Bidirectional causal associations between amphetamine use and mental health problems across adolescence and young adulthood: Findings from four Australasian cohort studies.

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**Introduction:** The use of amphetamines (including amphetamine and methamphetamine) has been consistently associated with common mental health problems (depression and anxiety); however, the direction of potential causal relationships has not yet been established.

Methods: Harmonised data from four population-level, Australasian cohorts participating in the Monitoring Illicit Substance Use (MISUse) Consortium were used to assess the direction of potential causal relationships between amphetamine use (≥monthly) and common mental health problems in adolescence (age 10-17 years) and young adulthood (age 18-30 years). Associations were estimated as Risk Ratios (RRs) with Confidence Intervals (CIs) using Poisson regression models with robust error variances and G-computation procedures, while accounting for up to 15 potential confounding factors.

**Results:** In the pooled sample (N = 7,527, 51% female) the risk of common mental health problems in young adulthood was 21% greater (RR= $1\cdot21$ , 95% CI= $1\cdot04$ ,  $1\cdot40$ ) for those that reported monthly or more frequent amphetamine use in adolescence. The risk of monthly or higher amphetamine use in young adulthood was 18% greater (RR= $1\cdot18$ , 95% CI= $0\cdot98$ ,  $1\cdot42$ ) in those who reported common mental health problems in adolescence. There was also some (more tentative) evidence to suggest that in males the strongest association was from amphetamine use to common mental health problems (RR= $1\cdot25$ , 95% CI= $0\cdot98$ ,  $1\cdot60$ ), while in females the strongest association was from common mental health problems to amphetamine use (RR= $1\cdot35$ , 95% CI= $1\cdot01$ ,  $1\cdot81$ ). In general, findings were consistent across the four cohorts supporting their generalisability.

**Discussions and Conclusions:** The finding of potential causal effects for both adolescent amphetamine use and adolescent common mental health problems on early adult outcomes supports the view that adolescent interventions that targeting both substance use and/or mental health could improve the young adulthood outcomes.

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