal in predicting craving and potential relapse (Dunbar, Scharf, Kirchner, & Shiffman, 2010). While the presence of symptoms of withdrawal has been identified in relation to khat in retrospective surveys, there have been no studies to date identifying the time course of their severity prospectively. The present study aimed to examine the time course of development and reduction of withdrawal symptoms (craving, negative affect, arousal, depression,
nervousness, irritability, restlessness, tiredness/fatigue, and poor motivation) over the first 2 weeks of a quit attempt.

**Methods**

**Participants**

Sixty participants were recruited mostly through online advertisements on social media and leaflets distributed at Adama Science and Technology University campus. To be eligible, interested applicants were required to demonstrate high motivation and overall interest to quit chewing during the study quit periods and to have a chewing frequency of at least one bundle of khat leaves for $\geq$ 3 days per week over the past 12-month duration. All participants had demonstrated khat dependence by self-report and Mini International Neuropsychiatric Interview (MINI) screen and reported high motivation to quit chewing. Participants were reimbursed ETB 950.00 (approximately USD $47) for a total of seven study visits.

**Materials**

Affective factors and energy level were assessed by using 17 items: focus, alert, angry/frustrated, loss of interest, excited, tired, passive, poor concentration, poor memory, happy, irritable, poor motivation, nervous/anxious, drowsy/sleepy, restless, depressed, and arousal (visual analog scales [VAS] anchors: 0 _ “No!!,” 100 _ “Yes!!”) derived from the circumplex model of affect (Shiffman, Ferguson, Gwaltney, Balabanis, & Shadel, 2006). Individual adjectives (e.g., “depressed”, “restless”) were presented on the screen one at a time. Ten items were used to form two factor scores: specifically, negative affect and arousal. The 10 items that were used to form the two factors were focus, alert, excited, passive, drowsy/sleepy, poor concentration, and poor memory, which formed *arousal factor scores* and angry/frustrated; loss of interest and happy (reverse).
formed *negative affect factor scores*. In addition, we reported the results from seven individual items (in addition to arousal and negative affect). These 7 items were selected as relating to the DSM stimulant withdrawal symptoms, as this was the topic of the paper. Craving was assessed on a single VAS item with anchors of 0 = “No!!” 100 = “Yes!!”.

**Procedures:**

The current study was the first to use Ecological Momentary Assessment (EMA) Techniques in a naturalistic context (Ferguson & Shiffman, 2011) to examine khat cravings and withdrawal syndrome among chronic khat users. Informed consent was obtained from each participant before providing training on the use of an electronic diary (ED) and on how to report every instance of khat chewing, withdrawal symptoms, and cravings during the monitoring period. Assessments were completed in English as there was no need to translate the survey into Amharic (native language), given the participants in our study were university graduates and students. Moreover, all participants were given enough training during enrolment sessions on the nature of the survey items, the psychological constructs and on how to use the EMA devices and complete the survey electronically.

Similar to previous smoking studies using ecological momentary assessment (Shiffman et al., 1997; Shiffman & Ferguson, 2008; Shiffman et al., 2006; Shiffman, Scharf, et al., 2006), in addition to participant-initiated data collection when khat was consumed, the ED was also designed to issue random prompts for assessments 4–7 times a day during waking hours. Both event and time sampling strategies were used in this study. Withdrawal scores collected on the three days prior to the quit date were averaged to form the baseline data. Data collected 24hr after
the actual quit day (Day 1) was used as 24-hr. point in time. Data collected on the seventh day post-quit was used as Day 7 time point whereas the data collected on the fourteenth day was considered as Day 14 time point. The points in time were chosen based on the evidence from previous research that withdrawal symptoms, including cravings, are likely to manifest within 24 hr, to reach peak at about the first week and decline around the second week and thereafter, which could provide sufficient evidence to quantify severity of withdrawal and compare the measures accordingly (e.g., nicotine withdrawal; Van Zundert, Boogerd, Vermulst, & Engels, 2009).

During both chewing random assessments, participants recorded their chewing status and current mood and social context. Participants monitored their chewing and related feelings on the ED for 10 (M = 10.8; SD = 1.2) days prior to cessation and met with the researcher in three study visits, scheduled on the second, fifth and tenth days after the initial screening visit. Each of the seven visits lasted on average 30 min. During study visit 1, the information sheet was read, consent forms were signed, participants were enrolled in database, and baseline surveys were conducted, EMA booklets were handed out, the phones (EMA devices) were set up, phones and chargers were provided, and the next appointments were booked. During visit 2, EMA data was downloaded, compliance was checked, additional training if needed was provided, participants were instructed to monitor chewing for 10 consecutive days and the next appointment was booked. During the third visit EMA data was downloaded, compliance was checked, and participants were instructed to quit chewing the following day (target quit day, TQD). Post-quit monitoring continued for up to 4 weeks after cessation (M =24.0, SD = 6.5) with an additional four visits scheduled approximately weekly. During visits 4 – 6, EMA data was downloaded, compliance was checked, and participants were instructed to quit chewing for the next four weeks and the
next appointment was booked. The first actual full day of abstinence (i.e., no chewing for 24 hr) was labeled as actual quit day. The Tasmania Human Research Ethics Network granted approval for the study (#H 0013347), with additional local ethical clearance obtained from Adama Science and Technology University.

**Data reduction and analytic plan**

Eligible subjects for analyses must have provided baseline data; reported khat abstention on the scheduled quit date and abstained from chewing for the first 24 hr. of their quit attempt. Additionally, while eligible participants were encouraged to maintain khat abstinence over the course of the study, this was not possible for many, and to obtain clean withdrawal measurements uncontaminated by days with any use of khat, we abandoned days of monitoring where any participant used khat during post-quit days. While 80% of participants achieved 7-day abstinence, less than a third (32%) maintained 14-day abstinence. We also plotted withdrawal symptoms separately for those who lapsed (68%) and those who did not (non-lapsers; 32%) and the results demonstrated that there were no substantial differences in the trends of withdrawal syndromes between the non-lapser and lapser groups (Supplemental material Figure S1).

Baseline ad libitum chewing data were collected from random prompts and khat use reports. Participants were instructed to chew ad libitum during the first 10 days of pre-quit monitoring. However, while 56% of participants reached 24-hr abstinence on the target quit day, 20% quit between Day 11 and Day 12. The remaining participants (24%) reached 24-hr abstinence a day before the target quit day. Only one participant dropped out 4 days prior to the target quit day and was hence not included in any analyses. Data was centered on actual quit day. EMA data were
collected from a total of 3,913 random prompts during both periods of abstinence and use (M = 3 random prompts per day, SD = 1.5).

While monitoring was conducted for approximately 28 days post-quit, 40 (68%) had lapsed or relapsed after 14 days post-quit day. As such, for the description of withdrawal symptom severity over time, only 14 days post-quit was included in analyses and for any day in which a participant reported chewing khat, all symptoms were removed from analysis for (only) that day. To determine the presence of specific changes in symptom severity between baseline, acute withdrawal (24-hr post-quit) and changes over time (7 and 14 days), we employed mixed models for repeated measures analyses using AR (1) covariance matrix to compare symptom endorsement from each of these time points. This procedure allowed us to include cases where we have incomplete data for this series of analysis (Table 2). The figures were constructed using least squared (LS) means generated from mixed models for repeated measures.

**Results**

**Substance Use Profile of Participants**

Of the 59 participants contributing data during periods of both use and abstinence, mean age was 24.8 years (range 20–32; SD = 2.8), and were predominantly male (n = 45, 75%). One-quarter were chewing daily and 38% were chewing near daily (M = 5.7; SD = 1.1; range = 4 – 7) when participants used khat, the majority consumed 1 bundle (approximately 100–200g of leaves; n = 44, 73.3%), with the remainder using 1.5 bundles (n = 16, 27%). Mean khat consumption was 1.3 (SD = 0.4) bundle of khat leaves per session. The majority had made prior quit attempts (n = 42, 70%), maintaining abstinence on average for 7.2 weeks (SD = 5.9).
None of the chewers had current significant medical disorders or history of severe mental illnesses. Scores on the Alcohol Use Disorders Identification Test (AUDIT; Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) suggested the absence of significant alcohol-related problems (M = 13.3, SD = 1.2, range = 11–15). All participants reported episodic tobacco smoking and scores on the Fagerstrom Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) suggested low dependence (M = 0.90; SD = 0.7, range = 0–2). The mean score on the Kessler Psychological Distress Scale (K10 (Andrews & Slade, 2001) was 20.4 (SD = 3.1; range = 14–27). No participants screened positively for high psychological distress (≥30), with the majority (35%) in the well (<20) or 58% in mild (20 – 24) range.

Table 1: Polynomial regression models describing changes in withdrawal symptoms from 3 days prior to, and 14 days following, khat cessation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intercept</th>
<th>Linear term Coefficient (95%CI)</th>
<th>t(p)</th>
<th>Quadratic term Coefficient</th>
<th>t(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craving</td>
<td>54.24</td>
<td>1.54 (1.02 – 2.07)</td>
<td>5.82***</td>
<td>-0.14 (-0.18 – -0.09)</td>
<td>5.71***</td>
</tr>
<tr>
<td>Negative affect^</td>
<td>-0.13</td>
<td>0.16 (0.14 – 0.18)</td>
<td>14.47***</td>
<td>-0.01 (-0.01 – -0.01)</td>
<td>11.58***</td>
</tr>
<tr>
<td>Arousal^</td>
<td>0.34</td>
<td>-0.18 (-0.20 – -0.16)</td>
<td>16.45***</td>
<td>0.01 (0.01 – 0.01)</td>
<td>10.61***</td>
</tr>
<tr>
<td>Tired</td>
<td>36.97</td>
<td>3.63 (3.15 – 4.12)</td>
<td>14.75***</td>
<td>-0.25 (-.29 – -0.20)</td>
<td>11.21***</td>
</tr>
<tr>
<td>Poor Motivation</td>
<td>36.73</td>
<td>3.03 (2.56 – 3.50)</td>
<td>12.70***</td>
<td>-0.21 (-.26 – -0.17)</td>
<td>9.97***</td>
</tr>
<tr>
<td>Nervous</td>
<td>37.80</td>
<td>2.87 (2.40 – 3.35)</td>
<td>11.89***</td>
<td>-0.21 (-0.26 – -0.17)</td>
<td>9.77***</td>
</tr>
<tr>
<td>Depressed</td>
<td>34.36</td>
<td>3.63 (3.15 – 4.11)</td>
<td>14.96***</td>
<td>-0.27 (-0.31 – -0.23)</td>
<td>12.45***</td>
</tr>
<tr>
<td>Irritable</td>
<td>41.02</td>
<td>1.98 (1.49 – 2.47)</td>
<td>7.91***</td>
<td>-0.15 (-0.20 – -0.11)</td>
<td>6.86***</td>
</tr>
<tr>
<td>Restless</td>
<td>39.64</td>
<td>2.18 (1.71 – 2.65)</td>
<td>9.14***</td>
<td>-0.18 (-0.22 – -0.13)</td>
<td>8.18***</td>
</tr>
</tbody>
</table>

Note. ^ Analyses involving arousal and negative affect performed on their factor scores, values ranging from – 1 to + 1; all other variables on scales 0–100.
***p < .001.

Withdrawal symptoms, trend and characteristics

The best-fitting model with quadratic terms for the average subjective scores of nine withdrawal symptoms over 3 days pre-quit chewing and 14 days of abstinence (n = 59) is summarized in Table 1 and portrayed graphically in Figure 1. For the sake of uniformity and clarity of the figures, the factor scores of Negative affect and Arousal (originally on a scale –1 to +1) were transformed
to a 0–100 scale consistent with other measures. Depression, craving, nervousness, tiredness, restlessness, poor motivation, irritability, and negative affect seem to increase substantially and reach peak in the first week around Day 7 and decline thereafter in some cases (craving, irritable, and restless) returning to near baseline values (Table 2). Arousal showed a sharp decrease in symptoms during the first week following the quit day and decreased slightly throughout the second week (Figure 1d). As can be seen from the plots, all withdrawal symptoms followed similar overall patterns with salient changes after the quit day and curvatures around the first week post-quit day.

**Figure 1 (a-i):** Trends of average withdrawal scores of the participants over 3 pre-quit and 14 post quit days (N=59).
Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Statistically significant change over time (p <0.001)
Table 2 shows the mean scores of the withdrawal items across the four points in time. The mixed effect repeated measure analysis revealed that overall all withdrawal symptoms examined in this study significantly change over the course of a quit attempt. There was an acute withdrawal effect at 24 hr. for each variable assessed and a significant increase in all symptoms from baseline on the first week of the post quit period. Withdrawal symptoms did not significantly change between the first and the second weeks of post quit periods. The majority of symptoms (negative affect,
arousal, fatigue, poor motivation, nervousness, and depression) remained significantly elevated from baseline at Day 14. Craving, irritability, and restlessness, however, had returned to levels comparable to baseline during the second week of the post-quit period.
Table 2: Mean withdrawal symptom scores at baseline, on quit day, 1st week post quit and at 2nd week post quit.

<table>
<thead>
<tr>
<th>Item</th>
<th>Baseline (day -3)</th>
<th>24h abstinent (day 1)</th>
<th>One week (day 7)</th>
<th>Two weeks (day 14)</th>
<th>Overall F</th>
<th>Is there an acute withdrawal effect? (baseline vs 24h), p</th>
<th>Does withdrawal increase? (baseline vs 7 days), p</th>
<th>Does withdrawal get worse over time? (24h vs day 7), p</th>
<th>Do symptoms reduce between day 7 and day 14? (day 7 vs day 14), p</th>
<th>Do symptoms revert to baseline at 14 days? (baseline vs day 14), p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craving</td>
<td>49.5 (10.8)</td>
<td>57.0 (15.4)</td>
<td>56.4 (15.9)</td>
<td>51.9 (15.7)</td>
<td>5.7**</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Negative affect</td>
<td>-0.6 (0.4)</td>
<td>0.2 (0.6)</td>
<td>0.3 (0.6)</td>
<td>0.1 (0.7)</td>
<td>32.5***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Arousal^</td>
<td>0.9 (0.3)</td>
<td>0.01 (0.7)</td>
<td>-0.2 (0.6)</td>
<td>-0.3 (0.6)</td>
<td>73.6***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Tired</td>
<td>25.6 (8.1)</td>
<td>43.5 (14.8)</td>
<td>50.0 (14.6)</td>
<td>45.8 (16.1)</td>
<td>39.7***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.100</td>
<td>0.949</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poor motivation</td>
<td>27.1 (8.2)</td>
<td>44.3 (14.1)</td>
<td>45.5 (13.2)</td>
<td>41.2 (14.2)</td>
<td>27.2***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>1.000</td>
<td>1.000</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nervous</td>
<td>28.2 (10.0)</td>
<td>42.4 (13.1)</td>
<td>45.6 (12.5)</td>
<td>39.1 (14.1)</td>
<td>19.0***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.965</td>
<td>0.378</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Depressed</td>
<td>22.6 (7.6)</td>
<td>44.2 (13.3)</td>
<td>44.4 (14.6)</td>
<td>37.2 (16.3)</td>
<td>35.1***</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>1.000</td>
<td>0.206</td>
<td>&lt;0.001</td>
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<tr>
<td>Irritable</td>
<td>34.8 (13.0)</td>
<td>46.3 (13.0)</td>
<td>46.3 (13.7)</td>
<td>41.0 (13.2)</td>
<td>7.0**</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>1.000</td>
<td>0.431</td>
<td>0.303</td>
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<tr>
<td>Restless</td>
<td>33.0 (12.3)</td>
<td>43.8 (14.1)</td>
<td>43.4 (12.4)</td>
<td>39.6 (14.3)</td>
<td>8.2***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>1.000</td>
<td>1.000</td>
<td>0.303</td>
</tr>
</tbody>
</table>

Note. ^Analyses involving arousal and negative affect performed on their factor scores, values ranging from +1 to –1; all other variables on scales 0–100. ** p <.01. *** p <.001.
Discussion

The main objective of the present study was to determine whether there were any meaningful and sustainable withdrawal symptoms present in a sample of frequent khat chewers who engaged on a motivated quit attempt. Withdrawal symptoms (craving, negative affect, tiredness, poor motivation, nervousness, depression, irritability, and restlessness) significantly changed on the designated quit day and continued at higher levels throughout the first week. During the second week, only some of the symptoms (craving, irritability, and restlessness) had reverted to the baseline levels.

