

**TITLE OF THE PROJECT: Depression and addiction**

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**SUMMARY****Background**

Major depression is one of the leading causes of disability worldwide and often co-occurs with substance use disorders. This comorbidity is associated with poorer outcomes for both conditions but potential mechanisms are not fully understood and may vary by type of substance used and differ in effects across subgroups of the population (e.g., sex, age and SES). Data are especially lacking for cannabis and, whatever the substance, for older adults. Like the other projects of the DEDALE research consortium, the present project will encompass both a cross-sectional and a longitudinal approach. Given the rapid aging of the French population, specific attention will also be paid to late-life depression.

**Objectives**

The specific aims of this project are:

1. To describe the prevalence of consumption of alcohol, tobacco and cannabis associated with depressive states in France according to gender, age and SES.
2. To examine simultaneously whether sex, age and SES disparities in the prevalence or effects of alcohol, tobacco and cannabis consumption contribute respectively to sex, age and SES differences in the prevalence of depressive states.
3. To determine the specificity of effects of each drug on depressive states.
4. To disentangle the causal relationships between consumption of alcohol, tobacco and cannabis and depressive states.

**Methods**

Depressive states will be measured at baseline and every three years by the CESD scale. General Linear Model (GLM) will be used to examine sex, age and SES differences in the prevalence of each substance and the conditional risk of depression by substance. Structural equation model (SEM) with moderated mediation will be used to test the presence of moderating effects while simultaneously taking into account age differences in the prevalence of substance types. Since substance use disorders often co-occur, we will combine confirmatory factor analysis (CFA) or exploratory factor analysis with SEM to determine the extent to which the association between substance use and depressive states is specific to each substance and the extent to which it is due to co-occurring use of more than one substance. The hypothesis that the predominant direction of the bidirectional association is from substance use to depressive states will be tested with both instrumental variable and propensity score methods.

**Perspectives**

Examining the reasons for the strong association between major depression and each substance use disorder would advance our understanding of the etiology of these disorders and help develop more effective treatment and preventive interventions. Examining whether this comorbidity is more frequent / more detrimental in particular subgroup(s) of the population and understanding the

reasons for this hypothesized heightened vulnerability in specific subgroups would be crucial to implement personalized interventions.

Note: this project is part of the research consortium 'DEDALE - Déterminants et évolution des états dépressifs : approche longitudinale en épidémiologie intégrative'