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 \cite{58} in 1968 which has a cutoff score from 2 to 1. A cutoff $\geq 2$ 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 $\alpha$ value of 0.05 (by repeating test 100 times, at least 95 times we will get same 15% difference) and a power ($1-\beta$) 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.