Craving showed significant growth on the designated quit day (24 hr) and remained high throughout the first week of the post quit monitoring period with the smallest magnitude of changes overtime returning to baseline rates around Day 14. This trend was also true for irritability and restlessness which continued at high levels after the quit day until roughly Day 8 and reverted back to baseline levels in the second week. These results partially support earlier studies which reported significant craving after cutting down or reducing khat chewing by 82% of chewers (Al-Motarreb, Baker, & Broadley, 2002) and significant increase in irritability, enhanced distress, emotional reactivity and nervousness among 53% of chewers (Bongard, al’Absi, Khalil, & Al Habori, 2011).

For most of withdrawal items, particularly negative affect, patterns of steady increase in elevation of withdrawal symptoms during pre-quit days and noticeable change around the quit day heading for greatest severity during the first week were observed. In addition, as revealed in the time course analysis (Table 2), for most withdrawal items maximum severity of symptoms was observed starting from the 24-hr. initial quit day throughout the first week of
Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

the 4-week quitting process. Taking this into account, it may be crucial to target withdrawal symptoms before the attempt is started as well as once 24-hr. abstinence is achieved.

The change in arousal/energy level was significant and the observed results were similar in terms of trend and elevation to all other symptoms. Pre-quit level was generally higher at baseline and was in a slightly decreasing trend toward the designated quit day. Eventually, there was nonsignificant trend for symptoms to continue to decline from Day 7 to Day 14. In this regard, although longer duration of follow up is necessary to clearly examine this, it may be reasonable to say that a prolonged reduction of arousal/energy level after the quit day might be a likely change that could be attributed at least in part from lack of access to the stimulant agent (khat) during the post-quit days.

The present study has some limitations given that it is the first study of withdrawal symptoms in relation to khat chewing and quit attempts using the method of EMA. First, because of lack of availability of the necessary equipment for urinalysis, we relied on participants’ self-reports of both khat chewing and cessation and were unable to conduct ongoing urine analysis to objectively verify these conditions during pre- and post-quit periods. So, it is possible that chewing participants might have reported false abstinence during post quit periods or vice versa. Second, because of the large difference in sample size between those who maintained continuous abstinence (n = 4) and those who lapsed (n = 55) we were unable to compare the difference in course of withdrawal symptoms and clearly examine its contribution to abstinence.

Despite these limitations, however, the present study has yielded new insights about the natural course of khat withdrawal symptoms over time in the process of a chewing cessation attempt.
Our results have demonstrated that the intensity of withdrawal symptoms associated with khat abstinence were significantly high, long lasting and meaningfully changed following a quit attempt. Given that many of the participants lapsed/relapsed after maintaining 7-day abstinence, the present finding has important implications, demonstrating that khat withdrawal symptoms may not indeed be mild as inferred by other authors (Kalix, 1988) and that chewers may experience significant discomfort following discontinuation, which may increase the risk of lapse and relapse. Although comparisons of the withdrawal symptoms between the groups to help justify that higher withdrawal leads to lapsing, were not made because of time limitations and very small cell size, taking the aforementioned idea into account, our findings provide an indication of the influence of withdrawal symptoms in the quitting process. Hence, supporting the need for interventions to reduce the presence of withdrawal symptoms or to enhance coping with withdrawal symptoms is indispensable to support individuals during the period of increased symptoms of dysphoria and to reduce the risk of relapse.
REFERENCES


http://www.who.int/iris/handle/10665/67205


SUPLIMENTAL MATERIAL

**Figure S1:** Trends of average withdrawal scores over 3 pre-quit and 14 post quit days for lapser and non-lapser groups.

Statistically significant change over time (p <0.001)

Statistically significant change over time (p <0.001)
Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Statistically significant change over time ($p < 0.001$)

Statistically significant change over time ($p < 0.001$)
Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Statistically significant change over time (p < 0.001)

**Nervousness** (0-100)

<table>
<thead>
<tr>
<th>Study day</th>
<th>Non-lapser</th>
<th>Lapser</th>
</tr>
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<tbody>
<tr>
<td>-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2</td>
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<tr>
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**Irritability** (0-100)

<table>
<thead>
<tr>
<th>Study day</th>
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<th>Lapser</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3</td>
<td></td>
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</table>

Statistically significant change over time (p < 0.001)
Chapter 5: Khat withdrawal symptoms among chronic khat users following a quit attempt: An Ecological Momentary Assessment study.

Statistically significant change over time (p < 0.001)

**Depression (0-100)**

**Arousal (1-100)**

Statistically significant change over time (p < 0.001)
Statistically significant change over time (p < 0.001)
General Discussion
General Discussion

In this chapter, the main findings with regard to the research questions are summarized and the general conclusions based on the findings of the studies presented in this thesis are described. Furthermore, the strengths and limitations of this thesis are considered and suggestions for further research in relation to khat use and its multiple consequences are provided. This chapter concludes with practical recommendations for concerned stakeholders in Ethiopia: policy makers, community members, teachers and students.

Khat (*Catha edulis Forsk*) is a natural stimulant plant and has become a public health concern due to adverse health risks and increased negative risks for social, financial, and mental health problems associated with chronic frequent chewing (Aden, Dimba, Ndolo, & Chindia, 2006; Al-Motarreb, Al-Habori, & Broadley, 2010; El-Wajeh & Thornhill, 2009; Tulloch, Frayn, Craig, & Nicholson, 2012). The population prevalence of past month use has been estimated to be 15.3% across the Ethiopian general population, and 7.7% among Ethiopian university students (n=3268) (Gebrehanna, Berhane, & Worku, 2014c). Although there are conflicting opinions with regard to the existence of dependence in relation to khat use, higher frequency of khat chewing has been associated with psychological dependence (Kassim, Islam, & Croucher, 2010). There is also accumulating evidence suggesting the presence of lack of control over use, withdrawal, craving and a degree of tolerance related to chronic khat chewing (Cox & Rampes, 2003), which might become significant barriers to cessation/reduction of problem drug use (Shoptaw, Kao, Heinzerling, & Ling, 2009). However, there has been inadequate systematic study of the nature of symptoms of substance use disorder relating to khat use. Likewise, very little has been done
with regard to the nature and time course of withdrawal symptoms during motivated quit attempts among frequent khat users.

The major aims of the studies in this thesis, therefore, were to examine the presence, structure, and external validity of a khat use disorder (KUD) syndrome using current Diagnostic and Statistical Manual (DSM-5) criteria, as well as the more clinically familiar DSM-IV dependence syndrome; to evaluate the use of the SDS as a potential screening tool for identifying people experiencing KUD; to describe the outcomes of unassisted khat cessation among frequent khat users who had motivation to quit and to examine the time course of development and reduction of withdrawal symptoms over the first two weeks of a quit attempt. Thus, this thesis contributes vital insight into the nature of khat use disorder, severity of use dependence and the nature of khat withdrawal symptoms, which ultimately would help in designing intervention strategies to handle consequences associated with problematic use.

The thesis has four cohesive chapters with distinct but unified objectives that focus on addressing potential psychological and health consequences in relation to khat use by examining the nature of khat dependence, the outcome of khat cessation attempts and the characteristics of withdrawal symptoms and craving during khat abstinence. The central aim of the studies reported in Chapters 2 and 3 was to examine the validity of khat use disorder and to determine if a brief screening tool could be validly identified to identify people experiencing problems with use. The principal aim of the studies presented in Chapters 4 and 5 was to explore how successful are frequent khat users in their khat cessation attempts and to examine the trends and characteristics of withdrawal symptoms in the quitting process. The data for Study 1 and 2 were collected by using a survey
questionnaire comprised a modified version of AUDADIS-IV for assessment of past year khat use disorder and items taken from the Composite International Diagnostic Interview (CIDI) for the assessment of withdrawal symptoms. Four hundred current khat chewers (aged 16 and above) recruited from khat markets and cafes provided valid answers either to the online version or the pencil and paper version of the khat survey.

The first study investigated the presence of khat use disorder syndrome using DSM-5 criteria and identified its relationship with increased experience of harms. Khat use disorder was evident among the majority (74%) of the participants; 10.5% were categorized as experiencing mild, 8.8%, moderate and 54.5% severe khat use disorder. Those identified as having khat use disorder experienced multiple harms associated with their use. More specifically, use of khat was associated with self-reported mental health problems and psychological distress. About a third of users reported life-time access to help-seeking largely from friends and relatives. The findings of this study support the existence of the substance use disorder syndrome for khat and clearly show that people experience problems and the syndrome structure matches with the findings of other drugs of dependence such as amphetamine. These provided unique contributions to substance use research by using DSM 5 criterion to validate khat use disorder.

The second study assessed the efficacy of the Severity of Dependence Scale (SDS) as a screening tool for Khat Use Disorder. The key finding of this study showed that nearly three quarters (73%) of the sample experienced some symptoms related to Khat Use Disorder. The SDS for khat had excellent discrimination for identifying cases of DSM-5 khat use disorder with an optimal cut-off score of 3 or above. Those individuals screening at 3 or greater had substantially higher rates of
adverse consequences associated with khat use than those with lower scores. Those that were screened positive reported greater frequency and quantity of khat use.

Study 3 and study 4 were quitting studies using Ecological Momentary Assessment (EMA) methodologies. Both studies involved the use of electronic diary (ED smart phones) to assess withdrawal symptoms, mood, and khat consumption at multiple random occasions of 10 days prior to, and 28 days following an attempt to discontinue regular khat chewing (a quit attempt). Study 3 involved data collection in a naturalistic setting from 59 daily and near daily khat consumers who were motivated and interested in khat abstinence. While 80% reached at least seven continuous days of abstinence, 93% lapsed after 11 post-quit days and only 7% maintained continuous abstinence for 28 post-quit days. These findings revealed that chewers who have the motivation to quit have difficulties maintaining abstinence. This is strongly suggestive that it is important to provide clinical attention and relevant support for interested quitters.

Study 4 using the same participants and research devices (Electronic Diary) as the previous study collected real time data of khat withdrawal symptoms and cravings. The data was used to evaluate the time course of the major withdrawal symptoms and craving during 3 pre-quit and 14 post-quit days. All withdrawal symptoms followed similar overall patterns with salient elevations after the quit day and curvatures around the first week of post quit period. Most symptoms reached peak level around day 7 and many remained elevated at 14 days from quitting. This finding indicates that withdrawal symptoms may be heavier than previously suggested (Kalix, 1988) and that frequent users may experience significant discomfort following discontinuation, which may increase the risk of lapse and relapse.
### Table 1: A Summary of Major Findings of this Thesis

<table>
<thead>
<tr>
<th>Central Aim</th>
<th>Findings</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 2 (Study 1) Aim 1: To identify cases of khat use disorder using DSM criteria.</td>
<td>Khat use disorder was identified in almost three-quarters of this general community sample of frequent chewers.</td>
<td>Khat-chewing is legal and culturally acceptable habit in Ethiopia. However, there is a clear evidence of the presence of khat use disorder among frequent khat chewers. Those with KUD were more likely to have issues with increase debts due to khat, poor access to treatment and poor cognition.</td>
</tr>
<tr>
<td>Chapter 2 (Study 1) Aim 2: To determine if khat use disorder symptoms produce a syndrome that performs in the same manner as other stimulants.</td>
<td>Confirmatory factor analysis demonstrated a good fit of a unifactorial model to both DSM-IV dependence and DSM-5 substance use disorder items.</td>
<td>The khat use disorder symptoms fell into a unifactorial structure and the presence of three latent symptom classes were consistent with a dimensional process, consistent with findings for amphetamines and other drugs of dependence such as cannabis. This provides further support for khat use disorder as a valid entity.</td>
</tr>
<tr>
<td>Chapter 2 (Study 1) Aim 3: To examine if khat use disorder performs as a valid syndrome, relating to an increased experience of harms.</td>
<td>Those with khat use disorder experienced significantly higher rates of psychological, social and cognitive problems than those without khat use disorder.</td>
<td>While khat chewing is a deep-rooted culturally acceptable habit and khat itself plays a substantial role in Ethiopia’s economy, it is associated with health and public safety problems which are not well addressed by legislative responses. Help-seeking was uncommon and mainly from untrained family/friends rather than from professional counseling centers.</td>
</tr>
</tbody>
</table>
### Chapter 3 (Study 2) Aim 1:
To determine the psychometric properties of the Severity of Dependence Scale in relation to khat

- **Confirmatory factor analysis** supported a unifactorial structure for the scale, and a wide spread of scores.
- **The total score on the Severity of Dependence scale** can be used as a measure of increasing problems associated with khat.

### Chapter 3 (Study 2) Aim 2:
To determine a useful cutoff score on SDS-khat to identify people likely to be experiencing Khat Use Disorder

- **Cutoff scores** of ≥3 and ≥4 were determined for identification of mild and moderate KUD (Khat Use Disorder/dependence), respectively.
- **While SDS scores** of 3 or above were appropriate for screening of cases of likely mild Khat disorder/dependence, SDS scores of 4 or greater were appropriate for cases of likely moderate Khat use disorder/dependence. SDS score of 5 or above was appropriate for screening severe KUD.

### Chapter 3 (Study 2) Aim 3:
To examine if the SDS cut-off scores validly identify group of individuals using khat at greater frequency and quantity and experiencing functional problems.

- **Overall the cut-off Scores have demonstrated construct validity** identifying a group with behaviors indicative of use dependence with higher quantity and frequency of use, greater rates of adverse consequences and harms associated with use.
- **The SDS is a 1-minute tool and scores are associated with an increased experience of problems associated with khat use.** The scale should be applied in routine screening processes in primary health care.

