EPIDEMIOLOGY OF PRESCRIPTION OPIOID ABUSE IN SIKKIM

A THESIS

submitted by

DEBRANJAN DATTA

(REG NO: 20081003)

for the award of the degree

of

DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHARMACOLOGY

(SIKKIM MANIPAL INSTITUTE OF MEDICAL SCIENCES)

SMU
Sikkim Manipal University

September , 2015

SIKKIM MANIPAL UNIVERSITY

FORMAT FOR FURNISHING PARTICULARS OF STUDENT THESIS

Department	:	PHARMACOLOGY
Institute	:	SIKKIM MANIPAL INSTITUTE OF MEDICAL SCIENCES, GANGTOK
Programme	:	PhD
Name of the Student	:	**DEBRANJAN DATTA**
Name of Guide	:	DR. AMIT CHAKRABARTI
Year of Submission of the Thesis		2015, SEPTEMBER
Title of the Thesis	:	EPIDEMIOLOGY OF PRESCRIPTION OPIOID ABUSE IN SIKKIM

Fax : 91-33-2367-6683

Phone : 2367-4390 / 4955
2367-3262

क्षेत्रीय व्यावसायिक स्वास्थ्य केन्द्र (पूर्वी)

Regional Occupational Health Centre (Eastern)

(Indian Council of Medical Research)

Block - DP-1, Sector - V, Bidhan Nagar (Salt Lake City), Kolkata - 700 091

Ref. no. Misc/ROHC/568/14-15 dated 31/10/14

THESIS CERTIFICATE

This is to certify that the thesis entitled "Epidemiology of prescription opioid abuse in Sikkim" submitted by Mr. Debranjan Datta to the Sikkim Manipal University (SMU) for the award of the degree of Doctor of Philosophy is a bonafide record of research work carried out by him at Sikkim Manipal Institute of Medical Sciences under my supervision. The content of this thesis, in full or in parts have not been submitted to any other Institute or University for the award of any degree or diploma.

Signature of the Guide:

Amit Chakrabarti

Dr. Amit Chakrabarti
Scientist "E" (Deputy Director – Medical),
Regional Occupational Health Centre, Eastern,
National Institute of Occupational Health,
Indian Council of Medical Research (ICMR),
Kolkata
Email: amitc@icmr.org.in
Cell: +91-9674566502

DR. AMIT CHAKRABARTI, M.D.
Scientist 'E' (Medical)
Regional Occupational Health Centre (ROHC), Eastern
National Institute of Occupational Health (NIOH)
Indian Council of Medical Research (ICMR)
Sector-V, Salt Lake, Kolkata-700091

Place: Kolkata, West Bengal
Date: 31/10/2014

THESIS CERTIFICATE

This is to certify that the thesis entitled "**EPIDEMIOLOGY OF PRESCRIPTION OPIOID ABUSE IN SIKKIM**" submitted by **Mr. Debranjan Datta** to the Sikkim Manipal University (SMU) for the award of the degree of Doctor of Philosophy is a bonafide record of research work carried out by him under my supervision. The content of this thesis, in full or in parts have not been submitted to any other Institute or University for the award of any degree or diploma.

Signature of the Co-Guides:

Dr. Sanjiba Datta

Professor & Head
Department of Psychiatry
SMIMS, Gangtok

Dr. Yogesh Verma

Associate Professor
Department of Pathology
SMIMS, Gangtok

DECLARATION BY THE RESEARCH SCHOLAR

This is to declare that the thesis entitled “Epidemiology of prescription opioid abuse in Sikkim” submitted by me to the Sikkim Manipal University for the award of the degree of Doctor of Philosophy is a bonafide record of research work carried out by me under the direct supervision of my Guide and co-guides. The content of this thesis have not been and will not be submitted to any other Institute or University for the award of any degree or diploma.

Date:
Place:

Signature of the Research scholar
(DEBRANJAN DATTA)

DECLARATION BY THE RESEARCH SCHOLAR

This is to declare that the thesis entitled **"EPIDEMIOLOGY OF PRESCRIPTION OPIOID ABUSE IN SIKKIM"** submitted by me to the Sikkim Manipal University, for the award of degree of Doctor of Philosophy is a bona fide record of research work carried out by me at Sikkim Manipal Institute of Medical Sciences under the supervision of **Dr. Amit Chakrabarti,** ROHC (E), NIOH, ICMR, Kolkata. The contents of the thesis have not been submitted and will not be submitted to any other Institute or University for the award of any degree or diploma.

Place:

Signature of the Research Scholar

Debranjan Datta

Date:

(Name of the Research Scholar)

Forwarded

Research Guide

Amit Chakrabarti
5/11/2014

Dr. Amit Chakrabarti

(Name of the guide)

DR. AMIT CHAKRABARTI, *M.D.*
Scientist 'E' (Medical)
Regional Occupational Health Centre (ROHC), Eastern
National Institute of Occupational Health (NIOH)
Indian Council of Medical Research (ICMR)
Sector-V, Salt Lake, Kolkata-700091

TABLE OF CONTENTS

ACKNOWLEDGEMENT

This dissertation would not have been possible without the guidance and the help of several individuals who in one way or another contributed and extended their valuable assistance in the preparation and completion of this study.

First and foremost I offer my sincere gratitude to my guide, Dr. Amit Chakraborty, who has supported me throughout my thesis with his patience, enormous knowledge and devoted scholarship. One simply could not wish for a better or friendlier supervisor. I consider it a huge honor to have conducted this research work under his able guidance.

I take this opportunity to express my sincere and deep sense of gratitude and sincere regards to my co-guides Dr. Sanjiba Datta, Professor, Head, Department of Psychiatry, Sikkim Manipal Institute of Medical Sciences, Gangtok and Dr. Yogesh Verma, Associate Professor, Pathology, SMIMS & former Medical Superintendent of STNM hospital, Gangtok for their invaluable guidance, constant supervision, constructive criticism and keen interest taken by them at every stage during the entire course of this study.

I am deeply indebted to Doctoral Committee members for their valuable inputs in every step of study and their every suggestions helped me to do better at every phase of the study.

I also offer my sincere thanks to Mr. Joseph Tamang, Director of Sikkim Rehabilitation and Detoxification Centre and all the staff members of rehabilitation centers of Sikkim whose selfless cooperation helped me in every aspect during site visit stages.

Heartfelt thanks to Dr. Supratim Datta, Associate Professor, Dr. Chandrakala Sharma, Associate Professor, Mr. Sunil Kumar Pandey, Lecturer, Dr. K.C. Swain, Ex-professor & Head, of the department of Pharmacology, SMIMS, Mrs. Judith Dorjee, Mr. R. C. Sharma and Mr. Krishna of department of pharmacology, Gangtok for their invigorating advice and unrelenting support whenever I found myself at an impasse in the study.

I take this moment also to thank all the respondents of this study for their active and co-operative participation in my thesis.

I would like to take this opportunity to express my gratitude, love and respect to my parents, daughter and wife for their enormous and continuous encouragement and moral support during this study and helping me at every stage and in every aspect of this study.

Last but not the least, I thank the almighty GOD with whose grace I exist and who gave me the opportunity to work for this profession.

-Debranjan Datta

ABSTRACT

Background:

Sikkim –a hilly state in Northeast India reports high prevalence of alcohol use with emerging substance abuse problems. Sikkim is emerging as an important area for prescription opioid abuse with frequent news of seizures and arrests due to possession of prescription opioids. Although substance use disorder is in alarming stage in north eastern states of India, till date there is little information on descriptive epidemiology, comorbid illnesses and high risk behaviour of prescription opioid dependents from Sikkim.

Aim:

Published report on increased incidences of prescription opioid abuse from other north eastern states of India urges to study and understand various socio-demographic profile, drug use characteristics, peer's role , pain pattern etc. of prescription opioid abusers from another north eastern states i.e. Sikkim. Aim of this study is to find out various socio-demographic variables such as age, sex, religion, marital status, community, occupation, income, education, role of migration etc., pain status, pattern of opioid analgesic use such as sources –for both initial and continued use, motives, and frequency of use as well as quality of life of prescription opioid abusers who reported for treatment at various treatment centres of Sikkim. It was also aimed to find out differences in pain interference, pain characteristics and correlations, among the pain severity groups.

Subjects and Methods:

Epidemiological data were collected by administering pre-devised questionnaires from n=224 prescription opioid abusers (main problem prescription opioids) reporting for treatment at five different drug abuse treatment centres across Sikkim. Several pre devised questionnaire on different domains were administered to 224 prescription opioid abusers after obtaining informed consent. The study protocol, instruments/questionnaire, informed consent was duly approved by Institutional Ethics Committee (IEC). For database development and analysis, SPSS-version 20 was adopted. For categorical variables chi-square test was used considering p value less than 0.05 as statistically significant.

Results:

Majority of subjects were male, of Nepalese ethnicity, urban resident, and never married, school dropout and/or illiterate, earning less than Rs. 5000 / month. The median age of prescription opioid abusers in Sikkim was 26 years. No role of migration on subject's prescription opioid use behaviour was reported. Prescription opioid abuse observed both in rural and urban settings of Sikkim. It is more prevalent among school dropouts and unemployed respondents. Peers influence on subject's prescription opioid use was observed. Commonly abused prescription opioids were dextropropoxyphene and codeine. Prescription opioid abusers also reported co-administration of alcohol, cannabis and benzodiazepines. Experimentation and euphoria were reported as major motives for initiation and continued use of its. Substance using friends and local dealers were noted as major source of prescription opioids in this study.

Injection sharing was more in urban whereas syringe exchange was observed equally among rural and urban prescription opioid abusers ($p>0.05$). Among urban injectors visits to commercial sex workers (CSWs), and multiple sex partners (MSPs) were also common in spite of knowledge about AIDS. Limited condom use was observed among rural respondents. Incidences of arrests, public intoxication, and violence under the influence of prescription opioids were also reported. Prescription opioid injection was found significantly associated with health problems, psychosocial problems and utilization of medical services.

Conclusions:

Existence of prescription opioid abuse problem was found both in urban and rural setting. It is more prevalent among school dropouts and unemployed youth. Alcohol problem was experienced by almost half of the prescription opioid abusers of Sikkim. First use of alcohol and prescription opioid started almost same time. Therefore poor education status, low literacy rate, more expenditure on substance use, peers substance use behaviour, more employment problems and moreover increased reporting of treatment admission at de-addiction centre indicates the need to study the socio-demographic profile, drug use characteristics and peer's influence on substance use of prescription opioid abusers of Sikkim. Trends of injection drug use (IDU), unsafe injection, high risk behaviour have also been observed.

Key words:

Sikkim, prescription opioid, substance abuse, injection drug use.

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

AA	Alcohol Anonymous
ACTH	Adreno Cortico Tropic Hormone
ADHD	Attention Deficit Hyperactive Disorder
AIDS	Acquired Immune Deficiency Syndrome
ANOVA	Analysis Of Variance
ARQ	Annual Reports Questionnaire
ASI LITE	Addiction Severity Index Lite
ASI-MV	Addiction Severity Index –Multimedia Version
ATP	Adenosine Tri Phosphate
ATS	Amphetamine Type Stimulant
BPI	Brief Pain Inventory
CEWG	Community Epidemiology Work Group
CI	Confidence Interval
CNS	Central Nervous System
CSW	Commercial Sex Worker
CVS	Cardio Vascular System
DAMS	Drug Abuse Monitoring System
DSM	Diagnostic & Statistical Manual Of Mental Disorder
DWI	Driving While Intoxicated
EMCDDA	European Monitoring Centre For Drugs And Drug Addiction
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICMR	Indian Council Of Medical Research

IDU	Injection Drug Use
IEC	Institutional Ethics Committee
LC	Lucullus Ceruleus
MSM	Male Having Sex With Male
MSP	Multiple Sex Partner
MTF	Monitoring The Future
NA	Narcotic Anonymous
NFHS	National Family Health Survey
NGO	Non Government Organizations
NHS	National Household Survey
NHSDA	National Household Survey On Drug Abuse
NIDA	National Institute On Drug Abuse
NIH	National Institute Of Health
NMDA	N-Methyl-D-Aspartate
NMUPD	Non Medical Use Of Prescription Drugs
NOP	Nociceptor Opioid Receptor
NRM	Nucleus Raphe Magnus
NSAIDS	Non Steroidal Anti-Inflammatory Drugs
NSDUH	National Survey On Drug Use Among Households
OR	Odds Ratio
PAG	Periaqueductal Grey
POAUH	Pain And Opioid Analgesic Use History
RAS	Rapid Assessment Survey
REM	Rapid Eyeball Movement
RPEC	Research Protocol Evaluation Committee

RR	Relative Risk
RSA	Rapid Situation Assessment
RSRA	Rapid Situation And Response Assessment
SADA	Sikkim Anti-Drug Acts
SAMHSA	Substance Abuse And Mental Health Services Administration
SD	Standard Deviation
SF36	Short Form 36
SG	Substantia Gelatinosa
SPSS	Statistical Package For Social Sciences
SRDS	Sikkim Rehabilitation & Detoxification Society
UNODC	United Nations Office Of Drugs And Crime
US	United States
WHO	World Health Organization

INTRODUCTION

Substance use pattern changes over time. Substance use includes use of licit substances such as alcohol, tobacco, diversion of prescription drugs as well as illicit substances. Both licit and illicit substance use can cause serious public health problems in our country. Continued use may lead to misuse or abuse and/or addiction. In general terms 'misuse' means use beyond medical and societal harm and according to the "lexicon of alcohol and drug terms" [1] by WHO, it is the use of substance for a purpose not consistent with legal or medical guidelines, as in the non-medical use of prescription medications. Sustained misuse can lead to abuse. Abuse means use causing physical, social, psychological and economic harm. Abuse describes the maladaptive pattern of substance use, not related to therapeutic purpose, resulting in recurrent and significant adverse consequences. DSM III R (Diagnostic & Statistical Manual of Mental Disorders), published by the American Psychiatric association defines "drug abuse" as 'a maladaptive pattern of use indicated by….continued use despite knowledge of having a persistent or recurrent social, occupational, psychological or physical problem that is caused or exacerbated by the use (or by) recurrent use in situations in which it is physically hazardous'. DSM IV defines substance/drug abuse as a 'problematic use without compulsive use, significant tolerance, or withdrawal'. Commonly abused classes of drugs include opioids (both prescription opioids such as buprenorphine and non-prescription opioids such as heroin), CNS stimulants and CNS depressants.

Prescription opioids are drugs that are prescribed by doctors for the management of chronic pain and thereby improve quality of life. Various prescription opioids are mainly meperidine, methadone, morphine, dextropropoxyphene, buprenorphine, codeine, fentanyl, tramadol, pentazocine etc. On the other hand, illicit opioids (e.g. heroin) are those that are obtained from

illegal source such as by prescription forgery –either by writing or buying fake prescriptions, from dealer, friend, family members, by stealing from pharmacy, obtaining from medical stores without prescription etc. The main purposes of using those substances are either to get relieve from physical pain, to enjoy euphoria, to get rid of depression, anxiety, bad memories etc. It varies from person to person.

Tolerance and dependence develops to the actions of opioid analgesics. Common withdrawal symptoms associated with opioid group of drugs include feeling of unpleasantness, muscle aches, mydriasis, diarrhoea, insomnia, dysphoria, lacrimation, rhinorrhoea piloerection etc. The relatively modest efficacy of buprenorphine can lead to the precipitation of withdrawal if it is administered to someone who is physically dependent on a higher efficacy opioid (e.g. heroin). Beyond the withdrawal syndrome, that mainly lasts no longer than a few days, individuals who have received opioids as analgesics only rarely develop addiction.

Central nervous system depressants which are used to treat anxiety, sleep disorders, control stress reaction can cause abuse and addiction. They are of two types –barbiturates and benzodiazepines. Abuse potential is mainly seen with medium duration of action barbiturates such as amylobarbitone, pentobarbitone, butobarbitone, etc. Benzodiazepines that have high abuse potential are diazepam, nitrazepam, chlordiazepoxide etc. In addition to opioids and CNS depressant drugs, there are various central nervous system stimulants, which also has high abuse and addiction potential. They are mainly amphetamines, methylphenidate, and cocaine. Amphetamine is a powerful CNS stimulant which elevates mood and makes the user feel energetic, alert and self-confident. Amphetamine reduces feeling of hunger and fatigue. There is

slow development of tolerance to its euphoric effect. Therefore abusers need to increase the dosage progressively to maintain its effect. There are developments of both physical as well as psychological dependence of amphetamine. Chronic amphetamine users experience intense craving and drug seeking behaviour. Abrupt withdrawal of this drug produces of fatigue, depression and hunger. The other CNS stimulant drug methylphenidate needs special attention as there is increased prescription of this drug in the treatment of ADHD. Cocaine is another powerful central nervous system stimulant which produces increased energy, wakefulness, confidence and facilitates social interchange. It produces euphoria i.e. great feeling of well-being. There are number of physical dependence symptoms following withdrawal of the cocaine. From low to high intensity, they are mainly lethargy, depression, social withdrawal, tremor, muscle pain, sleep as well as eating disturbances, anxiety, dysphoria and craving. Cocaine causes severe psychological dependence symptoms such as craving and drug seeking behaviour, psychosis, which disrupts their normal life.

Both licit and illicit substance use, affects in an adverse way not only the individual but also its family, community and society at large. Psychoactive substance users are at higher risk of medical complications and attend health care facilities more frequently than normal population.

Variety of diseases commonly co-occur with substance abuse and addiction (e.g., HIV, hepatitis C, cancer, cardiovascular disease).

Many people who regularly abuse drugs are also diagnosed with mental disorders and vice versa. The high prevalence of this comorbidity has been documented in several studies. Strong associations of substance use, abuse and dependence with a range of mental disorders has been observed in several studies by Langås et al, [2] Meyer D et al. [3]. Alcohol abuse results in gastrointestinal complications such as gastritis, hepatitis and

cirrhosis and other eventual complications. In comparison to alcohol, opiates (including prescription opioids) and cannabis cause less direct organ damage. It is their vehicle and route of administration, which is responsible for many health hazards. If smoked, users of both of these drugs are at risk of developing chronic smoking related complications. More significant problems are associated with parenteral modes of drug use where in the users exposes them to both local (at the injection site) and systemic infection besides running the risks of sudden death due to over dose. The growing incidence of injection drug use (which includes opioids, sedatives as well as stimulants) and the alarming finding of association of HIV transmission with Injection Drug Use (IDU) are increasingly being recognised as a major public health problem. Since drug use often imposes a significant financial burden on user, which soon is reflected in the family's financial status, and drag them to the lower socioeconomic strata of the society.

Prescription opioid abuse not only adversely affects the vitals of the society but also badly affects the economic growth of the country, because this is the trade which generates huge unaccounted money. The money generated is used for various purposes including antinational and terrorist activities. Opioids including prescription opioid abuse also impair thinking, understanding capabilities, and decrease interests towards school, among students.

Pain –both acute and chronic type is a most common symptom for which person always seeks treatment. One of the very common causes of pain recognised globally is musculoskeletal diseases. [4] The prevalence of chronic pain from India was reported 19% according to a World Health Organization study in 'primary care' [5] and that of musculoskeletal pain was found 25.9% in India [6]. Prescription opioids are drugs that are prescribed for management of chronic non-

cancer pain mainly. They are believed to be safer than illicit drugs of abuse and are also more easily available than illicit opioids such as heroin. This has resulted in increases in incidence of abuse of prescription opioids. Increased opioid prescribing trends has been observed globally.[7] UNODC World Drug Report 2015 estimated that in 2013, between 246 million people aged 15-64 years had used an illicit substance at least once in the previous year. Of which an estimated 27 million were problem drug users and an estimated 32.4 million people aged 15-64 years were opioid users.[8] In North America, Oceania, and in some of the European countries, abuse of fentanyl and buprenorphine observed more in comparison to heroin use according to UNODC report.[8] Prescription opioid misuse and diversion globally was also observed among 'high school students'[9], 'college students'[10], 'older persons'[11], and 'women'[12-13]. Most of who initially obtain prescription opioids via legitimate medical practices. The elderly as well as older populations are among those most vulnerable to prescription opioid problems (abuse or misuse). This is because adolescence is a period of experimentation and search for identity and that young people are more likely than adults to experiment with various things, including drugs like prescription opioids. In India, Bangladesh, Nepal, long standing problems with the licit control of pharmaceutical preparations has led to widespread abuse among all segments of the population. In general, pharmaceutical preparations are diverted from domestic distribution routes and are sold without prescription in pharmacies and various other retail outlets in the region. In South-Asian countries, abuse of buprenorphine, dextropropoxyphene and codeine based cough syrup observed more and incidences of unsafe practices including injection drug use was reported which remains one of the key factors for spread of HIV/AIDS in India, Nepal and Bangladesh.[14] Non-medical use of prescription opioids also reported by various surveys and

study settings such as ‘Drug abuse monitoring system’ study, ‘Rapid Situation Assessment survey’, ‘Rapid Situation and Response Assessment’ among Indian populations.[15-17] Injection prescription opioids use in India was initially acknowledged in the north east states of Manipur and Nagaland, mainly due to their proximity to the ‘Golden Triangle’ –Burma, Thailand, and Cambodia where abuse of prescription opioid is very common.[18] Sikkim, a small mountainous state in the eastern Himalayas, borders Nepal to the west, China's Tibet Autonomous Region to the north and east, and Bhutan to the southeast. The Indian state of West Bengal lies to the south. Sikkim is a multi-ethnic state, where Bhutias and Nepalese (approximately 70% of Sikkim’s population) have migrated from Tibet and Nepal, respectively. As a result, a lot of migration took place from its Border States and countries, with introduction of new substances of abuse including prescription opioids.

North East India is a major source of IDUs and associated HIV/AIDS. Sikkim observe changing cultural & societal values. While substantial epidemiological information on prescription opioid abuse is available globally and from India but until date, there is no systematic study available from Sikkim. The study of prescription opioid abuse in Sikkim is needed as there is increased reporting of abuse of prescription opioids from various treatment centres. In this context it is necessary to study the complete epidemiological profile of prescription opioid abusers of Sikkim, another state in north eastern India, with no information on this emerging public health problem.

NEED OF THE STUDY

A number of studies have reported presence of enormous variety of substance abuse including prescription opioids and associated public health problems from North-eastern states of India. National Family Health Survey-2, Government of India, has also highlighted a significant prevalence of alcohol use in Sikkim (32% and 17% among above 15 years of age males and females, respectively). Until date, any systematic information on epidemiology of non-medical prescription opioid use behaviour i.e. either extent as well as pattern of abuse in Sikkim is not available. However few arbitrary data on such is available from various detoxification centres of Sikkim. That shows increasing trends in both alcohol as well as drugs including prescription opioids. More over reports in media of Sikkim indicate increased incidences of arrests due to possession and violence due to influence of drugs especially prescription opioids.

Therefore, the information on epidemiology of prescription opioid abuse in Sikkim is needed for effective prevention and treatment of substance abuse related problems in Sikkim. The purpose of this research study is to get a better understanding of the relationship between pain and prescription opioid abuse i.e. whether prescription opioids are received as a first opiate analgesic treatment of pain and whether major reasons for continuing its use. This study will help to describe demographic variables (age, sex, religion, marital status, community, occupation etc.), socioeconomic variables (income, education, family information etc.) , drug use pattern (types of drug, duration, route of use etc.), high risk behaviour profile (crime, law infringement, injection sharing, visit to commercial sex workers, homosexuality etc.), quality of life, associated medical and psychiatric conditions, reasons for seeking treatment of prescription opioid abusers (overdose/withdrawal/accident/consequences etc.). This study will also help to find out any association if present among mental health disorders, blood borne diseases like HIV with the

injecting prescription opioid abuse. Thereby awareness regarding safe injection can be created. Information from this study will also help to find out the differences in various socio-behavioural characteristics like migration (either drug use started before or after migration), community (rural or urban setup), level of education etc. therefore results of my study will contribute in developing more effective strategies for prescription opioid abuse prevention and control.

REVIEW OF LITERATURE

Chronic pain is a pain that persists longer than normal stipulated time of cure, for which prescription analgesics are the preferred choice of treatment globally. Long-term prescription opioid use for the treatment of chronic pain can lead to abuse and addiction.

Opiates & Opioids:

Conventionally, the term 'opiate' indicates both naturally occurring substances and semisynthetic drugs which are derived from them (e.g. Heroin), whereas the term 'opioid' describes totally synthetic drugs (e.g. pethidine) with similar properties. But with the discovery of opioid receptors, the term 'opioid' describes collectively naturally occurring alkaloids, semisynthetic derivatives and totally synthetic drugs.

Discovery of various opioid receptors has helped understanding the mechanism of actions of various opioids a better way. These receptors are specialized sites on the cell membrane, with a very specific shape to which opioids binds. Three major categories of opioid receptors have been identified in various nervous system sites and in other tissues. They are mu (μ), kappa (κ) and delta (δ). A fourth receptor NOP (nociception opioid receptor), has also been identified. It has high sequence homology to these three opioid receptors (μ, δ, κ). Opioids do not bind to NOP receptor with high affinity, although it has structural similarity with opioid receptors. Each of the three major receptors has now been cloned. All are members of G protein-coupled receptor and show significant amino acid sequence homologies. Multiple receptor subtypes have been proposed based on pharmacologic criteria, including μ_1, μ_2; δ_1, δ_2; and κ_1, κ_2, κ_3. All the three types of receptors are found on presynaptic nerve terminals and they have inhibitory effect on transmission across synapses, by reducing the release of neurotransmitters. Since an opioid may

function as an agonist, partial agonist or antagonist at more than one receptor subtype, it is expected that these agents are capable of diverse pharmacologic effects. One of the important action of opioids i.e. their ability to induce analgesia but depending on the patient as well as condition, not necessarily the most important action of this class of drugs (loperamide for diarrhoea, codeine for cough…) is mediated by supraspinal activation of μ receptors and by the activation of κ receptors in the spinal cord. Opioids produce analgesic action not only through central action, but also through activation of peripheral opioid receptors by local application which was proven by promising results seen in patients undergoing arthroscopic knee surgery.[19] Euphoria –a pleasant floating sensation with lessened anxiety and distress, miosis, respiratory depression and decreased gastrointestinal motility are the other opioid effects due to stimulation of μ receptor, whereas stimulation of κ receptor is often associated with dysphoria. The effects of δ stimulation have not been yet fully established.

Endogenous ligands of opioid receptors i.e. the opioid peptides are termed as endogenous opioid peptides. They possess opioid like pharmacological properties. There are three distinct 'families' of endogenous opioid peptides. They are 1) the pentapeptide–enkephalins, 2) the endorphins, 3) dynorphin with 31 amino acids. The endogenous opioid peptides are derived from three major precursor proteins: prepro-opiomelanocortin, prepro-enkephalin and prepro-dynorphin. The prepro-opiomelanocortin contains met-enkephalin sequence, beta-endorphin and several non-opioid peptides such as ACTH, beta-lipoproteins and melanocyte-stimulating hormone. Prepro-enkephalin contains six copies of met-enkephalin and one copy of leu-enkephalin. Both of them have slightly higher affinity for δ receptor than for μ receptor. The endogenous peptides endomorphin-1 and endomorphin-2 has high affinity towards μ receptor. These endogenous

opioid peptides are secreted from immunocytes. They occupy opioid receptors on sensory nerves and produce analgesia by inhibiting either the excitability of these nerves or the release of excitatory pro-inflammatory neuropeptides (e.g. substance P). In contrast to the analgesic role of leu- and met-enkephalin, an analgesic action of dynorphin A –through its binding to κ receptor remains controversial. Chronic agonist action at μ or κ receptors can cause tolerance and physical dependence within the neural systems which are affected by these receptors. Thus precipitation of withdrawal syndrome is either due to withdrawal of agonist drug after a long period of administration, or due to its displacement by an antagonist. μ (mu) receptor physical dependence produces severe withdrawal manifestations with intense drug seeking behaviour. There is little cross tolerance between the different receptors so that a drug with κ (kappa) agonist properties cannot suppress the withdrawal syndrome caused by a μ agonist withdrawal. The outstanding property of opioid analgesic is to cure pain. Severe, constant pain is usually relieved with opioids, whereas sharp, intermittent pain does not get controlled effectively by opioids. The pain associated with cancer and other terminal illnesses are effectively treated by using opioid analgesics. The acute, severe pain of renal and biliary colic requires stronger opioids.

There are two components of pain perception. They are nociceptive component and affective component. The nociceptive component is an unpleasant sensation evoked by noxious thermal, chemical or mechanical stimuli and conveyed to CNS by ascending pathways. The chemical stimuli acting on nociceptor to cause pain are substance P, neurokinin A and B, bradykinin, serotonin, histamine, prostaglandins, ATP, and capsaicin. The affective component is the psychological response towards pain and conveyed from CNS to dorsal horn by descending

pathways. There are two types of pain pathways. They are the ascending and descending pathways. The ascending pain pathway transmits pain impulses from the dorsal horn of the spinal cord to the medulla, midbrain, thalamus, limbic structures and cortex. The pain activates the terminals of primary afferent neuron fibres (Aδ & C) which enters the spinal cord. The Aδ fibre alerts the person about the presence and location of intense and sharp somatic pain. Based on this, the person may use withdrawal reflexes to avoid noxious stimuli. The slow conducting C fibres medicate the motivational –affective (mood) response towards dull aching visceral pain (e.g. pain related to myocardial infarction), or burning neuropathic pain (e.g. pain of trigeminal neuralgia, diabetic nephropathy), thereby enable the person to bear with the pain, experience the discomfort and modify his/her emotional reaction to the pain. The descending pain pathway control pain transmission through dorsal horn by applying inhibitory effect on dorsal horn transmission. The descending neuronal tracts from periaqueductal grey (PAG) activate nucleus raphe magnus (NRM), and releases serotonin and enkephalin from NRM at substantia gelatinosa (SG) of dorsal horn to inhibit ascending pain transmission. From loculus ceruleus (LC), there is release of nor-epinephrine that also inhibits pain transmission from dorsal horn.

Opioid analgesics activate the descending PAG, NMR and LC neuronal pathways and also activate opioid receptors in the spinal cord and SG. They reduce both sensory and affective (emotional) components of pain. Neuropathic pain is less responsive to opioids than is nociceptive pain. The analgesic action of opioids is probably due not only to their direct action at one or more sites within the nervous system, but also to the way in which they make pain more tolerable. This in turn is related to the euphoriant effect i.e. their ability to induce a state of

mental detachment and feeling of wellbeing. However, dysphoria, an unpleasant state characterized by restlessness and malaise, may sometimes occur in some individuals.
Opioids also cause sedation, drowsiness and mental clouding. There is little or no amnesia. Sleep is induced by opioids more frequently in the elderly than in young, healthy individuals. In standard analgesic dose, opioid disrupts normal rapid eye ball movement (REM).

All the opioid analgesics can produce significant respiratory depression by inhibiting brainstem respiratory mechanisms at medulla. The respiratory depression is dose related and mediated by μ_2 receptor. Respiratory depression by opioids is not accompanied by depression of medullary centres controlling CVS functions. Therefore, respiratory depression by opioids is well tolerated. Opioid induced respiratory depression remains one of the most difficult clinical challenges in the treatment of severe pain. Higher doses cause respiratory arrest, unconsciousness and death.

Opioids also control cough by suppression of cough reflex. Suppression of cough reflex occurs at doses lower than that required to produce analgesia or respiratory depression. Codeine particularly has advantage in persons suffering from pathologic cough. However, cough suppression by opioids may allow accumulation of secretions and thus lead to airway obstruction and atelectasis.

The opioid analgesics initially activate the brainstem chemoreceptor trigger zone, later depress vomiting centre. Thereby produce emesis. There is role of vestibular component to nausea as vomiting occurs more frequently in ambulatory patients than in recumbent patients after giving potent opioid analgesic such as morphine.

Constriction of pupils (pin point pupil) is seen with practically all opioid agonists. It is due to μ and κ receptor induced stimulation of third cranial nerve nucleus. It has no direct action on radial or circular muscles of iris. Even in highly tolerant addicts, miosis is seen.

Constipation is a well-recognized effect of opioids which does not diminish with continued use. That means tolerance does not develop to opioid-induced constipation. This action is mediated through μ_2 opioid receptor effect on CNS and also action on enteric nervous system. In the large intestine opioid diminishes propulsive peristaltic waves and increases tone which delays passage of faecal mass and allows increased absorption of water leading to constipation. This action of opioid accounts for their use in antidiarrheal preparation.

Opioids constrict the urinary sphincter causing difficulty in urination (true for mu receptor agonists but not for kappa receptor agonists); on the other hand contract the detrusor muscle, causing urgency to urinate, which often is very troublesome to the patient. μ Opioids have been found to have antidiuretic effect in humans. Opioids also enhance renal tubular sodium reabsorption.

According to WHO, tolerance[20] is ‘a reduction in the sensitivity to a drug following its repeated administration in which increased doses are required to produce the same magnitude of effect previously produced by a smaller dose’. Although development of tolerance begins with the first dose of an opioid, tolerance normally does not become clinically apparent until after 2-3 weeks of frequent exposure to therapeutic doses. However ultra-potent opioid remifentanil have been shown to induce tolerance within hours. A very high degree of tolerance develops to the actions

of opioids that cause analgesia, mental clouding and respiratory depression (slow and shallow breathing) so that these effects of opiates are not apparent even when the individual is consuming a very high daily dose –as long as that dose level has been reached gradually. It is possible to produce respiratory arrest in a non-tolerant person with a dose of 60mg of morphine, whereas in addicts who are maximally tolerant to opioids, as much as 2000 mg of morphine taken over a period of 2-3 hour may not produce significant respiratory depression. Tolerance to sedating and respiratory effects of the opiates dissipates within a few days after the drugs are discontinued. Tolerance to emetic effect may persist for several months after withdrawal of drug. The degree of tolerance and rate of its development as well as disappearance differ among different opioid analgesics and among individuals using the same drug, for e.g., tolerance to methadone develops more slowly and to a lesser degree than to morphine. However, little or no tolerance develops to the action of opiates on the pupil of the eye or on the bowl so that the same individual usually displays a typically constricted pupil and suffers from constipation as well as to convulsing effect. Cross tolerance develops between different opioids. That means if an individual has become tolerant to the effects of heroin, he or she can take large doses of any other opiate but not of other classes of drugs. If heroin is withdrawn, the resulting abstinence syndrome can be relieved by the administration of any opiate but not by any other type or class of drug. Morphine and its congener's exhibit cross tolerance not only with respect to their analgesic actions but also to their euphoriant, sedative and respiratory effects. However the cross tolerance existing among the μ receptor agonists can often be partial or incomplete. This clinical observation has led to the concept of opioid rotation, which has been used in the treatment of cancer pain. A patient who is experiencing decreasing effects of one opioid analgesics is rotated to a different opioids (morphine to hydromorphone) thereby experiences significantly improved analgesia at a reduced

overall equivalent dosage. Another attitude is to 'recouple' opioid receptor function through the use of adjunctive nonopioid agents. NMDA receptor antagonists (ketamine) have shown promise in preventing or reversing opioid induced tolerance in both animals and humans. The novel use of δ receptor antagonist with μ receptor agonist is also emerging as a strategy to avoid the development of tolerance.

