DETERMINATION OF AN OVERCONSUMPTION 'S THRESHOLD FOR THE EVALUATION OF ABUSE AND DEPENDENCE POTENTIAL OF DRUGS

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Non-medical use of some medications like tranquilizers, hypnotics carries risks including development of abuse/dependence. The purpose of this study was to combine two different statistical approaches to help identifying, for a given treatment, abuse and/or dependence behaviours which are characterized by the patient's compelling search of the drug. The objective was to determine a threshold defining two groups of patients (over and normal consumption groups) and to investigate the demographic and clinical characteristics associated with the risk of over consumption of drugs. The criterion often employed to characterize the use of a drug is the ratio between the daily average consumption of the patient and the recommended daily dose as specified in the drug monograph, called F Factor. In theory, any patient having an F Factor> 1 is classified in the over consuming group; but in practice this threshold might not be very relevant.
Firstly, the threshold over which a patient, for a given drug, can be regarded as having a pathological or extreme behaviour is obtained using extreme value theory and more specifically Peaks Over Threshold (POT) Model. Then, in order to depict and identify predictors of abuse and /or dependence, a logistic regression model is constructed using a stepwise procedure to select important covariates. Lastly, the model performance is assessed by considering both calibration and discrimination with the ROC Curve. The combination of several statistical methods (POT model, logistic regression, ROC curve) is innovative in this domain of application, pharmacoepidemiology.
This procedure is applied to 2 different drugs (an antidepressant drug, tianeptime Stablon® and an hypnotic, zolpidem), in the population insured by the General Health Insurance Scheme in the Countries of the Loire in France having had at least 1 delivery of the drug studied between the 01/07/2005 and the 31/12/2005.

Keywords: extreme value theory, POT model, logistic regression, ROC curve, dependence, misuse, evaluation.