### Chapter 4 (Study 3) Aim 1:
To describe the outcomes of unassisted khat cessation among 60 khat users who were motivated to quit

- **All except one participant (n=59)** reached initial abstinence. However, the majority (93%) lapsed. Very few (7%) could maintain continuous abstinence throughout the study period.
- **Some chewers have problems arising from their use of khat and even motivated individuals have difficulties maintaining abstinence.** Hence, psycho-educational and peer/group support approaches might be helpful in reducing substance use and improving outcomes of quit attempts among khat consumers (Donovan & Wells, 2007).
| Chapter 4 (Study 3) Aim 2: To identify the predictors of success during a khat cessation attempt | Only quantity of khat consumed was a statistically significant predictor of successful abstinence for the continuous abstinence group. However, there was low power for these analyses. | None of the demographic variables examined but quantity of khat consumed predicted successful abstinence for the continuous abstinence group, counter-intuitively indicating that those in the continuous abstinence group, who usually consumed one and half bundle or more of khat per session, were more likely to maintain abstinence than those consumed one bundle or less of khat in the same group. However, due to the small number of individuals maintaining abstinence, these findings were preliminary and tentative. |
| Chapter 5 (Study 4) Aim 1: To examine the time course of development and reduction of withdrawal symptoms over a 14-day period spent without khat. | Significant withdrawal symptoms were apparent. There were salient elevations after the quit day, and symptoms peaked around the first week after quitting. Craving, irritability and restlessness returned to baseline ratings after 14 days. However, dysphoric symptoms (negative affect, depression and nervousness), fatigue and motivation did not return to return to baseline ratings after 14 days. | While craving, restlessness and irritability resolved in 14 days, dysphoria, fatigue and motivation did not resolve in 14 days. The influence of withdrawal symptoms is an important issue in the quitting process. To help quitting individuals during the period of increased symptoms of dysphoria and to reduce the risk of relapse, intervention strategies that aim to reduce withdrawal symptoms or to enhance coping with withdrawal symptoms are vital. |
Findings with regards to the research questions

Chapter 2 (Study 1)

Research question (Aim) 1 Are use disorder symptoms experienced in relation to khat? One of the main aims of study 1 was to identify cases of khat use disorder (KUD) syndrome using current Diagnostic and Statistical Manual (DSM-5) criteria. Almost three-quarters of the sample of frequent chewers had diagnosable khat use disorder. Half of the participants surveyed were identified as having severe khat use disorder (KUD) symptoms. Most chewers continued using khat despite having knowledge of physical and psychological harms from use. As khat chewing is a long process, usually lasting about 5-6 hours (Kalix, 1988) and mainly being conducted in special places intended for this purpose (khat café), most chewers failed to fulfil major role obligations in workplaces, schools, within the family and in the wider community, which resulted in interpersonal problems. The reported experience of prioritization of purchasing khat over basic personal and family needs may suggest loss of control over khat chewing (Griffiths et al., 1997; Kalix, 1990; Kassim & Croucher, 2006; Luqman & Danowski, 1976; Nencini, Grassi, Botan, Asseyr, & Paroli, 1989). Most chewers reported continuing to use khat despite interpersonal consequences. Previous studies of university and hospital staff in Ethiopia have revealed that half the khat consumers surveyed reported leaving work early or missing work entirely to chew khat (Gelaw & HaileAmlak, 2004).

In the present study, physical withdrawal symptoms and craving that were severe enough to interfere with functioning were apparent in half the participants and almost all had experienced at least one clinically significant withdrawal symptom. However, in regard to
the core requirements for stimulant withdrawal (concurrent dysphoria plus two other symptoms, severe enough to cause distress), only 28% of the participants met this criterion. Overall, in this sample of the current study, the presence of KUD was evident and khat use disorder was substantially linked to a number of behavioural problems.

**Research question (Aim) 2: Do these symptoms produce a syndrome that performs in the same manner as other stimulants?**

A confirmatory factor analysis was performed to determine if all symptoms relate to a shared latent process. Results established a good fit of a unifactorial model to both DSM-IV dependence and DSM-5 substance use disorder items. This is consistent with the syndrome structure for other drugs of dependence. A latent class analyses of DSM-5 khat use disorder symptoms determined a 3-class model, identifying three distinctive categories of participants in this sample: A “low-dependent consumers” with low probability of any use disorder symptoms (35% of this sample); a second group with khat abuse, physiological dependence, use in larger or longer amounts than planned, and continuing use despite experiencing physical/psychological harm (33%); and a third group (32%) with high probability of endorsement of all DSM-5 symptoms. The identified latent symptom classes were consistent with a dimensional process (i.e. severity of dependence), consistent with findings for amphetamines (Saha et al., 2012) and other drugs such as cannabis (Compton, Saha, Conway, & Grant, 2009).

**Research question (Aim) 3: Does the presence of a khat use disorder syndrome perform validly, relating to an increased experience of harms?**
To address this aim, differences between individuals identified with and without khat use disorder (KUD) in terms of variables such as patterns of consumption, mental health and financial and occupational problems were examined. Those classified with KUD were significantly more likely to use khat in larger amounts and more frequently compared to non-classified participants, with nearly half of them chewing khat on daily basis. One third of those categorized as KUD reported participating in life time ‘help-seeking’ for khat use from family members, teachers and friends.

Those identified as having KUD were significantly more likely to be male, daily alcohol consumers and dependent or daily tobacco smokers. Khat is typically chewed by groups of men in culturally sanctioned gatherings (Hoffman & Al'Absi, 2010). Traditionally, khat consumption by women is less likely as it is mostly considered socially unacceptable and discouraged by family and the community (Beckerleg, 2010). In support of this, recent epidemiological work in Ethiopia has demonstrated substantially greater prevalence of past-month khat-chewing among males than females (Haile & Lakew, 2015). This might have put males than females at a higher risk of developing khat dependence (Baer, Kivlahan, Blume, McKnight, & Marlatt, 2001).

Recent use of shisha was also more common among the group with KUD, as reported by half of individuals in this group. Although the use of other drugs (alcohol, cannabis and benzodiazepines) was uncommon, rates were elevated in the group with KUD. During khat chewing, other substances, mainly cigarettes, alcohol and, more recently, shisha are commonly consumed. The stimulating effects of cigarettes and shisha may enhance the
effect obtained during khat chewing and to reduce its bitter taste, while alcohol is widely used to ease the stimulatory effects of khat.

The group with KUD had increased rates of self-reported mental health problems, financial problems, psychological distress and poorer quality of life. Problems related to academic functioning were significantly more common among the group with KUD. This result is contrary to the widely reported expectation that khat enhances cognitive ability and concentration in academic activity. However, multiple studies of cognition (inhibition of response conflicts, monitoring of working memory, mental flexibility) in regular khat consumers have demonstrated impaired cognitive function when not actively intoxicated (Colzato, Ruiz, van den Wildenberg, & Hommel, 2011; Colzato, Sellaro, Ruiz, Sikora, & Hommel, 2013a; Hoffman & Al'absi, 2013a). Similarly, research results showed that khat chewing students have lower mean Cumulative Grade Point Average (CGPA) compared to non-chewers. Comparable negative effects on learning ability have also been found with regard to the use of amphetamine among individuals. Therefore, the current study clearly indicates that khat use disorder is substantially associated with multilevel adverse health and psychological effects and may be related to negative behavioural changes and significant impairments of mental health and cognitive functioning such as poor concentration and short-term memory.

Regarding financial problems, those in the KUD group were more likely to have made excuses about money spent on khat, to have sold their belongings to buy khat, to have worried about the amount of money they spent on khat, to have drug related debts and to have spent money that meant for other things on khat. In several surveys of khat using communities it was reported that time spent chewing as well as amount of money dedicated
to khat use were major factors for family breakdowns and conflict between spouses, contributing significantly to socioeconomic problems in the community (Omar et al., 2015).

Chapter 3 (Study 2)

Research question (Aim) 1: Does the Severity of Dependence Scale (SDS) for khat use perform in a similar way to existing diagnostic measures of khat use disorders?

The SDS is a short, easily administered instrument for measuring subjective concerns in relation to particular substance use. It is recognized as a robust and adaptable measure of screening for dependence across variety of substances of abuse in diverse populations and samples. Consistent with findings for the SDS in relation to amphetamine (Topp & Mattick, 1997) the findings from this study clearly support the use of SDS scale as a screening instrument for psychological dependence. Fit indices from confirmatory factor analyses were satisfactory indicating good fit of a unifactorial structure of the scale. This means that a total sum score on this scale is valid and also that the scale performs in a manner consistent with the nature of the dependence syndrome itself in relation to khat. The SDS has performed similarly in relation to other stimulant drugs such as methamphetamine (Topp & Mattick, 1997)

Research question (Aim) 2: What is an adequate cut-off score for case identification for screening purposes?

ROC analysis demonstrated that the SDS has high diagnostic utility in identifying the presence of DSM-5 Khat Use Disorder (KUD) and DSM-IV Khat Dependence. Cut off scores of 3 and 4 were identified as the most appropriate for the identification of likely cases of DSM-5 mild khat use disorder and DSM-5 moderate khat use disorder,
respectively, with good sensitivity and specificity. Moreover, a value of 5 was appropriate for screening severe khat use disorder. These cut-off values are similar to those identified for screening for ecstasy dependence (Bruno, Gomez, & Matthews, 2011), for amphetamine dependence (Topp & Mattick, 1997) and for cannabis dependence in adolescents (Martin, Copeland, Gates, & Gilmour, 2006). This spread of cut points on the scale may be useful for designing and providing the appropriate and stepped level assessments and interventions. While individuals scoring 3 may require brief motivational interviewing and interventions (Kaye & Darke, 2002), those scoring 5 or above may be referred to more formal assessment and support interventions (Kassim et al., 2010).

**Research question (Aim) 3: Are identified SDS cut-off scores valid in terms of identifying a group of individuals using khat at greater frequency and quantity, and experiencing functional problems?**

Independent logistic regression models using the groups above and below the two SDS cut-off scores (SDS ≥ 3 for likely Khat Use Disorder and SDS ≥ 5 for likely severe Khat Use Disorder) were used to examine the validity of these cut-off values in distinguishing groups with greater psychological and related harms. Previous studies indicated that frequent khat chewing was associated with anxiety and depression among users and suggested that heavier and frequent use was predominantly related to the severity of khat dependency (Kassim, Croucher, & al'Absi, 2013a). The current study has demonstrated that that the group above these cut-off scores were more commonly male, were using khat frequently and in larger volume and were experiencing a significantly greater amount of mental health problems, financial problems, cognitive problems and had poorer quality of life than those scoring below the cut-off. Male and female chewers had different patterns of khat use as
well as symptoms related to dependence. The finding of gender differences in correlates and patterns of khat use and dependence is consistent with previous studies (Nakajima & al'Absi, 2013). The group with SDS score above the cut-off scores had also engaged in greater rates of help-seeking for khat use. These findings are consistent with studies of similar substances (Ferri CP, 2000; Gonzalez-Saiz et al., 2008; Gossop et al., 1995; Kaye & Darke, 2002; Lawrinson, Copeland, Gerber, & Gilmour, 2007), and support the use of the SDS as a brief screening tool for identifying individuals potentially experiencing problems related to khat use.

Chapter 4 (Study 3)

Research question (Aim) 1: What is the outcome/success rate of unassisted quit attempts of frequent khat users who were motivated to quit?

The main aim of this study was to describe the outcome of unassisted khat quitting attempts in terms of the proportion of participants reaching four different end points – a proposed target quit date (TQD), initial 24-hr abstinence, 7-day abstinence and continuous abstinence over 28 days. The results of this study showed that all except one participant (n=59) reached the TQD and achieved 24-hr abstinence around the designated quit day. While 80% of the participants achieved, very few (7%) maintained continuous abstinence over 28 days of study. Among those who achieved initial abstinence, 93 % lapsed.

The findings suggest that without support for quitting khat, successful abstinence was very low, and lapse and relapse rates were high. The study implies that motivation to quit in the process of quit attempts may need to be supported with additional interventions to help the quitting process succeed.
Research question (Aim) 2: What are the demographic variables which are associated with success of abstinence?

In this study three demographic variables (gender, amount of khat used in bundle per session and the level of psychological distress as measured by the Kessler Psychological Distress Scale (K-10)) were examined as potential factors which might have association with rates of successful khat abstinence. Surprisingly, none of the demographic variables examined but quantity of khat consumed, predicted successful abstinence for the continuous abstinence group, counter-intuitively indicating that those in the continuous abstinence group, who usually consumed one and half bundle or more of khat per session, were likely to maintain abstinence than those consumed one bundle or less of khat in the same group. Although, this finding is somewhat puzzling, as the direction of the association is opposite to what we would expect based on work in other substances of addiction, it may be possible that the heavier users in our study were more committed to quitting, or that other factors might have explained this discrepancy. However, given the small number of ‘successful’ quitters in this study, there was poor power to identify correlates, and as such these findings merit replication in larger studies before speculating on the cause of the association.

Chapter 5 (Study 4)

Research question (Aim) 1: What are the trends and characteristics of the rate of withdrawal symptoms over the course of the first two weeks of a quit attempt?

There were overall significant changes in withdrawal symptoms following khat cessation. Most withdrawal symptoms followed overall similar trends, with moderate elevations that continued to be greater than baseline even 14 days following quitting. However, craving,
irritability and restlessness reverted to the levels recorded at baseline. Dysphoric symptoms (negative affect, depression and nervousness), fatigue and poor motivation did not return to baseline ratings. Peak severity of symptoms was observed between 24hr post-quit and day 7 indicating the importance of targeting withdrawal symptoms prior and after the designated quit days for successful khat cessation. Understanding the trend, nature and influence of withdrawal symptoms over the course of a quitting process is an important issue. Intervention strategies that aim at reducing and coping with withdrawal (mainly the dysphoric symptoms) are vital in order to help individuals successfully quit and to reduce the risk of relapse.

**Limitations**

The four studies in this thesis have used effective and well-designed sampling and research methods and employed a number of standard and validated measures to gather the necessary data from a relatively ‘hard-to-access’ population in which recruiting frequently consuming individuals for inclusion in the studies were challenging tasks. However, there were a number of limitations which might have potentially affected the results to some extent: The first study which attempted to examine khat use disorder as a valid diagnostic entity has the following important imitations: Firstly, a self-report survey (e. g. AUDADIS-IV) was used to collect diagnostic data rather than the gold standard of clinical diagnosis. In addition, survey responses may also be susceptible to social desirability and recall bias. However, we believe that the influence might be low since in multiple studies the AUDADIS-IV has demonstrated good to excellent reliability and validity (Chatterji et al., 1997; Grant, Harford, Dawson, Chou, & Pickering, 1995; Hasin, Carpenter, McCloud, Smith, & Grant, 1997) for the identification of illicit drug use disorders in similar applications to the current
study. Moreover, we used anonymous self-administered surveys which provided full anonymity to all participants. As such, we believe that the response biases have been kept to minimum.