Physical dependence is 'an adaptive state manifested by intense physical disturbances when the drug is withdrawn'.[21] The development and severity of physical dependence on opioids depends on the particular opioid being taken, the dose and the duration of chronic administration; but becomes apparent only if regular administration of the drug ceases. While opioids are being taken there is no subjective evidence of the existence or the severity of physical dependence. The symptoms and signs of the abstinence syndrome develop if the drug administration is interrupted, or in the presence of antagonists. Severity of abstinence syndrome is a measure of degree of physical dependence. As tolerance to opioids develops, the daily dose is increased, and the severity of dependence increases too. Beyond its ceiling effect, further increase of dose has little effect on the degree of physical dependence. Degree of physical dependence varies from opioid to opioid. Codeine and Dextropropoxyphene, even in high dosage, do not cause physical dependence to match that caused by morphine or heroin.

The signs and symptoms of opioid abstinence syndrome are graded from grade 0 to grade 3, depending on the severity. These are importantly drug craving, anxiety, drug seeking behaviour, running eye and noses, restless sleep, gooseflesh, muscle twitching, hot and cold flushes, loss of appetite, irritability, increased pulse as well as respiratory rate, weight loss etc. The time of

onset, severity and duration of abstinence syndrome depend on the drug previously used and biological half-life of opioid. An opioid with short duration of action, such as heroin, has an abstinence syndrome of earlier onset, shorter duration and greater intensity than the longer acting drug like methadone. Intensity of signs as well as symptoms of withdrawal increases with increased dosage of opioids. With morphine or heroin, withdrawal signs usually start within 6-10 hours after the last dose. Peak effects are seen at 36-48 hours, after which most of the signs and symptoms gradually subside. By 5 days, most of the effects have disappeared, but some may persist for months. In case of meperidine, the withdrawal syndrome largely subsides, within 24 hours, whereas with methadone several days are required to reach the peak of the abstinence syndrome, and it may last as long as 2 weeks. The slower subsidence of methadone effects is associated with a less intense immediate syndrome, which is reason for its use in the detoxification of heroin addicts. A transient abstinence syndrome can be induced in a subject physically dependent on opioids by administering naloxone or other antagonist. Within 3 minutes after injection of the antagonist, signs and symptoms similar to those seen after abrupt withdrawal appear, becomes maximum in 10-20 minutes and largely settling after 1 hour. Psychological dependence is the 'feeling of satisfaction and a psychic drive that requires periodic or continuous administration of the drug to produce pleasure or to avoid discomfort'.[21] Psychological dependence on opioid is severe & accounts for the desire and craving for drugs that eventually disrupt the addict's life, which may become wholly devoted to obtaining more drugs. There are various factors that promote compulsive use of opioid drugs. They are euphoria, indifference to stimuli, and sedation. The addict also experiences abdominal effects that have been linked to an intense sexual orgasm.[22] Craving[23] is a fundamental component of psychological dependence and implies a constant preoccupation with the drug with instructive

thoughts and obsessive thinking about everything to do with it –particularly its desired effects and the need to obtain it. When craving is severe, drug seeking behaviour dominates daily activity. Drug seeking behaviour involves literally searching for drugs, different activities –both legal and illegal, to obtain money to buy them, identifying the source of supply, purchasing them etc. Unfortunately, psychological dependence does not end when drug withdrawal has been achieved. It persists long after the abstinence syndrome has been subsided.

The intensity of withdrawal symptoms depends on physical condition of the user, type of drug abused, amount of drug intake and duration of abuse. Feeling of unpleasantness, body aches, pains all over the body, diarrhea, dilated pupil, insomnia are the common withdrawal symptoms of opioids which is discussed earlier. On the other hand, extreme fatigue, voracious appetite, moderate to severe depression, disturbed sleep are prominent withdrawal symptoms of stimulants such as oral amphetamines and snorted cocaine. Depressants such as sedative hypnotics, barbiturates, benzodiazepines, alcohol exhibit tremors, insomnia, irritability, restlessness, hallucinations, convulsions, and delirium tremens as major withdrawal symptoms. Withdrawal symptoms are not reported by hallucinogens such as lysergic acid diethylamide (LSD), phencyclidine, mescaline, psilocybin. While, Loss of appetite, irritability, tremors, sleep disturbances, prominent psychotic symptoms, depression are characterized as important withdrawal symptoms of cannabis/marijuana.

Comorbidity of substance abuse and mental health problems is at the heart of drug abuse in much of the world. Drug use disorders (abuse / dependence) often co-occur with other mental illnesses such as depression, anxiety, or schizophrenia. Population surveys show a high rate of co-

occurrence, or comorbidity, between drug abuse and other mental illnesses. Results from the South African Stress and Health (SASH) Survey shown significant associations between substance use and mood and anxiety disorders, with a particularly strong relationship between cannabis use and mental disorder. [24] The high prevalence of comorbidity between drug use disorders and other mental illnesses does not mean that one caused the other, even if one appeared first. According to reports from NIDA research report series (NIH Publication Number 10-5771, revised September 2010), substances of abuse can cause abusers to experience one or more symptoms of another mental illness. Reports from the Epidemiologic Catchment Area (ECA) study, [25] the National Comorbidity Study (NCS), [26] and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [27-29] establishes high prevalence of SUDs in those with mood disorders. Of these, the NESARC survey provides the most comprehensive, up-to-date data on psychiatric comorbidity. On the other hand, mental illnesses can lead to drug abuse. Individuals with overt, mild, or even subclinical mental disorders may abuse drugs in the form of self-medication. Both drug use disorders and mental illnesses are caused by some of the common factors such as overlapping genetic vulnerabilities, underlying brain deficits, etc.

Global scenario:

Physicians treating patients for chronic pain have limited means of determining whether a person is taking medications as prescribed or are not consuming extra medication. Over the past few decades, the prescription of opioid analgesics for the treatment of pain has increased globally from 75.5 million to 209.5 million.[7] Estimates from the U.S. National Survey on Drug Use

among Households (NSDUH)[30] from 1990 to 2006, reflect trends of increasing self-reported recent abuse of prescription opioids. Total cost of prescription opioid abuse in the United States was $8.6 billion in 2001 and this continues to grow. Direct health care cost for people who use opioids non-medically alone is more than eight times than those who do not use them for non-medical purposes. There are two major population based surveys on college students and younger adults of US population, which also supports the trends in increasing pattern of prescription opioid abuse among them. They are 'National Household Survey on Drug Abuse' (NHSDA) and 'Monitoring The Future' (MTF). The NHSDA, conducted by the Office of Applied Studies, Substance Abuse and Mental Health Services Administration, surveys a representative sample of households aged 12 years and older in the United States. On the other hand, the MTF study, which was conducted by the University of Michigan, with funding from the National Institute on Drug Abuse (NIDA), is an on-going study of the behaviours, attitudes, and values of American secondary school students, college students, and young adults since 1975. In 1991, the study was expanded to include 8th and 10th graders from representative samples of middle schools and high schools.

Based on the 1997 National Household Survey on Drug Abuse, it is estimated that 36.5 per cent of the Nation's household population aged 12 and older, had used an illicit drug at least once in their lives and 13.9 million people had used an illicit drug sometime in the month prior to the survey. According to report, 60 per cent had used only marijuana, 20 per cent had used marijuana and some other illicit drug, and 20 per cent had used a drug other than marijuana in past month. 1997 NHSDA showed that a prescription opioid –codeine was the most prevalent illicit drug used, after marijuana. Illicit use of analgesics, hallucinogens, inhalants, and

stimulants were also reported. This study also reported that illicit codeine use among those ages 12 and older has consistently been much higher for males than for females among US population. 30 per cent of the household population aged 12 and above, reported smoking cigarettes within the month prior to the 1997 NHSDA. The mean age at which persons started use of marijuana, cocaine, inhalants, hallucinogens, heroin, and daily cigarette smoking has decreased over time since the survey began, whereas the mean age of first use of alcohol and cigarettes has remained stable. [31] Apprehension for drug use among young people is supported by the findings from the December 1998 Community Epidemiology Work Group (CEWG) meeting, which is the major national surveillance system in the US, supported by NIDA. According to their report benzodiazepines and codeine (prescription opioid) abuse are emerging in US populations. Benzodiazepines abuse has been reported in Boston, Chicago, San Francisco, Seattle, and Texas and is used by heroin addicts mainly. On the other hand in Boston, Detroit, San Diego, San Francisco, and in Texas, codeine abuse is emerging as a major problem. Comparative data on 8th, 10th, and 12th grade students surveyed in 1997 and 1998 in the Monitoring the Future (MTF) Study reported a decrease in the proportions of young people using most illicit drugs including prescription opioids; the exceptions were crack cocaine and tranquilizers.

According to the MTF study, in 2009, hydrocodone was the most used substance after alcohol & marijuana among 12th grade students in United States and although its use fell significantly in 2010 to 8%, hydrocodone remains one of the most widely used illicit drugs among 12th graders. Whereas in 2008, methadone was implicated as the principal drug in 27 per cent of drug- related deaths among 16-24 year-olds in the United Kingdom.

In 1975, when MTF began, 55% of young people had used an illicit drug by the time they left high school. This figure increases to 66% in 1981 then declined to 41% in 1992. From there it rose to 55% in 1999, and then declined gradually to 47% in 2007 through 2009, and stands at 49% in 2012. There has been no significant change in use of other illicit drugs between 2011 and 2012. But, heroin use without using a needle declined significantly in 8th (down by 0.3%) and 12th grades (down by 0.4%), and remained unchanged in 10th grade in 2012.

MTF-2012 report also revealed that there is sharp increase in the use of narcotic drugs i.e. prescription opioids other than heroin in recent years. Significant use is reported only in 12th grade, because researchers considered that the data from 8th and 10th graders to be of questionable validity. Increase in OxyContin use observed in all grades from 2002 (when it was first measured) through 2011. MTF-2012 reported an increase in OxyContin use in all grades from 2002 through 2011. MTF-2014 reported a significant drop in OxyContin use among the 8th graders. Annual prevalence in 2014 was 1.0%, 3.0%, and 3.3% in grades 8, 10, and 12, respectively. On the other hand, use of Vicodin, remained fairly steady at somewhat higher levels since 2002, until its use declined after 2009 in all three grades till date. [32] MTF-2014 reported declining use of number of illicit & licit substances, this decline is mainly due to a decrease in annual prevalence of marijuana in 8th, 10th, and 12th graders.

Other than younger adults, women drug abusers are more likely than men to report psychiatric problems, (mental disturbances, suicidal behaviour) [33] and histories of 'physical, emotional, and/or sexual abuse' [34] which put them at greater risk of abuse of drugs. A retrospective study

by Traci C Green et al [13] on participants of 18 years and older attending substance abuse treatment centres across the United States, who completed the Addiction Severity Index-Multimedia Version® (ASI-MV®) Connect, revealed that there are gender differences persists at the most fundamental levels of prescription opioid use and abuse and women were more likely than men to report use of any prescription opioid in the past 30 days (29.8% females vs. 21.1% males, $p<0.001$) as well as abuse of prescription opioids in the past 30 days (15.4% females vs. 11.1% males, $p<0.001$). A Canadian study suggests that women between 12-16 years old in detention compare to men in detention of the same age are more likely to report injecting prescription opioids. [35]

Non-medical use of prescription opioids remains a major problem in the Americas. According to world drug report 2011, there are over 40 per cent of global opioid users in North America. This is because there is wide spread non medical use of prescription opioids in the North America which rose between 2002 and 2006, then fall was recorded until 2008 and rose again in 2009. In 2006, a behavioural surveillance study in Canada, reported injection morphine use in Canada. [36] In 2009, 1.9 million people in the USA were diagnosed with substance abuse or dependence on prescription opioids and prescription opioid misuse was reported at 0.5% in Canada.[37] In US, the non-medical use of prescription opioids (4.9%) now show higher annual prevalence rate than cocaine (1.9%). Among prescription opioids, oxycodone's non-medical use was reported to rise since 2005 in US and it was also observed that codeine based preparations are among the commonly abused prescription opioids in south and Central America. World Drug Report 2011 also reported high prevalence of non-medical use of prescription opioid in Costa Rica, Brazil and Chile. Increased incidences of overdoses from prescription opioid by 175% from 2001 to 2006 in

US has also been reported by both National prescription Drug threat Assessment 2009 report and National Drug threat Assessment 2010 report.[38]

Opium poppy –the parent drug grows largely in the South-East Asia and Middle-East i.e. Afghanistan, Iran, Myanmar, Thailand, Turkey etc. as well as in other parts of the world. Opium crop failure due to a disease of the opium poppy in Afghanistan in 2010 as well as heroin shortage in some European countries in 2010-11 might be the possible reasons for rapid build-up of parallel illicit market for prescription opioids. This encourages users to shift from heroin to other substances like desomorphine, acetylated opium and prescription opioids such as fentanyl and buprenorphine. Replacement of heroin by fentanyl was reported by Russian federations. [8] According to UNODC report, opioids remains the dominant drug type accounting for treatment demand both in Asia and Europe.

According to annual report 2010 of European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) [39], among European countries, only Denmark, Estonia and Finland show substantial non-medical use of prescription opioids than heroin, whereas benzodiazepines are the commonly abused there. Northern Ireland reports highest abuse of prescription opioids. Some of the European countries such as Estonia and Finland reported incidences of shift from heroin to prescription opioid mainly fentanyl and buprenorphine. EMCDDA annual report 2015 indicated high substance abuse related admission due to prescription opioids. A 75 percent of substance abuse related admission due to fentanyl in Estonia and 58 percent of drug abuse related admission due to buprenorphine in Finland were reported. [40]

According to UNODC report, seven out of fifty four African states reported an increasing trend in the use of opioids and opioid along with cannabis were the two main substances contributing to demand for treatment for illicit drug use. In South Africa, an average of 6.9% of people at substance abuse treatment reported prescription opioid as either their primary or secondary substance of abuse. [41] Annual Reports questionnaire (ARQ) data by UNODC evidenced non-medical use of buprenorphine and pentazocine in Africa. [42]

2012 World drug report indicated that cannabis, opioid (mainly heroin) and amphetamine type stimulant (ATS) are the major substance of abuse in Asia and there is an increasing trends of non-medical use of synthetic prescription drugs in Middle East. NIDA, UNODC and SAMHSA reports identified several drug use characteristics in Middle East such as decreasing age of starting drug use, increasing number of IDUs, more women drug users, contribution towards spread of HIV/AIDS.

Population based survey in Taiwan from 2002 to 2007 reported increased consumption of transdermal fentanyl and oral morphine. [43] The first national study on secular trends and characteristics of pethidine use in Taiwan conducted during 2002-2007, observes declining trends in the prevalence of pethidine users.[44] An increasing proportion of pethidine prescriptions from clinics, outpatient settings and operation patients with cancer diagnoses was also noted. Similar trend of pethidine use was also reported in Israel from 2000-2008. [45] Nepal which shares border with India, also reported significant use of prescription opioids such as dextropropoxyphene, buprenorphine and propoxyphene non medically.[46] According to Mapping and Size Estimation of Most at Risk Population survey, Nepal reported 30,000-34,000

(nearly 0.18 per cent of the adult population) injecting drug users among which most of them uses buprenorphine and propoxyphene non medically.[47]

Indian scenario:

Historical aspects:-

The traditional drugs of use in India were cannabis (bhang, ganja) and opium since ancient times. Their use has been continuing in rural areas of northern states of India. The Indian Hemp Drugs commission reviewed and discussed medical evidence given by 335 physicians throughout India from Bengal, Assam, North-Western Provinces, Punjab, Central Provinces, Madras, Bombay, Sind, Burma, and Berar regarding physical, mental and moral effects of marijuana. The Indian Hemp Commission Report (1893-94) states that occasional bhang use was almost universal in India and only 5% of the regular users were heavy users. In last few decades, there is rapid increase in the use of alcohol, tobacco and drugs. Since early 80's, heroin brown sugar effectively displaces opium and cannabis as the major substance of abuse. This was mainly due to stringent effects of Narcotics and Psychotropic Substances act 1985. [48] India ranks second to Afghanistan in licit production of opium. Opium was transported to India in the ninth century by Arab traders via the west coast and was primarily used for the medicinal purposes. By the next century, its use spreads all over the country. By the end of 14th century along the west coast at Cambay and Malwa full production and cultivation of opium has started. By 1757, the British East India Company started increasing revenue by cultivating opium mainly in Bengal. By the early 80's India became the main opium producing country and became the only supplier of licit opium for the world's requirements. Legally cultivated opium was being diverted and converted

into heroin by the 80's-90. In the beginning of 90's there were nearly five million opium addicts and 750,000 to one million heroin addicts in India. ICMR bulletin [49] also reports that since ancient times, opium was being used by wrestlers in battle fields to increase physical strength. This bulletin also states that in industrial areas of Kolkata, Mumbai, women factory workers used to give opium mixed with sweets to their children's to keep them docile. Opium is often mentioned in the Materia Medica section of Sharangadhar Samhita and Bhavaprakash and found in eight Ayurveda preparations such as Karpua rasa, Ahiphenasava, Brihat Gangadhar churna, Markandeya churna, Dugdha vati, Grahanikapta rasa (Rasendra sara sangraha), Akrakaravadi churna (Sarangadhara) and Sambhunath rasa (Bhaishajya tantra) in last two centuries. In the 19th century, smoking of opium became popular in India compare to oral consumption of it. By 1959, the sale as well as consumption of opium was completely prohibited by the government of India except for registered addicts. Various other substances other than opium, such as hypnotics, sedatives, stimulants, hallucinogens were being popular among younger population by the latter half of twentieth century. During the late 1980's and early 1990's, buprenorphine became very popular and its injectable form became popular throughout India. [49]

Indian epidemiological studies:

There are four major national surveys and five thematic studies which were carried out among general populations of India to determine the prevalence and pattern of major substance of abuse including prescription opioids amongst them. Each study differ in methodology.

Among these the first systemic study done on Indian population was National Household Survey on Drug and alcohol abuse (2000-2001). The National Household Survey (NHS) determines the prevalence of lifetime as well as current abuse of various licit and illicit substances for the country as a whole and studies the socio demographic correlates of drug abuse, where data were collected from 40,697 males aged 12-60 years in 25 states of India. National Household Survey on Drug and Alcohol Abuse, Government of India, observed the prevalence of opioids abuse of 0.7% after alcohol (21.4%) and cannabis (3%) among adult males. [15] The second major survey was National Family Health Survey (NFHS). It is a house to house survey. NFHS-3 (2005-2006) did not provide any information on prescription opioid abuse, whereas it provides information only about alcohol and tobacco use. [50]

The Drug abuse monitoring system (DAMS) evaluated the primary substance of abuse in inpatient treatment centres (de-addiction centres) which were funded by Ministry of Social Justice and Empowerment, Ministry of Health and family Welfare as well as various NGO's. They reported that alcohol (43.9%) was the major substance of abuse (n=16942) followed by opioids (26%). 14 per cent had used drugs through the injecting route at some point in time and about 9 per cent could be called current (used within last month) IDUs.[15]

The Rapid Situation Assessment (RSA) attempted to obtain data from inaccessible drug users in the community. It measures the pattern of substance use. Study was conducted by United Nations Office of Drugs and Crime (UNODC) in 2002 among 4648 drug users in 14 urban areas in India showed that cannabis (40%) was the major substance of abuse followed by alcohol (33%) and opioids (15%). However, the proportion of IDUs was higher in four major metros and Imphal. [16]

A Rapid Situation and Response Assessment (RSRA) of drugs and HIV among 5800 male drug users in India revealed that among prescription opioids, injection buprenorphine (76%) was primarily abused followed by propoxyphene (64%).[17]

A Rapid Assessment Survey of 1865 women drug users by 110 NGOs across the country revealed that 25% currently were heroin users, 18% used dextropropoxyphene, 11% used opioid containing cough syrups and 7% used buprenorphine. 25% respondents had history of lifetime injecting drug use. 87% concomitantly used alcohol. [51]

The NHS, DAMS and RAS had unique and exclusive information on various aspects such as socio demographic information, drug use pattern, sexual behaviour and knowledge on AIDS, on drug abuse from the particular city / state / region. Information on reasons for drug use is available from both the NHS and the RAS survey. Detailed information on injecting drug use in the form of reasons of use, reasons for shifting to IDU, frequency of sharing, cleaning habits, etc. is available from the NHS and the RAS surveys.

There are five focused thematic studies which were carried out on Indian population. They are Drug Abuse among Women, Burden on Women due to Drug Abuse by Family Members, Drug Abuse among Rural Population, Availability and Consumption of Drugs in Border Areas and Drug Abuse among Prison Population.

The study on Drug Abuse among Women studied individual characteristics, household characteristics and social support systems available to and accessed by women drug users from Delhi, Mumbai and Mizoram (Aizawl). This study included 75 women drug abusers enrolled in a snowball sampling technique from these cities. The Mumbai sample consisted of women drug users involved in sex work, the Delhi sample comprised mostly working women, and the Aizwal sample was constituted by women drug abusers in treatment. The women were mostly in their 3rd and 4th decades. Half the respondents from Mumbai and Delhi were illiterate. Very few had received any technical or professional training. Thirty one per cent of the women across the sites were single, 32% were separated or divorced. While a majority of women from Aizawl lived with their families of origin, Mumbai had a large number of women who had run away from home at an early age and were entrapped in the flesh trade. Friends had introduced drugs initially to 48% of the respondents, whereas in 16%, introduction to drug use was by the husband or partner. Thirteen per cent of women from Mumbai reported initiation of drug use on account of humiliation, shame, anger and powerlessness as a response to their situation. With the married women from Delhi, marital conflict and abuse of prescription pharmaceuticals (including prescription opioids) was a common initiation factor of drug abuse. Most of the women were using heroin or brown sugar. Other common or concomitant drugs of abuse were propoxyphene, alcohol, tranquilizers, cough syrups and cannabis. Propoxyphene was most preferred substance of abuse in Aizawl. IDU was reported in 41% among respondents. Study also stated that women from Aizawl who injected propoxyphene for their peers were able to receive their drug supply in exchange for 'fixing' their peers. Injecting drug users from Mizoram were regularly hospitalised for overdose and treatment of abscesses. There was reporting incidences of both physical and psychological problems associated with their drug use. About 10 had suffered miscarriages or

undergone medical terminations due to their drug use. Among Aizawl women, family cohesion was better than women respondents of Delhi and Mumbai. Domestic violence was often reported by non-drug abusing husbands of the women. Sexual intimacy within the relationship was reported as poor, as was emotional closeness. The drug abusing women received little support from their relatives, husbands or friends. In all three cities, specific issues that interfered with treatment included concerns for children unattended at home, fear of exploitation, fear of withdrawal, and a lack of supportive systems.

In the study on Burden on Women due to Drug Abuse by family members, adult women who were living with an affected close family member who was a current regular user of drug(s) (opioid and prescription opioids) other than exclusively alcohol or tobacco from various treatment centres, community or workplace of nine Indian cities were interviewed. This study indicated that women, both as substance users and partners of users were vulnerable to HIV infection through the sexual route.

Another thematic study on Availability and Consumption of Drugs in Indian Border Areas explored drug trafficking across the international borders of India (three sites at India - Pakistan border and one site at India – Nepal border, one site at India – Bangladesh border, one site at India – Srilanka border, two sites at India – Myanmar border) and availability and consumption of various drugs in these border areas. It examined both supply and demand of various drugs in these sites. Study revealed that 40 per cent reported using drugs through injectable routes. Injecting drug use was reported mostly from Tuensang (Nagaland) and Moreh (Manipur) on the Indo-Myanmar border. There were a few IDUs at Tuticorin (Tamil Nadu)-Indo-Sri Lankan

border, Sonauli (Uttar Pradesh) on the Indo-Nepal border and Lalgola, (West Bengal) on the Indo-Bangladesh border. The primary drug of abuse in Tuensang, Moreh and Attari (Punjab, Indo-Pakistan border) was heroin and propoxyphene. At times of inadequacy due to mainly heroin drought or escalating cost of heroin, they shift to injectable pharmaceutical drugs. In Tuticorin, pentazocine injection was prevalent. At Sonauli, Lalgola, and to a lesser extent in Attari, injectors used a cocktail of buprenorphine and antihistamines. At Moreh and Tuensang (Indo-Myanmar border), many injectors reported overdose and reuse of syringes and needles. [52] Seizure statistics as well as information from other sources also states that there is rapid increase in the use of the Tamil Nadu shore around Tuticorin as a staging point for heroin shipments to Sri Lanka. According to Narcotic Control Board, geographical proximity and ethnic links contribute to smuggling between coastal southern India, especially the southern Coromandel Coast and the north-western coast of Sri Lanka by sea, mainly by small craft. The smuggling of pharmaceuticals from India, especially prescription opioids such as dextropropoxyphene, injectable buprenorphine, and codeine based cough syrups as well as diazepam and nitrazepam is a major concern for India's neighbours, particularly Bangladesh, Nepal and Sri Lanka. During 2002, law enforcement authorities on the Indian side of the border seized 300,000 bottles of Phensidyl. [53]

IDU in India was initially acknowledged in the north east states of Manipur and Nagaland, mainly due to their proximity to the 'Golden Triangle' –Burma, Thailand, and Cambodia. In the Northeast Indian states of Manipur and Nagaland there has been an on-going HIV epidemic among injecting drug users (IDUs) since the mid-1990s. Of the eight north eastern states – Assam, Meghalaya, Sikkim, Tripura, Arunachal Pradesh, Manipur, Mizoram and Nagaland –the

last four share a common international border with Myanmar, the world's second largest illicit opium producing country. Heroin –commonly referred to brown sugar, enters the north eastern states from their respective borders with other Indian states as well as from Myanmar. Ephedrine, a precursor for the manufacture of Amphetamine Type Stimulants also moves into Myanmar from India. In mid-2006 a cross-sectional survey among 200 injecting drug users (IDUs) was undertaken in collaboration with local NGOs in (Imphal) Manipur and (Dimapur) Nagaland. According to their study, the primary drug of abuse was injection dextropropoxyphene (spasmoproxyvon) (65.5%), followed by heroin (30.5%). This study also states that injection drug use started at 20 years of age and there were evidences of significant peer influence. Among North East Indian states, Manipur has high prevalence of HIV among IDUs as evidenced by a study conducted by Agarwal AK et al, [54] where 100 blood samples were collected from Manipuri women of which seven were migrant from Myanmar. The HIV prevalence among IDU community sex workers of Manipur was found to be 9.4 times higher than non IDU community sex workers.

Information from Sikkim:

Sikkim, a small mountainous state in the eastern Himalayas, observed great changes in its political structure, social structure, economic life and cultural values during the past hundred years. The state borders Nepal to the west, China's Tibet Autonomous Region to the north and east, and Bhutan to the southeast. The Indian state of West Bengal lies to the south. Sikkim with a population of 6.11 lakh [55] is a multi-ethnic state, inhabited by ethnic population of Lepchas, Bhutias and Nepalese. Lepchas are traditional inhabitants of Sikkim, whereas Bhutias and

Nepalese (approximately 70% of Sikkim's population) have migrated from Tibet and Nepal, respectively. Sikkim was annexed to India as its 22nd state in 1975. As a result, a lot of migration took place from other parts of India, with introduction of new substances of abuse including prescription opioids. A retrospective study by Bhalla et al [56] on patients with history of current drug use seeking emergency services for any medical or surgical consequence incident to substance abuse in Sikkim from July 2000 to June 2005 revealed that the primary substance of abuse was alcohol (77.8%), followed by opioids (14.8%) mainly injection dextropropoxyphene and pentazocine. National Family Health Survey-3 (2005-06) by Govt. of India has shown a significant increase in alcohol abuse in Sikkim among both males (45.4%) and females (19.1%) of 15-49 yrs. age group from its previous report of NFHS-2. In order to control or regulate the use of drug and controlled substances with abuse potential being misused by addicts and traffickers, to make stringent provision to deal with the ever increasing phenomena abuse of medicinal preparations -'Sikkim anti-drug Acts (SADA)' was launched in 2006. There are many reports of arrests under SADA Act from both rural as well as urban areas of Sikkim, for consuming or carrying illicit substances including prescription opioids, barbiturates etc. This also shows a growing trend towards alcohol and drug abuse and addiction.

RESEARCH QUESTIONS

The study has following research questions:

(1) What are the sociodemographic characteristics of prescription opioid abusers?

Sociodemographic information of prescription opioid abusers includes –religion (Hinduism/Islamic/Buddhism/Christianity),ethnicity(Nepali/Bhutia/Lepcha/other),age, gender (male/female), marital status (single/married/separated/widower), level of education (10th standard pass / 12th standard pass /graduate/post graduate/school dropout & illiterate), occupation (business/skilled-semiskilled/unemployed), source of income (salaried/self-employed/unemployed), average monthly income, average monthly expenditure on prescription opioids).

(2) What is the relationship between pain and prescription opioid abuse?

This includes –whether prescription opioids are received as a first opiate analgesic treatment of pain and to find out what is the major reason for continuing its use i.e. either for relieving physical pain or to get high or euphoria or to improve sleep, to relieve depression, nervousness, anxiety or to avoid withdrawal effects?

(3) What are the high risk behaviour profile of prescription opioid abusers?

Injection drug use (IDU) and homosexuality are the high risk behaviour profile of prescription opioid abusers.

(4) What is the quality of life of prescription opioid abusers?

This includes their current general health status (either much better/somewhat better/same as past year), whether facing any limitations in doing physical activities like running, playing, walking, whether facing any limitations in doing regular activities/work due to emotional problem?

(5) Is there any differences in socio-behavioural and drug use characteristics among different drug using samples?

The aim is to find out the differences in various socio-behavioural characteristics like migration (either drug use started before or after migration), community (either from rural or urban setup), level of education, age group and differences in drug use characteristics like route of drug administration, frequency of use, among prescription opioid abusers and poly drug abusers.

SUBJECTS AND METHODS

Study settings:

A cross sectional, target population based study was conducted during the period of 2010 to 2013 among prescription opioid abusers who reported for treatment at five different substance abuse treatment centres located at different parts of Sikkim. n=224 subjects with clinically diagnosed prescription opioid abuse as the main problem participated in the study. Subjects were recruited from Sikkim Rehabilitation & Detoxification Society (SRDS), located at Nimtar, 32 mile, East Sikkim; Integrated Rehabilitation Centre for Addicts (Jagriti), located at Upper Sichey, Gangtok, East Sikkim; Hope Rehabilitation Centre and Sanjeevani Rehabilitation Centre, both located at Namchi, West Sikkim; and Serenity Home, located at Burtuk, East Sikkim. All treatment centres are non-profit organizations and registered under Government of Sikkim. They are residential treatment centres and affiliated with private and government hospitals for providing ancillary treatment to their patients. Duration of residential treatment varies from centre to centre (120-144 days). Among these treatment centres, SRDS, Nimtar provides the longest residential treatment. Detoxification schedule also varies among the treatment centres (25-30 days). Treatment-seeking drug abusers take admission to treatment centres through various drop-in centres located in rural as well as in urban areas of Sikkim.

Selection of subjects:

Subjects of either sex and of any age who were admitted for treatment of clinically diagnosed prescription opioid abuse as the main problem at treatment centres in Sikkim were included in my study. Those who had a history of abuse of only alcohol and/or only illicit opioids and/or any other drug were excluded. All instruments were administered to a participant in a single session following completion of informed consent procedure. All participants were interviewed by the same interviewer; thus excluding possibility of inter-rater error.

Study design:

Before enrolling for this study, an informed consent was explained and signed from each participant from all the five treatment centres of Sikkim. Participation for this study was voluntary. At any time participant has complete freedom to withdraw from this study if desired. Full confidentiality of personal details of each participant was maintained. Pre-devised questionnaires were then administered to prescription opioid abusers of respective treatment centres.

Instruments:

(1). Participant's socio-demographic information was recorded by administering 'Generic Instrument - Population Survey of Alcohol & Other Drug Use' questionnaire. Major Sociodemographic parameter recorded were age, race/ethnicity, religion, marital status, education, income, occupation etc.

(2). Risk Behaviour Survey questionnaire collected information on high risk behaviour profile of prescription opioid abusers, i.e., injection drug use pattern, injection sharing, frequency of sexual activity, condom use characteristics, visit to commercial sex workers, history of homosexuality etc.

(3). Participant's prescription opioid and alcohol use characteristics were recorded by administering 'Addiction Severity Index Lite' (ASI-Lite) questionnaire. ASI Lite [57] is a shortened version of ASI- 5th edition. It gathers information on seven domains of patient's life: medical, employment/ support, drug & alcohol use, legal, family, social relationship and psychiatric problems.

(4). Abbreviated Brief Pain Inventory & Brief Pain Inventory (short form) questionnaire collected information on pain status at this current time period and how much relief has pain treatments or medication provided. BPI assessed average, worst & least pain intensity at the time of interview as well as over the last 24 hours using 0 ("no pain") to 10 ("pain as bad as you can imagine") numeric rating scale. Participants identified location of pain on body map indicating

31 locations. A numeric rating scale from 0 (“does not interfere) to 10 (“completely interferes”) was used to find out degree at which pain interfered with seven activities (such as general activity, mood, walking ability, sleep, enjoyment of life, normal work and relations with others) over the past 24 hours.

