**Co-morbidity between mood and substance-related disorders: a systematic review and meta-analysis**

**Abstract (n=272)**

**Aims**

Evidence indicates that mood disorders often co-occur with substance-related disorders. However, pooling comorbidity estimates can be challenging due to heterogeneity in diagnostic criteria and in the overall study design. The aim of this study was to systematically review and, where appropriate, meta-analyse estimates related to the pairwise comorbidity between mood disorders and substance-related disorders, after sorting these estimates by various study designs.

**Methods**

We searched PUBMED (MEDLINE), Embase, CINAHL, Web of Science for publications between 1980 and 2017 regardless of geographical location and language. We meta-analysed estimates from original articles in four broadly defined mood, and 35 substance-related disorders (where data were available) after sorted by: (a) temporal ordering (lifetime, period, or temporally-ordered estimates), and (c) estimates with or without covariate adjustments.

**Results**

After multiple eligibility steps, we included 120 studies for quantitative analysis. In general, regardless of variations in diagnosis type, temporal order or use of adjustments, there was substantial comorbidity between mood and substance-related disorders. Based on 56 separate meta-analyses, all pooled ORs were above 1, and 46 were significantly greater than 1 (i.e. the 95% confidence intervals did not include 1). Additionally, we found 502 estimates that were not meta-analysed, of which most of the estimates were consistent with the overall findings from the meta-analyses.

**Conclusions**

This review found robust and consistent evidence of an increased risk of comorbidity between many combinations of mood and substance-related disorders. We also identified a number of under-researched mood and substance-related disorders, suitable for future scrutiny. This review reinforces the need for clinicians to remain vigilant in order to promptly identify and treat these common types of comorbidity.

**Keywords**: Systematic review, Mood disorder, substance use disorder, depression, bipolar disorder

**PROSPERO** registration: PROSPERO 2019 CRD42019080516 Available from: <https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019080516>