Secondly, since participants were all drawn from a defined geographical region (Adama, Ethiopia) and recruited using convenience sampling, primarily through khat cafes, it is clear that this has definitely increased the likelihood of the participation of frequent chewers who were at elevated risk of khat use disorder with greater base rates of symptoms identified. As such, the patterns of dependence identified here are clearly not reflective of rates in the general population, however, for the aims of the current study, where the presence and relationships between dependence symptoms was critical, a sample with elevated rates of problems was clearly appropriate for the aims of the study.

Thirdly, given the social context of khat use, polysubstance use, especially of cigarettes and shisha, is probably unavoidable. As a result, as polysubstance use often has the potential to contribute to the symptoms identified, there could be some potential interpretive problems arising from the presence of polysubstance use. However, the occurrence of a substantial inflating effect is unlikely, given the low proportion of frequent polysubstance use reported, the low levels of dependence and the finding that increased rates of adverse effects remained the same after controlling for polysubstance use.

The use of purposive sampling which increased the probability of recruiting frequent khat chewers could be considered as a limitation of study 2. However, as the ultimate objective of this work was to determine the efficacy of the severity of dependence scale (SDS) in
screening for khat use disorder, the use of this sampling method was appropriate in order to successfully achieve the intended goal.

Study 3 which aimed at describing the outcomes of an unassisted quit attempts made by motivated frequent khat users has also some limitations. First, due to the pilot nature of the study this was conducted on only a small sample of university students who used khat regularly, and results may not be generalizable to a larger population. Secondly, the lack of urine screening for verification of abstinence and relying merely on self-reported abstinence was also a limitation. However, the application of prospective recording of participants’ responses using electronic diaries, we believe, has substantially increased the reliability of the responses obtained. Thirdly, we used outcome variables selected from related smoking cessation literature. Theses variables might not be perfect fit for khat, given the marked difference between the process of khat chewing and tobacco smoking. Finally, the study procedure had required the study participants set their quit dates, which might have acted as assistance in terms of aiding their quit attempts. We cannot absolutely rule out the chance that our EMA monitoring procedures could have influenced the outcomes observed. However, considering the scarcity of research findings in this area the current findings undeniably shed light on this matter of substantial concern.

**General conclusion and future studies**

The global estimate of khat use is reported to be 20 million or higher, making it a public health concern nationally and internationally (Feyissa & Kelly, 2008). In Ethiopia, khat is consumed largely for recreational purposes and chewing of khat is a deep rooted socio-cultural tradition (Kalix & Braenden, 1985). The prevalence of past month khat use is
estimated to be 15% (Gebrehanna et al., 2014c). Khat chewing brings about a number of adverse health impacts that may include behavioral and mental health problems (Kassim, Croucher, & al'Absi, 2013b). Despite the health-related consequences identified in some studies, khat chewing is still a common practice among youths and adults in Ethiopia. While society’s knowledge, in general and chewers’ awareness, in particular, of the problems and adverse psychological effects associated with khat use have been increasing, it seems that there is still a need to further people’s understanding of clinically defined khat use disorders and ways of screening for khat use problems, which can help design effective strategies to minimize the potential harms and multifaceted consequences. Public health interventions need to aim at the increasing trend of khat use among the general population (primary prevention), and in particular to address the issue of problematic khat use (tertiary prevention) among youth and adult community members in Ethiopia.

The research reports presented in this thesis have enhanced the current understanding of the existence and nature of khat use disorders and the withdrawal profile of khat. The research has also answered key questions about khat chewing practices and potential adverse effects. The popularity of khat chewing and the escalation of the frequency of use among students and adults in Ethiopia were the important factors underlying the development of these studies. Although the survey studies were not restricted to university students, the relatively high prevalence of student chewers (Gebrehanna et al., 2014c) and the concentrations of khat supplies around university campus (Gebrehanna, Berhane, & Worku, 2014a), suggest that adopting comprehensive prevention strategies for substance use in colleges and universities may be warranted. This must extend beyond the simple prevention of use on campus grounds to use in the wider associated community. Khat supplies and khat chewing
facilities in the community around university campuses have been identified as liability factors for the spread of khat chewing, and increasing the potential for dependence among students (Gebrehanna, Berhane, & Worku, 2014b)

According to the findings of this research study, most of the withdrawal symptoms reach their peak at around day 7 after quitting and the majority of them, specifically dysphoria and fatigue, do not resolve or persist well after the first week of use discontinuation. Hence, the time frame for experience of withdrawal symptoms following discontinuation of khat chewing should be communicated to those considering quitting, and effective treatment options (e.g. behavioural resources and social support) should be developed in order to better support sustained cessation.

In the current study more than 50% of khat chewers endorsed’ interference with role obligations’ as one of khat use disorder symptoms. This supports the reports of other studies which suggested that khat chewing is not only interfering with full engagement of workers in work places but also is a barrier to gaining employment, due to considerable amount of time is spent in chewing and recovering from its after-effects (Nabuzoka and Badhadhe, 2000). Hence, it would be reasonable to suggest that the Ministry of Labour and Social Affairs should take appropriate measures to alleviate these.

It seems obvious that khat is socially, culturally and financially important crop in Ethiopia. It is one of the major cash crops well known for generating substantial income to the farmers and foreign currency earnings to the government (Amare Getahun & Krikorian, 1973; Lemessa, 2001). Therefore, considering the potential negative impact that chewing exerts
directly on the end users and on productivity of the work force, from policy perspectives, it may be reasonable to levy sales and use this for education and support through establishing primary care services and providing specific training to drug and alcohol service practitioners. This would increase the capacity of practitioners to deliver effective services that help increase community awareness of khat chewing and its multiple harms.

**Future directions**

The potential for further studies in this area remains very high, as research involving khat consumption involves human subjects and as it is relatively new area of research. One of the most important findings of the present study is that it has provided new understandings about the natural history of the course of khat withdrawal symptoms following cessation of regular khat use. The results suggest that understanding how withdrawal symptoms/craving develop and change over time and developing interventions to reduce these may help support successful khat cessation. However, the contributions of khat related environments in the development of withdrawal and risk of relapse were not studied. There is substantial evidence for the association of cue-induced cravings with the success of attempts to discontinue drug use (Ferguson & Shiffman, 2009). Attentional bias for drug-related stimuli in drug using individuals is likely to induce craving, exacerbate withdrawal and ultimately to relapse (Field & Cox, 2008; Field, Munafo, & Franken, 2009; Franken, 2003; Franken, Kroon, Wiers, & Jansen, 2000; Sayette et al., 2003; Waters et al., 2003). Therefore, future study may need to focus on investigating these potential factors using the methods of EMA amongst other diverse samples.
The current study has also identified a few self-reported cognitive problems such as trouble with short term memory and difficulty sustaining concentration among individuals classified as having khat use disorder. Previous findings suggested that impairments in the inhibition of response conflicts, monitoring of working memory and mental flexibility have been evident in abstinent khat consumers (Colzato et al., 2011; Colzato, Sellaro, Ruiz, Sikora, & Hommel, 2013b). Hence, future research work may need to focus on a well-designed human experimental study using psychological and neuropsychological measures for investigating the acute dose-related effects of khat use on a variety of cognitive functions (Hoffman & al’Absi, 2013b). This will assist in determining any causation in the cognitive problems associated with khat use identified in these studies. Similarly, a better understanding of the scope and range of residual cognitive impairments, and the time course of their reversibility, following use of khat is important. These may require large scale prospective longitudinal studies.

In conclusion, Khat brings great financial benefit and many people may chew without adverse problems. The socio-cultural aspect of khat chewing in terms of enhancing relationships with friends and peers is something to appreciate. However, some people do clearly experience significant problems in association with their khat use. Despite the prevailing view of khat as a mild stimulant, regular khat use is associated with significant negative impacts on mental health, emotional, relational and vocational roles. Hence, clearly there needs to be greater awareness of the risks and benefits in association to khat use, and it is a public health imperative for governments of countries where khat use is legal to implement demand reduction programs in addition to increasing supports for existing consumers by educating, training, and developing health and community services responsible for assisting those experiencing adverse consequences of khat use.
REFERENCES


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doi:10.1016/j.jsat.2008.06.005


Appendices

Appendices: A - T

Following is a copy of the study advertisements, information sheet, consent form and survey questionnaires presented to participants in Ethiopia in 2013 - 2014
Appendices

Appendix A: Khat use and experience Survey Questionnaire.

General information
How old are you?
Please write your answer here: _______________

Do you live in Ethiopia?
Please choose only one of the followings
• ☐ Yes
• ☐ No

Have you chewed any khat over the last twelve months? *
Please choose only one of the followings:
• ☐ Yes
• ☐ No

Thank you for your interest in this research. This study is being conducted in partial fulfilment of a PhD degree for Samson Duresso under the supervision of Dr. Raimondo Bruno at the University of Tasmania.

Demographic information
What is your gender? *
Please choose only one of the followings:
• ☐ Female
• ☐ Male

Are you a University student?
Please choose only one of the followings:
• ☐ Yes
• ☐ No

If yes, what is your year of higher education?
Please choose only one of the followings:
• ☐ Year I
• ☐ Year II
• ☐ Year III
• ☐ Year IV
• ☐ Year V
• ☐ Year VI
• ☐ Other

If you are not a student, which one best describes your employment status?
Please choose only one of the followings:
• ☐ Unemployed
• ☐ Self-employed
• ☐ Employed for wages or payments
• ☐ Looking for work
• ☐ Solely engaged in home duties
• ☐ Retired or a pension
• ☐ Volunteer or charity work
• ☐ Unable to work
• ☐ Other

What is the highest year of education you have completed?
Please choose only one of the followings:
• ☐ I did not go to school
• ☐ Grade 6 or below
• ☐ Grade 7 or equivalent
• ☐ Grade 8 or equivalent
• ☐ Grade 9 or equivalent
• ☐ Grade 10 or equivalent
• ☐ Grade 11 or equivalent
Appendices

- Grade 12 or equivalent
- Diploma
- 1st Degree
- 2nd degree and above
- Other

What is the highest qualification that you have achieved?

Please choose only one of the followings:
- Certificate
- TVET certificate (Level I & II)
- New answer option
- Diploma
- Advanced Diploma
- Bachelor’s degree
- Higher than a bachelor’s degree
- Other

The next questions ask about your ETHNICITY. The Ethnic groups are listed in Alphabetical order.

Please, select and mark the ethnic group that you belong to

Which one is your Ethnic group?

* Please choose only one of the followings:
- Afar
- Agew
- Amhara
- Benshangul
- Harari
- Oromo
- Gambella
- Somali
- SSPN
- Tigrai
- Other

The next questions ask about your PARENTS. If you were raised mostly by foster parents, step-parents or others, answer for them. For example, if you have both a stepfather and a natural father, answer for the one who was the most important in raising you. What is the highest level of schooling your father attained?

* Please choose only one of the followings:
- Completed primary school or less
- Some secondary school
- Completed secondary school
- Some college or university
- Completed college or university
- Don't know or does not apply
- Other

What is the highest level of schooling your mother attained?

Please choose only one of the followings:
- Completed primary school or less
- Some secondary school
- Completed secondary school
- Some college or university
- Completed college or university
- Don't know or does not apply
- Other

Which of the following people live in the same household with you?

Please choose only one of the followings:
- I live alone
- Father
Appendices

• Stepfather
• Mother
• Stepmother
• Brother(s) and/or sister(s)
• Grandparent(s)
• Other relative(s)
• Non-relative(s)
• Other

Khat Use and Dependency
The following questions ask about your khat use
In the last 12 months, how often did you chew khat? *
Please choose only one of the followings:
• Every day
• 3 times or more a week
• Twice a week
• Once a week
• Every few months
• Once or twice a year
• Other

On a typical day of khat chewing how much of the day do you feel excited or stoned? *
Please choose only one of the followings:
• 0 hours
• 1 to 2 hours
• 3 to 4 hours
• 5 to 6 hours
• 7 to 8 hours
• 9 or more hours
• Other

Which variety of khat have you often chewed during the past twelve months?
Please choose the appropriate response from:
(1 = Not at all; 2 = rarely; 3 = sometimes; 4 = often; 5 = most often) *
Please choose the appropriate response for each item:

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<th>Variety</th>
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It is assumed that the strength and stimulating effects of khat vary among the different varieties. Based on your experience and subjective evaluation, please, rate the strength of the khat variety you have ever used in the past twelve months:
Please choose the appropriate response from:
(1 = the least strong; 2 = fairly strong; 3 = strong; 4 = very strong; 5 = extremely strong) *
Please choose the appropriate response for each item:

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frequency of khat use

the following questions are based on the frequency of your khat use

how old where you the first time you used khat?
please, enter your age in years

please write your answer here: ____________

how did you typically access khat over last 12 months?
* 

please choose only one of the followings:

• purchased from khat shop
• purchased from open air khat market
• purchased from khat shop near the school
• have been given it by friends
• have my own supply
• other

how much did you spend for khat over the last four weeks?
* 

please choose only one of the followings:

• less than 50 birr
• 50 - 100 birr
• 100 - 150 birr
• 150 - 200 birr
• 200 - 300 birr
• over 300 birr
• other

on a typical day when you chew khat, on average, how much (in grams or bundles) of khat leaves do you normally have?
* 

please choose only one of the followings:

• 50gms /half a bundle or less
• 50gms - 100gms/half a bundle - quarter to a bundle
Appendices

- 100gms - 150gms/ quarter to a bundle - a bundle
- 150gms - 200gms / one bundle - a bundle and half
- 250gms or more/ 2 bundles or more
- Other

Over the past 12 months, have you tended to chew more on your own than you used to?
Please choose the appropriate response*
Please choose only one of the followings:

- Yes
- No

How khat affected your finances in the last 12 months?
Please choose the appropriate response (Yes or No) for the following items. *
Please choose the appropriate response for each item:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Have you spent money on khat that was meant for other things (e.g., rent, photocopying, food etc.) on khat?</td>
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<tr>
<td>Have you sold any of your belonging to buy khat?</td>
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<td>Have you found yourself worried about the amount of money you have been spending on khat?</td>
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<tr>
<td>Have you had any drug related debts?</td>
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<td>Did you find yourself making excuses about money?</td>
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Have you ever accessed services for your khat use (e.g. counselling)?
Please choose the appropriate response*
Please choose only one of the followings:

- Yes
- No

If Yes, what is the main type of drug treatment you have accessed? *
Please choose only one of the followings:

- Not in treatment
- Family treatment
- Rehabilitation Centre
- Community support center
- University counselling/psychiatric Centre
- Public psychiatric centre
- Other

DSM - V

The following questions about your khat use over the last 12 months.
Please, choose the appropriate response for each item:
In the last 12 months did you........... *
Please choose the appropriate response for each item:

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<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>Have job or school troubles as a result of your khat use - like missing too much work, not doing your work well, being demoted or losing a job, or being suspended, expelled, or dropping out of school?</td>
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<td>Have a period when your khat use (or recovering from your khat use) often interfered with taking care of your study or home or family?</td>
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<td>Accidentally injured yourself while under the influence of khat, for example, have a bad fall or cut yourself badly, get hurt in a traffic accident, or anything like that?</td>
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<td>More than once driven a car, motorcycle, truck, boat or other vehicle when you were under the influence of khat?</td>
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<tr>
<td>Find yourself under the influence of khat or feeling its after-effects in</td>
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situations that increased your chances of getting hurt “like swimming, using machinery, or walking in a dangerous area or around heavy traffic?