(5). Alcohol problem was measured by using CAGE questionnaire, which is a valid tool for detecting alcohol abuse and dependence. The CAGE questionnaire was developed by Ewing [58] in 1968which has a cutoff score from 2 to 1. A cutoff ≥ 2 is recommended to detect alcohol abuse or dependence.

(6). Pain and Opioid Analgesic Use History questionnaire collected information on types of pain treatment taken and source of treatment taken for opiate problems, routes of prescription opiate use, source of prescription opioids for addiction, reason for addiction, and their view on using prescription opiates at this time once rehabilitation gets over. Pain component of this questionnaire collected information on frequency and duration of pain, characteristics of pain, nature & pattern of pain.

(7). SF-36, i.e., questionnaire on quality of life, collected information on their current health condition comparing to one year on both physical and psychological domains.

(8). Fagerstrom Test for Nicotine Dependence, a six item questionnaire assessed the pattern and severity of tobacco use among prescription opioid abusers.

Ethical issues:

The study involved only interviewing the subjects and did not involve any intervention. The study protocol, instruments and informed consent were approved by Institutional Ethics Committee (IEC) and Research Protocol Evaluation Committee (RPEC) of Sikkim Manipal Institute of Medical Sciences, Gangtok.

Informed consent was explained & obtained from each participant before enrolment for this study. They were provided with a copy of informed consent form with contact information of investigators so that they can contact investigator or ask questions regarding their substance use problems and/or treatments. Questionnaire response were coded by numbers and at no time participants name / photo were associated with participant's responses to the questionnaire so that full confidentiality was maintained. Participation for this study was voluntary. At any time participant had complete freedom to withdraw from the study if desired so. Participants must be convinced that this study does not have any relation with police or with their employment.

Sample size estimation:

To detect a 15% (high 25 vs. low 10) difference in presence of a risk factor (e.g. lack of parental supervision/attachment, disintegration of old joint family, working parents, academic failure, social difficulties, poverty, easy availability of drugs, association with drug abusing peers, unwilling migration, etc.) with an α value of 0.05 (by repeating test 100 times, at least 95 times we will get same 15% difference) and a power (**1-β**) of 80%, which indicates how well test is working, the study needs to enrol a total of n=224 subjects.

Attempts were made to oversample by 20%, for getting required number of prescription opioid abusers. This allows for possible subgroup analysis.

All instruments are internationally standardized and used in drug abuse research. But still there is a need for reliability & validity analysis of mainly ASI- Lite & (POAUH) in Sikkim's population as ASI-Lite and POAUH were developed on American socio-demographic, drug use characteristics which differs from Indian standards (e.g., race, ethnicity differs).

Statistical analysis:

Statistical Package for Social Sciences (SPSS), version 20 was adopted for development of the databases as well as for carrying out statistical analysis.

Descriptive statistics of variables of interest are presented. The mean and SD are presented for continuous variables. The number and percent of study participants practicing a particular behaviour are presented for categorical variables. The Chi-Squared ($\chi 2$) test was used to test hypotheses between categorical variables. Significance level was set at $p < 0.05$.
Odds ratio, relative risk and 95% confidence interval (CI) were calculated to estimate associated risk.

Differences in pain interference, pain characteristics and correlations, among the pain severity groups were analysed by using one way ANOVA and Chi square tests. For categorical variable, post hoc test were done with Bonferroni procedure with considering P value of less than 0.05 for statistical significance.

Substance use type by different pain severity group were analysed by using chi square test considering p value less than 0.05 as statistically significant. Psychiatric comorbidity among those groups were analysed by Fisher's exact test.

RESULTS

Section 1: Sociodemographic profile of prescription opioid abusers.

1.1 Age & gender: Of the 224 study participants, only one was female. The mean age of prescription opioid abusers in Sikkim was 27 years, ranged from 17 to 51 years.

1.2 Ethnicity & religion: According to our findings 61.2% (n =137) respondents were of Nepalese ethnicity, only 6.3% (n=14) belonged to the Lepcha –the only traditional inhabitants of Sikkim. Majority of them were of Buddhist religion (43.3%, n= 97), followed by Hindu (42.9%, n= 96). Christianity contributed to 13.8% (n= 31) among the prescription opioid abusers.

1.3 Marital status: Majority of respondents were (62.9%, n=141) single/unmarried, while 27.7% were married and remaining 8.9% (n= 20) were either separated or divorced or widowed.

1.4 Education: Eighty-nine respondents (39.7%, n= 89) dropout from school even before completing the eighth standard, whereas sixty-nine respondents (30.8%, n= 69) completed intermediate level (12th standard) and eleven respondents (4.9%, n= 11) never attended school in life.

1.5 Living arrangements: Most (57.6%, n=129) prescription opioid abusers belong to urban community, whereas 42.4% (n=95) belong to rural community. About 97.8% (n=219) had lived in the same area since birth. Abuse was higher among different age groups in urban compared to rural, except in the age group of 30 and more (chi-square = 13.89, $p<0.05$).

1.6 Source of income & Occupation / employment status: Among all the respondents, nearly one-fourths were unemployed (26.8%, n=60) and 12.5% (n=28) were students. One thirty six respondents (60.7%) had regular income from either salary and or from business. Study revealed that forty per cent (n=88) respondents (including students) never had any kind of job in their lifetime, whereas similar number possess any kind of job of less than 5 years of duration in lifetime. Among 137 subjects (61.2%) who were employed in different types of jobs in the past three years, only 42 of 137 (31%) were engaged in part-time works(both regular and irregular works) whereas rest of them had full time job in past 3 years. About 26.3% (59 of 224) respondents were unemployed in past three years. Study revealed that more than one fourth (n=64, 28.6%) subjects had an employment problem of more than 20 days in the last month. It was found that majority were earning less than Rs. 5000 / month (26.8%, n=60) whereas 24.6% (n=55) earned Rs.10, 000 or more in last month. About half the respondents (54.9%, n= 123) took any kind of support from any one including family members for daily livings.

1.7 Peer's role or influence on subject's prescription opioid use: According to our study all the subjects' parents were regular drinker. Our study also found that parents, siblings and friends of the respondents had significant alcohol use behaviour. Use of both alcohol and prescription opioid in lifetimes was reported mainly by friends (n=182, 81.3%) of subjects. whereas it was also found that thirty-four respondents had friends (15.2%, n=34) who consumes only prescription opioids.

Table 1.1: Socio-demographic characteristics.

Variables		N	Percentages
Gender	Male	223	99.6
	Female	01	0.4
Level of education	Illiterate	11	4.9
	School dropout	89	39.7
	Class 10 pass	21	9.4
	Class 12 pass	69	30.8
	Graduate & Post Graduate	34	15.1
Source of income	Salaried	72	32.1
	Self employed	64	28.6
	Student	28	12.5
	Unemployed	60	26.8
Occupation	Business, office work-clerical	54	24
	Skilled, semi-skilled, unskilled	82	36.5
	Unemployed	59	26.3
Community	Urban	129	57.6
	Rural	95	42.4
Ethnicity	Lepcha	14	6.3
	Bhutia	43	19.2
	Nepali	137	61.2
	Others	30	13.4
Marital status	Single	141	62.9
	Married	62	27.7
	Separated & divorces	20	8.9
Religion	Hinduism	96	42.9
	Buddhism	97	43.3
	Christianity	31	13.8
Migration	Yes	05	2.2
Migration reason	Family	04	1.8
	Other reasons	01	.4
Parental substance use type	Alcohol only	100	44.6
	Both alcohol and prescription opioids	01	.4
Sibling substance use type	Alcohol only	62	27.7

	Prescription opioid only	06	2.7
	Both alcohol & prescription opioid	04	1.8
Friend's substance use type	Alcohol only	08	3.6
	Prescription opioid only	34	15.2
	Both alcohol & prescription opioid	182	81.3

Table 1.2: "Elaborated employment status of prescription opioid abusers":

Variables		N	Percentages
Longest full time job duration	No job	88	39.6
	1-5 years of job	89	40
	6-10 years of job	28	12.6
	More than 10 years of job	17	7.7
Majority of support, contributed by anyone	Yes	123	54.9
Income from employment in Rs, past 30 days	Up to 5000	60	26.8
	5001-10000	44	19.6
	More than 10000	55	24.6
Employment problem in days, past 30 days	1-10 days	26	11.6
	11-20 days	15	6.7
	More than 20 days	64	28.6

Figure 1: Employment status, past 3 years

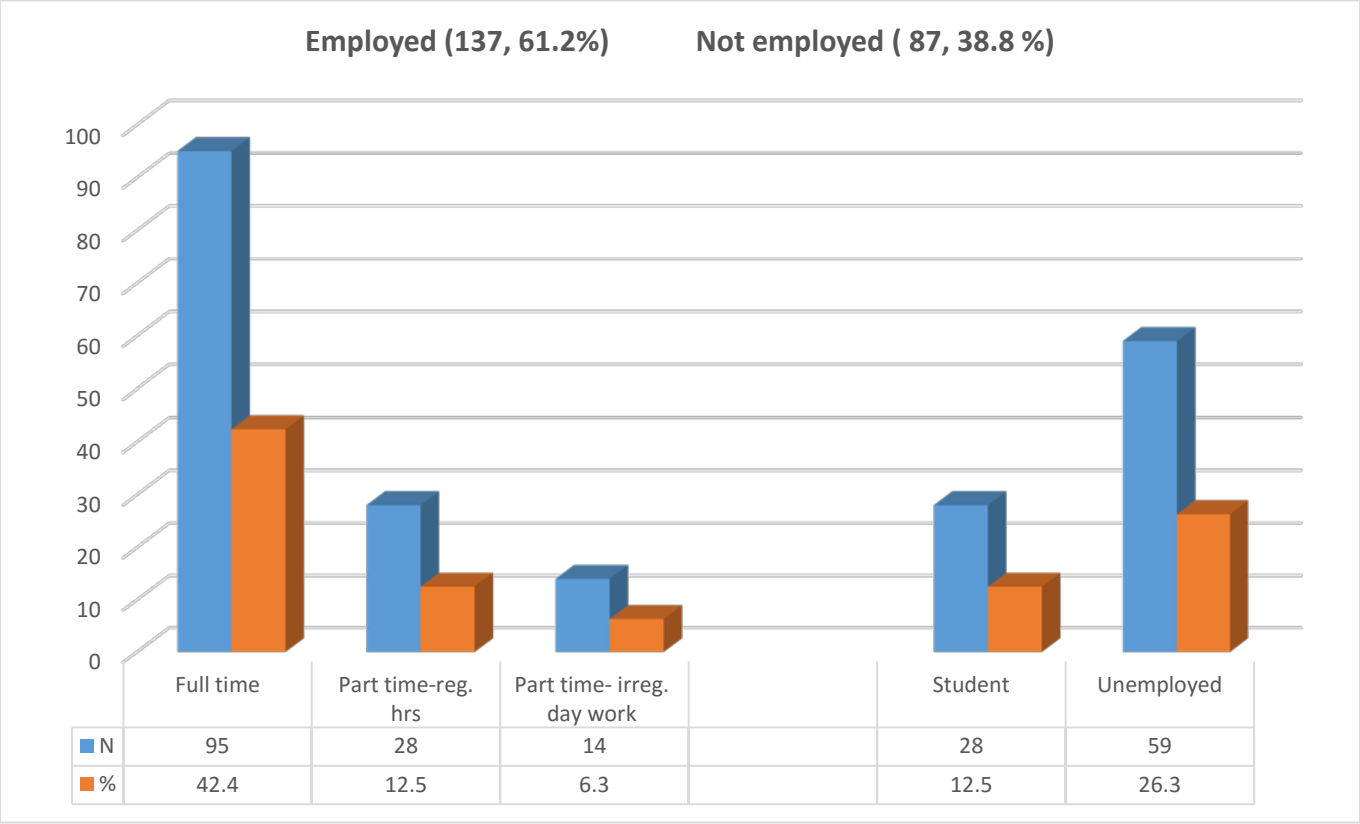
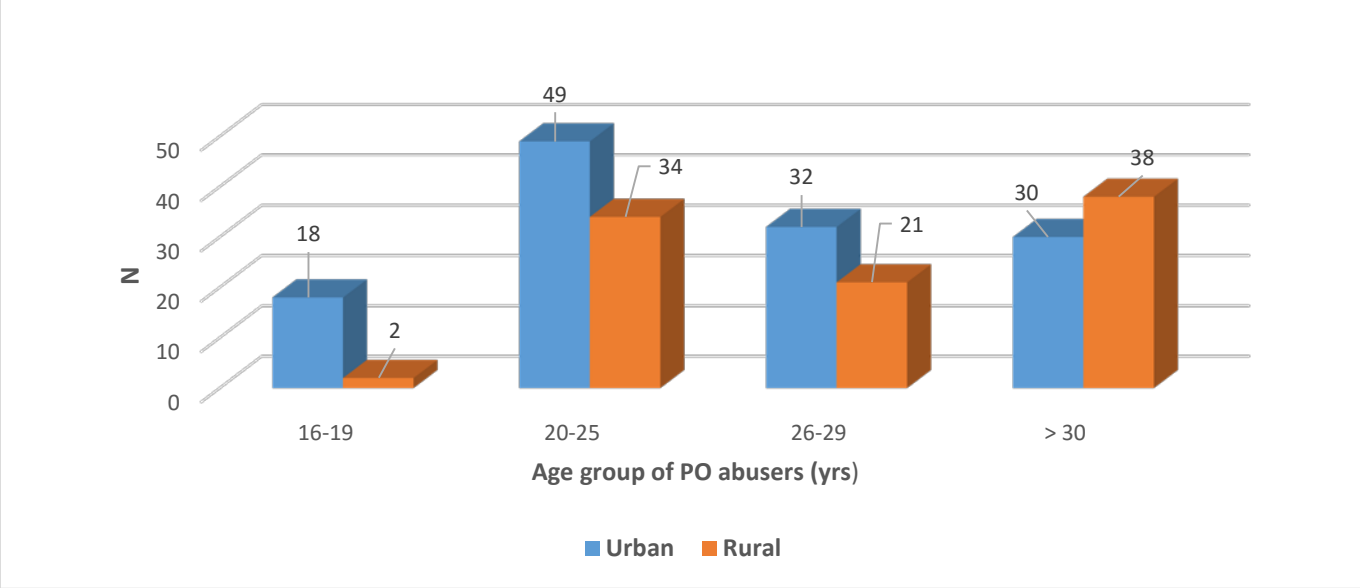


Figure 2: Age group distribution of prescription opioid abusers in the community



$\chi^2 = 13.9$, df = 3, p = 0.003

Section 2: Pattern of substance use of prescription opioid abusers.

2.1. Prescription opioid alone (without alcohol) was found to be the substance of major problem for 30.8% (n=69) respondents while prescription opioid along with alcohol was reported as a substance of major problem by majority of respondents (62.1%, n= 139). Very few respondents (7.1%, n=16) reported major problems with other opiates such as heroin. Lifetime use of heroin was reported by forty-four per cent (n=98) prescription opioid abusers. Majority of respondents (79%, n=177) were taking prescription opioids for a period of 20-30 days in the last month and majority of them had lifetime use of prescription opioid for 0-9 years (74.1%, n=166).Swallowing was found to be the preferred route of prescription opioids use. One seventy two respondents swallowed (76.8%) exclusively, while fifty-two (23.2%) respondents also injected it.

2.2. Study revealed that benzodiazepine (nitrazepam) tablet (79%, n=177) followed by alcohol (62.5%, n=140) and cannabis (55%, n=123) were the most common orally used substance used by the prescription opioid abusers in the last month. Cannabis (74.5%, n=167) was found to be the second most substance used by the respondents after benzodiazepines (64%, n=143) in their lifetime.

2.3 Findings of our study revealed that current as well as lifetime alcohol use was observed more by prescription opioid abusers aged 25 years and older. For both the instances difference was statistically significant with $p<0.05$. Past month use of alcohol by respondents that leads to intoxication was found more by subjects aged 25 years and older with p value 0.492, whereas

lifetime alcohol use that causes intoxication was observed more among 15-24 years age group respondents (p=0.165).

2.4. Study also reported both past month (2.9%, n= 07) as well as lifetime (21%, n= 49) use of inhalants by the prescription opioid abusers. All respondents reported regular and lifetime use of nicotine or tobacco products. Most of the respondents reported regular smoking of tobacco products by over 15 days in the past month.

2.5. Study reported an average monthly expenditure of Rs. 4896 (2798) {mean (SD)} on prescription opioids by the respondents.

Table 2.1. Pattern of drugs use.

Variables		Frequency	Percentages
Alcohol			
1. Any use, past 30 days	1-10 days	34	15.2
	11-20 days	40	17.9
	21-30 days	66	29.5
2. Any use, lifetime in yrs.	1-5 years	56	25.0
	6-10 years	44	19.6
	Over 10 years	43	19.2
3. Intoxication, 30 days	1-10 days	27	12.1
	11-20 days	26	11.6
	21-30 days	27	12.1
4. Intoxication, life time	1-5 years	65	29.0
	More than 5 years	20	8.9
Heroin/Brown Sugar		97	43.3
1. Past month use in days	1-10 days.	18	8.0
	11-20 days.	36	16.1
2. lifetime use (n=98)	1-5 yrs.	83	37.1
	More than 5 years	15	6.7
3. Route of administration	Smoking	95	42.4
	Intravenous injection	01	0.4
	Both of them	02	0.9
Prescription opioids		224	100
1. Past month use in days	0-9 days	07	3.1
	10-19 days	40	17.9
	20-30 days	177	79.0
2. Lifetime use	0-9 years	166	74.1
	10-19 years	56	25.0
	20-30 years	02	0.9
3. Route of administration	Oral	172	76.8
	Both oral and injectable route	52	23.2
Sedatives/hypnotics/tranquilizers			
1. Past month use in days	1-10 days	56	25.0

	11-20 days	69	30.8
	21-30 days	52	23.2
2. Lifetime use	1-5 years	113	50.4
	More than 5 years	69	30.8
Cannabis			
1. Past month use in days	1-10 days	79	35.3
	11-20 days	19	8.5
	21-30 days	25	11.2
2. Lifetime use	1-5 years	121	54.0
	More than 5 years	46	20.6
Inhalants			
1. Past month use in days	1-5 days	03	1.2
	6-10 days	04	1.7
2. Lifetime use	1-5 years	47	20.9
	More than 5 years	02	0.9
Nicotine/tobacco products			
1. Past month use in days	1-15 days	06	2.7
	16-30 days	218	97.3
2. Lifetime use	1-10 years	139	62.1
	More than 10 years	85	37.9
Substance of major problem	Other opiates	16	7.1
	Alcohol and one or more prescription opioid	139	62.1
	Prescription opioid but no alcohol	69	30.8
Money spent on alcohol, past month (Rs)	Upto 500	23	10.3
	501-1000	55	24.6
	More than 1000	58	25.9
Money spent on prescription opioids, past month (Rs)	Up to 3000	69	30.8
	3001-6000	89	39.7
	6001-10000	52	23.2
	More than 10001	14	6.2

Table 2.2: Alcohol use pattern among various age groups.

	15–24 years N (%)	25 years and older N (%)	Age group differences χ 2 (d.f.) p-value
Alcohol use, past month	47 (20.9)	93 (41.5)	11.600 (2) p = 0.003
Alcohol use, lifetime	48 (21.4)	95 (42.4)	40.625 (2) p = 0.001
Alcohol intoxication, past month	21 (9.37)	58 (25.8)	1.419 (2) p = 0.492
Alcohol intoxication, lifetime	23 (10.3)	62 (27.7)	1.927 (1) p = 0.165

Section 3: Characteristics of substance use by prescription opioid abusers.

3.1 Mean age of commencement of prescription opioid use by the respondents was found to be 20 years, ranges between 11-46 years. Mean duration of prescription opioids use by the respondents in last month was 23 days, ranging from 4-30 days. Mean years of lifetime prescription opioid use reported was 6 years, ranging from 1-20 years.

3.2 Respondents had used more than one substance of abuse per day for an average of 18 days in the last month while it was 5 years in lifetime.

3.3 Age of first alcohol use of prescription opioid abusing subjects ranged from 11-28 years with a mean of 19.55 years. Mean duration of alcohol use in last month was 20.81 days ranging from 4-30 days and mean years of alcohol use reported 8.39 years by respondents. Subjects experienced alcohol problem in an average of 13 days in last month.

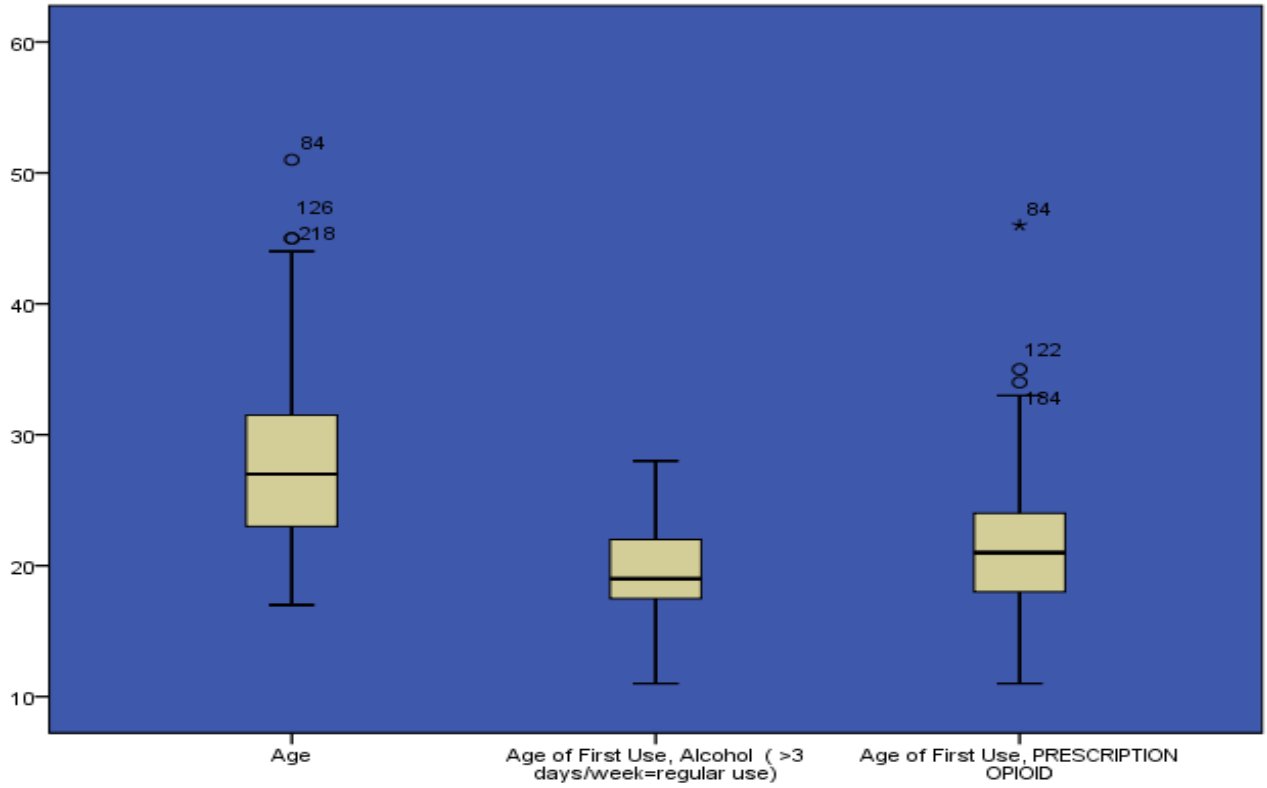
Table 3.1. Prescription opioid use characteristics of respondents:

Variables	Range	Mean (SD)
Age of respondents (years)	17-51	27.03 (6.11)
Age of First Use, prescription opioids (years)	11-46	20.40 (5.08)
Prescription opioids use, past month (Days)	4-30	23.92 (6.51)
Prescription opioid, lifetime use (exclude last 30 days)	1-20	06.31 (4.08)
> 1 substance/day used (including alcohol, excluding nicotine), past month	-	18.09 (9.51)
>1 substance /day used (including alcohol, excluding nicotine), life time	-	05.62 (3.96)

Table 3.2. Alcohol use characteristics of respondents:

Variables	Range	Mean (SD)
Age of first use, alcohol (years)	11-28	19.55 (3.25)
Alcohol use, past month (days)	4-30	20.81 (8.75)
Alcohol, lifetime use (exclude last 30 days)	1-35	8.39 (5.64)
Days experienced alcohol problem, past month	2-25	13.41 (6.8)

Figure 3: Distribution of respondents' age and age of fist use of alcohol user and PO users. (BOX PLOT)



Section 4: Opioid analgesic use history of prescription opioid abusers.

4.1 Among the opiates, prescription opioid alone was the major problem for concern to 75.9% respondents (n=170). For nearly one fourth of respondents (24.1%, n= 54), both prescription opioid and heroin were of biggest problem causing opiates.

4.2 Dextropropoxyphene (84.4%, n=189) followed by codeine (15.6%, n=35) were the most commonly abused prescription opioids by the respondents in the last month. Morphine was consumed by only one (0.4%) subject.

4.3 Several goals for using prescription opioids at the time of interview were stated by the respondents. Among those, majority (69.6%, n=156) wanted to quit using prescription opioids once and for all and to be totally abstinent from it and never use it in life. However several other versions were also recorded such as having no clear goal in mind at present (13.8%, n=31); want to quit once and for all, may slip up and use in a while (8.9%, n=20); want to be totally abstinent for a period, then take a new decision (4%, n=09); lastly, continue to use in a controlled manner (3.6%, n=08).

4.4 Study revealed that only 4% (n=09) respondents had used prescription opioid for a period of 6 months to less than one year for other than relief of occasional short term pain. One hundred and forty (62.5%) respondents used prescription opioids for a period of more than four years in their lifetime.

4.5 Friends were the first source from whom majority of subjects (67.9%, n=152) received their first prescription opioid at free of cost. Drug peddlers/dealers (8.5%, n=19) and medical shops (8%, n= 18) contributed equally as the first source of prescription opioids of the respondents. It was also reported that dealers (95.08%, n=213), friends (92.32%, n=207) and medical shops (without prescription) (88.75%, n=199) were the various major sources from where subjects obtained their prescription opioids during the last six months. Among these sources, about half of the respondents (55.4%, n= 124) procured prescription opioids most of the times from local dealers only. Only 04 of 224 subjects reported to obtain prescription opioids sometimes to frequently from doctors without legitimate medical reason in the past six months. It was also noted that, half of the respondents (51.8%, n= 116) also had purchased prescription opioids frequently to most of the time from medicine shops of nearest city (not from same place of living) without prescription.

4.6 Euphoria (54.5%, n=122) followed by curiosity/peer pressure (35.7%, n=80) were reported as the major reasons of first use of prescription opioids by the respondents. However there were several reasons for continued use of prescription opioids. Among those, 'being in good mood and feelings of getting high' & having good time with others (100%, n=224) were most important reasons. "Being in good mood" and "experiencing once the effects of prescription opioids"were reported as extremely important reasons for continued use of prescription opioids by 56.2% and 37.1% respondents respectively. Getting tempted to use prescription opioid was recorded as very important reason by majority of the respondents (74.6%, n= 167) among other reasons.

4.7 Study reported two major reasons for which subjects seek treatment for their prescription opioid use problems. The major reasons for treatment needs were –notto be dependent of prescription opioids (95.9%, n=215) & getting irritated by side effects (94.9%, n=213) of it. Among these, not to be dependent of prescription opioids was reported as very important reason by 44.2% (n=99) respondents.

Table 4.1: Opioid analgesics use history

Variables		N	%
Biggest opiate problem at present	Prescription opioid only	170	75.9
	Both PO & heroin	54	24.1
Goal about using PO at this time	Want to quite, never use in life	156	69.6
	No clear goal in mind	31	13.8
	Want to quite, may slip up and use in a while	20	8.9
	Want to be totally abstinent for a period, then will make a new decision	09	4.0
	Want to use in controlled manner	08	3.6
Most used POs, past month	Dextropropoxyphene	189	84.4
	Codeine	35	15.6
Other used POs, past month	Morphine	01	0.4
	Dextropropoxyphene	11	4.9
	Codeine	113	50.4
First source of prescription opioids	Dealer	19	8.5
	Sold by family member or friend	35	15.6
	Given by friends at free of cost	152	67.9
	Medicine shop	18	8.0
Major reason of first use of PO	Euphoria	122	54.5
	Relief from depression,	13	8
	Relief from anxiety, nervousness	09	4
	Others (peer pressure)	80	35.7
Reasons for continued use of prescription opioids	Anger	209	93.21
	Felt bore	133	59.32
	Felt anxious	198	88.31
	Saw prescription opioids	214	95.45
	Felt sad	202	90.09
	Felt ill or in pain because wanted prescription opioids	191	85.19
	Was in good mood, felt getting high	224	100
	experimentation	217	96.78
	Felt tempted to use it	220	98.12
	Someone offered	223	99.46
	Having good time with others and felt like getting high together	222	99.01
	Felt worried about owns relationship with someone	188	83.85
	Felt ill or in pain but not due to prescription opioid withdrawal	37	16.50
	Others were being critical of myself	197	87.86
	Saw others using it	217	96.78

Figure 4: Most used PO's, past month.

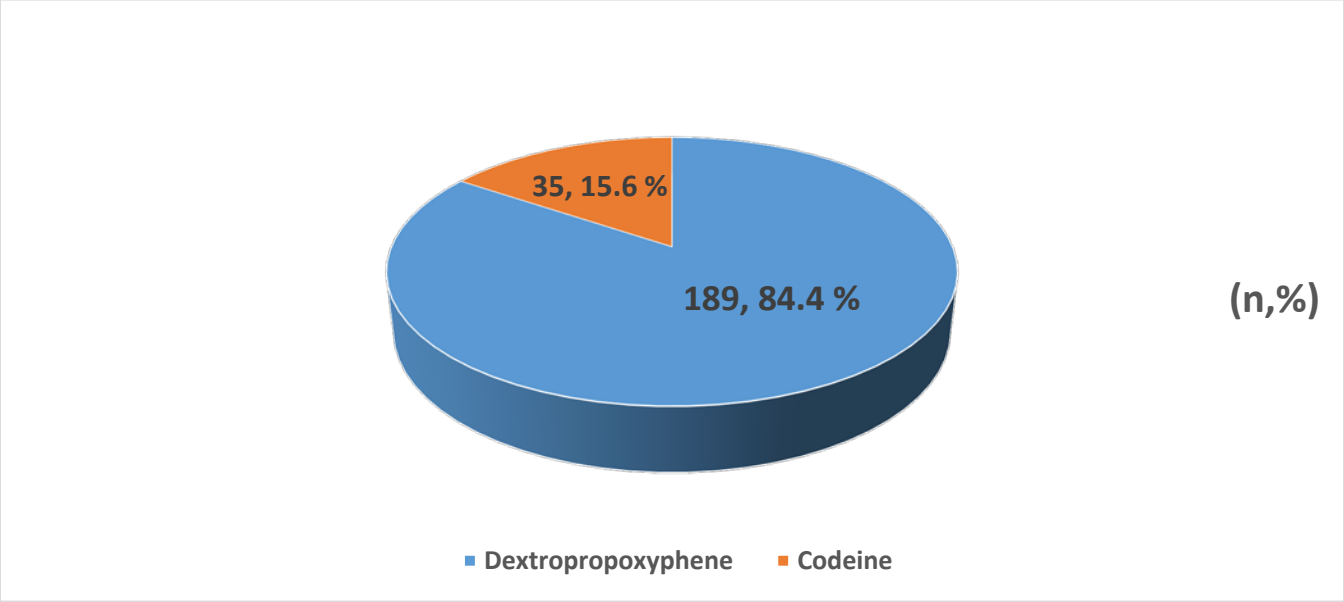
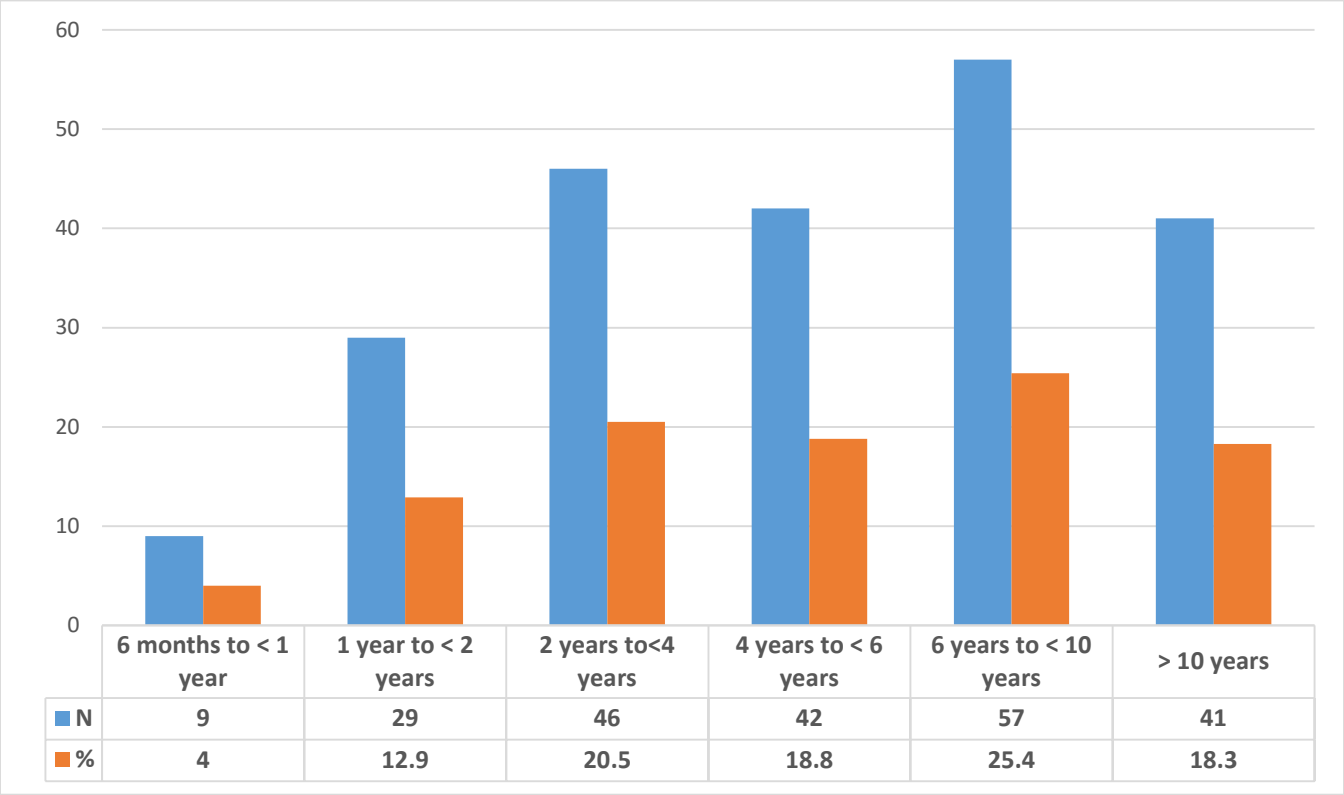


Figure 5: Duration of PO use, for other than relief of occasional short term pain.