--------- Get arrested, get held at a police station, or have any other legal problems because of your khat use?

--------- Have arguments with your spouse, boyfriend/girlfriend, family, friends or teachers as a result of your khat use?

--------- Get into physical fights while under the influence of khat?

*In the last 12 months did you……..
Continue to use khat even though you knew it was causing you trouble with your family or friends? *
Please choose only one of the followings:
• ☐ Yes
• ☐ No

Now I’m going to ask you about some OTHER experiences you may have had with khat.

*In the last 12 months did you……..
More than once want to stop or cut down on using khat? *
Please choose only one of the followings:
• ☐ Yes
• ☐ No

In the last 12 months did you……..
More than once try to stop or cut down using khat but found you couldn’t do it? *
Please choose only one of the followings:
• ☐ Yes
• ☐ No

**DSM-V4**

OTHER experiences you may have had with khat.

*Now I’m going to ask you about some OTHER experiences you may have had with khat. In the last 12 months did you…….*

Please choose the appropriate response for each item:

…… Often use khat in larger amounts or for a much longer period than you meant to?

…… Often use khat in large amounts or for a much longer period than you meant to?

…… Have a period of a month or more when you spent a lot of time using khat or getting over its bad after-effects?

…… Have a period of a month or more when you spent a lot of time making sure you always had enough khat available?

…… Find that your usual amount of khat had much less effect on you than it once did?

…… Find that you had to use much more khat than you once did to get the effect you wanted?

…… Give up or cut down on activities that were important to you in order to use khat like work, school, or associating with friends or relatives?

…… Give up or cut down on activities that you were interested in or that gave you pleasure in order to use khat?

(Now I’m going to ask you about some OTHER experiences you may have had with khat. In the last 12 months did you……
…… give up or cut down on activities that you were interested in or that gave you pleasure in order to use khat?)

Please choose only one of the followings:
• ☐ Yes
• ☐ No
Now I’m going to ask you about some OTHER experiences you may have had with khat.

In the last 12 months did you…….*

Please choose the appropriate response for each item:

…… Continue to use khat even though it was making you feel depressed, uninterested in things, or suspicious and distrustful of other people?  
……. Continue to use khat even though you knew it was causing you a health problem or making a health problem worse?

In the last 12 months, did you have any of the following bad aftereffects when the effects of khat were wearing off? This includes the morning after using it or in the first few days after stopping or cutting down on it. For example, did you….*

Please choose the appropriate response for each item:

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep more than usual?</td>
<td></td>
<td></td>
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<tr>
<td>Feel weak or tired? (not due to insufficient sleep or rest)</td>
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<td></td>
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<tr>
<td>Feel depressed?</td>
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<td></td>
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<tr>
<td>Eat more than usual or gain weight? (increase in appetite)</td>
<td></td>
<td></td>
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<tr>
<td>Feel anxious or nervous?</td>
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<tr>
<td>Become so restless you fidgeted paced or couldn’t sit still?</td>
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<tr>
<td>Move or talk much more slowly than usual?</td>
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<tr>
<td>Have unpleasant dreams that often seemed real?</td>
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<tr>
<td>See, feel or hear things that weren’t really there?</td>
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<tr>
<td>Have trouble falling sleep or staying asleep?</td>
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<tr>
<td>Have very bad headaches?</td>
<td></td>
<td></td>
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<tr>
<td>Become irritated more easily than usual?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eat less than usual or lose weight? (appetite decrease)</td>
<td></td>
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<tr>
<td>Have trouble concentrating?</td>
<td></td>
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<tr>
<td>Have a strong desire or craving for more khat</td>
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</tbody>
</table>

…… was there ever a time where two or more of these problems occurred together for two days or more because of stopping, cutting down on, or going without khat? *

Please choose only one of the followings:

- Yes
- No
In the last 12 months did you......

...... did you take more khat or a similar drug to get over or avoid any of these bad aftereffects? *

Please choose only one of the followings:

- ☐ Yes
- ☐ No

### Khat Expectancy and Reason

*The following questions ask about what impact Khat has on you. Please indicate how true each statement is of you*

Please, choose the appropriate response for each item from:

(1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree) *

<table>
<thead>
<tr>
<th>I have better ideas when I am chewing khat</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have better concentrations when I am chewing khat</td>
<td></td>
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<tr>
<td>Little things annoy me less when I am chewing khat</td>
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<tr>
<td>I have more self-confidence when chewing khat</td>
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<tr>
<td>I chew khat to get full enjoyment out of life</td>
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<tr>
<td>Chewing khat makes me passive</td>
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<tr>
<td>When I chew khat I withdraw from others</td>
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<tr>
<td>When I chew khat it is easier to express my feelings</td>
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<tr>
<td>Chewing khat makes me more easily irritated</td>
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<tr>
<td>When I chew khat my mood feels flat</td>
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<tr>
<td>Chewing khat makes me happy</td>
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<tr>
<td>Chewing khat makes me feel insecure</td>
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<tr>
<td>When I chew khat I feel panicky</td>
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<tr>
<td>When I chew khat I feel excited</td>
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<tr>
<td>When I chew khat I feel jumpier and more agitated</td>
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<tr>
<td>Chewing khat makes me lose sexual interest</td>
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<tr>
<td>When I chew khat I have more energy</td>
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<tr>
<td>When I chew khat I do things that I do not really mean to do</td>
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<tr>
<td>Chewing khat makes me feel insecure</td>
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<tr>
<td>I become clumsier when I chew khat</td>
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<tr>
<td>When I chew khat I tend to avoid sex</td>
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<tr>
<td>When I chew khat I can speak my mind</td>
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<tr>
<td>Chewing khat makes me talk more</td>
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<tr>
<td>When I chew khat I tend to avoid people for fear of embarrassment</td>
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<tr>
<td>Chewing khat helps me feel normal again</td>
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<tr>
<td>When I chew khat I become less shy</td>
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<tr>
<td>When I chew khat I will be more easily irritated</td>
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<tr>
<td>I tend to adopt who cares attitude when I chew khat</td>
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<tr>
<td>When I chew khat I become less motivated</td>
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<tr>
<td>Chewing khat makes me serious</td>
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<tr>
<td>Chewing khat increases my tension</td>
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<td>I feel restless when I chew khat</td>
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<tr>
<td>When I chew khat I become more aware of what I say and what I do</td>
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<tr>
<td>Chewing khat ultimately makes me confused</td>
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<tr>
<td>When I chew khat I become more sexually responsive</td>
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</tbody>
</table>
Chewing khat makes me outgoing and friendly
I become more worried about what others say about me when I chew khat

The following questions ask about the reasons why you smoke khat. Please mark from 1 (not true of me) to 10 (very true of me) how true each statement is for you*

Please choose the appropriate response for each item from:

- In the last 12 months….
- I use khat because I want to stay motivated for my work or study
- I use khat because I want to stay awake or alert
- I use khat because I want to achieve better
- I use khat because I want to use other drugs and alcohol
- I use khat as it helps me escape from my problems and worries
- I use khat as it helps me to interact with others
- I use khat as it helps me to increase my thinking and reasoning
- I use khat as I enjoy how it changes my perception
- I use khat as it enhances my concentration on my study
- I use khat as I prefer it to everything else
- I use khat to avoid experiencing psychotic symptoms
- I use khat as it makes me more alert or energetic
- I use khat as it helps me escape from my problems and worries
- I use khat, so I do not have to interact with others
- I use khat because I want to use other drugs and alcohol
- I use khat because I want to achieve better
- I use khat because I want to feel more confident and enthusiastic
- I use khat because I want to stay awake or alert
- I use khat because I want to stay motivated for my work or study

Severity of Dependence (SDS - Khat)
In the last 12 months….
Please, choose the appropriate response for each item from:
(1 = Never or almost never, 2 = Sometimes, 3 = rarely, 4 = Often 5 = Always or nearly always) *

Did you ever think your use of khat was out of control?
Did the prospect of missing khat make you very anxious or worried?
Do you worry about your khat use?
Do you wish you could stop using khat?

How difficult would you find it to stop or go without? *
Please choose only one of the followings:
- Not difficult
- Quite difficult
- Very difficult
- Impossible
Appendices

- Other

K - 10

Please indicate what best represents how you have been over the past four weeks.
During the last four weeks about how often did you...........

Please, choose the appropriate response for each item from:
(1 = none of the time, 2 = A little of the time, 3 = some of the time, 4 = Most of the time, 5 = All of the time) *

<table>
<thead>
<tr>
<th>Question</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>.....feel fatigued out for no good reason?</td>
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<tr>
<td>.....feel nervous?</td>
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<tr>
<td>.....feel so anxious that nothing could calm you down?</td>
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<tr>
<td>.....feel hopeless?</td>
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<tr>
<td>.....feel restless or fidgety?</td>
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<tr>
<td>.....feel so restless you could not sit still?</td>
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<tr>
<td>.....feel depressed?</td>
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<tr>
<td>.....feel that everything was an effort?</td>
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<tr>
<td>.....feel so sad that nothing could cheer you up?</td>
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<tr>
<td>.....feel worthless?</td>
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</tbody>
</table>

The following questions ask about things in the last 12 months.
In the last 12 months ......

Please, choose the appropriate response (Yes or No) for each item: *

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>.....have you ever had any mental health problems, such as depression, anxiety, or psychosis? This could include any issues you haven’t spoken to a health professional about.</td>
<td></td>
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</tr>
<tr>
<td>.....have you attended an appointment with a health professional for mental health problems?</td>
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<tr>
<td>.....have you been prescribed any medication for a mental health problem?</td>
<td></td>
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</tr>
</tbody>
</table>

What was the mental health problem(s)? *

Please choose all that apply:
- Depression
- Phobia
- Posttraumatic stress disorder
- Other psychosis
- Other: 

SF - 12

The following questions ask about your health. In general, would you say your health is: *

Please choose only one of the followings:
- Excellent
- Very good
- Good
- Fair
- Poor

The following questions ask about your activities you might do during a typical day.

Does your health limit you in these activities? *

Please choose the appropriate response for each item:  

| Yes | No |
Moderate activities such as moving a table, cleaning a house, playing football
Climbing several stairs

During the past 4 weeks, have you had any of the following problems with your work, study or other regular activities as a result of your physical health? *
Please choose the appropriate response for each item:

Accomplished less than you would like
Were limited in the kind of work or other regular daily activities

During the past 4 weeks, have you had any of the following problems with your work, study or other regular activities as a result of your emotional problems (such as feeling depressed or anxious)?
Please, choose the appropriate response (Yes or No) for each item: *

Accomplished less than you would like?
Did work or other regular daily activities less carefully than usual?

During the past 4 weeks...........
Please, choose the appropriate response for each item from:
(1 = Not at all, 2 = A little bit, 3 = moderately, 4 = Quite a bit, 5 = extremely) *

How much did pain interfere with your normal work (including both work outside the home and housework)?

The next questions are about how you feel and how things have been with you during the past 12 months.
As you read each question, please indicate one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks ........?
Please, choose the appropriate response for each item from:
(1 = none of the time, 2 = A little bit of the time, 3 = some of the time, 4 = A good bit of the time, 5 = All the time) *

……have you felt calm and peaceful?
……did you have a lot of energy?
……have you felt downhearted and blue?

During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?
(1 = none of the time, 2 = A little bit of the time, 3 = some of the time, 4 = Most of the time, 5 = All of the time) *
Please choose only one of the followings:
• 
  ○1
• 
  ○2
• 
  ○3
• 
  ○4
• 
  ○5
OTHER DRUGS
The following questions are interested in your experience with drugs other than khat.
Of the drugs listed below, which (if any) was the FIRST one you ever tried in the past twelve months? *
Please choose only one of the followings:

- I've never tried any of the substances listed below
- Tranquillizers or sedatives (without a doctor or medical worker telling you to do so)
- Marijuana or hashish
- Khat
- Shisha
- Tobacco
- I don't know what it was
- Other

In the past 12 months, of the drugs listed below, which (if any) was the FIRST one you tried? *
Please choose only one of the followings:

- I've never tried any of the substances listed below
- Tranquillizers or sedatives (without a doctor or medical worker telling you to do so Phobia)
- New answer option
- Marijuana or hashish
- Khat
- Shisha
- Tobacco
- I don't know what it was
- Other

How often do you have a drink containing alcohol? *
Please choose only one of the followings:

- Never
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week
- Daily or nearly daily
- Other

How many drinks (in Bottles/glasses of drinks) containing alcohol do you have on a typical day when you
are drinking? *
Please choose only one of the followings:

- 1 to 2
- 3 to 4
- 5 to 6
- 7 to 9
- 10 or more
- Other

How often do you have six or more drinks (in Bottles/glasses) containing alcohol on one occasion? *
Please choose only one of the followings:

- Never
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week
- Daily or nearly daily
- Other
Do you smoke tobacco? *
Please choose only one of the followings:
- Yes
- Yes, only when I chew khat
- No
- Other

How often do you smoke tobacco? *
Please choose only one of the followings:
- Never
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week
- Daily or nearly daily
- Other

Do you smoke shisha? *
Please choose only one of the followings:
- Yes
- Yes, when I chew khat
- No
- Other

How often do you smoke shisha? *
Please choose only one of the followings:
- Never
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week
- Daily or nearly daily
- Other

Have you used tranquillisers and/or sleeping pills (e.g. benzos, valium, alprazolam, temazepam) for non-medical purposes in the last 12 months? *
Please choose only one of the followings:
- Yes
- Yes, when I chew Khat
- No
- Other

In the last 12 months, how often did you use tranquillisers and/or sleeping pills for non-medical purposes? *
Please choose only one of the followings:
- Never
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week
- Daily or nearly daily
- Other

Have you used inhalants (e.g. glue) in the last 12 months? *
Please choose only one of the followings:
- Yes
- No

In the last 12 months, how often did you use inhalants? *
Please choose only one of the followings:
- Never
- Monthly or less
- 2 to 4 times a month
Fagerstrom Nicotine Dependence Scale (FTND)
How soon after you wake up do you smoke your first cigarette? *
Please choose only one of the followings:
- Within 5 minutes
- 6-30 minutes
- 31-60 minutes
- After 60 minutes

Do you find it difficult to refrain from smoking in places where it is forbidden for example at church, at the library, in the cinema, and so on? *
Please choose only one of the followings:
- Yes
- No

Which cigarette would you hate to give up? *
Please choose only one of the followings:
- The first one in the morning
- All others

How many cigarettes do you smoke a day? *
Please choose only one of the followings:
- 10 or less
- 11-20
- 21-30
- 31 or more

Do you smoke more during the first two hours than during the rest of the day? *
Please choose only one of the followings:
- Yes
- No

Do you smoke if you are so ill that you are in bed most of the day? *
Please choose only one of the followings:
- Yes
- No

Personal Wellbeing Index (PWI)
The following questions ask how satisfied you feel, on a scale from zero to 10. Zero means you feel completely dissatisfied and 10 means you feel completely satisfied. The middle of the scale is 5, which means you feel neutral, neither satisfied nor dissatisfied.

Thinking about your own life and personal circumstances, how satisfied are you……
Please, choose the appropriate response for each item from:
Â(1 = completely dissatisfied, 2 ... 3...... 4.... 5 = Neutral, 6.... 7 ....8....9.... 10 = completely satisfied) *

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>......with your personal relationships?</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
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<tr>
<td>......with your standard of living?</td>
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<tr>
<td>......with your life as a whole?</td>
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<tr>
<td>......with your personal relationships?</td>
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<td>......with your health?</td>
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<tr>
<td>......with what you are achieving in life?</td>
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<td>......with how safe you feel?</td>
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<td>......with feeling part of your community?</td>
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<td>......with your future security?</td>
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</tbody>
</table>
**Cognitive and Academic experiences (CGAC)**

The following questions ask about your learning and academic experiences, on a scale from zero to 3. Zero means that experience happens to you none of the times and 4 means that experience happens all of the times describes you very well.

During the last 12 months……Please, choose the appropriate response for each item from:
(0 - doesn't describe me at all, 1 - describes me somewhat, 2 - describes me pretty well, 3 - describes me very well) *

Please choose the appropriate response for each item:

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<th>0</th>
<th>1</th>
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<tbody>
<tr>
<td>......I have Trouble listening in lectures</td>
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<tr>
<td>......I trouble making study plans</td>
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<td>......I spent lot of time doing nothing</td>
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<td>......I unable to do two or three tasks in a row</td>
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<tr>
<td>......I have trouble remembering things to do</td>
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<tr>
<td>.... I don’t stick to tasks to completion</td>
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<td>.... I often have lack of attention</td>
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<tr>
<td>.... I have trouble with short term memory</td>
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<td>.... I don't stick to tasks that are optional</td>
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<tr>
<td>.... I have difficulty sustaining concentration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>.... I often have lack of concentration on studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The following questions ask about your overall academic achievement. Please indicate your response by selecting one number from:
1(exremely lower) 2....3....4 (a bit lower), 5 (same) 6 (a bit higher) 7.... 8....9...to 10 (Extremely higher)  
*If you are a College student.............

Please choose the appropriate response for each item:

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>compared to your high school GPA, your current college GPA is</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What was your high school GPA?

Please, enter your GPA in figures*

Please write your answer here:

What is your current college GPA?

Please, enter your GPA in figures*

Please write your answer here: ____________________

**Social approval**

The following questions ask about your attitudes concerning drug use. Individuals differ in whether or not they disapprove of people doing certain things.

DO YOU DISAPPROVE of people doing any of the following?

Please, choose the appropriate response for each item from
(Don't disapprove/Disapprove/Strongly disapprove/Don’t Know) *

Please choose the appropriate response for each item:

<table>
<thead>
<tr>
<th></th>
<th>Don't disapprove</th>
<th>Disapprove</th>
<th>Strongly disapprove</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chewing Khat every day</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Chewing khat more than 100gms (a bundle) per session</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoking 10 or more cigarettes a day</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Having five or more drinks* in a row each weekend</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>
### Drug risk

The following questions ask about your thoughts of risks associated with different drug related activities. How much do you think people risk harming themselves (physically or in other ways), if they do the following?

Please, choose the appropriate response for each item from (No Risk, Slight Risk, Moderate Risk, Great Risk, and Don’t Know) *

<table>
<thead>
<tr>
<th>Activity</th>
<th>No Risk</th>
<th>Slight Risk</th>
<th>Moderate Risk</th>
<th>Great Risk</th>
<th>Don’t Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chewing khat occasionally</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Chewing khat frequently</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Chewing chat on daily basis</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Chewing one or more bundle of khat per session</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoke cigarettes occasionally</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoke one or more packs of cigarettes per day</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Have one or two drinks nearly every day</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Have four or five drinks in a row nearly every day</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Have five or more drinks in a row each weekend</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Try marijuana or hashish (cannabis, pot, grass) once or twice</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoke marijuana or hashish occasionally</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoke marijuana or hashish regularly</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoking shisha everyday</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Smoking shisha occasionally</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

Thank you for your time and effort in completing this survey!
Appendices

If you would like to contact someone if you are feeling at all worried, anxious, or distressed, you can contact:
Adama Science & Technology University Counselling Health Services Centres at http://www.astu.edu.et/index.php/services/medical-and-clinical-services/health-center

Further participation

Research is only possible due to the generous nature of those who volunteer to participate. As researchers, we are constantly indebted to those who give up their time and resources to participate.

If you are interested in participating in further research on Khat Chewing and Cognitive Functioning, and you are a university student between the ages of 18 and 35, and frequently chew khat (at least 3 times a week over the last 12 months) please:

✓ If you are completing the survey by hand using the pencil and paper version of the survey, complete the attached Further Research Participation and seal it in the white envelope titled Further Research Participation and post it back to us separately from your survey
✓ If you are completing the survey electronically, click here

While we do appreciate any expressions of interest, please do not feel obliged to complete this form, your current contribution has already added to this research project significantly.

Submit your survey.
Thank you for completing this survey.
Appendices

Appendix B — Information Sheet and Consent Form/electronic version

Thank you for your interest in this research. This study is being conducted in partial fulfillment of a PhD degree for Samson Duresso under the supervision of Dr. Raimondo Bruno at the University of Tasmania. Before you decide to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please contact the researchers by email at Samson.Duresso@utas.edu.au if you would like more information.

1. What is this study about?
This study aims to better understand the ways people consume khat, and how any problems may develop. In particular, we aim to better understand the possible positive and negative psychological, emotional, health, cognitive and social implications that may arise from different degrees of khat use. This study will help with the development of ways of identifying khat problems and the interventions needed to manage khat dependency. You are invited to participate if you are over the age of 16 years old, live in Ethiopia, and have chewed khat in the past 12 months.

2. What will I be asked to do?
As a participant in this survey, you would be asked to complete an anonymous online or paper-pencil survey on the positive and negative effects of chewing khat, including questions regarding your health, lifestyle, other drug use, physical health, mental health, cognitive/academic influences and social interaction. This will take about 30-40 minutes to complete. It is important that you understand that your involvement in this study is voluntary. If you decide to discontinue participation at any time, you can do so by simply closing your web browser or withholding the questionnaire. No information will be submitted to the researchers until you have completed the survey.

3. Where will the data be kept?
All of the survey information/data we obtain from participants will be kept on a password protected computer in the School of Psychology, University of Tasmania, for a period of five years.

4. How will the data be kept secure?
All survey data will be stored on a password-protected computer.

5. How and when will the data be destroyed?
All data relating to the study will be electronically stored for five years. After this period, all survey data will be deleted, following secure data destruction processes.

6. Are there any possible benefits from participation in this study?
Participating in this study may result in individuals having a greater understanding of their khat use and the possible effects that this may have on their wellbeing. By participating in this study, you are providing important and valuable information in an area of research that is relevant to you. Your participation will help us gain important information that will assist us to better understand the positive and negative effects that Ethiopians experience from their khat use and
how this relates to different levels of dependence and withdrawal problems. This information will be valuable in the development of community intervention programs aimed at reducing the harms some people may experience with khat.

Additionally, to thank you for your time, upon completion you may choose to enter a draw to win an Apple iPad.

7. Are there any possible risks involved in participating in this study?
There are no specific risks anticipated with taking part in this study. However, should you become uncomfortable or upset whilst completing the survey, or feel you’d like to talk to someone about your khat use, below are some contact details of services that are available during office hours 5 days a week:

8. How will your confidentiality and privacy be protected?
Our server uses a 128bit encryption, which is backed by Verisign, the world largest security certificate provider. This is the same level of encryption used by banks and the Australian Tax Office. Therefore, the responses you provide will remain completely anonymous and confidential, as the risk of identification is negligible. However, you may also choose to use an anonymiser, which will mask your IP address. This will mean that both the computer you are using, as well as the responses you provide will be completely unidentifiable. Anonymisers work by inserting a fake computer between your computer and our server, therefore, masking your IP address. For more information, see: http://www.livinginternet.com/i/is_anon.htm

On completion of the survey, you will be asked if you would like to take part in the prize draw. If you wish to take part, you will be redirected to a different website, where you will be asked to provide an email address. In order to protect your confidentiality, we would recommend using an email address that is not associated with your name in any way, such as bowwow@google.com rather than your.name@myworkplace.com. Free email addresses are available at mail.google.com or mail.yahoo.com, and many other sites. No connection is made between completed questionnaires and submitted email addresses, as these are stored on independent servers and no timestamps are taken.

9. What if I have questions or concerns about this research?
If you would like to discuss any aspect of this study please feel free to contact either of the researchers by email at Raimondo.Bruno@utas.edu.au or Samson.Duresso@utas.edu.au. If you would like to view the results of this research, this can occur at the conclusion of this research and the results will be published online at the survey website. Additionally, if the participants require further information or want to discuss the results they are encouraged to call or email the researchers.

This study has been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study, you should contact the Executive Officer of the HREC (Tasmania) Network on +61(0)36226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote [HREC project number: H0013036].

10. How do I participate?
By clicking the "Next" button below, you indicate that you have read the information on this page and you are agreeing to participate in this survey. If you do not wish to participate, we thank you for your time and you can close this browser window to end this session.
Consent

1. I have read and understood the 'Information Sheet' for this study.
2. I have understood the nature and possible effects of this study.
3. I have understood that this study involves answering questions about khat and other drug use, physical health, mental health, and social interactions.
4. I am 16 years of age or older.
5. I have understood that all questions are optional and that I may choose to not answer any questions that I am uncomfortable with.
6. I have understood that all research data will be securely stored on a password protected server at the University of Tasmania.
7. I have understood that my participation is voluntary and that I cannot be identified in any way.

I agree with the above statements and wish to participate in the survey by clicking “Next”

Thank you for taking the time to consider this study and we hope you are interested in participating.
Appendix C—Information Sheet and Consent Form/Pencil paper version

Thank you for your interest in this research. This study is being conducted in partial fulfillment of a PhD degree for Samson Duresso under the supervision of Dr. Raimondo Bruno at the University of Tasmania. Before you decide to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please contact the researchers by email at Samson.Duresso@utas.edu.au if you would like more information.

1. What is this study about?
This study aims to better understand the ways people consume khat, and how any problems may develop. In particular, we aim to better understand the possible positive and negative psychological, emotional, health, cognitive and social implications that may arise from different degrees of khat use. This study will help with the development of ways of identifying khat problems and the interventions needed to manage khat dependency. You are invited to participate if you are over the age of 16 years old, live in Ethiopia, and have chewed khat in the past 12 months.

2. What will I be asked to do?
As a participant in this survey, you would be asked to complete an anonymous online or paper-pencil survey on the positive and negative effects of chewing khat, including questions regarding your health, lifestyle, other drug use, physical health, mental health, cognitive/academic influences and social interaction. This will take about 30-40 minutes to complete. It is important that you understand that your involvement in this study is voluntary. If you decide to discontinue participation at any time, you can do so by simply closing your web browser or withholding the questionnaire. No information will be submitted to the researchers until you have completed the survey.

3. Where will the data be kept?
All of the survey information/data we obtain from participants will be kept on a password protected computer in the School of Psychology, University of Tasmania, for a period of five years.

4. How will the data be kept secure?
All survey data will be stored on a password-protected computer.

5. How and when will the data be destroyed?
All data relating to the study will be electronically stored for five years. After this period, all survey data will be deleted, following secure data destruction processes.

6. Are there any possible benefits from participation in this study?
Participating in this study may result in individuals having a greater understanding of their khat use and the possible effects that this may have on their wellbeing. By participating in this study, you are providing important and valuable information in an area of research that is relevant to you. Your participation will help us gain important information that will assist us to better
understand the positive and negative effects that Ethiopians experience from their khat use and how this relates to different levels of dependence and withdrawal problems. This information will be valuable in the development of community intervention programs aimed at reducing the harms some people may experience with khat.

Additionally, to thank you for your time, upon completion you may choose to enter a draw to win an Apple iPad.

7. Are there any possible risks involved in participating in this study?
There are no specific risks anticipated with taking part in this study. However, should you become uncomfortable or upset whilst completing the survey, or feel you’d like to talk to someone about your khat use, below are some contact details of services that are available during office hours 5 days a week:

8. How will your confidentiality and privacy be protected?
Our server uses a 128bit encryption, which is backed by Verisign, the world largest security certificate provider. This is the same level of encryption used by banks and the Australian Tax Office. Therefore, the responses you provide will remain completely anonymous and confidential, as the risk of identification is negligible. However, you may also choose to use an anonymiser, which will mask your IP address. This will mean that both the computer you are using, as well as the responses you provide will be completely unidentifiable. Anonymisers work by inserting a fake computer between your computer and our server, therefore, masking your IP address. For more information, see: http://www.livinginternet.com/i/is_anon.htm

On completion of the survey, you will be asked if you would like to take part in the prize draw. If you wish to take part, you will be redirected to a different website, where you will be asked to provide an email address. In order to protect your confidentiality, we would recommend using an email address that is not associated with your name in any way, such as bowwow@google.com rather than your.name@myworkplace.com. Free email addresses are available at mail.google.com or mail.yahoo.com, and many other sites. No connection is made between completed questionnaires and submitted email addresses, as these are stored on independent servers and no timestamps are taken.

9. What if I have questions or concerns about this research?
If you would like to discuss any aspect of this study please feel free to contact either of the researchers by email at Raimondo.Bruno@utas.edu.au or Samson.Duresso@utas.edu.au. If you would like to view the results of this research, this can occur at the conclusion of this research and the results will be published online at the survey website. Additionally, if the participants require further information or want to discuss the results they are encouraged to call or email the researchers.

This study has been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study, you should contact the Executive Officer of the HREC (Tasmania) Network on +61(0)36226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote [HREC project number: H0013036].

10. How do I participate?
By clicking the "Next" button below, you indicate that you have read the information on this page and you are agreeing to participate in this survey. If you do not wish to participate, we thank you for your time and you can close this browser window to end this session.
Consent

1. I have read and understood the *Information Sheet* for this study.
2. I have understood the nature and possible effects of this study.
3. I have understood that this study involves answering questions about khat and other drug use, physical health, mental health, and social interactions.
4. I am 16 years of age or older.
5. I have understood that all questions are optional and that I may choose to not answer any questions that I am uncomfortable with.
6. I have understood that all research data will be securely stored on a password protected server at the University of Tasmania.
7. I have understood that my participation is voluntary and that I cannot be identified in any way.