	6 months to < 1 year	1 year to < 2 years	2 years to<4 years	4 years to < 6 years	6 years to < 10 years	> 10 years
N	9	29	46	42	57	41
%	4	12.9	20.5	18.8	25.4	18.3

Figure 6: Sources of PO, past six months

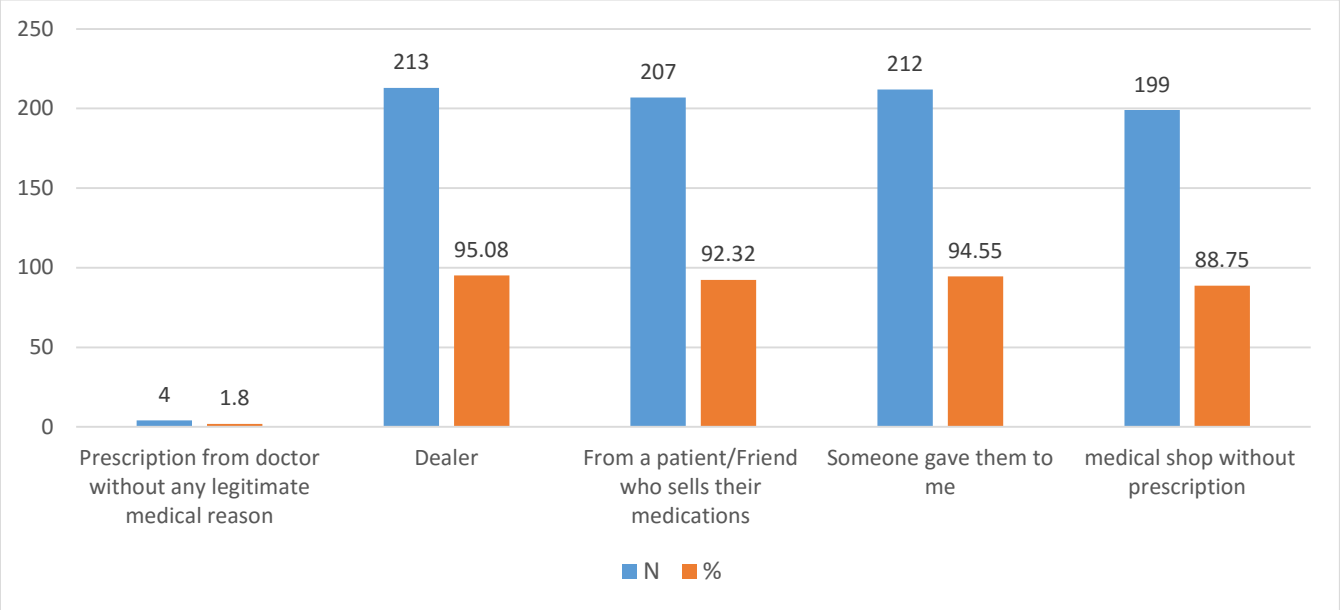


Table 4.2: Importance of reasons for using prescription opioids, past six month (n=224).

Variables	Slightly important N (%)	Moderately important N (%)	Very important N (%)	Extremely important N (%)
Felt angry either with myself or because things were not going own way	40 (17.9)	104 (46.4)	65 (29.0)	-
Felt bore	56 (25.0)	52 (23.2)	25 (11.2)	-
Felt anxious	67 (29.9)	94 (42.0)	37 (16.5)	-
Saw prescription opioids	25 (11.2)	73 (32.6)	116 (51.8)	-
Felt sad	53 (23.7)	62 (27.7)	87 (38.8)	-
Felt ill or in pain because wanted prescription opioids	38 (17.0)	91 (40.6)	62 (27.7)	-
Was in good mood and felt getting high	10 (4.5)	22 (9.8)	66 (29.5)	126 (56.2)
Wanted to see what would happen if tried prescription opioids one time	04 (1.8)	24 (10.7)	106 (47.3)	83 (37.1)
Felt tempted to use it	8 (3.6)	24 (10.7)	167 (74.6)	21 (9.4)
Offered by someone	9 (4.0)	45 (20.1)	159 (71.0)	10 (4.5)
Having good time with others and felt like getting high together	6 (2.7)	22 (9.8)	116 (51.8)	78 (34.8)
Felt worried about owns relationship with someone	53 (23.7)	62 (27.7)	73 (32.6)	-
Felt ill or in pain but not due to prescription opioid withdrawal	26 (11.6)	08 (3.6)	03 (1.3)	-
Others were being critical of me	51 (22.8)	76 (33.9)	70 (31.3)	-
Saw others using it	29 (12.9)	67 (29.9)	121 (54)	-

Table 4.3: Frequency of obtaining prescription opioids from various sources, past six month (n=224).

Variables		N	Percentages
Prescription from doctor without legitimate medical reason	Sometimes	02	0.9
	Frequently	02	0.9
From a dealer	Sometimes	12	5.4
	Frequently	35	15.6
	Most of the time	124	55.4
	Always	41	18.3
From a patient/friend who sells their medications	Rarely	19	8.5
	Sometimes	55	24.6
	Frequently	94	42.0
	Most of the time	39	17.4
Someone gave them to me	Rarely	38	17.0
	Sometimes	91	40.6
	Frequently	74	33.0
	Most of the time	09	4.0
Purchased from medical shop without prescription	Rarely	40	17.9
	Sometimes	36	16.1
	Frequently	49	21.9
	Most of the time	67	29.9
	Always	07	3.1

Table 4.4: Importance of seeking treatment for prescription opioid abuse (n=224).

Variables		Frequency	Percentages
Don't like being dependent	Somewhat important	12	5.4
	Important	78	34.8
	Very important	99	44.2
	Extremely important	26	11.6
Physical side effects are annoying	Somewhat important	82	36.6
	Important	126	56.2
	Very important	1	0.4
	Extremely important	4	1.8

Section 5: Medical and psychiatric problem experienced by prescription opioid abusers.

5. 1. Present study reported that among all the prescription opioid abusers, twenty-eight respondents (12.5%) had chronic medical problems in lifetimes and sixteen subjects (7.1%) were hospitalised four or more times in lifetimes. These excluded admission to detox, alcohol/drug, psychiatric treatment and childbirth. A chronic medical condition was considered as a serious physical or medical condition that requires regular care. Medical problems ever troubles to 34% respondents from slight to moderate intensity. Need of treatment for self's medical problem was reported by almost 33% respondents. For 19.2% (n=43) respondents, treatment need was moderately important for their medical problems.

5. 2. It was also reported that prescription opioid abusers of my study experienced serious depression either due to sadness, hopelessness, which consequences loss of interest, difficulty performing in daily functions for both last month (55%, n=124) and lifetime (68.3%, n=153). Besides these psychiatric problems, serious anxiety, tension were experienced by 76.8% (n=172) & 96.9% (n=217) of respondents in last month and lifetime respectively.

Table 5.1. Self-reported medical conditions and problems of prescription opioid abusers (n=224).

Variable `		N	Percentage
Controlled environment, 30 days	For alcohol/drug treatment	224	100
Times hospitalised for medical problems, lifetime	1-3 times	101	45.1
	4 or more times	16	7.1
Chronic medical problem any	Yes	28	12.5
Medical problem ever troubles or bothers, 30 days	Slightly	27	12.1
	Moderately	49	21.9
	Considerably	13	5.8
	Extremely	5	2.2
Importance of treatment needed	Slightly	19	8.5
	Moderately	43	19.2
	Considerably	7	3.1
	Extremely	7	3.1

Table 5.2 Self-reported psychiatric problems by prescription opioid abusers (n=224).

Variables		Frequency	Percentages
Serious depression	Past month	124	55.4
	Lifetime	153	68.3
Serious anxiety/tension, unreasonably worried	Past month	172	76.8
	Lifetime	217	96.9
Thoughts of suicide	Past month	11	4.9
	Lifetime	48	21.4

Section 6: Criminal offences by prescription opioid abusers (n=224).

6. 1. Study reported that, only 4.9% (n=11) respondent's admission to rehabilitation centre was prompted or suggested by the criminal justice system as post release supervision (on parole). Seventy eight respondents were charged for possession of opiates including prescription opioids for 1 to 5 times in their lives and one hundred and seventeen (52.23%) prescription opioid abusers were charged for other crimes. For other offences such as disorderly conduct, vagrancy or public intoxication under the influence of prescription opioids, an eighteen respondents were charged for one and/or more times in their lives. Other than these, a 3.5% (n=08) prescription opioid abusers were charged with driving while intoxicated (DWI) more than once in their lives and 1.3% were charged with major driving violations under the influence of prescription opioids. Sixty two reported to get incarcerated from months to years due to criminal offences due to either dealing with or crimes under the influences of prescription opioids. Findings of the study reported that respondents with prescription opioid use history of more than 10 years were either charged or arrested more than one time in their lives due to dealing or possessing prescription opioids than those who are using prescription opioids non medically for less than 10 years in their lives. Although this finding was not statistically significant (Chi square = 5.12, df= 2, p = 0.077).

Table 6.1: Status regarding criminal justice system of prescription opioid abusers attending de-addiction centres of Sikkim (n=224)

Category	Frequency	Percentages
Admission prompted or suggested by the criminal justice system	11	4.9
On parole or post release supervision	11	4.9
How many times in your life have you been charged for possession and dealing of drugs?	78	34.8
1. One time	48	21.4
2. 2-3 times	25	11.2
3. 4-5 times	05	2.2
How many times in your life have you been charged for other crimes	117	52.23
How many times in your life have you been charged with disorderly conduct, vagrancy or public intoxication?	18	8.0
1. One time	08	3.6
2. More than one time	10	4.4
How many times in your life have you been charged with driving while intoxicated?	18	8.0
1. One time	10	4.5
2. More than one time	08	3.5
How many times in your life have you been charged with major driving violations?	03	1.3
How many months were you incarcerated in your life?	62	27.7
1. 1-5 months	37	16.5
2. 6-10 months	17	7.6
3. More than 10 months	08	3.6

Section 7: Treatment history.

7.1 It was observed that all the respondents of this study had taken several types of treatments such as detoxification, outpatient counselling, AA, NA, residential treatment etc. for their prescription opioid related problems. Majority (96.9%, n=217) reported to take such treatments for 1-5 times in their lives. All the 224 respondents of this study went through medical detoxification treatment several times in their lives. Most of them (96.6%, n=216) had participated medical detoxification for 1-4 times. Study also found that, 67 of 224 subjects (29.9%) were prescribed outpatient counselling, whereas only 5.8% (13 of 224) availed day hospital treatment. Residential treatment was opted by sixteen subjects (7.1%).

7.2 Respondents aged 24 years and above reported to participate in medical detoxification for more than once in their lives in comparison to younger adults of 15-24 years of age ($p < 0.005$).

Table 7.1. Treatment history of prescription opioid abusers attending de-addiction centres of Sikkim.

Variable `		N	Percentages
Alcohol abuse treatment, lifetimes	1-4 times	132	58.9
	5 and more times	09	4.01
Alcohol how many detox	1-2 times	114	50.9
	3-4 times	21	9.4
	More than 5 times	06	2.6
Prescription opioid abuse treatment, lifetime	1-5 times	217	96.9
	more than 5 times	07	3.1
Prescription opioids, how many detoxes	1-2 times	187	83.4
	3-4 times	29	12.9
	5 times & more	08	3.56
Types of treatment	Medical detoxification	224	100
	Outpatient-counselling	67	29.9
	Intensive-Outpatient/day hospital treatment	13	5.8
	Inpatient/ Residential treatment	16	7.1
	AA/NA/SHG programme	41	18.3
	Other medications for addictions	74	33.0
Medical detoxification, Times participated	1- 4 times	216	96.6
	5-9 times	08	3.4

Section 8: Pain status of prescription opioid abusers.

8.1 Study showed that majority of subjects had intermittent pain (32.6%, n=73), of sharp nature (21.4%, n=48) and of three to less than twelve month of duration (17.4%, n=39). At the day of interview, 89(39.7%) respondents reported to have pain other than everyday kind of pain. Of them thirty two subjects (14.3%) suffered by moderate (grade 2-3) and five (2.2%) subjects suffered by severe (grade 4-6) intensity pain.

8.2 There were several activities such as general day to day activity, mood, sleep pattern, enjoyment of life etc. of the recruited prescription opioid abusers were affected by several grades (1 to 10). Of these enjoyment of life, sleep, mood, performing normal work and maintaining cordial relationship with others were affected by 29%, 23.63%, 22.2%, 18.73% and 14.3% respondents respectively from moderate to severe intensity. It was noted that only 6.3% (n=14) of them had taken other pain medications like NSAIDs for pain relief, whereas majority (24.1%, n=54) did not tried any pain interventions. It was also reported that none of the respondents had taken or prescribed any prescription opioids for the purpose of relief of pain.

8.3 Differences in pain characteristics among pain severity groups: Most participants (98%) were categorized as having pain of less than a year duration and 35% reported chronic pain (> 12 month). Significant differences in the occurrence of pain of up to 6 month duration (p=0.02) and occurrence of chronic pain (p=0.008) were found among the three pain severity groups. Post hoc Bonferroni analysis demonstrated that a higher percentages of subjects of moderate

pain groups reported chronic pain than the mild pain group ($p<0.05$). It was also noted that, a higher percentage of subjects in the moderate pain group suffered pain of less than 6 months duration ($p<0.05$). Significant differences in all the brief pain intensity scores were found among the three pain intensity groups. Subjects in the moderate pain group reported more than one number of pain locations than the mild pain group (Chi square = 6.197, df = 2, p = 0.045). A total of six pain qualities were experienced by the subjects of all the three pain severity groups. Among them sharp (54%) and heavy pain (35%) were experienced by most of them.

8.4 Differences in pain interference among pain severity groups: Subjects reported several activities which were affected from mild to severe intensity in the past 24 hours due to pain. All major activities were affected more in moderate pain severity group subjects. Significant differences in all of the interference items were found among all the pain severity groups except general work, mood and relationship ($p<0.05$). Post hoc analysis demonstrated that for both the normal work and enjoyment activity, mean difference was found statistically significant ($p<0.05$) among mild and moderate severity pain groups, whereas for sleep, it was found significant among moderate and severe intensity pain groups ($p=0.01$).

8.5 Difference in substance use characteristics among pain severity groups: The majority of prescription opioid abusers were using more than one substance of abuse per day both in past month (94.4%, n=84) & lifetime (96.6%, n=86) and all of them were current smokers. Overall, 64% reported alcohol use in last month. A small percentage of subjects (27%) reported past month use of heroin. No significant differences in any of the substance use

characteristics (among past month users) were found among the three pain severity groups. On the other hand, 78.7% prescription opioid users reported lifetime cannabis use. More participants in the moderate pain group reported that they were using more than one substance of abuse per day in lifetime ($p = 0.002$) than mild and severe pain group. It was also reported that lifetime prescription opioid abuse was significantly associated with pain level ($p = 0.011$).

8.6 Differences in self-reported psychiatric conditions among pain severity groups: Higher percentages of participants in the severe pain groups reported both depression & anxiety compared to mild and moderate pain severity groups. However the difference was not found statistically significant.

Table 8.1. Pain status/characteristics

Variables		Frequency	Percentages
Pain right now/today		89	39.7
	Mild (Grade 1)	52	23.2
	Moderate (Grade 2-3)	32	14.3
	Severe (Grade 4 –6)	05	2.2
Duration of pain	< 1 month	14	6.3
	1 to < 3 months	20	8.9
	3 to < 6 months	24	10.7
	6 to < 12 months	15	6.7
	1 year to< 2 years	10	4.5
	More than 2 years	06	2.6
Characteristics of pain	Constant/ always there	16	7.1
	Intermittent	73	32.6
Nature of pain	Sharp	48	21.4
	Heavy	31	13.8
	Other	10	4.4

Table 8.2: Sufferings by pain and treatment measures taken.

Variables		Frequency	Percentages
Activities affected by pain, past 24 hrs.			
1. General Activity		80	35.7
2. Mood		82	36.6
3. Normal work		88	39.3
4. Relations with other people		66	29.4
5. Sleep		86	38.4
6. Enjoyment of life		88	39.3
Pain interventions you tried	Other pain medicines	14	6.3
	None	54	24.1
First PO received for treatment of pain:		0	0

Table 8.3. Difference in pain characteristics among pain severity groups.

Pain characteristics	Overall (n=89)	Mild pain (n=27)	Moderate pain (n=52)	Severe pain (n=10)	P value
Frequency & duration		*N (%)*	*N (%)*	*N (%)*	
Up to 6 month	58 (98%)	21 (78%)	33 (49%)	04 (40%)	0.02
Chronic (more than 06 months)	31 (35%)	06 (22%)	19 (36.5%)	06 (60%)	0.008
Brief pain intensity	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	
Pain right now	0.64 (0.974)	5.4 (3.9)	10.4 (6.1)	2.0 (0.71)	<0.0001
Average past-week pain	0.92 (1.268)	4.5 (2.4)	8.6 (3.6)	1.7 (0.42)	0.001
Worst past- week pain	1.78 (2.195)	3.4 (1.5)	6.5 (2.1)	1.3 (0.41)	0.005
Area where experiencing pain	*N (%)*	*N (%)*	*N (%)*	*N (%)*	0.045
More than one joint	55 (62%)	15 (55.5%)	35 (67%)	5 (50%)	
Middle back/thoracic	08 (8.9%)	6 (22%)	2 (3.8%)	0 (0%)	
Lower back/lumbar	13 (15%)	4 (14.8%)	5 (9.6%)	4 (40%)	
Pain quality	*N (%)*	*N (%)*	*N (%)*	*N (%)*	
Sharp	48 (54%)	16 (59%)	27 (52%)	05 (50%)	0.765
Heavy	31 (35%)	10 (37%)	18 (35%)	03 (30%)	
Other	10 (11%)	01 (3.7%)	07 (13%)	02 (20%)	

Table: 8.4. Difference in pain interference among pain severity groups.

Activities affected by pain, past month	Mild pain	Moderate pain	Severe pain	P value
	Mean (SD)	Mean (SD)	Mean (SD)	
General activities	1.57 (0.57)	1.75 (0.62)	2.00 (0.66)	0.172
Mood	1.62 (0.64)	1.72 (0.64)	2.10 (0.87)	0.176
Normal work	1.33 (0.48)	1.58 (0.63)	2.00 (0.81)	0.015
Relation with others	1.65 (0.58)	1.50 (0.68)	1.75 (0.71)	0.524
Sleep	1.88 (0.71)	1.74 (0.77)	2.55 (0.88)	0.017
Enjoyment in life	1.88 (0.43)	1.84 (0.72)	2.50 (0.71)	0.016

Table 8.5. Substance use

Substance type	Mild pain (n=27)	Moderate pain (n=52)	Severe pain (n=10)	Total (n=89)	Chi-square P value
Past month user	*N (%)*	*N (%)*	*N (%)*	*N (%)*	
Alcohol	17 (62.9%)	33 (63.5%)	7 (70%)	57 (64%)	0.227
Heroin	6 (22.2%)	17 (32.7%)	1 (10%)	24 (27%)	0.214
Prescription opioid	27 (100%)	52 (100%)	10 (100%)	89 (100%)	0.106
Cannabis	11 (40.7%)	35 (67.3%)	5 (50%)	51 (57.3%)	0.505
Nicotine	27 (100%)	52 (100%)	10 (100%)	89 (100%)	0.069
More than one substance per day	25 (92.6%)	50 (96.2%)	9 (90%)	84 (94.4%)	0.189
Lifetime user	*N (%)*	*N (%)*	*N (%)*	*N (%)*	
Alcohol	10 (37%)	27 (51.9%)	7 (70%)	44 (49.4%)	0.325
Heroin	10 (37%0	25 (48.1%)	3 (30%)	38 (42.7%)	0.958
PO	27 (100%)	52 (100%0	10 (100%)	89 (100%)	0.011
Cannabis	14 (51.8%)	48 (92.3%)	8 (80%)	70 (78.7%)	0.747
Nicotine	27 (100%)	52 (100%)	10 (100%)	89 (100%)	0.136
More than one substance per day	25 (92.6%)	52 (100%)	9 (90%)	86 (96.6%)	0.002

Table 8.6. Self-reported psychiatric problems of prescription opioid abusers among three pain severity groups.

Psychiatric problems, past month	Mild (n=27)	Moderate (n=52)	Severe (n=10)	*P value
	N (%)	N (%)	N (%)	
Depression	16 (59.2%)	34 (65.4%)	8 (80%)	1.000
Anxiety	20 (74%)	44 (84.6%)	9 (90%)	

*Fisher's exact test

Section 9: Quality of life of prescription opioid abusers (n=224).

9.1 Thirty-three per cent respondents reported fair to poor health at the time of interview. Most of the respondents (89.3%, n=200) experienced any improvement of their health status than the previous year, whereas 10.7% (n=24) subjects reported to have same health condition as previous years. Present health status did not limit most of the respondents' day-to-day activities, whereas strenuous activities like climbing several flights of stairs (38.8%, n=87), moderate to vigorous activities (34.8%, n=78) were limited a lot due to their current health problems. Study revealed that about 79% & 75% respondents faced problems such as cutting down time on work or activity and accomplishing less work than usual respectively due to their poor physical health conditions whereas 85.8% & 84% respondents faced problems such as accomplishing less work than usual and performing works/activities less carefully due to emotional problems, in the past month from little to most of the times respectively. On the whole, it was observed that, 150 of 224 respondents (67%) normal social activity was affected by both their physical health and emotional problems from moderate to quite a bit in the past month.

9.2 Study reported that most of the prescription opioid abusers (62%, n=139) felt full of life from little to some of the times in the past month. Quality of life survey also reported that, 67%, 65.1%, 57.2% respondents felt down in the dumps that nothing could cheer them, felt tired and felt downhearted & depressed in the past month respectively. Forty six respondents reported to get sick a little easier than other people. 8.9% (n=20) respondents reported that they expect their health to get worse.

Table 9.1: Quality of life –Health status.

Variable		Frequency	Percentages
General health condition	Excellent	04	1.8
	Very good	40	17.9
	Good	104	46.4
	Fair	69	30.8
	Poor	07	3.1
Compared to one year ago, health condition now	Much better now than one year ago	92	41.1
	Somewhat better now than one year	108	48.2
	About the same as one year ago	24	10.7

Table 9.2: Quality of life –Problems faced due to physical & emotional problems

Variable		N	Percentages
Activities limited by health, now			
1. Vigorous activity	Limited a lot	46	20.5
	Limited a little	62	27.7
	Not limited at all	116	51.8
2. Moderate activities	Limited a lot	32	14.3
	Limited a little	62	27.7
	Not limited at all	130	58.0
3. Lifting or carrying groceries	Limited a lot	18	8.0
	Limited a little	46	20.5
	Not limited at all	160	71.4
4. Climbing several flights of stairs	Limited a lot	87	38.8
	Limited a little	113	50.4
	Not limited at all	24	10.7
Problems faced in past month due to physical health			
1. Cut down time work/activity	Most of the time	48	21.4
	Some of the time	98	43.8
	A little of the time	32	14.3
	None of the time	46	20.5
2. Accomplish less work	Most of the time	68	30.4

	Some of the time	71	31.7
	A little of the time	28	12.5
	None of the time	57	25.4
Problems faced in past month due to emotional problem			
1. Accomplish less work	Most of the time	19	8.5
	Some of the time	94	42.0
	A little of the time	79	35.3
	None of the time	32	14.3
2. Workor other activities done less carefully than usual	Most of the time	109	48.7
	Some of the time	66	29.5
	A little of the time	13	5.8
	None of the time	36	16.1
Extent of physical health or emotional problem interfered with normal social activity, past 4 weeks			
	Not at all	12	5.4
	Slightly	62	27.7
	Moderately	112	50.0
	Quite a bit	38	17.0

Table 9.3: Pain and other activities affected

Variable		N	Percentages
Intensity of bodily pain, past 4 weeks	Very mild	14	6.2
	Mild	33	14.7
	Moderate	48	21.4
Pain interfered with normal work, past 4 weeks	A little bit	35	15.6
	Moderately	57	25.4
	Quite a bit	11	4.9
Felt full of life, past 4 weeks	All of the time	01	0.4
	Most of the time	01	0.4
	Some of the time	13	5.8
	A little of the time	126	56.2
Been very nervous, past 4 weeks	Most of the time	01	0.4

	Some of the time	24	10.7
	A little of the time	64	28.6
	None of the time	135	60.3
Felt down in the dumps, past 4 weeks	All of the time	39	17.4
	Most of the time	111	49.6
	Some of the time	55	24.6
	A little of the time	14	6.2
	None of the time	5	2.2
Felt calm and peaceful, past 4 weeks	Some of the time	21	9.4
	A little of the time	132	58.9
	None of the time	71	31.7
Extent of having lots of energy, past 4 weeks	Most of the time	19	8.5
	Some of the time	55	24.6
	A little of the time	118	52.7
	None of the time	32	14.3
Felt downhearted & depressed, past 4 weeks	All of the time	38	17.0
	Most of the time	90	40.2
	Some of the time	75	33.5
	A little of the time	16	7.1
	None of the time	5	2.2
Felt worn out, past 4 weeks	Some of the time	61	27.2
	A little of the time	29	12.9
	None of the time	134	59.8
Have you been happy, past 4 weeks	All of the time	1	0.4
	Most of the time	11	4.9
	Some of the time	75	33.5
	A little of the time	95	42.4
	None of the time	42	18.8
Felt tired, past 4 weeks	Most of the time	76	33.9
	Some of the time	70	31.2
	A little of the time	56	25.0
	None of the time	22	9.8
Physical health or emotional problem times interfered with social activities, past 4 weeks	All of the time	5	2.2

	Most of the time	88	39.3
	Some of the time	75	33.5
	A little of the time	46	20.5
	None of the time	10	4.5
Get sick a little easier than other people	Definitely true	08	3.6
	Mostly true	38	17.0
	Mostly false	81	36.2
	Definitely false	83	37.1
	Don’t know		14
Expect my health to get worse, how true	Definitely true	01	.4
	Mostly true	19	8.5
	Don’t know	119	53.1
	Mostly false	77	34.4
	Definitely false	8	3.6
Excellent health	Definitely true	2	.9
	Mostly true	61	27.2
	Don’t know	22	9.8
	Mostly false	102	45.5
	Definite false	37	16.5

Section 10: Socio-demographic characteristics and type of drug use among prescription opioid abusers (n=224).

10.1. This study reported that most of the male respondents (92.9%, N=208) were poly drug user. Use of more than one substance was prevalent among school dropout & illiterates with a p value of 0.30 and among salaried respondents than students and unemployed ones with a p value of < 0.005. Findings of my study reported that business (n=06) was the major occupation for respondents who were using prescription opioids only (p=0.02) whereas poly substance abuse was commonly practised by skilled workers (36%, n=81). Abuse of both the only prescription opioid as well as poly substance was reported more by urban respondents. It was also found that poly substance abuse was prevalent among urban respondents than rural respondents. Poly substance abuse was common among all major ethnic groups of Sikkim. It was also reported that in both the categories Nepalese dominates. Unmarried respondents were found to abuse more than one substance (57%) than only prescription opioids (5.8%).Prescription opioid abusers of all the religious group reported to abuse other substances also. Only prescription opioid abuse was reported more by the Hindu's whereas poly substance abuse was found prevalent among Buddhists & Hindus (p=0.60). Those who migrated from own place were reported to abuse more than one substances. Poly drug users reported to have more alcohol using siblings in comparison to only prescription opioid abusing siblings with a p <0.005. Subjects who abuse only prescription opioids reported to have less friends with substance use problem than those of poly drug users.

Table 10.1. Sociodemographic characteristics and type of drug use among prescription opioid abusers (n=224).

Variables		**Study Groups**		**Significance**
		Only PO	Poly drug	
Gender	Male	15 (6.7%)	208 (92.9%)	p=1.0
	Female	00 (0%)	01(0.5%)	
Education level	School dropout, illiterate	04(1.8%)	96(42.3%)	χ^2=3.0, df=3, p=0.30
	Class 10 pass	02(0.9%)	19(8.5%)	
	Class 12 pass	05 (2.2%)	64(28.9%)	
	Graduate & Post Graduate	04(1.8%)	29 (12.9%)	
Income source	Salaried	06 (2.7%)	66 (29.5%)	χ^2=13.77, df=3, p=0.003
	Self employed	02 (0.9%)	62 (27.7%)	
	Student	06 (2.7%)	22 (9.8%)	
	Unemployed	01(0.5%)	59(26.3%)	
Occupation	Business, office work	06(2.7%)	48(21.4%)	χ^2=7.30, df=2,p=0.02
	Skilled/semiskilled/unskilled	02(0.9%)	81(36.2%)	
	Unemployed	01(0.5%)	58 (25.9%)	
Community	Urban	11(4.9%)	118 (52.7%)	p=0.28
	Rural	04(1.8%)	91(40.6%)	
Ethnicity	Lepcha	00(0%)	14(6.3%)	
	Bhutia	03(1.3%)	40(17.9%)	
	Nepali	09(4.02%)	128(57.1%)	
	Others	03(1.3%)	27(12.1%)	
Marital status	Single	13(5.8%)	128(57.1%)	p=0.06
	Married	01(0.5%)	61(27.2%)	
	Separated,	00(0%)	11(4.9%)	
	Divorced	01(0.5%)	08(3.6%)	
Religion	Hinduism	08(3.6%)	88(39.3%)	χ^2=1.05, df=2, p=0.60
	Buddhism	06(2.7%)	91(40.6%)	
	Christianity	01(0.5%)	30(13.4%)	
Migration	Yes	01(0.5%)	04(1.8%)	
Migration reason	Family	00(0%)	01(0.5%)	p=0.20
	Other reasons	04(1.8%)	00(0%)	
Parental use of	Only alcohol	03 (1.3%)	97 (43.3%)	P=0.1
	Both alcohol & PO	00 (0%)	01 (0.5%)	
Sibling	Only alcohol	00 (0%)	62 (27.7%)	χ^2=17.24, df=2,p=0.0002
	PO only	00 (0%)	06(2.7%)	
	Both PO & alcohol	01 (0.5%)	03 (1.3%)	
Friends	Only alcohol	00(0.0%)	08(3.6%)	χ^2=2.10, df=2, p=0.35
	PO only	04(1.8%)	30(13.4%)	
	Both PO & alcohol	11(4.9%)	171(76.3%)	

Section 11: Risk behaviour pattern of prescription opioid abusers.

11.1. Present study found that injection prescription opioid use, injection sharing, needle exchange, unprotected sex, sexual practices with commercial sex worker (CSW), and homosexuality were the various high-risk behaviour of prescription opioid abusers. Study reported that, thirteen respondents (5.8%) injected prescription opioids in the past month, of which six subjects injected for a period of 5-15 days. Only two subjects cleaned injection with bleach after someone's use. Among all the injection prescription opioid users (13 of 224), ten subjects (77%) fixed prescription opioids with another person's in the past month. It was also reported that among 224 prescription opioid abusers, 48.2 % (n=108) had history of sexual intercourse in the past month. They mostly practised vaginal sex. Frequency of vaginal sex with female partners reported mostly was 'once a week' (n=45, 20.1%), and that of oral sex was mainly 'once or irregular' (n=09, 4%) in the last month. 13.8% (n=31) respondents used condom more than half the time in last month during vaginal sex with female partners.

11.2. Injection sharing was more in urban (n=31, 24%) whereas syringe exchange was observed equally among rural (n=6) and urban (n=7) prescription opioid abusers ($p>0.05$). Among injection drug users (IDUs), commercial sex worker (CSW), multiple sex partner (MSP) behaviour, knowledge about AIDS and its transmission were present in urban respondents whereas limited condom use was practiced by rural respondents.

11.3. Prescription opioid abusers who were living with family members, showed a risk of developing sexual practices with CSWs 5.8 times than those who were staying with their friends (OR=5.8, RR=4.1, p=0.03).

11.4. Mean age of precocious sexual activity of prescription opioid abusers was 16 years, where that of prescription opioid abusers who had sexual practices with commercial sex worker (CSW) was 19.5 years and 20 years for those who had multiple sex partners (MSP). A significant 47.3% (n=106) had multiple sex partner, 37.5% (n=84) had reported any visit to CSW whereas only 0.4% (n=1) had reported involvement in MSM (male having sex with male) behaviour in lifetime.

Table 11.1. Risk behaviour pattern (n=224).