*Thank you for taking the time to consider this study and we are hope you are interested in participating.*
Appendix D: Further Research Participation Form/ Electronic version

Further participation

Research is only possible due to the generous nature of those who volunteer to participate. As researchers, we are constantly indebted to those who give up their time and resources to participate.

If you are interested in participating in further research on Khat Chewing and Cognitive Functioning, and you are a university student between the ages of 18 and 35, and frequently chew khat (at least 3 times a week over the last 12 months) please:
If you are completing the survey by hand, complete the attached “Further Research Participation” and seal it in the white envelope titled “Further Research Participation” and post it back to us.
If you are completing the survey electronically, [click here](#)

While we do appreciate any expressions of interest, please do not feel obliged to complete this form, your current contribution has already added to this research project significantly.
Appendix E: Further Research Participation Form/ Envelop version

PARTICIPATION IN FURTHER RESEARCH

Survey of Khat use and experiences

Thank you for participating in our survey.

If you are a University student between the ages of 18 and 35 consume khat frequently (3 or more days per week) and are interested in volunteering to participate in further research on khat chewing and impacts on cognitive control functions, please provide a contact number and/or email address below:

Your phone number: ............................................
Confirm phone number: ............................................

Email address: ............................................
Confirm email address: ............................................

We will contact you in early January 2014 to determine your continued interest and eligibility for subsequent studies.

Thank you!
Appendix F: General Survey Email Preamble

Survey Khat Use & experience

Dear,

At the University of Tasmania, we are conducting research examining the effect of chronic khat consumption on emotional and cognitive functioning. We are currently seeking volunteers to participate and would be most appreciative if you would consider distributing the attached flyer to members of your business/organisation/society.

Participants are asked to fill in a 30-40-minute survey which examines history, rate of khat use, current consumption patterns, motivations for, and perceived emotional and cognitive consequences of use.

Volunteers must have at least some history and exposure of khat use to participate. Participants will have the opportunity to go into a prize draw to win an Apple IPad. Data collection will be complete by January 2014. So please feel free to remove the flyer at this point.

The survey is available online at [www.khatuse.utas.edu.au](http://www.khatuse.utas.edu.au) or a paper version can be requested by emailing [Samson.Duresso@utas.edu.au](mailto:Samson.Duresso@utas.edu.au) or calling +251 .

Please feel free to contact me further with any queries. Thank you in advance for your assistance.

Kind regards

Samson Duresso
School of Psychology
University of Tasmania
Temporary Psychology Research office (Adama Science & Technology University)
P. O. Box 456
Oromia, Ethiopia

Ph: +251 .
Email: [Samson.Duresso@utas.edu.au](mailto:Samson.Duresso@utas.edu.au)
Appendix G: General Survey Noticeboard Advertisement

Khat use & experience

Are you interested in the effects of khat chewing?

Researchers at the University of Tasmania (Australia) are seeking volunteers over the age of 16 to take part in a study examining khat chewing and experiences in Ethiopia.

Participation involves completing a 30-40 minute anonymous online or pencil and paper survey which examines consumption rate, antecedents and consequences of use, perceived positive and negative effects of khat chewing, including questions about health and life styles. **People with at least moderate history of khat use are welcome to participate.**

Participants have the opportunity to enter a prize draw to win an Apple iPad.

The survey can be completed online at: [www.khatsurvey.utas.edu.au](http://www.khatsurvey.utas.edu.au) or you can request a postal paper version by phoning +25 or emailing: Samson.Duresso@utas.edu.au
**Appendix H: General Survey Noticeboard Advertisement (Amharic version)**

**University of Tasmania (Australia)**  
**School of Psychology**  
**ልሚስሚያ የማወቅ ፍላጎት አሎዎት**

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**Appendix H**: General Survey Noticeboard Advertisement (Amharic version)

**University of Tasmania (Australia)**  
**School of Psychology**  
**ልሚስሚያ የማወቅ ፍላጎት አሎዎት**

_

<table>
<thead>
<tr>
<th>Text in English</th>
<th>Amharic Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of concentration on studies</td>
<td>ለማወቅ ፍላጎት ከወረቀት ለማወቅ ፍላጎት ከወረቀት</td>
</tr>
<tr>
<td><a href="http://www.khatsurvey.utas.edu.au">www.khatsurvey.utas.edu.au</a></td>
<td>ልብስ ለማወቅ ፍላጎት ከወረቀት ለማወቅ ፍላጎት ከወረቀት</td>
</tr>
</tbody>
</table>

**Survey: Khat use & Experiences**  
**www.khatsurvey.utas.edu.au**  
**Ph: 093605535**  
**Email: Samson Duresso@utas.edu.au**
Title of Project: *Khat Withdrawal, Craving and Relapse among Chronic Khat Users*

You are invited to participate in a study that investigates KHAT WITHDRAWAL, CRAVING AND RELAPSE. The aim of this study is to examine the *nature of withdrawal syndromes in chronic khat users, the role it plays in craving over the course of a cessation attempt and the extent of craving during quit attempts and its relationship with environmental cues*. The research is being conducted by Samson Duresso in partial fulfilment of the requirements of a PhD in Psychology. Samson is being supervised by Dr. Raimondo Bruno, Dr. Allison Matthews, from the school of Psychology and Dr. Stuart Ferguson from the School of Medicine/Pharmacy, University of Tasmania. Samson Duresso can be contacted on +25192362504 or email: Samson.Duresso@utas.edu.au.

1. ‘What is the purpose of this study?’

The purpose is to examine the nature of withdrawal syndromes in chronic khat users, the role it plays in craving over the course of a cessation attempt and the extent of craving during quit attempts and its relationship with environmental cues.

2. ‘Why have I been invited to participate in this study?’

You are eligible to participate in this study because you are a student at Adama Science & Technology University and frequent khat user who is interested in quitting chewing.

3. ‘What does this study involve?’

If you choose to participate in this study, you will be required to monitor your chewing habit for 10 days before you begin to quit chewing, and for four [4] weeks after you quit; to take part in up to five [5] study visits at Adama Science & Technology University campus. Visit 1 will take approximately 30-45 minutes to complete, during which you will be assigned a quit date that will fall 10 days after this initial enrolment visit. For these first 10 days of the study, you will be...
asked to monitor your chewing using a simple to use hand-held computer - similar in appearance to a mobile telephone. You will need to return this device at the end of the study (visit – 5). You will be asked to carry this device with you at all times until Visit 5. Each day you will be asked to indicate, by pressing a button on the phone, each time you chew khat, you will also be asked to complete 4-5 assessments at random times throughout your waking day. Each assessment will take approximately 1-2 minutes to complete. The researcher will provide training on how to use the study device and will be able to answer any questions that you might have regarding study participation.

After Visit 1, each further study visit will take approximately 15-20 minutes, during which your study data will be downloaded from the monitoring device; and you may be required to provide urine sample. During the quit day study visit (Visit 4), you will be instructed to quit chewing completely. At your final visit (Visit 5), you will be asked about your experiences in the study. In addition, participants who complete the entire study will be reimbursed $66, 50 for their time and out-of-pocket expenses. Your involvement in this study is not linked to your success at quitting khat – if you complete the study you will be reimbursed for your time regardless of whether you quit successfully or not.

It is important that you understand that your involvement in this study is voluntary. While we would be pleased to have you participate, we respect your right to decline. There will be no consequences to you if you decide not to participate. If you decide to discontinue participation at any time, you may do so without providing an explanation. All information will be treated in a confidential manner, and your name will not be used in any publication arising out of the research. All of the research data will be kept in a locked cabinet at the School of Psychology (Tasmania), and on a password protected computer. Hard copy data will be kept for at least five (5) years from the date of the first publication of the study results. Electronic data will be securely stored until it is no longer necessary.

4. Are there any possible benefits from participation in this study?

It is possible that you may quit chewing as a part of this study. Due to the negative effects of continued chewing, this may lead to an improvement in your general health. Furthermore, the information we gather may be beneficial to other chewers who want to quit chewing.
5. Are there any possible risks from participation in this study?

There are no specific risks anticipated with participation in this study aside from those associated with quitting chewing (for example, it is possible that you will experience khat withdrawal symptoms and craving as a result of quitting chewing). However, if you find that you are becoming distressed you will be advised to talk to your regular GP (at Adama University) or alternatively, you may choose to contact a counsellor who you can talk to about your experiences. In Adams Science & Technology University, counselling services can be obtained via http://www.astu.edu.et/index.php/services/medical-and-clinical-services/health-center.

6. What if I have questions about this research?

If you would like to discuss any aspect of this study please feel free to contact Dr. Raimondo Bruno (Raimondo.Bruno@utas.edu.au) or Dr Stuart Ferguson (stuart.ferguson@gmail.com) or Dr. Allison Matthews (Allison.Matthews@utas.edu.au) or Samson Duresso (Samson.Duresso@utas.edu.au or +251 ). The researchers would be happy to discuss any aspect of the research with you. When the study has been finalized the main outcomes will be published on the University of Tasmania’s website.

This study has been approved by the Tasmanian Health and Medical Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study, you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote [REF.NO: H0013347].

Thank you for taking the time to consider this study. If you wish to take part in it, please sign the attached consent form. This information sheet is for you to keep.
APPENDIX J: Consent Form

UNIVERSITY OF TASMANIA

CONSENT FORM

Title of Project: Khat Withdrawal, Craving and Relapse among Chronic Khat Users

1. I have read and understood the ‘Information Sheet’ for this project.
2. The nature and possible effects of the study have been explained to me.
3. I understand that the study involves monitoring my chewing using a simple to use hand-held computer for 10 pre-quit and 28 post-quit days (explained below).
4. In this study, I understand that I will be asked to carry this device with me at all times for the 10 pre-quit and 28 post-quit days of the study.
5. I understand that I am required to return the study device at the end of the study (at visit 5).
6. I understand that I will also be required to visit Adama Science & Technology University Research Centre up to five [5] times for study visits: once to enrol (this current visit), and a further four times over the course of the study. Aside from this enrolment visit (which will take up to 45 minutes), each future study visit will take approximately 15-20 minutes to complete. During each study visit I will also be required to provide a sample of my urine.
7. I understand that if I complete the entire study I will receive $66, 50 as compensation for my time.
8. I understand that participation involves the risk(s) that I may quit chewing as a part of this study and hence potentially experience withdrawal symptoms and craving.
9. I understand that all research data will be securely stored on the University of Tasmania premises for at least five years and will then be destroyed when no longer required.
10. Any questions that I have asked have been answered to my satisfaction.
11. I agree that research data gathered from me for the study may be published provided that I cannot be identified as a participant.
12. I understand that the researchers will maintain my identity confidential and that any information I supply to the researcher(s) will be used only for the purposes of the research.
13. I agree to participate in this investigation and understand that I may withdraw at any time without any consequence, and if I so wish I may request that any data I have supplied to date be withdrawn from the research.
14. I understand that this research has been approved by the Tasmanian Health and Medical Human Research Ethics Committee [project number: H0013347].
Name of Participant: ____________________________

Signature: ____________________________ Date: ____________________________

**Statement by Investigator**

☐ I have explained the project & the implications of participation in it to this volunteer and I believe that the consent is informed and that he/she understands the implications of participation.

If the Investigator has not had an opportunity to talk to participants prior to them participating, the following must be ticked.

☐ The participant has received the Information Sheet where my details have been provided so participants have the opportunity to contact me prior to consenting to participate in this project.

Name of investigator ____________________________

Signature of investigator ____________________________ Date ____________________________
## APPENDIX K: Baseline Questionnaires

### Khat Chewing Habit

The following questions ask about your use of khat in the **last 6 months**.

<table>
<thead>
<tr>
<th>How often do you chew khat?</th>
<th>Never (Skip to Alcohol Use section)</th>
<th>Monthly or less</th>
<th>2 to 4 times a month</th>
<th>2 to 3 times a week</th>
<th>4 or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much (in grams or in bundle) khat leaves do you consume on a typical day when you are chewing khat?</td>
<td>25 – 50gms (about half a bundle)</td>
<td>50 – 100gms (about a bundle)</td>
<td>100 – 150gms (about 1 and half bundle)</td>
<td>150 – 200gms (about 2 bundles)</td>
<td>More than 200gms (2 bundles and more)</td>
</tr>
<tr>
<td>How often do you chew 150gms/a bundle or more khat in a single session?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>What is the greatest amount of khat you have consumed in a single session?</td>
<td>______ gms. Or _____ bundle</td>
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</tbody>
</table>
The following questions ask about your use of alcohol in the *last 12 months*. Please use number of bottles (330ml) or glasses (400ml) to help with your estimation. All information provided will be kept confidential.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never (Skip to Inclusion Question 4)</th>
<th>Monthly or less times a month</th>
<th>2 to 4 times a month</th>
<th>2 to 3 times a week</th>
<th>4 or more times a week</th>
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</thead>
<tbody>
<tr>
<td>How often do you have a drink containing alcohol?</td>
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<tr>
<td>How many drinks containing alcohol do you have on a typical day when you are drinking?</td>
<td>1 or 2 Bottles, 3 or 4 Glasses, 5 or 6 Bottles, 7 to 9 Glasses, 10 or more Bottles</td>
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<tr>
<td>How often during the last year have you found that you were not able to stop drinking once you had started?</td>
<td>Never, Less than monthly, Monthly, Weekly, Daily or almost daily</td>
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<tr>
<td>How often during the last year have you failed to do what was normally expected of you because of drinking?</td>
<td>Never, Less than monthly, Monthly, Weekly, Daily or almost daily</td>
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</tr>
<tr>
<td>How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?</td>
<td>Never, Less than monthly, Monthly, Weekly, Daily or almost daily</td>
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<tr>
<td>How often during the last year have you had a feeling of guilt or remorse after drinking?</td>
<td>Never, Less than monthly, Monthly, Weekly, Daily or almost daily</td>
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<tr>
<td>How often during the last year have you been unable to remember what happened the night before because of your drinking?</td>
<td>Never, Less than monthly, Monthly, Weekly, Daily or almost daily</td>
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<tr>
<td>Question</td>
<td>No</td>
<td>Yes, but not in the last year</td>
<td>Yes, during the last year</td>
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<tr>
<td>Have you or someone else ever been injured because of your drinking?</td>
<td>No</td>
<td></td>
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<tr>
<td>Has a relative or friend or a doctor or other health worker, ever been concerned about your drinking or suggested you cut down?</td>
<td>No</td>
<td></td>
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</tbody>
</table>
APPENDIX M: Baseline Questionnaires

University of Tasmania

Other Drugs Use

Do you, or have you ever used marijuana in the past two weeks? Yes ☐ No ☐

Have you used marijuana in the last two weeks? Yes ☐ No ☐

Have you used any form of illicit drug (apart from marijuana) in the last two weeks? Yes ☐ No ☐

Have you participated in another study within the last three months for which you had to consume any drugs? Yes ☐ No ☐

If yes, what drugs did you consume:

..........................................................................................................................
..........................................................................................................................