Variables		**n**	%
Prescription opioid injection (days)	1-4 days	7	3.1
	5-15days	6	2.7
Number of injection shared	1-10	8	3.6
	>10	5	2.2
Times cleaned injection with bleach after someone used		2	0.9
Times fixed drugs with another person , then split, 30 days		10	4.3
Vaginal/anal/oral sex with number of people	1-2no	71	31.7
	3-4	32	14.3
	≥ 5	05	2.2
Condom use frequency, vaginal sex with female	< half the time	12	5.4
	half the time	16	7.1
	> half the time	31	13.8
	Always	19	8.5
Vaginal sex frequency, male clients	< once a week	25	11.2
	once a week	45	20.1
	2-6 times a week	31	13.8

Table 11.2. Sexual behaviour among prescription opioid abusers (n=224)

Variable			**N**	**Percentage**
History of precocious sexual activity, lifetime				
Yes			95	42.4
Mean age of first activity in years		16		
Frequency, past year	Monthly		67	29.9
	Weekly		26	11.6
	Daily		02	0.9
CSW behaviour in lifetime				
Yes			84	37.5
Mean age of first activity in years		19.55		
Frequency, past year	< once a month		36	16.1
	1-3 times a month		25	11.2
	About once a week		04	1.8
	2-3 times a week		02	0.9

MSP behaviour in lifetime				
Yes			106	47.3
Mean age of first activity in years		20.08		
Frequency, past year	Less than once a month		11	4.9
	1-3 times a month		42	18.8
	About once a week		16	7.1
	2-3 times a week		23	10.3
	4-6 times a week		06	2.7
MSM behaviour in lifetime				
Yes			1	0.4
Mean age of first activity in years		26		
Frequency, past year	<once a month		01	0.4
Frequency condom use with non primary sexual partner	Never		70	31.3
	< once a week		19	8.5
	About half the time		28	12.5
	> half the time		41	18.3
	Always		41	18.3
	Don't know/unsure		09	4.0

Section 12: CAGE questionnaire for alcohol problems.

12.1. More than half respondents (53.2%, n=119) reported having alcohol problem with a CAGE score of 2 or more. Only twenty four (10.7%) had a score of 1. Sixty seven respondents (29.9%) felt that they need to cut down their regular drinking, whereas majority (61.6%, n=138) were annoyed due to their alcohol problems.

Table 12.1. CAGE report.

Variables	Frequency	Percentages
Ever felt to cut down on drinking	67	29.9
Ever annoyed by criticism of your drinking	138	61.6
Ever felt bad or guilty about drinking	88	39.3
Ever needed for get rid of hangover (eye opener)	68	30.4

Table 12.2. CAGE score

Score	Frequency	Percentage
.00	03	1.3
1.00	24	10.7
2.00	47	21.0
3.00	45	20.1
4.00	27	12.1

Section 13: Nicotine dependence of prescription opioid abusers.

13.1. It was noted that all the respondents smoked cigarette in their lifetimes. Majority of them (63%, n=141) had smoked first cigarette within five minutes after wakeup in the morning. 60% (n=135) respondents had difficulty to refrain from smoking in forbidden places like market places, movie hall etc. 57.6% (129) respondents hated most to give up their first cigarette smoking in the morning. 44.2% (n=99) respondents smoked up to 10 cigarette per day, whereas 13.4% (n=30) respondents smoked more than 20 cigarette per day. A 23.2% (n=52) respondents smoked more in first hour after waking than rest of the day and about 44% (n=99) respondents smoked while in bed rest due to illness.

Table 13.1 Fagestrom test for nicotine dependence.

Variables		Frequency	Percentages
Onset of first cigarette	Within 5 minutes	141	62.9
	Within 6-30 minutes	64	28.6
	Within 31-60 minutes	15	6.7
	After 60 minutes	04	1.8
Difficult to refraining from smoking in forbidden places		135	60.3
Cigarette that you hate most to give up	The first one in the morning	129	57.6
	All others	95	42.4
Number of cigarettes smokes per day	10 or less	99	44.2
	11-20	95	42.4
	More than 20	30	13.4
Smokes more in first hr. after waking than rest of the day		52	23.2
Smokes while in bed rest due to illness		99	44.2

DISCUSSIONS

A number of reports have shown that abuse of alcohol and other substances such as opiates, sedatives has reached alarming proportions in north eastern states of India including Sikkim. [59-65] There are reports to evident analgesic abuse among youths of Sikkim [56, 59], but to my knowledge, this is the first broad structured study to understand the epidemiology of prescription opioid abuse in Sikkim.

This study is an attempt to reveal the socioeconomic, demographic profile, pattern of substance use, employment status, high risk behaviour profile and quality of life of prescription opioid abusers in Sikkim and also to study their pain status, comorbid medical and psychiatric conditions etc. The current study brought out several trends & patterns of prescription opioid abuse which are of appreciable concern.

Study found that prescription opioid users of this study belonged to 17–51 years age group and mean age of first use of prescription opioid started around the age of 20 years, ranged between 11-46 years, when 43.3% (n=97) of the subjects had onset of prescription opioid use in the 15-20 years age range. This finding correlates with the 2006 NSDUH report [66] –which confirms initiation of prescription opioid use non medically at adolescent age (12 years and older) and also correlates with Basu D et al [67] study which documents lower age of subjects reporting for substance abuse treatment. Adolescent is a period in human growth and development that occurs after childhood and before adulthood from ages 10 to 19. Adolescence is also a period during which they have every possibility to put them in high risk behaviour either intentionally or unintentionally. Adolescents are different from young children and adults. Researchers from the University of Pittsburgh recorded neuron activity in the brains of adolescent rats while they

performed a reward-driven task, and found that adolescents' brains react to rewards with much greater excitement than adults' brains. The researchers found that the stimulation in adolescent brains varied throughout the study and with a greater degree of disorganization, whereas the adult brains processed their rewards with a more consistent balance of stimulation and inhibition. This could help explain why adolescents are more vulnerable to drug addiction, rash decisions, and mental health problems. [Source: Science Daily, Teen Brains Over-Process Rewards, Suggesting Root of Risky Behaviour, Mental Ills, January 26, 2011]. A behavioural-temperamental trait (often termed disinhibition), characterized by difficulty of inhibiting behavioural impulses, resulting in aggressive or otherwise problematic behaviour has been widely recognized as an important risk factor for alcohol and other substance use disorders. Childhood aggression predicts substance use problems in adulthood. While on the other hand, affective traits such as anxiousness may increase the risk for problematic substance use. Adolescents' substance abuse problem is important to address because it causes several harmful consequences such as physical deterioration, psychiatric problems, intellectual impairment, personality deterioration, increased risks of accidents, legal risks and higher susceptibility to high risk behaviour in the form of unprotected sex or use of unsterile needles.

The present study also found that adults 25 years of age and older are more likely than young adults 15–24 years old to report co-occurrence of alcohol use and prescription opioid use non medically. This finding does not counterparts with SE McCabe et al [68] study which compared past-year drinking behaviours and nonmedical use of prescription drugs (NMUPD) in a nationally representative samples of United States.

Number of female respondents in this study (0.04%) is too small to draw any meaningful conclusion on them. No significant gender differences in the use of prescription opioids were revealed. Finding indicates that there is limited turnover of women abusers at de-addiction centre for seeking treatment. Low turnover of female respondents to the treatment centre for treatment of any substance abuse is observed in several studies. [69] This low prevalence of women abusers reported at de-addiction centre is supported by the finding of Drug Abuse Monitoring Survey (DAMS) with percentage of treatment seeking female substance abusers at 2.8%. Our finding indicates that women of Sikkim are less likely than men to have prescription opioid problems. This low turnover can be explained by the fact that drug abusing women receive little support from their relatives, husbands and other family members. Fear that people will identify them as addict, fear of withdrawal and concerns about social acceptability of their children as well as fear of losing custody of their children are also the other reasons for which drug abusing women did not sought treatment from drug de-addiction centres. Several studies have identified these possible reasons as barriers to treatment, leading to low turnover of women substance users at treatment centre in countries like Australia, India, Canada and six European countries.[70-72] Lack of awareness, lack of resources and negative attitudes are therefore responsible for inadequate availability of gender related epidemiological data on prescription opioid abuse in Sikkim. This is of great concern because there are studies to indicate that women who inject opioids seem to be at higher risk of HIV infection [73,74] and women who use heroin and other opioids during pregnancy has risk of miscarriage, preterm delivery [75]and women drug abusers are more likely than men to report psychiatric problems [33,76].

This study found higher rates of prescription opioid abuse and abuse related problems among Nepalese ethnic subjects and abuse observed almost equally by Hindu (42.9%) and Buddhist (43.3%) subjects. Only traditional inhabitants of Sikkim i.e. Lepcha's contributed to only 6.3% to the total recruited subjects of this study. This can be explained by the fact that Nepalese [77] comprise major ethnic population (70%) in Sikkim and both 'Hindu and Buddhist' [78] are predominant religions in Sikkim. The findings are also in line with past researches that has shown high substance abuse rate by Nepalese in Sikkim.[56,79] This increased incidences of prescription opioid abuse by Nepalese Hindu and Buddhists are of particular concern because they are the dominant ethnic religion in the state who form society.

Study finds that over half of the prescription opioid abusers were unmarried. This was similar to a study from China [80, 81] with 54.7% unmarried opioid users seeking treatment for opioid dependence. Our finding is supported by findings of Amit Goel et al [79] study in 2009 on substance use in rural community in Sikkim representing 57.3% unmarried substance user. Only 20 of 224 (8.9%) prescription opioid abusers were either separated or divorced or widowed. This observation primarily indicates that the effect of divorce or separation was not the cause of subject's prescription opioid abuse. Further studies are needed to establish it.

Subjects of our study had poor literacy rate, higher unemployment status. Majority of respondents either never attended school or dropped out of school even before completing eight standards. These finding were different from a similar kind of study from Amit Goel et al [79] as well as Nebhinani et al [82] study. It was also observed that mean age of first use of prescription opioid was lower among school dropouts than those who had any kind of formal education. Employment problems are found quite common among individuals receiving treatment for

prescription opioid abuse. It was observed that unemployed and student respondents had started first use of prescription opioid at much lower age than those who were involved in any kind of employment such as business and skilled work. A severe employment problem or difficulties such as inability to find work, problems with present job of over 20 days in current time and over half of the respondent's dependency on family members for daily living were noticed in this study. Finding suggests that low rate of employment of prescription opioid abusers may be either due to lack of motivation to work and/or due to functional impairment directly related to prescription opioid abuse.

In our study prescription opioid abuse was found more among urban respondents. This is supported by the results of a meta-analysis by 'Reddy & Chandrasekhar' [83] indicating an overall substance use prevalence of 6.9/1000 for India with urban and rural rates of 5.8 and 7.3/1000 population. Our study also reported that there was no effect of migration on their pattern of prescription opioid abuse as most of them lived in and had started taking prescription opioid in the same place where they were born. Only 2.2% prescription opioid abusers had a history of migration.

Drinking of alcoholic beverages is very common and popular among Sikkim's population. All the parents of the respondents reported to drink alcoholic beverages either occasionally or regularly. Regular use of substances such as opiates and others were not found more by them. Parents and siblings alcohol use was significantly higher than their prescription opioid use. On the other hand it was found that friends of the respondents were frequent user of both alcohol and prescription opioids. Therefore it can be said that 'family history' [84] and drug use by 'friends' [85] are two important risk factors for study respondents' substance use. Study also revealed that

urban respondents have more friends with prescription opioid and alcohol use history. This is found statistically significant (Chi square = 13.38, df = 2, p = 0.0012).

In this study both prescription opioid and alcohol were reported as substance of major problem by more than half of the respondents, whereas prescription opioid alone was found to be the substance of major problem for over one fourth (30.8%) of respondents. Most commonly abused prescription opioids reported were dextropropoxyphene and codeine in both rural and urban Sikkim. Respondents did not report any shift or migration from their non-medical prescription opioid use to other illicit substance use. Rather reported concomitant alcohol and other substance use such as cannabis, heroin and nitrazepam. Prescription opioid abusers reported experiencing alcohol problems for nearly half a month (mean = 13 days) in past month. Alcohol problem or dependence was determined by using CAGE questionnaires. Study revealed that half of the subjects (53%) had alcohol problem (score ≥2). Although their biggest opiate problem at present recorded was prescription opioid only –i.e. opioids analgesics which are designed and used clinically for the treatment of severe / chronic pain.[86-88] This is a clear indication of diversion from pharmaceutical shops. Although there are studies indicating shift from OxyContin (a prescription opioid) use to heroin use.[89] Past month frequency of use of only prescription opioid was 79% in 20-30 days use group and majority reported to abuse prescription opioid for a period of 10 years or less in lifetimes. This shows that primary attention and concern about prescription opioid abuse and related harms has been in Sikkim-a north eastern state of India, where data from other parts of India also have documented increase in nonmedical use and abuse of prescription opioids in general populations. This correlates with findings of Basu D et al [67] study indicating a decrease in use of natural opioids over three decades (1978-88, 1989-98, 1999-

2008) while there is increase use of newer and prescription opioids such as buprenorphine, codeine and dextropropoxyphene in north India. In recent years, misuse and abuse of prescription opioids has been highlighted as a major and growing health problem globally. [90, 91] Examination of various routes of administration revealed that all participants were taking prescription opioids orally in pill form and 23.2% were also taking by injection form. This is similar to the Sudie E et al [92] study findings (orally, 100%) which collected information to help inform the design of a NIH-sponsored laboratory investigation to examine stress- and cue-induced craving among individuals with prescription opioid dependence. Proportion of IDUs of our study (23.2%, n=52), ranges between the findings of National Household Survey (0.1%) and that of Rapid Assessment survey of Drug Abuse (43%).[16] Unmarried respondents reported higher rates of injecting prescription opioids (16.5% vs 4%) than the married respondents. But this difference did not reach statistical significance (Fisher's exact test P value = 0.0712). Injecting prescription opioid was observed less by the students in comparison to skilled workers. This was not found statistically significant (Fisher's exact, p value = 1.00). The average monthly expenditure on prescription opioid (mean = 4896) was found almost half of the average past month income (mean = 9075) and was almost six times to the average monthly expenditure on alcohol (mean = 737). Past month expenses of Rs 5000 & above on prescription opioid was reported more by salaried and self-employed respondents in comparison to students and unemployed subjects (82.7% vs 17.2%). This was found statistically significant (Chi square = 31.27, df = 3, p =000). Average frequency of more than one substance use per day (including alcohol, excluding nicotine) in past month was 18 days. All the subjects endorsed either chewing or smoking nicotine products. Most of the prescription opioid abusers also endorsed using other illicit drugs (e.g. heroin, cannabis, benzodiazepines) in lifetimes, whereas only a limited (21%)

number of respondents had used any inhalants in lifetimes. Such types of patterns of poly substance use correlates with Sudie E et al [92] study.

Respondents identified initial and current reasons for their prescription opioid use. Half of the respondents mentioned that they had started using prescription opioids for the first time in order to experience ecstasy, but only few of the respondents said that they took prescription opioids for relief from depression, nervousness and anxiety. A significant number also reported to use it for the first time due to peer pressure. It was also found that none of the respondent had first received prescription opioids by physicians for the relief from chronic pain. Only 2.6% respondents among those who were interviewed reported to have pain for more than 2 years duration. Therefore it can be concluded that treatment need for the pain, coping with physical pain were not established in this study as important reasons or risk factors for subjects initiation of prescription opioid use. This research finding completely differ from Weiss RD et al [93] study where participants with chronic pain were more likely to report pain as their primary initial reason for use of prescription opioid. Our research noted that few subjects (16.5%) had used prescription opioids to get rid of pain which was not due to prescription opioid withdrawal symptoms in addition to other reasons. Many of them related that pain was not the reason why they were using prescription opioids. We found several reasons/motives such as anger, temptation to use, and craving, get rid of withdrawal symptoms and depressions etc. which were associated with subjects continued use of prescription opioids. Therefore, one of the major findings of this study is that this population often reports experiencing pain, although pain was not as an initial causal factor in why they sampled opioids and the fact that pain and

hypersensitivity can be manifestations of even mild opioid (or alcohol) withdrawal. Thereby, relationship of pain due to withdrawal symptoms can be established here.

In comparison to rural respondents, urban respondents were significantly more likely to report using prescription opioids in order to cope with depression and bad memories than anxiety and nervousness (Chi Square = 1.431, df = 2, p = 0.48). While grading the importance of motives of prescription opioid use by the subjects, we found that negative feelings such as feelings of pain, sadness, depression, and anger were not recognised as extremely important reasons rather their importance laid between moderate to very important reasons. On the other hand, only positive feelings of illicit substance use such as feelings of good mood, feelings of getting high either alone or along with peers were described as extremely importance reasons for continued use of prescription opioids either alone or along with other illicit substances like cannabis, benzodiazepines.

Respondents of the study reported that they first received their prescription opioids mostly from their substance using friends only at free of cost. It was reported that local drug peddlers were later introduced to the subjects by their friends who purchase prescription opioids regularly from them. Majority of the respondents had received prescription opioids most of the times from them. This establishes dealer's role as major supplier or source of prescription opioids to both rural and urban Sikkim's substance users in the next six months. It must be noted that dealer were not the first introducer. Simultaneously it was observed that friend's initial free supply changed to paid supply in subsequent six months. At the same time more number of respondents reported to

purchase prescription opioids from medical shops without having legitimate prescription for such in the subsequent months than their initial period.

Pain status, health and psychiatric problems of prescription opioid abusers who reported for substance abuse treatment at various detoxification centres of Sikkim were studied and compared among various pain severity groups in our study. Subjects from all the pain severity group experienced pain at more than one joint than pain at any single site. It was also observed that moderate severity pain group had higher mean for both average as well as worst pain experienced in the past month category. Our study also evaluated pain qualities across pain severity groups and no significant differences were found. A higher percentage of subjects of all the three pain severity group (mild, moderate, severe) reported serious anxiety, tension both in past month and life time. Differences in current illicit substance use among the three pain severity groups were not found statistically significant. It was observed that all the prescription opioid abusers belonging to moderate pain group were using more than one illicit substance per day in the last month in comparison to mild and severe pain groups. Smoking was reported by all the subjects of all three pain severity groups for both past month and life time use history.

According to findings of this study, prescription opioid abuse can be linked with numerous morbidity indicator, e.g. health problems and consequences –both physical and mental health problems for which treatment demand generates. Chronic medical problems (12.5%), frequent hospitalisation (52%) and moderate to extreme intensity sufferings due to these problems were reported. Co-occurrence of mental health problems such as serious depression (lifetime, 68%), anxiety (lifetime, 96%) and thoughts of suicide both in lifetimes and past month, reported in this

study correlates with results of OPICAN [94] study (depression, 49.2%) which compared social, health and drug use characteristics of untreated non-medical prescription opioid using populations in five cities of Canada and Sproule B et al [95] study (depressive symptoms, 53%; anxiety, 25%) where a high mental health/psychiatric problem levels of Toronto's non-medical prescription opioid users than the general population average was recorded. Reports of serious anxiety in lifetimes at Sproule B et al [95] study (25% vs 96%) was found far below than this study report. Male female ratio in this study is 223:1. All the prescription opioid abusing female had co morbid mental illness.

Our study also recorded several incidences of criminal charges due to either possession or dealing with prescription opioids and other illicit substance as well as numbers of incarcerations for the same. Incidences of major driving violations, disorderly conduct and public intoxications under the influence of alcohol and other illicit substances including prescription opioids were also reported. Therefore it can be concluded that ill effects of prescription opioid abuse –i.e. both physical & mental health problems as well as legitimate problems, were well observed in this study and correlates with several other studies as mentioned above. This increases concerns over illicit substance abuse related problems in Sikkim. This urges needs of education among general populations about deleterious effects of illicit substance use.

Entry into treatment were found to be influenced by a host of factors, including mandates from criminal justice proceedings (on parole, 4.9%) and perceptions of risk of continued illicit substance use (withdrawal symptoms and physical side effects) and the perceived benefits of treatment. Several subjects of this study availed inpatient and outpatient counselling, various

alcohol anonymous (AA) and narcotic anonymous (NA) programmes in addition to treatment at detoxification centre.

During the treatment course, majority reported to have somewhat to much better health condition in comparison to last year, which was confirmed by grading their ability to perform moderate to vigorous activities. Most of them reported to perform physical activities without much limitations.

IDU's are subject to dual risk of unsafe injections and sexual practices with non-primary sex partners. Needle sharing was found common among IDU's (8 of 13) in past month. First visit to CSW was reported at the age of 19.5 years. Lifetime history of precocious sexual activity (42%), MSP behaviour (47.3%), and unprotected sex (31.3%) were reported in this study. Majority reported to have sexual intercourse with 1-4 numbers of female partners in past month, whereas homosexuality (MSM) was reported only in 0.4% of prescription opioid abusers. This low reporting of MSM behaviour by respondents may be due to response bias. Past month safe intercourse practice rate with their female was found very low (8.5%).This indicates unprotected sex practices with partners other than spouse were quite common, which supports the similar findings of Rapid Assessment Survey of Drug Abuse (RAS) with percentages of 4-24%.[16] Vaginal sex was reported mostly than oral sex by respondents during past month. Lifetime history of CSW behaviour (37.5%), MSP behaviour, unsafe sexual practices and needle sharing are recognised as important risk factors. This is life-threatening because injection-related problems may result in increased likelihood of Blood-spills and poor injection practices. These along with CSW behaviour and unprotected sex can aggravate transmission of blood borne

diseases. [88] Research has shown that IDU who share needles are significantly more likely to have unsafe sex than IDU with safe needle practices, contributing to the risk to needle sharing.[89] While comparing socio-demographic characteristics and type of drug use among prescription opioid abusers, we found some significant associations. Non-medical use of more than one substance was found prevalent among salaried respondents ($p<0.005$) and also among those who have business ($p<0.05$).

Our study has several strengths and limitations. Subjects that fulfill criteria according to my protocol were only accessible / available from de-addiction centers of Sikkim. As the study planned to enroll only clinically diagnosed PO abusers; therefore subjects selected from rehabilitation centers only can broadly represent the population of Sikkim. Secondly, all the subjects were interviewed by same interviewer, thus eliminates inter-rater error.

Several limitations of this study need to be acknowledged. We relied on subjects self-report for all the data including their health and mental status. However psychiatric status of the subject was not verified/confirmed by health care provider or by doing psychiatric clinical diagnosis. Detailed information was collected regarding subjects various characteristics of pain, however further studies needed to determine the exact cause of pain. Area that hurt most by pain was recorded by showing body map containing various sites. Therefore, chances of under reporting for above parameters and misclassification in body map by subjects may arise. A detailed note was also taken regarding substance use pattern and characteristics but data were not verified with urine toxicology testing. This study fails to capture the full extent of the opioid abuse problem in Sikkim because of the underrepresentation of women in the sample (and that fact that,

apparently, women too are abusing opioids and alcohol). While it is understandable why there was not a greater representation of women, -this inherent bias is a limitation of this study. At the end the findings of our study may not be generalized to other parts of north eastern states of India even though there is geographical and socio cultural similarities exists among them. This is because substance use type and health care facilities widely varies among north eastern states. In our study alcohol problem was determined by analyzing CAGE questionnaire. We relied only on subjects self-report regarding data of alcohol intoxication and it was not assessed clinically.

CONCLUSION

Sikkim's all available substance abuse treatment centres contributing data to this study represent a complete census of substance abuse including prescription opioids abuse related problems. Data of this study reflect information on people who have both life time and current prescription opioid abuse problem.

Both the rural and urban areas of Sikkim show increasing rates of substance abuse, especially prescription opioids. It is more prevalent among school dropouts. Dextropropoxyphene and codeine were reported the most commonly abused prescription opioids. They were mainly abused by oral route. Significant percentages of prescription opioid abusers had simultaneous and concurrent alcohol use problem both in current time as well as lifetimes. Respondents started using both the substances i.e. alcohol & prescription opioids around same time frame in their life and lastly peers influence on subjects drug and alcohol using behaviour was established in our study. Trends of IDU, unsafe injection, high risk behaviour, unprotected sex with non-primary partners also has been observed in both the areas. Report from UNODC states that there is an increased incidence of use of prescription opioids, syringe exchange, injection sharing as well as non-sterile practices in Nepal, with whom Sikkim shares its border in west. Therefore Sikkim's border with Nepal at west and changing socio-cultural values, proximity with other north eastern states of India, increased migration of people and stringent law at border (Rangpo check post) controls for illicit drugs like cocaine, heroin makes Sikkim vulnerable for abuse of prescription opioids. Rapid increase in such drug abuse along with presence of hidden populations of sex workers engaged in drug use and high risk behaviour are risk factors for spread of hepatitis B (HBV), hepatitis C (HCV) and HIV. Therefore it is important to study the socio-demographic profile, risk behaviour profile of prescription opioid abusers of Sikkim.

Cannabis was the second most substance used after benzodiazepines among the respondents in their lifetime. It was also found that all the respondents used any form of nicotine/tobacco products both lifetimes as well as in last month. Incidence of crime, arrests due to dealing with prescription opioids, driving violations under the influence of prescription opioids were reported in my study. Comorbid psychiatric problem, medical consequences were also reported. There was clear reporting of diversion of prescription opioids from pharmaceutical shops. All the respondents underwent detoxification treatment at rehabilitation centre. Pain status of all the respondents was studied which revealed that none of the respondents started using prescription opioids due to their pain treatment and pain was relieved progressively by the detoxification treatment.

Findings of this study suggests that significant percentages of prescription opioid abusers experience moderate severity pain that is associated with decrements in physical, emotional and social well beings. Therefore it can be concluded that unrelieved average to worst pain is a major problem which is experienced to a greater extent by moderate to severe pain group subjects and more than one illicit substance use was evidenced by all the three pain severity groups who also reported incidences of depression and anxiety, thoughts of suicide in both current time and lifetime.

REFERENCES

1. WHO. Lexicon of alcohol and drug terms. Geneva: 1994.

2. Anne-Marit Langås, Ulrik Fredrik Malt and Stein Opjordsmoen. In-depth study of personality disorders in first-admission patients with substance use disorders. BMC Psychiatry 2012, 12:180.

3. Meyer D. Glantz, James C. Anthony, Patricia A. Berglund, Louisa Degenhardt, PhD, Lisa Dierker, Amanda Kalaydjian, Kathleen R. Merikangas, Ayelet Meron Ruscio, Joel Swendsen, and Ronald C. Kessler. Mental disorders as risk factors for later substance dependence. Estimates of optimal prevention and treatment benefits. Psychol Med. 2009 Aug; 39(8): 1365–1377.

4. Muriden K. The Origins, evolution and future of COPCORD. APLAR J Rheumatology. 1997;6:44-8.

5. Gurejee D,Vonkoff M, Smion GE. Persistent pain and well being. A World Health Organization study in primary care. JAMA. 1998;280:147-51.

6. Bihari V, Kesavachandran C, Pangtey BS, Srivastava AK. Musculoskeletal pain and its associated risk factors in residents of National Capital Region. Indian J Occup Environ Med. 2011;15:59-63.

7. Volkow N. Scientific research on prescription drug abuse, before the Subcommittee on Crime and Drugs, Committee on the Judiciary and the Caucus on International Narcotics Control United States Senate. Available from: www.drugabuse.gov/Testimony/3-12-08Testimony.html. Accessed April 2010.

8. UNODC. World drug report. 2015.

9. Generation Rx: National Study Reveals New Category of Substance Abuse Emerging: Teens Abusing Rx and OTC Medications Intentionally to Get High 2005. Available from: http://www.drugfree.org/Portal/DrugIssue/Research/Generation_Rx_National_Study_Reveals_New_Category/Teens_Abusing.

10. McCabe SE. Nonmedical use of prescription opioids among US college students: Prevalence and correlates from a national survey. Addictive Behaviors. 2005;30(4):789–805.

11. SAMHSA. 2004 National Survey on Drug use and health: Results. U.S Department of Health and Human Services Office of Applied Studies: 2005.

12. Manchikanti L. Drug abuse: What is being done to address this new drug epidemic? Pain Physician.2006;287-321.

13. Traci C Green, Jill M Grimes Serrano, Andrea Licari, Simon H. Budman SFB. Women Who Abuse Prescription Opioids: Findings from the Addiction Severity Index-Multimedia Version® Connect Prescription Opioid Database. Drug Alcohol Depend. 2009;103(1-2):65-73.

14. INCB. Report of the International Narcotics Control Board for 2006. New York: 2007.

15. Ray R. The extent, Pattern and Trends of drug abuse in India, National Survey. 2004.

16. Kumar M. A Rapid Assessment survey of Drug abuse in India New Delhi UNODC Regional Office for South Asia and Ministry of Social Justice and Empowerment -Govt of India; 2002. Available from: www.unodc.org/india/ras.html.

17. UNODC. A Rapid Situation and Response Assessment (RSRA) of drugs and HIV in Bangladesh, Bhutan, India, Nepal and Srilanka. A regional report 2005. Available from: www.unodc.org/pdf/india/26th_june/RSRA report (24-06-08).pdf

18. Gammelgaard J. Shifts in drug-taking threaten Asia. WorldAIDS. 1992;21(3).

19. HL Sharma, KK Sharma. Principles of Pharmacology. 2 ed: Paras; 2011.

20. WHO. WHO Expert Committee on drug dependence. Sixteenth Report (Technical Report series 407). Geneva: 1969.

21. EddyNB, Halbach H, Isbell H,Seevers MH. Drug dependence: its significance and characteristics. Bull World Health Organ. 1965;32(5):721–33.

22. Katzang MT. Basic and clinical Pharmacology. 11 ed: Tata Mc Graw-Hill; 2009. 544 p.

23. Ghodse Hamid. Drugs and addictive behaviour- a guide to treatment. 3 ed: Cambridge university press; 2002. 4 p.

24. Amina Saban, Alan J Flisher, Anna Grimsrud, Neo Morojele, Leslie London, David R Williams, Dan J Stein. The association between substance use and common mental disorders in young adults: results from the South African Stress and Health (SASH) Survey. Pan Afr Med J. 2014; 17(Supp 1):11.

25. Reiger DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. JAMA. 1990; 264:2511-2518.

26. Kessler RC, Crum R, Warner L, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry. 1997; 54:313-321.

27. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2004; 61:807-816.

28. Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of Major Depressive Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2005; 62:1097-1106.

29. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2007; 64:830-842.

30. Dasgupta N, Kramer ED, Zalman MA, Carino S, Jr, Smith MY, Haddox JD. Association between non-medical and prescriptive usage of opioids. Drug Alcohol Depend. 2006;82:135-42.

31. SAMHSA. Preliminary Results from the 1997 National Household Survey on Drug Abuse. Rockville, MD: 1998 Contract No.: DHHS Publication No. (SMA) 98-3251.

32. L loyd, D Johnston, Patric M, O'Malley, Jerald G, Bachman JES. MONITORING THE FUTURE NATIONAL RESULTS ON DRUG USE 2014-Overview Key Findings on Adolescent Drug Use;2014.

33. SK Lin, D Ball, CC Hsiao, YL Chiang, SC Ree. Psychiatric comorbidity and gender differences of persons incarcerated for methamphetamine abuse in Taiwan. Psychiatry Clin Neurosci. 2004;58(2):206-12.

34. Galaif ER, Stein JA, Newcomb MD. Gender differences in the prediction of problem alcohol use in adulthood: exploring the influence of family factors and childhood maltreatment. J Stud Alcohol. 2001;62(4):486-93.

35. Miller C, Strathdee S, Kerr T, Li K,Wood E. Factors associated with early adolescent initiation into injection drug use: implications for intervention programs. Journal of Adolescent Health. 2006;38:462-4.

36. Enhanced survilleilance of Risk Behaviours among injecting drug users in Canada, Phase 1 report. Public health agency of Canada., 2006.

37. UNODC. World Drug Report 2011-based on 1% prevalence of injecting drug use (estimated 220,690 IDU in 2004) reported by the Reference group to the UN on HIV and injecting drug use. 2011.

38. National Prescription Drug threat Assessment 2009 and National Drug threat Assessment 2010. U.S department of Justice, Drug Enforcement Admiinistration NDIC, 2010.

39. EMCDDA. The State of Drugs Problem in Europe, Annual report. 2010.

40. EMCDDA. The State of the Drugs Problem in Europe, Annual Report. 2015.

41. SACENDU. Monitoring Alcohol and drug abuse trends in South Africa. Research brief. 2010 Contract No.: 13 (1)

42. UNODC. World Drug report. 2011.

43. Pan HH, Ho ST, Lu CC, Wang JO, Lin TC. Trends in the consumption of opioid analgesics in Taiwan from 2002 to 2007: a population-based study. J Pain Symptom Manage. 2012.

44. Pan H, Li C, Lin TC, Wang JO, Ho ST, Wang KY. Trends and characteristics of pethidine use in Taiwan : a six-year-long survey. Clinics (Sao Paulo). july, 2012;67(7):749-55.

45. Ponizovsky AM, Maron E, Zeldin A CN. Trends in opioid analgesics consumption, Israel, 2000-2008. Eur J Clin Pharmacol. 2011;67(2):165-68.

46. Profile, Drug Use Pattern, Risk Behaviour and Selected Bio-Markers of Women Drug Users from Seven Sites in Nepal. UNODC, Nepal Ministry of Health Administration, 2011

47. Mapping and Size Estimation of Most-at-Risk Population in Nepal. Kathmandu 2011 Contract No.: NCASC & HSCB, 21.

48. Shekhar Saxena, Hem Raj Pal. Text book of Alcohol and Drug abuse: New Age International Publishers; 2003.

49. ICMR Bulletin. Pattern and process of drug and alcohol use in India.38(1-3).

50. National Family Health Survey India-3: International Institute for Population Sciences, India; [cited 3]. Available from: http://www.nfhsindia.org/nfhs3.html.

51. Murthy P. Women and Drug use in India. Substance, women and high risk assessment study. UNODC,Ministry of Social justice and empowerment , Govt. of India and United Nations Development Fund for women, 2008.

52. UNODC. Injecting Drug Use and HIV/AIDS in India: An Emerging Concern 2006 Available from: www.unodc.org/pdf/india/publications/idu_and_HIVAIDS_in_India-Monograph/14_iduhiv-aidsamongspecialpopulations.pdf.

53. Narcotics Annual Report 2002. NCB, Ministry of Home Affairs, Government of India, 2002.

54. AK Agarwal, GB Singh, KC Khundom, ND Singh, T Singh. The prevalence of HIV in female sex workers in Manipur, India. J Commun Dis. 1999;30(1):23-8.

55. Selected Socio Economic Statistics, India: Ministry of Statistics and Programme Implementation Govt of India; 2011 Available from: www.mospi.gov.in.

56. Bhalla A, Dutta S, Chakrabarti A. A profile of substance abusers using the emergency services in a tertiary care hospital in Sikkim. Indian J Psychiatry. 2006;48(4):243-7.

57. McLellan AT, Luborsky L, Woody GE. An improved diagnostic evaluation instrument for substance abuse patients: the Addiction Severity Index. J Nerv Ment Dis. 1980;168:26-33.

58. Ewing J. Detecting Alcoholism; The Cage Questionnaire. JAMA. 1968;252:1905-7.

59. Ahongshangbam S, Chakrabarti A. Current analgesic use predicts low emotional quality of life in youth: a cross-sectional survey among university students in Sikkim, North East India. IJMR. 2013;137(6):1199-203.

60. Kermode M, Songput CH, Sono CZ, Jamir TN, Devine A. Meeting the needs of women who use drugs and alcohol in North-east India - a challenge for HIV prevention services. BMC Public Health. 2012 sep 26;12:825.

61. Kermode M, Longleng V, Singh BC, Bowen K. Killing time with enjoyment: a qualitative study of initiation into injecting drug use in north-east India. Subst Use Misuse. 2009;44(8):1079-89.

62. Kermode M, Devine A, Chandra P, Dzuvichu B, Gilbert T, Herrman H. Some peace of mind: assessing a pilot intervention to promote mental health among widows of injecting drug users in north-east India. BMC Public Health. 2008 august 22;8:294.

63. Eicher AD, Crofts N, Benjamin S, Deutschmann P, Rodger AJ. A certain fate: spread of HIV among young injecting drug users in Manipur, north-east India. AIDS Care. 2000 Aug;12(4):497-504.

64. Sarkar S, Das N, Panda S, Naik TN, Sarkar K, Singh BC, Ralte JM. Rapid spread of HIV among injecting drug users in north-eastern states of India. Bull Narc. 1993;45(1):91-105.

65. Sarkar K, Bal B. Epidemic of HIV coupled with hepatitis C virus among injecting drug users of Himalayan West Bengal, Eastern India, Bordering Nepal, Bhutan and Bangladesh. Substance use Misuse. 2006;41(3):341-52.

66. Nonmedical users of pain relievers: Characteristics of recent initiates. Office of Applied Studies, The NSDUH Report, Issue 22: Substance Abuse and Mental Health Services Administration; 2006. Available from: www.samhsa.gov/data/2k6/pain/pain.pdf

67. Basu D, Agarwal M, Das PP, Mattoo SK, Kulhara P, Varma VK. Changing pattern of substance abuse in patients attending a de-addiction centre in north India (1978-2008). Indian J Med Res. 2012 June;135(6):830-6.

68. SE McCabe, James A, Cranford CJB. The relationship between past-year drinking behaviors and nonmedical use of prescription drugs: Prevalence of cooccurrence in a national sample. Drug Alcohol Depend. 2006;84(3):281-8.

69. Amiegheme F. Psychosocial factors affecting adolescent alcohol abuse in Edo State,Nigeria. Archives of Applied Science Research. 2013;5(1):88-92.

70. Copeland J. A qualitative study of barriers to formal treatment among women who self-managed change in addictive behaviours. Journal of Substance Abuse Treatment. 1997;14(2):183-90.

71. Murthy P. Women and Drug Abuse: the Problem in India. India, Ministry of Social Justice and Empowerment and United Nations International Drug Control Programme, Regional Office for South Asia, 2002.

72. Isaac N. Apprehensions: Barriers to Treatment for Substance-Using Mothers: Vancouver, Canada, British Columbia Centre of Excellence for Women's Health; 2001. Available from: www.bccewh.bc.ca/PDFs/apprehensions.pdf.

73. Barnard M. Needle sharing in context: patterns of sharing among men and women injectors and HIV risks. Addiction. 1993;88(6):805-12.

74. Latkin CA, MW, Knowlton AR, Doherty MC, Vlahov D, Suh T. Gender differences in injection-related behaviors among injection drug users in Baltimore, Maryland. AIDS Education and Prevention. 1998;10(3):257-63.

75. Fischer G. "Special issues in services for pregnant and parenting women", presentation at the meeting of the UNODC entitled "Women's Drug Treatment: Lessons Learned". Vienna: December 15-17,2003

76. Milani RM, Parrott AC, Turner JJ. Gender differences in self-reported anxiety, depression, and somatization among ecstasy/MDMA polydrug users, alcohol/tobacco users, and nondrug users. Addict Behav. 2004;29:965-71.

77. Information and Public relation Department-Govt. of sikkim. Available from: http://www.sikkimipr.org/sikkim_people.aspx.

78. National Family Health Survey-2, India, 1998-1999: Sikkim, Mumbai, India. International Institute for Population Sciences and ORC macro, 2001.

79. Goel Amit, Chakrabarti A. Prevalence and sociodemographic correlates of substance use in a rural community in Sikkim, North East India: Results from a pilot population survey. Journal of substance use. 2010;15(1):13-23.

80. Manchikanti L. National drug control policy and prescription drug abuse : facts and fallacies. Physician. 2007;10:399-424.

81. Reports of drug surveillance 2003. Beijing: National Institute on Drug Dependence & National Drug abuse Surveillance Centre, 2003.

82. Nebhinani N, Siddharth SS, Gupta S, Mattoo SK, Basu D. Demographic and clinical profile of substance abusing women seeking treatment at a de addiction center in north India. Industrial Psychiatry Journal. 2013;22(1):12-6.

83. Reddy M. Prevalence of mental and behavioural disorders in India: A meta-analysis. Indian J Psychiatry. 1998;40(149-157).

84. Hartman CA, Lessem JM, Hopfer CJ. The family transmission of adolescent alcohol abuse and dependence. Journal of studies of alcohol. 2006;67:657-64.

85. Bjorkqvist K, Batman A. Adolescents' use of tobacco and alcohol: coorelation with habits of parents and friends. Psychological repots. 2004;95:418-20.

86. Chou R, Fanciullo G, Fine P, Miaskowski C, Passik S. Opioids for chronic noncancer pain: Prediction and identification of aberrant drug-related behaviors: A review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain. 2009;10:131-46.

87. Martell B, O'Connor P, Kerns R B, Morales K, Kosten T. Systematic review: Opioid treatment for chronic pain: Prevalence, efficacy, and association with addiction. Ann Intern Med. 2007;146:116-27.

88. Manchikanti L, Vallejo R, Manchikanti KN,Benyamin RN,Datta S. Effectiveness of long-term opioid therapy for chronic non-cancer pain. Pain Physician. 2011;14:E133-E56.

89. Levy M. An exploratory study of OxyContin use among individuals with substance use disorders. J Psychoactive Drugs. 2007 Sep;39(3):271-6.

90. UNODC. World Drug Report 2010. Vienna, Austria: Division for Policy Analysis and Public Affairs: 2010 Contract No.: E.10.XI.13. 2010. .

91. UNODC. World Drug Report 2011. Vienna: United Nations Office on Drugs and Crime: 2011.

92. Sudie E Back, Katie Lawson, Lauren Singleton, KTB. Characteristics and Correlates of Men and Women with Prescription Opioid Dependence. Addict Behav. 2011;36(8):829-34.

93. Weiss RD, Potter JS, Griffin ML, McHugh RK, Haller D, Jacobs P, Gardin J 2nd, Fischer D. Reasons for opioid use among patients with dependence on prescription opioids: the role of chronic pain. J Subst Abuse Treat. 2014,Aug;47(2):140-5.

94. Fischer B, Rehm J, Brissette S BS, Bruneau J, El-Guebaly N, Noël L T, M, Wild C. Illicit opioid use in Canada: Comparing social, health and drug use characteristics of untreated users in five cities (OPICAN study). J Urban Health. 2005;82:250-66.

95. Sproule B, Brands B, Li S C. Changing patterns in opioid addiction. Characterizing users of oxycodne and other opioids. Can Fam Physician. 2009;55:68-9.

96. Maher L, Dixon D, Lynskey M, Hall W. Running the risks: heroin health and harm in South West Sydney (Research Monograph 38). Sydney, Australia: National Drug and Alcohol Research Centre, University of New South Wales, 1998.

97. Booth R. Gender differences in high-risk sex behaviours among heterosexual drug injectors and crack smokers. American Journal of Drug and Alcohol Abuse. 1995;21(4):419-32.

ANNEXURE

ANNEXURE 1-A

INFORMED CONSCENT FORM: ENGLISH VERSION

INFORMED CONSENT FORM

Title of the study:

"**Epidemiology of prescription opioid abuse in Sikkim."**

You are invited to participate in a research study regarding characteristics of prescription opioid abuse in Sikkim. This study will be conducted among prescription opioid abusers and illicit opioid abusers of Sikkim from treatment centres like Central Referal Hospital (CRH), Voluntary Counselling and Treatment Centre (VCTC), Sir Thutop Namgyal Memorial (SNTM) hospital, de-addiction centres etc. Prescription opioids (e.g. codeine) are those that are prescribed by doctors for pain management and bring important improvement in quality of life, whereas illicit opioids (e.g. heroin) are those that are obtained from illegal source mainly to relief physical pain and also to get euphoria, to improve sleep. You are selected as a possible participant because you have told me that you live in Sikkim and you frequently take opioids nonmedically. I request you to read this form carefully and ask any questions that arise to you, before agreeing to participate in this study. This study is being conducted by Mr. Debranjan Datta, Lecturer, Department of Pharmacology, Sikkim Manipal Institute of Medical Sciences under the guidance of Dr. Amit Chakrabarti, Professor, Department of Pharmacology and co-guidance of Dr. Sanjiba Datta, Professor, Department of Psychiatry, Sikkim Manipal Institute of Medical Sciences and Dr. Yogesh Verma, Department of Pathology, Sikkim Manipal Institute of Medical Sciences & STNM hospital, Gangtok.

Purpose of the study: The information on epidemiology of prescription opioid abuse in Sikkim is needed for effective prevention and treatment of substance abuse related problems in Sikkim. The purpose of this research study is to get a better understanding of the relationship between pain and opioid abuse. This community based survey will help to describe socio-demographic characteristics (age, gender, education, income etc) of prescription opioid and illicit opioid abusers. This study will provide information regarding types of drug use, frequency, route, duration of use. The quality of life of drug abusers as well as high risk behaviour pattern can also be studied.

Study procedure: if you agree to participate in this study, you will be asked to reply to the questions asked to you from the questionnaire sheet regarding your socio-demographic information, drug use, characteristics of pain, quality of life by using following eight questionnaires: a) Socio-demographic information, b) Risk behaviour Survey, c) Addiction Severity Index-Lite, d) Brief Pain Inventory, d) Pain & Opiate analgesic use history, e) SF-36, Quality of life, f) CAGE for Alcohol dependence and g) Fagerstorm Test for Nicotine dependence. This procedure should take maximum of one to one and half hour. The response sheet will be filled by me. The study does not involve administration of any drug, procedure, techniques or drawing of blood for any investigative purpose. You will be given a duplicate copy of this informed consent, which includes follow-up contact information.

Expected risks: There are no foreseeable risks either in terms of physical or psychological harm or injury to you by completing this survey. No confidential questions will be asked. You are free to withhold a response to any question asked to you.

Expected benefits: There will be no direct personal benefit to you, but your participation will help the investigator to better understand drug use behaviour, socio-medical characteristics and high risk behaviour of prescription opioid and illicit opioid abusers in Sikkim, which will help elevating effective prevention and treatment of substance abuse related problems in Sikkim.

Study compensation: You will not be entitled to receive any financial compensation for participation in this study, but I do value your input and information.

Confidentiality: Only a code number will identify your questionnaire responses. The results will be stored separately from the consent form, which includes your signature or any other identifying information. At no time your name will be associated with your responses to the questionnaire.

Voluntary participation: Participation in this study is voluntary. You may choose not to participate. If you do decide to participate, you can change your mind at any time and withdraw from the study without negative consequences.

Use of research results: Results will be presented in comprehensive form only. No names or individually identifying information will be revealed. Results will be presented as a part of doctoral dissertation being conducted by me, also may be presented in scientific publications.

Contacts and Questions: The researchers conducting this study are Mr. Debranjan Datta, Lecturer, and Dr. Amit Chakrabarti, Professor, Dept of Pharmacology, Sikkim Manipal Institute of Medical Sciences, Gangtok. You may ask any questions you have now or if you have questions late, you are encouraged to contact them at 9062356954 (Mr. Debranjan Datta), and 9674566502 (Dr. Amit Chakrabarti).

Statement of Informed Consent: I have read or had read to me all of the above information about this research study. All my questions, at this time, have been answered. I hereby consent to participate in the study.

Signature of participant: _____

Date: _____

Signature of investigator: _____

Date: _____

ANNEXURE 1-B

INFORMED CONSCENT FORM: NEPALI VERSION

सूचनांबद्ध सहमती प्रपत्र

अध्ययनको शीर्षक :

सिक्किममा प्रिसकाइभ दुर्व्यवसनकारीको व्यापकता (महामारी)

सिक्किममा प्रिसक्राइभ दुर्वयवसनकारीको लक्षणहरूमाथि अध्ययन गर्न तपाईंहरूलाई एउटा शोध अध्ययनमा सहभागी बन्ने आमन्त्रण गर्छौं। यो शोध अध्ययन ती उपचार केन्द्रहरू जस्तै सेन्ट्रल रेफरल अस्पताल (सीआरएच), भोलियूनटरी काउन्सलिङ एण्ड ट्रीटमेन्ट सेन्टर (भीसीटीसी), सर थूटोप नामग्याल मेमोरियल (एसटीएनएम) अस्पताल आदि उपचाराधीन सिक्किममा प्रिसक्राइभ दुर्वयवसनकारी अनि गैर-प्रिसक्राइभ दुर्व्यवसनकारीहरूमाथि गरिनेछ। प्रिसक्रिभ दुर्व्यवसनकारी भन्नाले उनीहरूलाई बुझिन्छ, जसलाई डाक्टरले प्रिसक्राइभ गरेको हुन्छ अनि गैर-दुर्व्यवसनकारी भन्नाले उनीहरूलाई बुझिन्छ जसले गैर-कानूनी स्रोतबाट शारीरिक पीड़ाबाट मुक्ति पाउन अथवा मौजमस्ती र निद्राको निम्ति लागू पदार्थ ग्रहण गर्छन्। हामीले तपाईंलाई एक सम्भावित सहभागीको रूपमा छनौट गरेका छौं किनभने तपाईंले मलाई भन्नुभएको छ, तपाईं सिक्किममा हुन र डाक्टरको प्रेसक्रिप्शन बिना लागू पदार्थको सेवन गर्नुहुन्छ। यस अध्ययनमा सहभागी बन्नअघि ध्यानपूर्वक सहमती पत्र पढ्ने र तपाईंको मनमा उब्जिएका प्रश्नहरू मलाई गर्ने अनुरोध गर्दछु।

डा० अमित चक्रवर्ती, प्रोफेसर, डिपार्टमेन्ट अव् फार्मालोजीका मर्गदर्शन अनि डा० सञ्जीभा दत्त, प्रोफेसर, डिपार्टमेन्ट अव् साइक्रेट्री, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्स तथा डा० योगेश वर्मा, डिपार्टमेन्ट अव् पेथोलोजी, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्स अनि एसटीएनएम अस्पताल, गान्तोकको सहमार्गदर्शनमा श्री देवरञ्जन दत्त, लेक्चरर, डिपार्टमेन्ट अव् फार्माकोलोजी, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्सले यस शोध अध्ययनको सञ्चालन गर्नेछन्।

अध्ययनको उद्देश्य : सिक्किममा प्रिसक्राइभ दुर्वयवसनकारी व्यापकताको जुन सूचना छ यसलाई ध्यानमा राख्दा प्रभावकारी रोकथामको अत्यन्त जरूरी छ। यसबाहेक दुर्व्यवसनकारीहरूले जुन मात्रामा लागू पदार्थको प्रयोग गरिरहेका छन्, त्यसलाई पनि हेर्दा उपचारको पनि अत्यन्त जरूरी छ। यस शोध अध्ययनको मुख्य उद्देश्य दुर्व्यवसनकारी अनि पीड़ा पाइरहेको सुहाउँदिलो तालमेल बुझ्नु हो। समाज आधारित यस शोध अध्ययन मार्फत् प्रिसक्राइभ दुर्व्यवसनकारी अनि गैर-प्रिसक्राइभ दुर्व्यवसनकारीहरूका लक्षणहरू जस्तै (उमेर, लिङ, शिक्षा, आय आदि) बारे वर्णन गर्नमा मद्दत पाइन्छ। यस अध्ययनले हामीलाई ड्रग्स प्रयोगको प्रकार, यसको मात्रा, रूट अनि प्रयोगको अवधिबारेमा सूचनाहरू उपलब्ध गराउँछ। शोध अध्ययन अन्तर्गत दुर्व्यवसनकारीहरूमा जीवन स्तर अनि व्यवहारमा आएको जोखिमपूर्ण परिवर्त्तन बारेमा अध्ययन गरिन्छ।

अध्ययनको प्रक्रिया : तपाईं यदि यस शोध अध्ययनमा सहभागी बन्न चाहनुहुन्छ भने तपाईंले एउटा प्रश्न पत्रमा तपाईंको सामाजिक जीवनको तथ्याङ्क, ड्रग्सको प्रयोग, पीड़ाको लक्षणहरूबारे गरिएको प्रश्नहरूको जवाब दिनुपर्छ। विशेष गरेर निम्नलिखित आठ प्रश्नहरूको :- (क) सामाजिक तथ्याङ्कबारे सूचना, (ख) व्यवहारिक जोखिमको सर्वेक्षण, (ग) दुर्व्यवसन आवश्यकताको सूचकाङ्क, (घ) पीड़ाको संक्षिप्त सूचीपत्र, (ङ) पीड़ा अनि पीड़ानाशक प्रयोगको इतिहास, (च) एसएफ-३६, जीवनको स्तर, (छ) एल्कोहल निर्भरताको निम्ति सीजीई र (ज) निकोटिन निर्भरताको निम्ति टेस्ट।

यो प्रक्रिया एक अथवा डेढ़ घण्टासम्ममा पूरा हुनुपर्छ। प्रत्युत्तर पत्र मद्वारा पूरा गरिनेछ। यस अध्ययनको अवधिमा कुनै पनि प्रकारको ड्रग्सको व्यवहार गरिनेछैन औ न त ड्रग्स सेवन प्रक्रियाको प्रदर्शन गरिनेछ। यसबाहेक जाँचको नाममा यसैबाट रक्त संग्रह गरिनेछैन। अध्ययनमा सहभागी गराउनअघि तपाईंलाई सूचनाबद्ध

सहमती प्रपत्रको प्रतिलिपि प्रदान गरिनेछ जसमा क्रमिक सम्पर्क सूचनाहरू सम्मलित रहनेछन्।

अपेक्षाकृत जोखिम : यो शोध अध्ययन पुरा गर्दा कुनै प्रकारको शारीरिक अथवा मनोवैज्ञानिक चोट अथवा नोक्सान पुग्ने कुनै सम्भावना छैन। तपाईंलाई कुनै पनि प्रकारको गोपनीय प्रश्न गरिनेछैन। तपाईंलाई सोधिएको प्रश्नको तपाईंले उत्तर नदिन पनि सक्नुहुन्छ।

अपेक्षाकृत फाइदा : यस शोध अध्ययनबाट तपाईंलाई कुनै प्रत्यक्ष फाइदा हुँदैन तर सिक्किममा प्रिसक्राइभ दुर्व्यवसनकारी अनि गैर-प्रिसक्राइभ दुर्व्यवसनकारीहरूमा व्याप्त लागू पदार्थ प्रयोगको प्रचलन, सामाजिक-चिकित्सकीय लक्षण अनि उच्च जोखिमता बारेमा जाँचकर्त्ताहरूलाई जानकारी बटुल्न ठूलो मद्दत पुग्नेछ। यसले गर्दा प्रभाकारी रोकथाम अनि उपचारको उचित मार्ग निकाल्नमा पनि मद्दत पुग्नेछ।

अध्ययनको क्षतिपूरण : यस शोध अध्ययनमा सहभागी बन्नको निम्ति कुनै प्रकारको आर्थिक क्षतिपूरण प्रदान गरिनेछैन तर तपाईंको सुझाउ अनि सूचनाको हामी कदर गर्नेछौं।

गोपनीयता : केवल एउटा कोडद्वारा तपाईंको प्रश्नहरूको प्रत्युत्तरको पहिचान हुनेछ। शोधको परिणाम तपाईंको सहमती प्रबत्रदेखि अलग राखिनेछ जसमा तपाईंको हस्ताक्षर अथवा अन्य कुनै पहिचान सूचना सामेल रहनेछ। कुनै पनि अवस्थामा तपाईंको नाम तपाईंको प्रत्युत्तरसँग जोड़िनेछैन।

स्वेच्छिक सहभागी : यस अध्ययनमा सहभागिता स्वेच्छिक रहनेछ। तपाईं यसमा सहभागी नहुन पनि सक्नुहुन्छ। यदि तपाईं सहभागी बन्न सहमत हुनुहुन्छ भने पनि तपाईंले कुनै पनि समय आफ्नो सहभागिता छोड़ेर शोध अध्ययनबाट निस्केर जान सक्नुहुन्छ।

शोध परिणामको उपयोगिता : शोधको परिणाम एउटा विस्तृत प्रपत्रमा पेश गरिनेछ। कुनै नाम अथवा व्यक्तिगत पहिचान सूचना प्रकाशित गरिनेछैन। शोधको परिणाम पूर्णत चिकित्सकीय विवेचनाको आधारमा पेश गरिनेछ जसको सञ्चालन मद्वारा हुनेछ। शोधको परिणाम वैज्ञानिक प्रकाशनहरूमा पनि पेश गरिनेछ।

सम्पर्क अनि प्रश्न : यो शोध अध्ययनमा शोधकर्त्ताहरू हुन् - श्री देवरञ्जन दत्त, लेक्चरर अनि डा० अमित चक्रवर्ती, प्रोफेसर डिपार्टमेन्ट अव् फार्माकोलोजी, सिक्किम मणिपाल इन्स्टिच्युट अव् मोडिकल साइन्स, गान्तोक। यदि तपाईंमा कुनै जिज्ञासा छ भने तपाईंले कुनै पनि प्रकारको प्रश्न सोध्न सक्नुहुन्छ। तपाईंलाई उनीहरूका नम्बर ९०६२३५६६५४ (श्री देवरञ्जन दत्त) अनि ९६७४५६६५०२ (डा० अमित चक्रवर्ती) मा सम्पर्क गर्न सक्नुहुन्छ।

सूचनाबद्ध सहमतीको विवरण : मैले यस शोध अध्ययनबारे अध्ययन गरेको छु अथवा गरेको थिएँ। मैले मेरो सबै प्रश्नहरूको जवाब पाएको छु। यस शोध अध्ययनमा सहभागी बन्ने मेरो मतामत प्रदान गर्दछु।

सहभागीको नाम :.....

तारीख :.....

जाँचकर्त्ताको हस्ताक्षर :.....

तारीख :.....

द्वारा ग्रहण : http://www.research.umn.deu/irb/consent/medical consent template.rtf

इण्डियन काउन्सील अव् मेडिकल रिसर्च (आईसीएआर), नयाँ दिल्ली, भारतद्वारा ग्रहण गरिएको सिद्धान्त अनुसार तथा युनिभर्सिटी अव् माइनेसोटा, माइनेयिपोलिस, यूएसएद्वारा गृहित।

ANNEXURE 1-C

INFORMED CONSCENT FORM: HINDI VERSION

सूचनाबद्ध सहमती प्रपत्र

अध्ययन का शीर्षक :

सिक्किम में प्रिसकाइभ दुर्व्यवसनकारियों का व्यापकता (महामारी)

सिक्किम में प्रिसंक्राइभ (सिफारिश) दुर्वयवसनकारियों के लक्षणों का अध्ययन हेतू आपको एक अनुसन्धान अध्ययन में सहभागी बन्ने के लिए आमन्त्रण किया जाता है। यह अनुसन्धान सेन्ट्रल रेफरल अस्पताल (सीआरएच), भोलेन्टेरी काउन्सेलिङ एण्ड ट्रीटमेन्ट सेन्टर (भीसीटीसी), सर थूटोप नामग्याल मेमोरियल (एसटीएनएम) अस्पतालों में चिकित्साधीन सिक्किम के प्रिसक्राइभ दुर्वयवसनकारी और गैर-प्रिसक्राइभ दुर्व्यवसनकारियों के ऊपर किया जाएगा। प्रिसक्राइभ दुर्व्यसनकारी उन लोगों को कहा जाता है जो डाक्टर द्वारा प्रिसक्राइभ किया गया हो और गैर-दुर्व्यवसनकारी उसे कहा जाता है जो गैर-कानूनी माध्यम से शारीरिक पीड़ा से मुक्ति, या मौजमस्ती अथवा दिन्द के लिए लागू पदार्थ व्यवहार करते हैं।

हमने आपको एक सम्भावित सहभागी के रूप में चयन किये है। क्योंकि आपने हमसे कहा है कि आप डाक्टर की सिफारिश के बगैर लागू पदार्थ सेवन करते है। इस अध्ययन में सहभागी होने से पहले ध्यानपूर्वक सहभागी पत्र को पढ़ें और अनुरोध यह भी करता हूँ कि आपके मन में उब्जे हुए सवालों को हमारे सामने रखें।

डा० अमित चक्रवर्ती, प्रोफेसर, डिपार्टमेन्ट अव् फार्मालोजी, मर्गदर्शन, प्रो० डा० सञ्जीभा दत्त, प्रोफेसर, डिपार्टमेन्ट अव् साइक्रेट्री, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्स, डा० योगेश वर्मा, डिपार्टमेन्ट अव् पेथोलोजी, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्स और लेक्चरर श्री देवरञ्जन दत्त, एसटीएनएम अस्पताल के सहमार्गदर्शन, डिपार्टमेन्ट अव् फार्माकोलोजी, सिक्किम मणिपाल इन्स्टीच्यूट अव् मेडिकल साइन्स द्वारा इस अनुसन्धान अध्ययन का सञ्चालन किया जायेगा।

अध्ययन का उद्देश्य : सिक्किम में प्रिसक्राइभ दुर्वयवसनकारियों में हुए बढ़ोत्तरी का जो सूचनाएँ हैं उसे मध्ये नजर रखते हुए प्रभावकारी रोकथाम की आवश्यकताएँ है। उसके अलावा दुर्व्यवसनकारियों ने जिस मात्रा मे लागू पदार्थ प्रयोग कर रहे हैं उसे देखते हुए सठीक चिकित्सा की जरूरत और भी बढ़ गई है। इस अनुसन्धान का मुख्य उद्देश्य दुर्व्यवसनकारी और पीड़ा के बीच में होनेवाला सामाञ्जस्य के तालमेल को समझना अथवा परखना है। समाज आधारित इस अनुसन्धान के मार्फत् प्रिसक्राइभ दुर्व्यवसनकारी और गैर-प्रिसक्राइभ दुर्व्यवसनकारियों के लक्षण जैसे (उम्र, लिङ्ग, शिक्षा और आय) बारे वर्णन करने में मद्दत मिल सकेगा। इस अध्ययन के द्वारा हमें ड्रग्स प्रयोग के प्रकार, इसकी मात्रा, रूट और प्रयोग अवधि बारे आवश्यक सूचनाएँ उपलब्ध होंगे। अनुसन्धान अध्ययन के तहत् दुर्व्यवसनकारियों के जीवन स्तर और व्यवहार में आनेवाले खतरनाक परिवर्त्तन को बारिकी से अध्ययन किया जायेगा।

अध्ययन की प्रक्रिया : यदि आप इस अनुसन्धान अध्ययन में सामेल होने की इच्छा रखते हैं तो आपको एक प्रश्नपत्र में अपनी सामाजिक जीवन की तथ्याङ्क और ड्रग्स प्रयोग से होनेवाले पीड़ा की लक्षणों के बारे में पूछा गया सवालों का जवाब देने होंगे। विशेषकर आठ प्रश्नों का जो इसप्रकार है - (क) सामाजिक तथ्याङ्क बारे सूचनाएँ, (ख) व्यवहारिक जोखिम के खतरे, (ग) दुर्व्यवसन लत् के सुचनाएँ, (घ) पीड़ा के संक्षिप्त सूचीपत्र, (ङ) पीड़ा और पीड़ानाशक प्रयोग के इतिहास, (च) एसएफ-३६, जीवन के स्तर, (छ) एल्कोहल के लिए सीएजीई और (ज) निकोटिन निर्भरता के लिए परीक्षण।

इस प्रक्रिया को एक से डेड़ घण्टे के अन्दर पूरा कर्ना होगा। लेकिन इसे प्रत्युत्तर पत्र के द्वारा पूरा करना होगा। इस अध्ययन के अवधि किसी प्रकार की ड्रग्स के व्यवहार नहीं किया जायेगा और ना ही ड्रग्स प्रक्रिया की प्रदर्शन। इसके अलावा जाँच के नाम में किसी भी प्रकार की खुन के नमूने नहीं लिया जायेगा। अध्ययन

में सामेल होने से पहले आपको सूचनाबद्ध सहमति प्रपत्र की प्रतिलिपि दिय जायेगा। जिसमें क्रमिक सूचनाएँ सम्मिलित होंगे।

अपेक्षाकृत जोखिम : इस अनुसन्धान अध्ययन पूरा करने से किसी प्रकार की शारीरिक अथवा मनोवैज्ञानिक चोट पहुँचने की कोई सम्भावना नहीं है। आपको किसी प्रकार की गोपनीय प्रश्न नहीं पूछा जायेगा। यदि आप चाहे तो किसी भी प्रकार का प्रश्न का उत्तर आप नहीं भी दे सकते हैं।

अपेक्षाकृत फाइदा : इस अनुसन्धान अध्ययन से हो सकता है आपको कोई फाइदा ना हो लेकिन सिक्किम में प्रिसक्राइभ दुर्व्यवसनकारी और गैर प्रिसक्राइभ दुर्व्यवसनकारियों में व्याप्त लागू पदार्थ के व्यवहारिक प्रचलन, सामाजिक-चिकित्सकीय लक्षण और उच्च-जोखिम के बारे में अनुसन्धानकर्त्ताओं को जानकारीआ एकत्रित करने में मद्दत मिलेगा। इससे प्रभावकारी उपचार का मार्ग प्रशस्त होंगे।

अध्ययन के क्षतिपूरण : इस अनुसन्धान अध्ययन में सहभागी बन्ने के लिए किसी प्रकार की आर्थिक क्षतिपूरण नहीं दिया जायेगा, लेकिन आपके द्वारा दिए गये परामर्श और सूचनाएँ के लिए हम आपके प्रति आभारी रहेंगे।

गोपनीयता : आप के द्वारा भेजे गए प्रत्युत्तर को एक विशेष कोड के माध्यम से पहिचान होगा। अनुसन्धान परिणाम को आपके प्रपत्र से अलग रखा जायेगा। जिसमें केवल आपके हस्ताक्षर या अन्य कोई पहिचान की सूचनाएँ सामेल होंगे। भेजे गये प्रत्युत्तर में आपके नाम को सामेल नहीं किया जायेगा।

स्वेच्छिक सहभागी : इस अध्ययन में आपका सहभागिता स्वेच्छिक रहेगा। आप इस अभियान में सहभागी नहीं भी हो सकते है। यदि सहभागी बनकर बीच में ही अनुसन्धान अध्ययन छोड़ने का मन किया तो आप इससे सहर्ष अलग हो सकते हैं।

अनुसन्धान परिणाम के उपयोगिता : अनुसन्धान के परिणाम को एक विस्तृत प्रपत्र में पेश किया जायेगा। किसी का नाम या व्यक्तिगत पहिचान एवं सूचनाएँ को प्रकाशित नहीं किया जायेगा।अनुसन्धान का परिणाम पूर्णतयः चिकित्सकीय विवेचना की आधार में पेश किया जायेगा। जिसके सञ्चालन मेरे माध्यम से होंगे। अनुसन्धान परिणाम को वैज्ञानिक प्रकाशनों मे भी पेश किया जायेगा।

सम्पर्क और सवाल : इस अनुसन्धान अध्ययन में शोधकर्त्ताओं इस प्रकार हैं - श्री देवरञ्जन दत्त, लेक्चरर अनि डा० अमित चक्रवर्ती, प्रोफेसर डिपार्टमेन्ट अव् फार्माकोलोजी, सिक्किम मणिपाल इन्स्टिच्युट अव् मोडिकल साइन्स, गान्तोक। यदि आपके मन में किसी प्रकार की जिज्ञासा हो तो आप कोई भी सवाल पूछ सकते हैं। सम्पर्क नम्बर इस प्रकार है - श्री देवरञ्जन दत्त - ९०६२३५६९५४ और डा० अमित चक्रवर्ती - ९६७४५६६५०२

सूचनाबद्ध सहमती का विवरण : मैंने इस अनुसन्धान बारे अध्ययन किया है अथवा कर लिया है। इस अनुसन्धान अध्ययन में सहभागी बन्ने के लिए मेरा मतामत प्रदान करता हूँ।

सहभागी का नाम :.....

तारीख :.....

जाँचकर्त्ता का हस्ताक्षर :.....

तारीख :.....