Thank you for your participation
APPENDIX N: Baseline Questionnaires

University of Tasmania

**The Kessler Psychological Distress Scale [K-10]**

Please indicate what best represents how you have been over the past four weeks. Please, choose the appropriate response for each item from:

(1 = none of the time, 2 = A little of the time, 3 = some of the time, 4 = most of the time, 5 = All of the time)

During the **last four weeks** about how often did you...........

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<td>....... feel fatigued out for no good reason?</td>
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<td>....... feel nervous?</td>
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<td>...... feel so anxious that nothing could calm you down?</td>
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<tr>
<td>...... feel hopeless?</td>
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<tr>
<td>...... feel restless or fidgety?</td>
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<td>...... feel so restless you could not sit still?</td>
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<td>...... feel depressed?</td>
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<td>...... feel that everything was an effort?</td>
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<td>...... feel so sad that nothing could cheer you up?</td>
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<tr>
<td>...... feel worthless?</td>
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</tbody>
</table>
APPENDIX O: Baseline Questionnaires

University of Tasmania
Fagerström Nicotine Dependence Scale (FTND)

Please mark only one of the following:

1. How often do you smoke tobacco (please mark)?
   - Never
   - Less than monthly
   - 2–4 times a month
   - 2–4 times a week
   - Daily or almost daily

2. How soon after you wake up do you smoke your first cigarette? *
   - Within 5 minutes
   - 6–30 minutes
   - 31–60 minutes
   - After 60 minutes

3. Do you find it difficult to refrain from smoking in places where it is forbidden for example at church, at the library, in the cinema, and so on? *
   - Yes
   - No

4. Which cigarette would you hate to give up? *
   - The first one in the morning
   - All others

5. How many cigarettes do you smoke a day? *
   - 10 or less
   - 11–20
   - 21–30
   - 31 or more

6. Do you smoke more during the first two hours than during the rest of the day? *
   - Yes
   - No

7. Do you smoke if you are so ill that you are in bed most of the day? *
   - Yes
APPENDIX P: Ethics approval letter 1

29 April 2013

Dr Raimondo Bruno
School of Psychology
Private Bag 30

Student Researcher: Samson Duresso
Sent via email

Dear Dr Bruno

Re: MINIMAL RISK ETHICS APPLICATION APPROVAL
Ethics Ref: H0013198 - Academic Functioning Questionnaire: A pilot study

We are pleased to advise that acting on a mandate from the Tasmania Social Sciences HREC, the Chair of the committee considered and approved the above project on 26 April 2013.

This approval constitutes ethical clearance by the Tasmania Social Sciences Human Research Ethics Committee. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approval of other bodies or authorities is required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

Please note that this approval is for four years and is conditional upon receipt of an annual Progress Report. Ethics approval for this project will lapse if a Progress Report is not submitted.

The following conditions apply to this approval. Failure to abide by these conditions may result in suspension or discontinuation of approval.

1. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval, to ensure the project is conducted as approved by the Ethics Committee, and to notify the Committee if any investigators are added to, or cease involvement with, the project.

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES
2. **Complaints:** If any complaints are received or ethical issues arise during the course of the project, investigators should advise the Executive Officer of the Ethics Committee on 03 6226 7479 or human.ethics@utas.edu.au.

3. **Incidents or adverse effects:** Investigators should notify the Ethics Committee immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.

4. **Amendments to Project:** Modifications to the project must not proceed until approval is obtained from the Ethics Committee. Please submit an Amendment Form (available on our website) to notify the Ethics Committee of the proposed modifications.

5. **Annual Report:** Continued approval for this project is dependent on the submission of a Progress Report by the anniversary date of your approval. You will be sent a courtesy reminder closer to this date. Failure to submit a Progress Report will mean that ethics approval for this project will lapse.

6. **Final Report:** A Final Report and a copy of any published material arising from the project, either in full or abstract, must be provided at the end of the project.

Yours sincerely

Katherine Shaw  
Ethics Officer  
Tasmania Social Sciences HREC
APPENDIX Q: Ethics approval letter 2

20 August 2013

Dr Raimondo Bruno
C/- Psychology

Sent via email

Dear Dr Bruno

REF NO: H0013347
TITLE: Khat withdrawal, craving and relapse among chronic khat users

- Application Form – Low Risk
- Participant Information Sheet
- Consent Form
- Appendix E – Participant Recruitment Materials/Baseline Questionnaires
- Recruitment Flyer
- Wording for Webpage link
- Alcohol and Substance use disorder Questionnaire (AUDIT)

The Tasmanian Health and Medical Human Research Ethics Committee considered and approved the above documentation on 20 August 2013 to be conducted at the following site(s):

Adama Science & Technology University (ASTU) (Ethiopia)

Please ensure that all investigators involved with this project have cited the approved versions of the documents listed within this letter and use only these versions in conducting this research project.

This approval constitutes ethical clearance by the Health and Medical HREC. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approval of other bodies or authorities are required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

All committees operating under the Human Research Ethics Committee (Tasmania) Network are registered and required to comply with the National Statement on the Ethical Conduct in Human Research (NHMRC 2007 updated 2009).
Therefore, the Chief Investigator's responsibility is to ensure that:

(1) The individual researcher's protocol complies with the HREC approved protocol.

(2) Modifications to the protocol do not proceed until approval is obtained in writing from the HREC. Please note that all requests for changes to approved documents must include a version number and date when submitted for review by the HREC.

(3) Section 5.5.3 of the National Statement states:

Researchers have a significant responsibility in monitoring approved research as they are in the best position to observe any adverse events or unexpected outcomes. They should report such events or outcomes promptly to the relevant institution/s and ethical review body/ies and take prompt steps to deal with any unexpected risks.

The appropriate forms for reporting such events in relation to clinical and non-clinical trials and innovations can be located at the website below. All adverse events must be reported regardless of whether or not the event, in your opinion, is a direct effect of the therapeutic goods being tested.


(4) All research participants must be provided with the current Patient Information Sheet and Consent Form, unless otherwise approved by the Committee.

(5) The Committee is notified if any investigators are added to, or cease involvement with, the project.

(6) This study has approval for 4 years contingent upon annual review. A Progress Report is to be provided on the anniversary date of your approval. Your first report is due 20 August 2014. You will be sent a courtesy reminder closer to this due date.

(7) A Final Report and a copy of the published material, either in full or abstract, must be provided at the end of the project.

Should you have any queries please do not hesitate to contact me on (03) 6226 2764.

Yours sincerely

Heather Vail
Ethics Administrator
Office of Research Services
Email: Heather.vail@utas.edu.au
University of Tasmania
Private Bag 01 Hobart Tas 7001
APPENDIX R: Ethics approval letter 3

09 April 2013

Dr Raimondo Bruno
Psychology
Private Bag 30

Dear Dr Bruno

Re: FULL ETHICS APPLICATION APPROVAL
Ethics Ref: H0013036 - Survey of khat use and experience

We are pleased to advise that the Tasmania Social Sciences Human Research Ethics Committee approved the above project on 09 April 2013.

This approval constitutes ethical clearance by the Tasmania Social Sciences Human Research Ethics Committee. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approval of other bodies or authorities is required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

Please note that this approval is for four years and is conditional upon receipt of an annual Progress Report. Ethics approval for this project will lapse if a Progress Report is not submitted.

The following conditions apply to this approval. Failure to abide by these conditions may result in suspension or discontinuation of approval.

1. It is the responsibility of the Chief investigator to ensure that all investigators are aware of the terms of approval, to ensure the project is conducted as approved by the Ethics Committee, and to notify the Committee if any investigators are added to, or cease involvement with, the project.

2. Complaints: If any complaints are received or ethical issues arise during the course of the project, investigators should advise the Executive Officer of the Ethics Committee on 03 6226 7479 or human.ethics@utas.edu.au.

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES
3. **Incidents or adverse effects:** Investigators should notify the Ethics Committee immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.

4. **Amendments to Project:** Modifications to the project must not proceed until approval is obtained from the Ethics Committee. Please submit an Amendment Form (available on our website) to notify the Ethics Committee of the proposed modifications.

5. **Annual Report:** Continued approval for this project is dependent on the submission of a Progress Report by the anniversary date of your approval. You will be sent a courtesy reminder closer to this date. **Failure to submit a Progress Report will mean that ethics approval for this project will lapse.**

6. **Final Report:** A Final Report and a copy of any published material arising from the project, either in full or abstract, must be provided at the end of the project.

Yours sincerely,

Lauren Townsend  
Ethics Administrator  
Office of Research Services  
Tel: +61 (03) 6226 2764  
Email: Lauren.Townsend@utas.edu.au  
University of Tasmania  
Private Bag 01 Hobart Tas 7001

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A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES
APPENDIX S: Khat survey Questionnaire (Amharic Version)
Appendices

Survey of Khat Use and Experience in Ethiopia

(Appendix A (General information))

1. BAHACA

2. HABUR

3. NAHUR

(Appendix B (Demographic information))

4. ETHNICITY

5. LANGUAGE

6. OCCUPATION

7. MARITAL STATUS

8. EDUCATION

9. RELIGION

10. PLACE OF BIRTH

11. PLACE OF WORK

3 | Page
Appendices

12. ያለው መረጃ ይሆን ከአምላው ለሆኑነኝ የጭብጥነት ይሆን? በሌለበ רואה የጭብጥነት ይሆን

13. ያለው መረጃ ይሆን ግር ይገኝ? በአማርኛ በአማርኛ መረጃ

**Khat Use and Dependency**

1. ያለው-12 የሆኔ ይገኝ ይህ ግር ይገኝ ይጭብጥነኝ?

2. ያለው መረጃው ይኖራ ይህ ግር ይገኝ ይጭብጥነኝ?

3. ያለው-12 የሆኔ ይገኝ ይስ ይገኝ ይህ ግር ይገኝ ይጭብጥነኝ?

4. ያለው መረጃ ይኖራ ይስ ይገኝ ይስ ይገኝ ይህ ግር ይገኝ ይጭብጥነኝ?
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6. ይ_splits በሚንግላት ወደ ውስጥ በሚካከል በሚካከል እንዲከታተለሁ?

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11. ይ_splits በሚንግላት ወደ ውስጥ በሚካكاتب በሚካكاتب እንዲከታተለሁ?

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13. ይ_splits በሚንግላት ወደ ውስጥ በሚካكاتب በሚካكاتب እንዲከታተለሁ?
Appendices

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5. ኢ. እ. አ. - V / DSM - V

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*Note: Table content is placeholders for demonstration purposes.*
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<tr>
<td>4. 12345</td>
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</table>

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### Appendices

2.  აღწერა თურქული ადგილი ოთახში თავისუფალ ზომისა და სხეულის უფლებითი პირდაპირობა.

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<tr>
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</tbody>
</table>

### Severity of Dependence (SDS - Khat)

1. თავისი თურქული ადგილი ოთახში თავისი ზომისა და სხეულის უფლებითი პირდაპირობა.

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3. თუ თანამედროვე ხელი დაანაგება სხვა შემთხვევა.

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### ტაგმო - ტაგმო (1-10)

1. თანამედროვე ხელი დაანაგება სხვა შემთხვევა.

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9 | Page |
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Appendices

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Appendices

   - Description of methods and results.
   - Discussion on implications for public health policies.

12. **Appendix 12**: The relationship between smoking and economic outcomes. 
   - Analysis of data from different countries.
   - Implications for intervention strategies.

13. **Appendix 12**: The effectiveness of smoking cessation interventions. 
   - Overview of various programs and their outcomes.
   - Recommendations for future research.

---

### Fagerstrom Nicotine Dependence Scale (FTND)

1. **Smoking History**: In 12 months, how often have you smoked?
   - Never
   - Less than once a day
   - Once a day
   - Twice a day
   - More than twice a day

2. **Cigarettes per Day**: How many cigarettes do you smoke per day?
   - Less than 5
   - 5 to 10
   - 11 to 20
   - More than 20

3. **Nicotine Dependence**: How strong is your nicotine dependence?
   - None
   - Mild
   - Moderate
   - Severe

4. **Smokeless Tobacco**: Have you ever used smokeless tobacco?
   - Yes
   - No

5. **Smoking Cessation**: Have you ever tried to quit smoking?
   - Yes
   - No

---

### Personal Wellbeing Index (PWI)

1. **Health Status**: In the past 12 months, were you bothered by your health? 
   - Not at all
   - A little
   - Quite a bit
   - Very much

2. **Energy**: How much energy do you have today?
   - None
   - Some
   - Most
   - Full

3. **Sleep**: How satisfied are you with your sleep?
   - Very dissatisfied
   - Dissatisfied
   - Satisfied
   - Very satisfied

4. **Social Support**: How much social support do you receive?
   - None
   - Some
   - A lot

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<table>
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<th>1</th>
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12 |
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### Appendices

#### Personal Wellbeing Index (PWI)

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<th>10</th>
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</table>
**Appendices**

### Academic Functioning Questionnaire

1. **Questions & Instructions:**

   - **Please rate your level of agreement with the following statements:**

<table>
<thead>
<tr>
<th>Item</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
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<tbody>
<tr>
<td>Item 1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Item 2</td>
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<td></td>
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<tr>
<td>Item 3</td>
<td></td>
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<tr>
<td>Item 4</td>
<td></td>
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</table>

2. **Helpful Feedback:**

   **(Optional) Feedback:**

   - Please provide any additional comments or suggestions.

3. **Additional Notes:**

   **(Optional) Additional Notes:**

   - Please include any other relevant information.

---

The end.

---

**Instructions:**

- Please use the rating scale provided to indicate your level of agreement.
- **Strongly Disagree:** I strongly disagree with this statement.
- **Disagree:** I disagree with this statement.
- **Agree:** I agree with this statement.
- **Strongly Agree:** I strongly agree with this statement.

---

Thank you for completing this survey.

---

[Link to Survey](https://surveys.psychol.utas.edu.au)

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Info line 1300 363 864
### APPENDIX T: Withdrawal Questionnaire

School of Medicine (Psychology)
University of Tasmania

**Wakeup Report: Please mark (X)**

**DATE: __________________ TIME: __________**

<table>
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<tr>
<th></th>
<th>&lt;15 mins</th>
<th>15 - 30 mins</th>
<th>30 - 60 mins</th>
<th>&gt;60 mins</th>
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<td>Good Morning! How long ago did you wake up?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>How long did it take for you to sleep?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</table>

<table>
<thead>
<tr>
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<th>20</th>
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<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>100 (High)</th>
</tr>
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<td>Quality of sleep?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4</td>
<td>How refreshed do you feel?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5</td>
<td>Have you had vivid and unpleasant dreams?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
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<td>6</td>
<td>Increased appetite?</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>Decreased appetite?</td>
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<td>☐</td>
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<tr>
<td>8</td>
<td>Khat craving?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
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<td>Cigarette craving?</td>
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Right now, your FEELINGS?

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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Very bad</th>
<th>Bad</th>
<th>Neutral</th>
<th>Good</th>
<th>Very good</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Last time you had khat, how many (in bundle)?</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>