द्वारा ग्रहण : http://www.research.umn.deu/irb/consent/medical consent template.rtf

इण्डियन काउन्सील अव् मेडिकल रिसर्च (आईसीएआर), नयाँ दिल्ली, भारतद्वारा ग्रहण गरिएको सिद्धान्त अनुसार तथा युनिभर्सिटी अव् माइनेसोटा, माइनेयिपोलिस, यूएसएद्वारा गृहित।

ANNEXURE 2

QUESTIONNAIRES

Generic Instrument - Population Survey of Alcohol & Other Drug Use

1	ID				
2	Gender	M / F			
3	Age				
4	Education				
5	Source of income	Student / Salaried / Self employed / Unemployed			
6	Occupation				
7	Community	Urban / Rural			
		Type of accommodation			
8	Ethnicity				
9	Marital status	Single / Married / Separated / Widow(er)			
10	Religion				
11	Socioeconomy	Average monthly incor me			
		Average monthly expenditure on alcohol / drugs			
12	Settlement	Migration	Yes / No	From	
		When		Why	
		Settlement of 1st alcohol / drug use			
13	Parental status	Both / Single	F / M		
14	Pregnancy status	Yes / No		Number	
15	Living with whom				
	Father's occupation (For students)				
16	Lifetime use (Years)		Alcohol	Other	
17	Past 30 days use		Alcohol	Other	
18	Alcohol to intoxication past 30 days				
19	Age of first use		Alcohol	Other	
20	Parental alcohol / drug	Yes / No	Father / Mother / Both		
		Frequency		Duration	
21	Sibling alcohol / drug u	Yes / No	Brother / Sister / Both		
		Frequency		Duration	
22	Friends' alcohol / drug	Yes / No	Number	Out of	
			Frequency	Duration	
23	Availability			Where	
24	Attitudes	Danger	Yes / No	Why	
		Disapproval	Yes / No	Why	
		Friends' disapproval	Yes / No	Why	
		Use in school / work	Yes / No	Why	
25	Family	Absence from home			
		Time at home			
26	Religion	Yes / No	Attending ceremonies		
			Rated importance		
27	Other deviances	Property crimes		Yes / No	
		Interpersonal aggression		Yes / No	
		Precocious sexual activity		Yes / No	Age

			Frequency	
Drunk driving		Yes / No		
Law enforcement		Yes / No	Why	
			Frequency	

28 Knowledge & attitude about HIV & other high risk behavior

CSW	Yes / No	Age since		Frequency	
Multiple sex partner	Yes / No	Age since		Frequency	
MSM	Yes / No	Age since		Frequency	
Condom use	Yes / No	Age since		Frequency	
Injection sharing	Yes / No	Age since		Frequency	
		Exchange	Yes / No	Frequency	

Knowledge about AIDS	Yes / No
Knowledge about transmission	Yes / No

29 Treatment	Yes / No	First treatment initiator		When	
		Treatment source			
		Expenses source	Amount		
		Risk behavior education	Yes / No	Source	
		Frequency			

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-Lite (ASL): General Information

G14 **How long have you lived at your current address?** ___ ___ / ___ ___ (years / months)

G16 **Date of birth:** ___ ___ /___ ___ /___ ___ ___ ___ (month / day / year)

G17 In which religion do you consider yourself?

- ☐ 1 Hinduism
- ☐ 2 Buddhism
- ☐ 3 Islamic
- ☐ 4 Christianity
- ☐ 5 Others

G18 What is your ethnicity?

- ☐ 1 Lepcha
- ☐ 2 Bhutia
- ☐ 3 Nepali
- ☐ 4 Others

G19 **Have you been in a controlled environment in the past 30 days?** *(A place, theoretically, without access to drugs/ alcohol)*

- ☐ 1 No
- ☐ 2 Jail
- ☐ 3 Alcohol or drug treatment
- ☐ 4 Medical treatment
- ☐ 5 Psychiatric treatment
- ☐ 6 Other *(specify)*: _____

G20 **How many days?** *(Refers to total number of days detained in the past 30 days)*

___ ___ days **OR** ☐ 96 NA

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Medical Status

M1 **How many times in your life have you been hospitalized for medical problems?**

_____ _____ times **OR** ☐ 97 Not answered

- *Include O.D.'s and D.T.'s. Exclude detox, alcohol/drug, psychiatric treatment and childbirth (if no complications).*
- *Enter the number of **overnight** hospitalizations for medical problems.*

M3 **Do you have any chronic medical problems which continue to interfere with your life?**

☐ 97 Not answered
☐ 0 No
☐ 1 Yes → **If Yes: Specify:** _____

- *A chronic medical condition is a serious physical or medical condition that requires regular care (i.e., medication, dietary restriction), preventing full advantage of their abilities.*

M4 **Are you taking any prescribed medication on a regular basis for a physical problem?**

☐ 97 Not answered
☐ 0 No
☐ 1 Yes → **If Yes: Specify:** _____

- *Medication prescribed by a M.D. for medical conditions; **not psychiatric medicines**.* • *Include medicines prescribed, whether or not the patient is currently taking them.*
- *The intent is to verify chronic medical problems.*

M5 **Do you receive a pension for a physical disability?**

☐ 97 Not answered
☐ 0 No
☐ 1 Yes → **If Yes: Specify:** _____

- *Include Workers' Compensation, exclude psychiatric disability.*

M6 **How many days have you experienced medical problems in the past 30 days?**

___ ___ days **OR** ☐ 97 Not answered

- *Do not include ailments directly caused by drugs/alcohol.*
- *Include flu, colds, etc. Include serious ailments related to drugs/alcohol, which would continue even if the patient were abstinent (e.g., cirrhosis of liver, abscesses from needles, etc.).*

For questions M7 & M8, please ask patient to use the Patient Rating Scale.

M7 **How troubled or bothered have you been by these medical problems in the past 30 days?**

☐ 0 Not at all
☐ 1 Slightly
☐ 2 Moderately
☐ 3 Considerably
☐ 4 Extremely
☐ 97 Not answered

- *Restrict response to problem days of question M6.*

M8 **How important to you ***now*** is treatment for these medical problems?**

☐ 0 Not at all
☐ 1 Slightly
☐ 2 Moderately
☐ 3 Considerably
☐ 4 Extremely
☐ 97 Not answered

- *Refers to the need for new or additional medical treatment by the patient.*

Confidence Ratings: Is the above information **significantly** distorted by:

M10 **Patient's misrepresentation?**

☐ 0 No
☐ 1 Yes

M11 **Patient's inability to understand?**

☐ 0 No
☐ 1 Yes

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Employment/Support Status

E1 Education completed:

___ ___ / ___ ___ **OR** ☐97 Not answered
A-Years B-Months

- *GED = 12 years*
- *Include formal education only.*

E2 Training or technical education completed:

___ ___ / ___ ___ **OR** ☐97 Not answered
A-Years B-Months

- *Formal/organized training only. For military training, only include training that can be used in civilian life, i.e., electronics or computers.*

E4 Do you have a valid driver's license?

☐0 No
☐1 Yes
☐97 Not answered

- *Valid license; not suspended/revoked.*

E5 Do you have an automobile available?

☐0 No
☐1 Yes
☐97 Not answered

- *If answer to E4 is "No", then E5 must be "No". Does not require ownership, only requires availability on a regular basis.*

E6 How long was your longest full time job?

___ ___ / ___ ___ **OR** ☐97 Not answered
A-Years B-Months

- *Full time = 35+ hours weekly; does not necessarily mean most recent job.*

E7 Usual *(or last)* **occupation?**

Specify: _____
OR ☐97 Not answered

- *Use Hollingshead Categories Reference Sheet.*

E9 Does someone contribute the majority of your support?

☐0 No
☐1 Yes
☐97 Not answered

- *Is patient receiving any regular support (i.e., cash, food, housing) from family/friend? • Include spouse's contribution; exclude support by an institution.*

E10 Usual employment pattern, past three years:

- *Answer should represent the **majority** of the last 3 years, not just the most recent selection. If there are equal times for more than one category, select that which best represents the more current situation.*

☐1 Full time *(35+ hrs/week)*
☐2 Part time *(reg. hrs)*
☐3 Part time *(irreg. day work)*
☐4 Student
☐5 Military service
☐6 Retired/disability
☐7 Unemployed
☐8 In controlled environment
☐97 Not answered

E11 How many days were you paid for working in the past 30 days?

___ ___ days **OR** ☐97 Not answered

- *Include "under the table" work, paid sick days, and vacation.*

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Employment/Support Status (continued)

For questions E12–E17: How much money did you receive from the following sources in the past 30 days?

Comments: _____

E12 Employment: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered
- *Net or "take home" pay, include any "under the table" money.*

E13 Unemployment compensation: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered

E14 Welfare: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered
- *Include food stamps, transportation money provided by an agency to go to and from treatment.*

E15 Pensions, benefits, or Social Security: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered
- *Include disability, pensions, retirement, veteran's benefits, SSI & workers' compensation.*

E16 Mate, family or friends: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered
- *Money for personal expenses, (i.e., clothing), include unreliable sources of income (e.g., gambling). Record cash payments only, include windfalls (unexpected), money from loans, gambling, inheritance, tax returns, etc.*

E17 Illegal: $ ___ ___ ___ ___ ___ **OR** ☐97 Not answered
- *Cash obtained from drug dealing, stealing, fencing stolen goods, gambling, prostitution, etc.*
- *Do not attempt to convert drugs exchanged to a dollar value.*

E18 How many people depend on you for the majority of their food, shelter, etc.? ___ ___ max = 99 **OR** ☐97 Not answered
- *Must be regularly depending on patient; do include alimony/child support; do not include the patient or self-supporting spouse, etc.*

E19 How many days have you experienced employment problems in the past 30 days? ___ ___ days **OR** ☐97 Not answered
- *Include inability to find work, if they are actively looking for work, or problems with present job in which that job is jeopardized.*

For questions E20-E21: Please ask patient to use the Patient Rating Scale.
The patient's ratings in questions E20 and E21 refer to question E19. Stress help in finding or preparing for a job, not giving them a job.

E20 How troubled or bothered have you been by these employment problems in the past 30 days?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered
- *If the patient has been incarcerated or detained during the past 30 days, they cannot have employment problems.*

E21 How important to you **now** is counseling for these employment problems?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

Confidence Ratings: Is the above information **significantly** distorted by:

E23 Patient's misrepresentation? ☐0 No ☐1 Yes

E24 Patient's inability to understand? ☐0 No ☐1 Yes

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Alcohol/Drugs (continued)

Route of Administration:

1 = Oral **2** = Nasal **3** = Smoking **4** = Non-IV injection **5** = IV Injection

*Note the **usual or most recent route**. For more than one route, choose the most severe. The routes are listed from least severe to most severe.*

Comments: _____

Substance	A Past 30 (Days)	B Lifetime Use (Years)	Route of Administration
D1 Alcohol *(any use at all)*:	___ ___	___ ___	
D2 Alcohol *(to intoxication)*:	___ ___	___ ___	
D3 Heroin:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D4 Methadone/LAAM *(prescribed)*:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D4a Methadone/LAAM *(illicit)*:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D5 Other opiates/ analgesics:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D6 Barbiturates:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D7 Other sedatives/ hypnotics/tranquilizers: (Benzodiazepines)	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D8 Cocaine:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Alcohol/Drugs (continued)

Route of Administration:

1 = Oral **2** = Nasal **3** = Smoking **4** = Non-IV injection **5** = IV Injection

*Note the **usual or most recent route**. For more than one route, choose the most severe. The routes are listed from least severe to most severe.*

Comments: _____

Substance	A Past 30 (Days)	B Lifetime Use (Years)	Route of Administration
D9 Amphetamines:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D10 Cannabis:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D11 Hallucinogens:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D12 Inhalants:	___ ___	___ ___	☐2 Nasal ☐96 Not applicable ☐97 Not answered
D36 Nicotine *(tobacco products)*:	___ ___	___ ___	☐1 Oral ☐4 Non IV injection ☐2 Nasal ☐5 IV injection ☐3 Smoking ☐96 Not applicable ☐97 Not answered
D13 More than 1 substance per day *(including alcohol, excluding nicotine)*:	___ ___	___ ___	

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Alcohol/Drugs (continued)

D14 According to the interviewer, which substance(s) is/are the major problem?

_____ _____ **OR** ☐97 Not answered

- Interviewer should determine the major drug or drugs of abuse (excluding Nicotine use). Code the number next to the drug in questions D1–12 (code prescribed or illicit methadone as **04**). **00** = no problem, **15** = alcohol and one or more drugs; **16** - more than one drug but no alcohol. Ask patient when not clear.

D17 How many times have you had Alcohol DT's?

_____ _____ **OR** ☐97 Not answered

- Delirium Tremens *(DT's): Occur 24–48 hours after last drink, or significant decrease in alcohol intake. Characterized by shaking, severe disorientation, fever, hallucinations; they usually require medical attention.*

How many times in your life have you been treated for:

D19 Alcohol abuse:

_____ _____ **OR** ☐97 Not answered

- *Include detoxification, halfway houses, in/outpatient counseling and AA or NA (if 3+ meetings within one month period.*

D20 Drug abuse:

_____ _____ **OR** ☐97 Not answered

- *Include detoxification, halfway houses, in/outpatient counseling and AA or NA (if 3+ meetings within one month period.*

How many of these were detox only:

D21 Alcohol:

_____ _____ **OR** ☐97 Not answered

D22 Drugs:

_____ _____ **OR** ☐97 Not answered

How much money would you say you spent during the past 30 days on:

D23 Alcohol:

$ _____ _____ _____ _____ **OR** ☐97 Not answered

- *Only count actual money spent. What is the financial burden caused by alcohol?*

D24 Drugs:

$ _____ _____ _____ _____ **OR** ☐97 Not answered

- *Only count actual money spent. What is the financial burden caused by drugs?*

D25 How many days have you been treated in an outpatient setting for alcohol or drugs in the past 30 days?

_____ _____ days **OR** ☐97 Not answered

- *Include AA/NA*

D26 How many days in the past 30 have you experienced alcohol problems?

_____ _____ days **OR** ☐97 Not answered

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Alcohol/Drugs (continued)

For questions D28–D31, please ask patient to use the Patient Rating Scale. The patient is rating the need for additional substance abuse treatment.

D28 **How troubled or bothered have you been within the past 30 days by alcohol problems?**

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

D30 **How important to you *now* is treatment for alcohol problems?**

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

D27 **How many days in the past 30 have you experienced drug problems?**

_____ _____ days **OR** ☐97 Not answered

- *Include: Craving, withdrawal symptoms, disturbing effects of use, or wanting to stop and being unable to.*

D29 **How troubled or bothered have you been within the past 30 days by drug problems?**

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

D31 **How important to you *now* is treatment for drug problems?**

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

Confidence Ratings: Is the above information **significantly** distorted by:

D34 **Patient's misrepresentation?** ☐0 No ☐1 Yes

D35 **Patient's inability to understand?** ☐0 No ☐1 Yes

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Legal Status

L1 Was this admission prompted by the criminal justice system? ☐0 No ☐1 Yes ☐97 Not answered
• *Judge, probation/parole officer, etc.*

L2 Are you on probation or parole?
☐0 No, neither
☐2 Yes, parole or post release supervision
☐3 Yes, probation or pre-sentencing diversion
☐97 Not answered
• *Note duration and level in comments.*

How many times in your life have you been arrested and charged with the following *(include total numbers of counts, not just convictions. Do not include juvenile [pre-age, 18] crimes, unless they were charged as an adult. Include formal charges only)*:

L3 Shoplifting/vandalism: ___ ___ **OR** ☐97 Not answered

L4 Parole/probation violations: ___ ___ **OR** ☐97 Not answered

L5 Drug charges: ___ ___ **OR** ☐97 Not answered

L6 Forgery: ___ ___ **OR** ☐97 Not answered

L7 Weapons offense: ___ ___ **OR** ☐97 Not answered

L8 Burglary ___ ___ **OR** ☐97 Not answered

L9 Robbery: ___ ___ **OR** ☐97 Not answered

L10 Assault: ___ ___ **OR** ☐97 Not answered

L 11 Attempt to murder __ __ OR 97 Not answered

L12 Rape: ___ ___ **OR** ☐97 Not answered

L13 Homicide/manslaughter: ___ ___ **OR** ☐97 Not answered

L14 Prostitution: ___ ___ **OR** ☐97 Not answered

L15 Contempt of court: ___ ___ **OR** ☐97 Not answered

L16 Other *(specify)*: _____ ___ ___ **OR** ☐97 Not answered

L17 How many of these charges resulted in convictions? ___ ___ **OR** ☐97 Not answered
Do not include misdemeanor offenses from questions L18–L20 below. Convictions include fines, probation, incarcerations, suspended sentences, and guilty pleas.

How many times in your life have you been charged with the following:

L18 Disorderly conduct, vagrancy, public intoxication: ___ ___ **OR** ☐97 Not answered

L19 Driving while intoxicated *(DWI)*: ___ ___ **OR** ☐97 Not answered

L20 Major driving violations: ___ ___ **OR** ☐97 Not answered
• *Moving violations: speeding, reckless driving, no license, etc.*

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Legal Status (continued)

L21 How many months were you incarcerated in your life?

___ ___ **OR** ☐97 Not answered

- *If incarcerated 2 weeks or more, round this up to 1 month. List total number of months incarcerated (up to 99). If more than 99, code 99 and enter the number in comments.*

L24 Are you presently awaiting charges, trial or sentence?

☐0 No ☐1 Yes ☐97 Not answered

L25 What for *(refers to L24)*?

___ ___ ☐97 Not answered ☐96 Not applicable

Use code 03–16, 18–20. If more than one, choose most severe. Don't include civil cases, unless a criminal offense is involved.

03 = Shoplift	12 = Rape
04 = Probation violation	13 = Homicide
05 = Drug	14 = Prostitution
06 = Forgery	15 = Contempt
07 = Weapons	16 = Other
08 = Burglary	18 = Disorderly conduct
09 = Robbery	19 = DWI
10 = Assault	20 = Major driving violation

L26 How many days in the past 30 were you detained or incarcerated?

___ ___ days **OR** ☐97 Not answered

- *Include being arrested and released on the same day.*

L27 How many days in the past 30 have you engaged in illegal activities for profit?

___ ___ days **OR** ☐97 Not answered

- *Exclude simple drug possession. Include drug dealing, prostitution, selling stolen goods, etc. May be cross checked with question E17 under Employment/Family Support section.*

For questions L28–29: Please ask patient to use the Patient Rating Scale.

L28 How serious do you feel your present legal problems are?

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

- *Exclude civil problems.*

L29 How important to you now is counseling or referral for these legal problems?

☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

- *Patient is rating a need for additional referral to legal counsel for defense against criminal charges.*

Confidence Ratings: Is the above information **significantly** distorted by:

L31 Patient's misrepresentation? ☐0 No ☐1 Yes

L32 Patient's inability to understand? ☐0 No ☐1 Yes

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Family/Social Relationships

F1 Marital status:

☐1 Married ☐5 Divorced
☐2 Remarried ☐6 Never married
☐3 Widowed ☐97 Not answered
☐4 Separated

• Common-law marriage=1: Specify in comments.

F3 Are you satisfied with this situation?

☐0 No ☐1 Yes ☐3 Indifferent ☐97 Not answered

• Satisfied = Generally liking the situation. Refers to question F1.

F4 Usual living arrangements *(past 3 yrs.)*:

☐1 With sexual partner and children
☐2 With sexual partner alone
☐3 With children alone
☐4 With parent
☐5 With family
☐6 With friend
☐7 Alone
☐8 Controlled environment
☐9 No stable arrangements
☐97 Not answered

• Choose arrangements most representative of the past 3 years. If there is an even split in time between these arrangements, choose the most recent arrangement.

F6 Are you satisfied with these arrangements?

☐0 No ☐1 Yes ☐3 Indifferent ☐97 Not answered

• Refers to response in question F4.

Do you live with anyone who:

F7 Has a current alcohol problem?

☐0 No ☐1 Yes ☐97 Not answered

F8 Uses non-prescribed drugs?

☐0 No ☐1 Yes ☐97 Not answered

F9 With whom do you spend most of your free time?

☐1 Family ☐3 Alone
☐2 Friends ☐97 Not answered

• If a girlfriend/boyfriend is considered as family by patient, then they must refer to them as family throughout this section, not as a friend. Family is not to be referred to as "friend."

F10 Are you satisfied with spending your free time this way?

☐0 No ☐1 Yes ☐3 Indifferent ☐97 Not answered

• A satisfied response must indicate that the person generally likes the situation. Refers to question F9.

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Family/Social Relationships (continued)

Have you had significant periods in which you have experienced serious problems getting along with:

- *Serious problems mean those that endangered the relationship.*
  A "problem" requires contact of some sort, either by telephone or in person.

Comments: _____

	A Past 30 Days	B Lifetime
F18 Mother:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F19 Father:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F20 Brother/sisters:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F21 Sexual partner/spouse:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F22 Children:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F23 Other significant family *(specify)*: _____ _____	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F24 Close friends:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F25 Neighbors:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
F26 Co-workers:	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable	☐0 No ☐97 Not answered ☐1 Yes ☐96 Not applicable
Did anyone abuse you?	**A Past 30 Days**	**B Lifetime**
F28 Physically *(cause you physical harm)*?	☐0 No ☐97 Not answered ☐1 Yes	☐0 No ☐97 Not answered ☐1 Yes
F29 Sexually *(force sexual advances/acts)*?	☐0 No ☐97 Not answered ☐1 Yes	☐0 No ☐97 Not answered ☐1 Yes

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Family/Social Relationships (continued)

F30 How many days in the past 30 have you had serious conflicts with your family? ___ ___ days **OR** ☐97 Not answered

For questions F32 and F34, please ask patient to use the Patient Rating Scale.

F32 How troubled or bothered have you been in the past 30 days by these family problems?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

F34 How important to you now is treatment or counseling for these family problems?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

F31 How many days in the past 30 have you had serious conflicts with other people *(excluding family)*? ___ ___ days **OR** ☐97 Not answered

For questions F33 and F35, please ask patient to use the Patient Rating Scale.

F33 How troubled or bothered have you been in the past 30 days by these social problems?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

F35 How important to you now is treatment or counseling for these social problems?
☐0 Not at all ☐3 Considerably
☐1 Slightly ☐4 Extremely
☐2 Moderately ☐97 Not answered

- *Include patient's need to seek treatment for such social problems as loneliness, inability to socialize, and dissatisfaction with friends. Patient rating should refer to dissatisfaction, conflicts, or other serious problems. Exclude problems that would be eliminated if patient had no substance abuse.*

Confidence Ratings: Is the above information **significantly** distorted by:

F37 Patient's misrepresentation? ☐0 No ☐1 Yes

F38 Patient's inability to understand? ☐0 No ☐1 Yes

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Psychiatric Status

How many times have you been treated for any psychological or emotional problems?

• Do not include substance abuse, employment, or family counseling. Treatment episode = a series of more or less continuous visits or treatment days, not the number of visits or treatment days. Enter diagnosis in Comments if known.

Comments: _____

P1	**In a hospital or inpatient setting?**	___ ___ **OR** ☐97 Not answered
P2	**As an outpatient or private patient?**	___ ___ **OR** ☐97 Not answered
P3	**Do you receive a pension for a psychiatric disability?**	☐0 No ☐1 Yes ☐97 Not answered

Have you had a significant period of time (that was not a direct result of drug/alcohol use) **in which you have:**

		A Past 30 Days	B Lifetime
P4	**Experienced serious depression—sadness, hopelessness, loss of interest, difficulty with daily function?**	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P5	**Experienced serious anxiety/tension—uptight, unreasonably worried, inability to feel relaxed?**	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P6	**Experienced hallucinations—saw things or heard voices that other people did not hear or see?**	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P7	**Experienced trouble understanding, concentrating, or remembering?**	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
	For questions P8–P10, patient could have been under the influence of alcohol/drugs		
P8	**Experienced trouble controlling violent behavior including episodes of rage, or violence?**	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P9	**Experienced serious thoughts of suicide?** *• Patient seriously considered a plan for taking his/her life.*	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P10	**Attempted suicide?** *• Include actual suicidal gestures or attempts.*	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered
P11	**Been prescribed medication for any psychological/emotional problem?** *• Prescribed for the patient by MD. Record "Yes" if a medication was prescribed **even if** the patient is not taking it.*	☐0 No ☐1 Yes ☐97 Not answered	☐0 No ☐1 Yes ☐97 Not answered

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

ASI-LITE (ASL): Psychiatric Status (continued)

P12 How many days in the past 30 have you experienced these psychological or emotional problems?

- *This refers to problems noted in questions P4–P10.*

___ ___ OR ☐$_{97}$ Not answered

For questions P13–P14, please ask patient to use the Patient Rating Scale.

P13 How much have you been troubled or bothered by these psychological or emotional problems in the past 30 days?

☐$_0$ Not at all
☐$_1$ Slightly
☐$_2$ Moderately
☐$_3$ Considerably
☐$_4$ Extremely
☐$_{97}$ Not answered

P14 How important to you now is treatment for these psychological or emotional problems?

☐$_0$ Not at all
☐$_1$ Slightly
☐$_2$ Moderately
☐$_3$ Considerably
☐$_4$ Extremely
☐$_{97}$ Not answered

- *Include patient's need to seek treatment for such social problems as loneliness, inability to socialize, and dissatisfaction with friends. Patient rating should refer to dissatisfaction, conflicts, or other serious problems. Exclude problems that would be eliminated if patient had no substance abuse.*

Confidence Ratings: Is the above information **significantly** distorted by:

P22 Patient's misrepresentation? ☐$_0$ No ☐$_1$ Yes

P23 Patient's inability to understand? ☐$_0$ No ☐$_1$ Yes

Comments: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

Abbreviated Brief Pain Inventory

Please rate your pain by checking the one number that best describes your pain.

0 = No pain and 10 = Pain as bad as you can imagine *(check only one)*:

		No pain										Pain as bad as you can imagine
1	**Worst pain in last 7 days:**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
2	**Least pain in last 7 days:**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
3	**Average pain in last 7 days:**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
4	**Pain right now:**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10

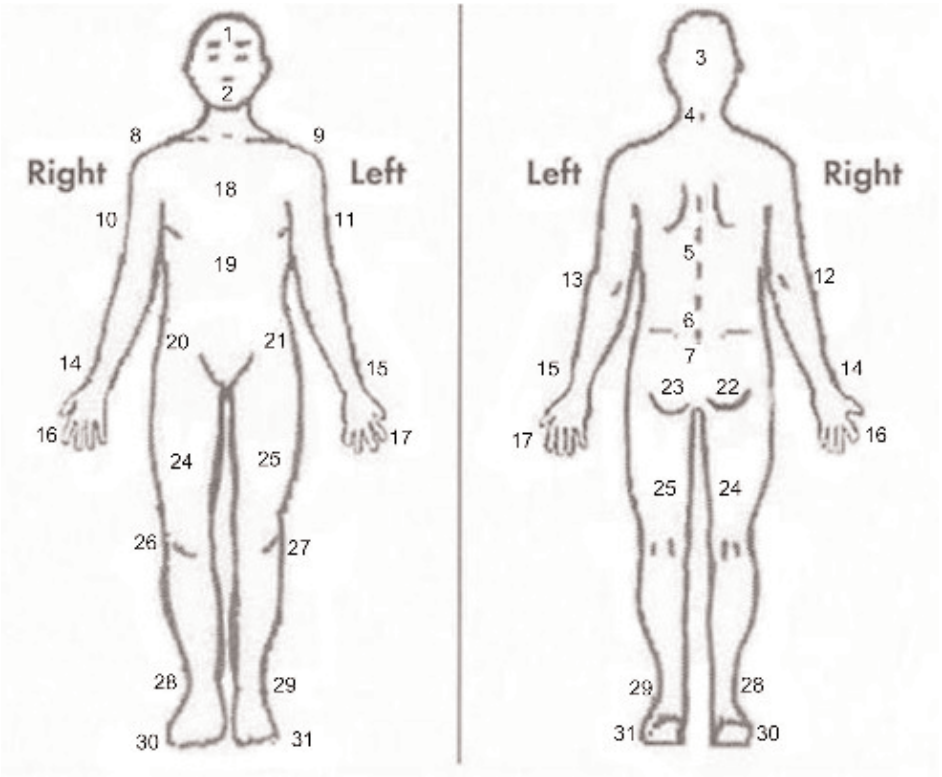
Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Brief Pain Inventory©—Short Form

1 **Throughout our lives, most of us have had pain from time to time** *(such as minor headaches, sprains, and toothaches)***. Have you had pain other than these everyday kinds of pain today?** ☐$_0$ No ☐$_1$ Yes

2a **Please identify and select the number(s) that correspond to the area(s) where you are experiencing pain** *(check all that apply)*:



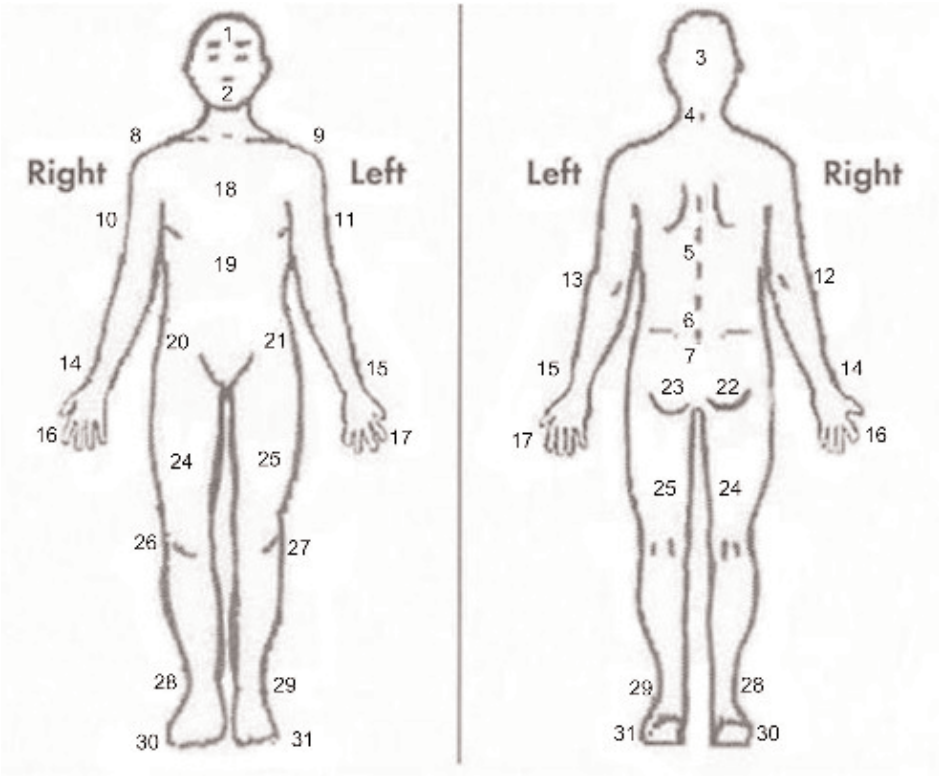
☐$_1$ Upper face
☐$_2$ Lower face
☐$_3$ Head
☐$_4$ Neck *(cervical spine)*
☐$_5$ Middle back *(thoracic)*
☐$_6$ Lower back *(lumbar)*
☐$_7$ Sacrum
☐$_8$ Right shoulder
☐$_9$ Left shoulder
☐$_{10}$ Right arm
☐$_{11}$ Left arm
☐$_{12}$ Right elbow
☐$_{13}$ Left elbow
☐$_{14}$ Right wrist
☐$_{15}$ Left wrist
☐$_{16}$ Right hand
☐$_{17}$ Left hand
☐$_{18}$ Upper trunk *(chest)*
☐$_{19}$ Lower trunk *(chest)*
☐$_{20}$ Right hip
☐$_{21}$ Left hip
☐$_{22}$ Right buttock
☐$_{23}$ Left buttock
☐$_{24}$ Right leg
☐$_{25}$ Left leg
☐$_{26}$ Right knee
☐$_{27}$ Left knee
☐$_{28}$ Right ankle
☐$_{29}$ Left ankle
☐$_{30}$ Right foot
☐$_{31}$ Left foot

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Brief Pain Inventory©—Short Form (continued)

2b Please identify and select the number that corresponds to the area that HURTS the MOST *(check only one)*:



☐ 1 Upper face	☐ 8 Right shoulder	☐ 14 Right wrist	☐ 20 Right hip	☐ 26 Right knee
☐ 2 Lower face	☐ 9 Left shoulder	☐ 15 Left wrist	☐ 21 Left hip	☐ 27 Left knee
☐ 3 Head	☐ 10 Right arm	☐ 16 Right hand	☐ 22 Right buttock	☐ 28 Right ankle
☐ 4 Neck *(cervical spine)*	☐ 11 Left arm	☐ 17 Left hand	☐ 23 Left buttock	☐ 29 Left ankle
☐ 5 Middle back *(thoracic)*	☐ 12 Right elbow	☐ 18 Upper trunk *(chest)*	☐ 24 Right leg	☐ 30 Right foot
☐ 6 Lower back *(lumbar)*	☐ 13 Left elbow	☐ 19 Lower trunk *(chest)*	☐ 25 Left leg	☐ 31 Left foot
☐ 7 Sacrum				

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Brief Pain Inventory©—Short Form (continued)

3 Please rate your pain by marking the box beside the number that best describes your pain at its **worst** in the past 24 hours.

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

No Pain — **Pain As Bad As You Can Imagine**

4 Please rate your pain by marking the box beside the number that best describes your pain at its **least** in the last 24 hours.

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

No Pain — **Pain As Bad As You Can Imagine**

5 Please rate your pain by marking the box beside the number that best describes your pain on the **average**.

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

No Pain — **Pain As Bad As You Can Imagine**

6 Please rate your pain by marking the box beside the number that tells how much pain you have **right now**.

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

No Pain — **Pain As Bad As You Can Imagine**

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Brief Pain Inventory©—Short Form (continued)

8 In the last 24 hours, how much relief have pain treatments or medications provided? Please mark the box below the percentage that most shows how much **relief** you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
No Relief										Complete Relief

9 Mark the box beside the number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

B. Mood

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

C. Walking ability

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

E. Relations with other people

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

F. Sleep

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

G. Enjoyment of life

☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10
Does Not Interfere										Completely Interferes

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History

1 Have you ever used heroin?

☐0 No → **If No: Skip to question 3.**

☐1 Yes

2 In the past 30 days, how many days did you use heroin? _____

2a How many different ways have you EVER used heroin *(check all that apply)***:**

☐ Smoking

☐ Inhaling

☐ Snorting or sniffing

☐ Injection

☐ Some other way → **If Some other way: Specify:** _____

Opiate analgesics are sometimes called painkillers. Some common examples are:

Codeine, Methadone, or Fentanyl, Morphine , dextropropoxyphen, buprenorphine, pentazocine,

Opiate analgesics do not include sedatives or benzodiazepines.

3 In the past 30 days, how many days did you use opiate analgesics? _____

4 In your opinion, what is your biggest opiate problem at present *(check only one)*

☐1 Opiate Analgesics

☐2 Heroin

☐3 Opiate analgesics AND heroin

5 Have you ever been in any kind of treatment for opiate problems?

☐0 No

☐1 Yes → **If Yes: Which ones have you participated in** *(check all that apply)***?**

5a	Medical detoxification:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5b	Methadone maintenance:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5c	Suboxone maintenance:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5d	Naltrexone:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5e	Outpatient - counseling:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5f	Intensive outpatient/ day hospital treatment:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5g	Inpatient/residential treatment:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5h	AA/NA or other self-help groups:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____
5i	Other medications for addictions *(specify below)*:	☐0 No	☐1 Yes →	**If Yes: How many different times?** _____

Specify other medications: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

The remainder of the interview will be ONLY about opiate analgesics, NOT heroin or any other drug.

6 What are the different ways you have ever used opiate analgesics:

- ☐ Swallowing
- ☐ Chewing
- ☐ Smoking
- ☐ Inhaling
- ☐ Snorting or sniffing
- ☐ Injection
- ☐ Sublingually *(under the tongue)*
- ☐ Wearing a patch
- ☐ Lollipop *(method for administering analgesics)*
- ☐ Some other way → **If Some other way: Specify:** _____

7 How helpful do you feel that the buprenorphine will be in helping you change your opiate analgesic use behavior?

☐ Not at all ☐ Slightly ☐ Moderately ☐ Considerably ☐ Extremely

8 How helpful do you feel that the counseling will be in helping you change your opiate analgesic use behavior?

☐ Not at all ☐ Slightly ☐ Moderately ☐ Considerably ☐ Extremely

9 What GOAL have you chosen for yourself about using opiate analgesics at this time?
(Please pick only one of the following that best describes your goal)

- ☐ I really don't have a clear goal in mind.
- ☐ I would like to use opiate analgesics *(only when I am in physical pain)*.
- ☐ I want to use opiate analgesics in a controlled manner – to be in control of how often I use and how much I use.
- ☐ I want to be totally abstinent from opiate analgesics for a period of time, after which I will make a new decision about whether or not I will use opiate analgesics again in any way.
- ☐ I want to quit using opiate analgesics once and for all, even though I realize I may slip up and use opiate analgesics once in a while.
- ☐ I want to quit using opiate analgesics once and for all, to be totally abstinent, and never use opiate analgesics ever again for the rest of my life.
- ☐ None of the above applies exactly to me.

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

10 What opiate analgesic have you used the MOST in the past 30 days *(check only one)***?**

- ☐ Meperidine
- ☐ Methadone
- ☐ Morphine
- ☐ Propoxyphene
- ☐ Buprenorphine
- ☐ Codeine
- ☐ Fentanyl
- ☐ Tramadol
- ☐ Pentazocine
- ☐ Dextropopoxyphen
- ☐ Don't know

☐ 98 Other → **If Other: Specify:** _____

11 What OTHER prescription opiate analgesics have you used in the past 30 days *(check all that apply)***?**

- ☐ Meperidine
- ☐ Methadone
- ☐ Morphine
- ☐ Propoxyphene
- ☐ Buprenorphine
- ☐ Codeine
- ☐ Fentanyl
- ☐ Tramadol
- ☐ Pentazocine
- ☐ Dextropopoxyphen
- ☐ Don't know

☐ Other → **If Other: Specify:** _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

12 How long have you been using opiate analgesics for purposes other than relief of occasional short term pain (check only one)**?**

- ☐ 1 Less than 6 months
- ☐ 2 6 months to less than 1 year
- ☐ 3 1 year to less than 2 years
- ☐ 4 2 years to less than 4 years
- ☐ 5 4 years to less than 6 years
- ☐ 6 6 years to less than 10 years
- ☐ 7 More than 10 years

13 Please think back to when you first started to have a problem with taking more opiate analgesics than prescribed or misusing opiate analgesics. What was your first source of opiate analgesics (check only one)**?**

- ☐ 1 Prescription from a doctor for actual pain or a legitimate medical reason
- ☐ 2 Prescription from a doctor although I had no legitimate medical reason
- ☐ 3 Prescriptions from multiple doctors *(from several doctors or emergency services)*
- ☐ 4 Prescription from a doctor who prescribes illegally
- ☐ 5 Prescription forgery *(writing or buying fake prescriptions)*
- ☐ 6 Bought from a dealer
- ☐ 7 Bought from a patient who sells their medications
- ☐ 8 Bought from a family member or friend who sells their medications
- ☐ 9 Internet
- ☐ 10 Someone gave them to me
- ☐ 11 Stolen/taken from someone who won't miss a couple of pills
- ☐ 12 Stolen from work *(hospital, nursing home, clinic, pharmacy, etc.)*
- ☐ 13 Stolen from stranger, store, or some other source
- ☐ 98 From medicine shop, without prescription

14 What was the major reason you first used opiate analgesics (check only one)**?**

- ☐ 1 To relieve physical pain → **Ask question 15 next.**
- ☐ 2 To get high/for euphoria
- ☐ 3 To improve sleep
- ☐ 4 To relieve depressed, sad feelings
- ☐ 5 To relieve nervousness, anxiety
- ☐ 6 To deal with bad memories

→ **Skip to question 16.**

- ☐ 98 Other → **Specify:** _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

15 What is the major reason you continue to take opiate analgesics (check only one)**?**

- ☐ 1 To relieve physical pain
- ☐ 2 To get high/for euphoria
- ☐ 3 To improve sleep
- ☐ 4 To relieve depressed, sad feelings
- ☐ 5 To relieve nervousness, anxiety
- ☐ 6 To deal with bad memories
- ☐ 7 To avoid withdrawal
- ☐ 98 Other → **If Other: Specify:** _____

16 The following questions are a list of reasons why people may use opiate analgesics. Please rate these on how important each reason was for you in the past six months. Zero (0) means the reason was not at all important for you, and ten (10) means that the reason was very important for you. Please circle one number on the scale for each reason below.

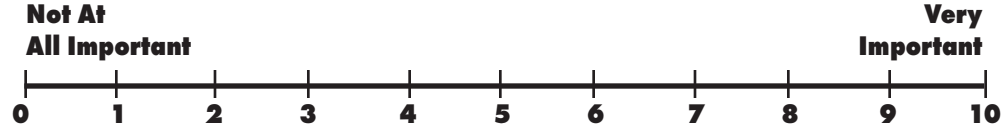
16a I felt angry or frustrated, either with myself or because things were not going my way:

16b I felt bored:

16c I felt anxious or tense:

16d When I saw opiate analgesics I just had to give in:

16e I felt sad:



Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

16f I felt ill or in pain or uncomfortable because I wanted opiate analgesics:

16g I was in a good mood and felt like getting high:

16h I wanted to see what would happen if I tried opiate analgesics one time:

16i I just felt tempted to use out of the blue and used:

16j Someone offered me opiate analgesics:

16k I felt angry or frustrated because of my relationship with someone else:

16l I was with others having a good time and we felt like getting high together:

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

16m I felt worried or tense about my relationship with someone else:

16n I felt ill or in pain or uncomfortable but this was NOT due to withdrawal from opiate analgesic:

16o I felt others were being critical of me:

16p I saw others using:

16q Other reason: Specify other reason: _____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

17 In the past six months, have you obtained opiate analgesics from the following sources?

	Never	Rarely	Some-times	Frequently	Most of the Time	Always
Prescription from a doctor for actual pain or a legitimate medical reason	☐	☐	☐	☐	☐	☐
Prescription from a doctor although I had no legitimate medical reason	☐	☐	☐	☐	☐	☐
Prescriptions from multiple doctors *(from several doctors or emergency services)*	☐	☐	☐	☐	☐	☐
Prescription from a doctor who prescribes illegally	☐	☐	☐	☐	☐	☐
Prescription forgery *(writing or buying fake prescriptions)*	☐	☐	☐	☐	☐	☐
Bought from a dealer	☐	☐	☐	☐	☐	☐
Bought from a patient who sells their medications	☐	☐	☐	☐	☐	☐
Internet	☐	☐	☐	☐	☐	☐
Someone gave them to me	☐	☐	☐	☐	☐	☐
Stolen/taken from someone who won't miss a couple of pills	☐	☐	☐	☐	☐	☐
Stolen from work *(hospital, nursing home, clinic, pharmacy, etc.)*	☐	☐	☐	☐	☐	☐
Stolen from stranger, store, or some other source	☐	☐	☐	☐	☐	☐
From Medicine shop, without prescription	☐	☐	☐	☐	☐	☐

18 How important, at this time, are the following reasons for why you are seeking treatment for opioid dependence?

	Not At All Important	Somewhat Important	Important	Very Important	Extremely Important
Don't like being dependent/withdrawal	☐	☐	☐	☐	☐
Physical side effects annoying	☐	☐	☐	☐	☐
Can't control my use of the meds	☐	☐	☐	☐	☐
The medications are controlling my life	☐	☐	☐	☐	☐
My physician wants me to stop	☐	☐	☐	☐	☐
Too much trouble getting the medications	☐	☐	☐	☐	☐
Family or friends want me to stop	☐	☐	☐	☐	☐
I've had legal problems	☐	☐	☐	☐	☐
I'm afraid of encountering legal problems	☐	☐	☐	☐	☐
I'm afraid of the long-term medical dangers	☐	☐	☐	☐	☐
Other *(specify)*: _____	☐	☐	☐	☐	☐

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

Pain:

19 Throughout our lives, most of us have had pain from time to time *(such as minor headaches, sprains, and toothaches)***. Have you had pain other than these everyday kinds of pain today?**

☐0 No → **If No: End the interview now**

☐1 Yes

20 How long have you been experiencing this pain *(check only one)***?**

☐1 Less than 1 month
☐2 1 month to less than 3 months
☐3 3 months to less than 6 months
☐4 6 months to less than 12 months
☐5 1 year to less than 2 years
☐6 2 years to less than 4 years
☐7 4 years or greater

21 How would you characterize your pain *(check only one)***?**

☐1 Constant/always there

☐2 Intermittent/comes and goes

22 Please indicate the level of your pain for each word, or not applicable if this does not apply to you:

	Mild	Moderate	Severe	Not Applicable
Throbbing	☐	☐	☐	☐
Shooting	☐	☐	☐	☐
Stabbing	☐	☐	☐	☐
Sharp	☐	☐	☐	☐
Cramping	☐	☐	☐	☐
Gnawing	☐	☐	☐	☐
Hot-burning	☐	☐	☐	☐
Aching	☐	☐	☐	☐
Heavy	☐	☐	☐	☐
Tender	☐	☐	☐	☐
Splitting	☐	☐	☐	☐
Tiring—exhausting	☐	☐	☐	☐
Sickening	☐	☐	☐	☐
Fearful	☐	☐	☐	☐
Cruel–punishing	☐	☐	☐	☐

23 What is the likelihood that your pain will improve during this treatment *(check only one)***?**

☐1 Not at all
☐2 Very low
☐3 Low
☐4 Moderate
☐5 High
☐6 Very high

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Pain and Opiate Analgesic Use History (continued)

Pain *(continued)*:

24 What pain interventions have you tried *(check all that apply)*?

- ☐ Organized pain program
- ☐ Injections
- ☐ Surgery
- ☐ Opiate analgesics *(If opiate analgesics, continue to question 25)*
- ☐ Biofeedback
- ☐ Other pain medicines *(NSAIDS, etc.)*
- ☐ Hypnosis training
- ☐ Physical therapy
- ☐ Acupuncture
- ☐ Hydro or water therapy
- ☐ TENS (Transcutaneous electrical nerve stimulation)
- ☐ Holistic health care *(herbs, yoga)*
- ☐ Psychosocial treatment/Psychotherapy *(group or individual)*
- ☐ Spinal cord stimulator
- ☐ Morphine pump
- ☐ Other → **If Other: Specify:** _____

25 Which opiate analgesic(s) did you receive for your <u>first</u> opiate analgesic treatment of pain *(check all that apply)*?

- ☐ Meperidine
- ☐ Methadone
- ☐ Propoxyphene
- ☐ Buprenorphine
- ☐ Codeine
- ☐ Morphine
- ☐ Fentanyl
- ☐ Tramadol
- ☐ Pentazocine
- ☐ Dextropopoxyphen
- ☐ Don't know
- ☐ Other → **If Other: Specify:** _____

Date of Assessment: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

SF-36 (Your Health and Well-Being)

Instructions: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for your completing this survey!
For each of the following questions, please mark an "X" in the one box that best describes your answer.

1 In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐1	☐2	☐3	☐4	☐5

2 Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐1	☐2	☐3	☐4	☐5

3 The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, Not limited at all
a Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐1	☐2	☐3
b Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐1	☐2	☐3
c Lifting or carrying groceries	☐1	☐2	☐3
d Climbing several flights of stairs	☐1	☐2	☐3
e Climbing one flight of stairs	☐1	☐2	☐3
f Bending, kneeling, or stooping	☐1	☐2	☐3
g Walking more than a mile	☐1	☐2	☐3
h Walking several hundred yards	☐1	☐2	☐3
i Walking one hundred yards	☐1	☐2	☐3
j Bathing or dressing yourself	☐1	☐2	☐3

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

SF-36 (Your Health and Well-Being) (continued)

4 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the **amount of time** you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b **Accomplish less** than you would like	☐1	☐2	☐3	☐4	☐5
c Were limited in the **kind** of work or other activities	☐1	☐2	☐3	☐4	☐5
d Had **difficulty** performing the work or other activities *(for example, it took extra effort)*	☐1	☐2	☐3	☐4	☐5

5 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems *(such as feeling depressed or anxious)*?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the **amount of time** you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b **Accomplish less** than you would like	☐1	☐2	☐3	☐4	☐5
c Did work or other activities **less carefully than usual**	☐1	☐2	☐3	☐4	☐5

6 During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐1	☐2	☐3	☐4	☐5

7 How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
☐1	☐2	☐3	☐4	☐5	☐6

Date of Assessment: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

SF-36 (Your Health and Well-Being) (continued)

8 **During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work** *(including both work outside the home and housework)***?**

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐1	☐2	☐3	☐4	☐5

9 **These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>...**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Did you feel full of life**?**	☐1	☐2	☐3	☐4	☐5
b Have you been very nervous**?**	☐1	☐2	☐3	☐4	☐5
c Have you felt so down in the dumps that nothing could cheer you up**?**	☐1	☐2	☐3	☐4	☐5
d Have you felt calm and peaceful**?**	☐1	☐2	☐3	☐4	☐5
e Did you have a lot of energy**?**	☐1	☐2	☐3	☐4	☐5
f Have you felt downhearted and depressed**?**	☐1	☐2	☐3	☐4	☐5
g Did you feel worn out**?**	☐1	☐2	☐3	☐4	☐5
h Have you been happy**?**	☐1	☐2	☐3	☐4	☐5
i Did you feel tired**?**	☐1	☐2	☐3	☐4	☐5

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

SF-36 (Your Health and Well-Being) (continued)

10 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.)*?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐1	☐2	☐3	☐4	☐5

11 How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a I seem to get sick a little easier than other people	☐1	☐2	☐3	☐4	☐5
b I am as healthy as anybody I know	☐1	☐2	☐3	☐4	☐5
c I expect my health to get worse	☐1	☐2	☐3	☐4	☐5
d My health is excellent	☐1	☐2	☐3	☐4	☐5

CAGE Questionnairer

ID

1 Have you ever felt you should **C**ut down on your drinking?

1 Yes
2 No

2 Have people **A**nnoyed you by criticising your drinking?

1 Yes
2 No

3 Hve you ever felt bad or **G**uilty about drinking?

1 Yes
2 No

4 Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (**E**ye-opener)?

1 Yes
2 No

Date of Assessment: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
day *month* *year*

Participant ID #: ___ ___ ___ ___

Is the participant a smoker?

☐ 0 No

☐ 1 Yes → **If Yes: Please have the participant complete the Fagerström (FTND) Assessment.**

Fagerström Test for Nicotine Dependence (FTND)

Please read each question below. For each question enter the answer choice which best describes your responses.

1 **How soon after you wake do you smoke your first cigarette** *(check only one)***?**

☐ 1 Within 5 minutes
☐ 2 Within 6 - 30 minutes
☐ 3 Within 31 - 60 minutes
☐ 4 After 60 minutes

2 **Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, at the movies, etc.** *(check only one)***?**

☐ 0 No
☐ 1 Yes

3 **Which cigarette would you hate most to give up** *(check only one)***?**

☐ 1 The first one in the morning
☐ 2 All others

4 **How many cigarettes per day do you smoke** *(check only one)***?**

☐ 1 10 or less
☐ 2 11-20
☐ 3 21-30
☐ 4 31 or more

5 **Do you smoke more frequently during the first hours after waking than during the rest of the day** *(check only one)***?**

☐ 0 No
☐ 1 Yes

6 **Do you smoke if you are so ill that you are in bed most of the day** *(check only one)***?**

☐ 0 No
☐ 1 Yes

Date of Assessment: __ __ /__ __ __ /__ __ __ __
day month year

Participant ID #: __ __ __ __

Risk Behavior Survey (RBS)

Interviewer: The RBS contains sensitive information on drug use and sexual behavior. Please ensure that you have developed rapport with the participant before asking these questions.

A Drug Use

I'm going to ask you some questions about your drug use. I'll ask what types of drugs you've used and how often you use them.	a				b	c	d	e	f
	Have you ever used? *(If no use, skip to next drug)*				How many days did you use ____ in the last 30 days? *(If 00, do not ask parts c–f, and skip to next drug)*	How many days did you inject ____ in the last 30 days? *(If 00, skip to part e)*	How many times a day did you inject _____ ? *(Average # of injections/day)*	How many days did you use _____ without injecting *(smoking, snorting, swallowing)* in the last 30 days? *(If 00, then skip to next drug class)*	How many times a day did you use _____ without injecting?
	No	Yes	Unk	Ref					
1 Cocaine by itself *(injected or snorted)*:	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____
2 Heroin by itself:	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____
3 Heroin and cocaine mixed together *(Speedball)*:	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____
4 Other opiates	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____
5 Amphetamines *(Speed, Methamphetamine, Crank)*:	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____
6 Benzodiazepines (nitrazepam)	0	1	9	7	____ ____	____ ____	____ ____	____ ____	____ ____

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Risk Behaviors Survey (RBS) (continued)

B Drug Injection *(If no injection use in past 30 days, skip to Section C)*

1 **In the last 30 days, how many times** *(number of injections)* **did you inject using works** *(needle/syringes)* **that you know had been used by somebody else?** ..... ___ ___ ___

(If 000, then skip to B3)

2 **Of the times you injected after someone, how many times did you clean the works with full-strength bleach?** ___ ___ ___

(Number cannot exceed total number of times used after a friend [question B1])

3 **How many times in the last 30 days did you use a cooker/cotton/rinse water that had been used by another injector?** ..... ___ ___ ___

4 **How many times in the last 30 days did you fix drugs with another person, then split the drug solution** *(through use of the same cooker/spoon or through front or back loading)***?** ..... ___ ___ ___

C Sexual Activity

Now I'm going to ask you some questions about sex. I'm referring here to anybody you've had sex with in the last 30 days.

1 **During the last 30 days, with how many people did you have vaginal, oral, or anal sex?** ..... ___ ___ ___

(If none, enter 000, and the questionnaire is completed)

2 **How many of your partners were female?** ..... ___ ___ ___

(Number cannot exceed total number of people [question C1])

3 **How many of your partners were male?** ..... ___ ___ ___

(Number cannot exceed total number of people [question C1])

4 **Interviewer: Code gender of respondent:**
- ☐ 1 Male → **If male, complete sections D, E, F, G, and I**
- ☐ 2 Female → **If female, complete sections D, G, H, and I**
- ☐ 9 Don't know → **If Don't Know, ask ALL sex/gender specific questions and allow client to answer as they like**

D Ask Male/Female Clients who had Female Partners

1a **How many women performed oral sex** *("went down")* **on you?** ..... ___ ___ ___

(If 000, then skip to question 2a. Number cannot exceed total number of female partners [question C2])

1b **How often did your partner(s) perform oral sex** *("go down")* **on you** *(check only one)***?**

☐ 1 Once or irregularly ☐ 2 Less than once a week ☐ 3 About once a week ☐ 4 2–6 times a week ☐ 5 About once a day
☐ 6 2–3 times a day ☐ 7 4 or more times a day ☐ 99 Don't know/unsure ☐ 77 Refused

1c **How often did you use condoms/dental dams when your partner(s) performed oral sex** *("went down")* **on you** *(check only one)***?**

☐ 0 Never ☐ 1 Less than half the time ☐ 2 About half the time ☐ 3 More than half the time
☐ 4 Always ☐ 9 Don't know/unsure ☐ 7 Refused

2a **How many women did you perform oral sex** *("go down")* **on?** ..... ___ ___ ___

(If 000, then skip to next section appropriate for the sex of this client. Number cannot exceed total number of female partners [question C2])

2b **How often did you perform oral sex** *("go down")* **on your partner(s)** *(check only one)***?**

☐ 1 Once or irregularly ☐ 2 Less than once a week ☐ 3 About once a week ☐ 4 2–6 times a week ☐ 5 About once a day
☐ 6 2–3 times a day ☐ 7 4 or more times a day ☐ 99 Don't know/unsure ☐ 77 Refused

2c **How often did you use condoms/dental dams when you performed oral sex** *("went down")* **on your partner(s)** *(check only one)***?**

☐ 0 Never ☐ 1 Less than half the time ☐ 2 About half the time ☐ 3 More than half the time
☐ 4 Always ☐ 9 Don't know/unsure ☐ 7 Refused

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Risk Behaviors Survey (RBS) (continued)

E Ask Male Clients who had Female Partners:

1a How many women have you had vaginal sex with? ..... ___ ___ ___

(If 000, then skip to question 2a. Number cannot exceed total number of female partners [question C2])

1b How often did you have vaginal sex *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

1c How often did you use a condom *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

2a How many women did you have *(insertive)* **anal sex with?** ..... ___ ___ ___

(If 000, then skip to next section appropriate for the sex of this client. Number cannot exceed total number of female partners [question C2])

2b How often did you have *(insertive)* **anal sex** *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

2c How often did you use a condom *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

F Ask Male Clients who had Male Partners:

1a How many men did you have *(insertive)* **anal sex with?** ..... ___ ___ ___

(If 000, then skip to next section appropriate for the sex of this client. Number cannot exceed total number of male partners [question C3])

1b How often did you have *(insertive)* **anal sex** *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

1c How often did you use a condom *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

G Ask Male/Female Clients who had Male Partners

1a How many men performed oral sex *("went down")* **on you?** ..... ___ ___ ___

(If 000, then skip to question 2a. Number cannot exceed total number of male partners [question C3])

1b How often did your partner(s) perform oral sex *("go down")* **on you** *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

1c How often did you use condoms/dental dams when your partner(s) performed oral sex *("went down")* **on you** *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐99 Don't know/unsure ☐77 Refused

Date of Assessment: ___ ___ /___ ___ ___ /___ ___ ___ ___
day month year

Participant ID #: ___ ___ ___ ___

Risk Behaviors Survey (RBS) (continued)

G Ask Male/Female Clients who had Male Partners *(continued)*

2a How many men did you perform oral sex *("go down")* **on?** ..... ___ ___ ___

(If 000, then skip to next section appropriate for the sex of this client. Number cannot exceed total number of male partners [question C3])

2b How often did you perform oral sex *("go down")* **on your partner(s)** *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

2c How often did you use condoms/dental dams when you performed oral sex *("went down")* **on your partner(s)** *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

H Ask Female Clients who had Male Partners

1a How many men have you had vaginal sex with? ..... ___ ___ ___

(If 000, then skip to next question appropriate for the sex of this client. Number cannot exceed total number of male partners [question C3])

1b How often did you have vaginal sex *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

1c How often did you use a condom *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

I Ask Male/Female Clients who had Male Partners

1a How many men did you have *(receptive)* **anal sex with?**..... ___ ___ ___

(If 000, end questionnaire. Number cannot exceed total number of male partners [question C3])

1b How often did you have *(receptive)* **anal sex** *(check only one)***?**

☐1 Once or irregularly ☐2 Less than once a week ☐3 About once a week ☐4 2–6 times a week ☐5 About once a day
☐6 2–3 times a day ☐7 4 or more times a day ☐99 Don't know/unsure ☐77 Refused

1c How often did you use a condom *(check only one)***?**

☐0 Never ☐1 Less than half the time ☐2 About half the time ☐3 More than half the time
☐4 Always ☐9 Don't know/unsure ☐7 Refused

ANNEXURE *3*

IEC & RPEC CERTIFICATES

SMU
Sikkim Manipal University
Sikkim Manipal Institute of Medical Sciences

Sikkim Manipal Institute of Medical Sciences
5th Mile, Tadong, Gangtok - 737102, Sikkim, India
Ph : +91-3592-270535 ♦ Fax : + 91-3592-231496
E-mail : smims_dean@yahoo.com ♦ Website : www.smuhmts.edu

Communication of Decision of the Institution Ethics Committee (IEC)

IEC No: SMIMS/IEC/2011-PhD-3

Protocol title: Epidemiology of prescription opioid abuse in Sikkim
Principal Investigator: Mr. Debranjan Datta
Name & Address of Institution: Sikkim Manipal Institute of Medical Sciences, 5th Mile, Tadong, Gangtok, Sikkim – 737 102
☑ New review ☐ Revised review ☐ Expedited review
Date of review (D/M/Y): 30/05/2011 Date of previous review, if revised application: NA
Decision of the IEC: ☑ Recommended ☐ Recommended with suggestions ☐ Revision ☐ Rejected
Suggestions/ Reasons/ Remarks: 1. Reliability and validity analysis of instruments should be carried out.
Recommended for a period of : One (1) year from date of approval

Please note *

- **Inform IEC immediately in case of any Adverse events and Serious adverse events**
- **Inform IEC in case of any change of study procedure, site and investigator**
- **This permission is only for period mentioned above. Annual report to be submitted to IEC**
- **Members of IEC have right to monitor the trial with prior intimation**

Signature of Chairperson, IEC

Proforma as prescribed by ICMR

SMU
Sikkim Manipal University
Sikkim Manipal Institute of Medical Sciences

Sikkim Manipal Institute of Medical Sciences
5th Mile, Tadong, Gangtok - 737102, Sikkim, India
Ph : +91-3592-270535 ♦ Fax : + 91-3592-231496
E-mail : smims@smu.edu.in ♦ Website : www.smu.edu.in

SMIMS RESEARCH PROTOCOL EVALUATION COMMITTEE

Ref No: SMIMS/RPEC/2014-70 **Dated:** 28th July 2014.

SMIMS RPEC Registration No: RPEC/090/14-44.
Protocol Title: Epidemiology of prescription opioid abuse in Sikkim
Principal Investigator: Mr. Debranjan Datta, Lecturer – Pharmacology.
Name & Address of the Institution: Sikkim Manipal Institute of Medical Sciences, 5th Mile, Tadong, Gangtok, Sikkim – 737102.
Date of Review: 19.07.2014 **Date of Previous Review, if revised application:** NA
Decision of the RPEC: [✓] Recommended [×] Recommended with suggestions [×] Revision [×] Rejected
Suggestion / Reasons / Remarks: PhD pre-synopsis report
Recommended for a period of: One Year.

Please note:

1. Inform RPEC immediately in case of any adverse events.
2. Inform RPEC the change of any study procedures, site and investigator.
3. This permission is only for the period mentioned above. Half-yearly report should be submitted to RPEC.
4. Members of RPEC have right to monitor the trial with prior intimation.

Dr. T Shanti Kumar Singh,
Professor & Head – Microbiology &
Member Secretary – SMIMS RPEC.

Dr. T.S.K. Singh
Professor & HOD
Deptt. of Microbiology
SMIMS

ANNEXURE 4

LIST OF PAPERS PUBLISHED ON THE BASIS OF THESIS

PAPERS IN JOURNALS

1. Datta Debranjan, Pandey Sunil. Socio-demographic characteristics of prescription opioid abusers from various treatment centres in Sikkim: A cross-sectional study. Annals of Biological Research, 2014, 5 (5):85-88.
2. Sunil Pandey, Debranjan Datta. Socio-economic and demographic characteristics of alcohol and other substance abusers, undergoing treatment in Sikkim, a north east state of India. Archives of Applied Science Research, 2014, 6 (2):106-110.
3. Sunil Kumar Pandey, Debranjan Datta, Sanjiba Dutta, Yogesh Verma, and Amit Chakrabarti. Socioeconomic characteristics of alcohol and other substance users, seeking treatment in Sikkim, North East India. J Pharm Bioallied Sci. 2015 Apr-Jun; 7(2): 151–155.
4. Debranjan Datta, Sunil Pandey, Sanjiba Dutta, Yogesh Verma, and Amit Chakrabarti. Descriptive epidemiology and high risk behaviour of prescription opioid abusers: Cross-sectional study from Sikkim, North East India. Indian Journal of Psychiatry 57(3), Jul-Sep 2015

PRESENTATION IN CONFERENCE:

1. Presented (oral presentation) “Socio-demographic correlates and sexual practices among prescription opioid abusers in rural and urban Sikkim” at 1st Epidemiological research for advanced nursing practice –a global health scenario” on Pondicherry Institute of Medical Sciences, Puducherry, dated 26-27 July, 2013.

ANNEXURE 5

PROFILE OF RESEARCH SCHOLAR

Debranjan Datta

Debranjan Datta did his post graduation in medical pharmacology (MSc medical) from Kasturba medical college, Manipal, Karnataka, India in 2006 and graduated in Pharmacy from Rajiv Gandhi University of health Sciences, Bangalore, Karnataka, India in 2001. He also completed post graduate diploma in Clinical Research and Regulatory Affairs from Sikkim Manipal University (DDE) in 2014. He is currently working as lecturer of pharmacology at Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim. He has three conference presentations and five publications in indexed national and international journals. He accomplished Indo-US Training in Chronic Non-Communicable Disorders & Diseases Across The Lifespan"- organised by Fogarty international centre, University of Florida at Gangtok, Sikkim. His area of interest are substance abuse and regulatory affairs. He can be reached at debranjandatta@gmail.com.

ANNEXURE 6

PROFILE OF RESEARCH GUIDE

Dr. Amit Chakrabarti

Dr. Amit Chakrabarti, is currently working as Scientist E (Deputy Director – Medical) at Regional Occupational Health Centre, Eastern; National Institute of Occupational Health, Indian Council of Medical Research, India. Prior to this, Dr. Amit Chakrabarti, worked in the Department of Pharmacology, Sikkim Manipal Institute of Medical Sciences, Gangtok from 2000 to 2013. He worked as visiting faculty at the Division of Behavioral Neuroscience, Department of Psychology, Arizona State University, Tempe, USA and at the Institute of Reproductive and Developmental Biology, Imperial College London, Hammersmith Campus, London, UK. He was also associated with Harvard Medical School, Boston & McLean Hospital, Belmont, USA as Research Fellow; Fulbright / Hubert H. Humphrey Fellow at Bloomberg School of Public Health, Johns Hopkins University and as Special Volunteer, National Institutes of Health (NIH) at the Intramural Research Program, National Institute on Drug Abuse, Johns Hopkins Bay view Medical Center, Baltimore, USA; INVEST Fellow at the Division of Alcohol and Drug Abuse, McLean Hospital, Belmont, USA. He completed his MD Pharmacology from Institute of Medical Sciences, Banaras Hindu University, India. He has varied experience in clinical research. His area of research interest is substance abuse. He participated in a number of international and national conference sessions. He has conducted quite a number of seminars, workshops and training programs in above areas and published 33 papers in various indexed national and international journals and 9 papers in books and proceedings. He is a member of National Academy of Medical Sciences, India, International Brain Research Organization, Indian Pharmacological Society, Association of Physiologists and Pharmacologists of India, Association of Indian Humphrey Fellows and International Harm Reduction Association. He can be reached at amitc@icmr.org.in or amitchakrabarti@hotmail.com.

ANNEXURE 7

PROFILE OF COGUIDES

Dr. Yogesh Verma

Dr. Yogesh Verma, MD Pathology, is currently working as Principal Chief Consultant and Medical Superintendent, S.T.N.M Hospital, Gangtok. He is also serving as chairman of state medical board and director of the State Blood Transfusion Council. He is a member of institutional ethics committee of Sikkim Manipal Institute of medical sciences and Sikkim University. Dr. Verma was associated with Integrated Counselling and Testing Centres for HIV in the State of Sikkim and also with state HIV Sentinel Surveillance since 1998. He participated in a number of international and national conference sessions. He has conducted quite a number of workshops and training programs and published numerous papers in various indexed national and international journals. He was awarded by several fellowship for his contribution to research in cancer epidemiology. He can be reached at yogeshverma58@gmail.com.

Dr. Sanjiba Dutta

Dr. Sanjiba Dutta is currently working as Professor and Head of the department of psychiatry at Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim. He has a more 18 years of teaching & research experience. He is also holding positions as member of Sikkim State Mental Health Authority, member of journal committee of Eastern Journal of Psychiatry and executive council member of Indian Psychiatric Society, Eastern Zonal Branch. Dr. Dutta has various research publications on substance abuse in indexed national and international journals. He has more than 10 paper presentations in several conferences. He also chaired several sessions in various zonal as well as national seminars and conferences. He can be reached at sanjibadutta@rediffmail.com

ANNEXURE 8

RESEARCH PROGRESS COMMITTEE MEMBERS

Research Progress Committee Members

1. Prof. (Dr.) Amit Chakrabarti

   MD Pharmacology, DNB, MNAMS

   Scientist "E" (Deputy Director – Medical),
   Regional Occupational Health Centre (ROHC), Eastern,
   National Institute of Occupational Health (NIOH),
   Indian Council of Medical Research (ICMR), Kolkata,

2. Prof. (Dr.) K.C Swain

   MD Pharmacology, FCGP(I), FRSH(London)

   Ex- Prof and Prof. Emeritus,
   Pharmacology, Sikkim Manipal Institute of Medical Sciences,
   Gangtok.

3. Prof. Dr. Sanjiba Dutta

   MD Psychiatry

   Prof. and HoD, Department of Psychiatry,
   Sikkim Manipal Institute of Medical Sciences,
   Gangtok.

4. Prof (Dr.) Yogesh Verma

   MD Pathology

   Medical Superintendent, STNM Hospital,
   Prof. Department of Pathology,
   Sikkim Manipal Institute of Medical Sciences,
   Gangtok.