The opioid epidemic started with misusing prescription opioid. Studies found that adverse childhood experience (ACE) is a significant predictor of prescription opioid misuse. Studies also showed that resilience is a protective factor of health-risk behaviors. But few studies have investigated the effects of resilience on mediating the association between ACEs and prescription opioid misuse. To discover the possible mechanism, this study examined if resilience may mediate the aforementioned association. Based on the Connor-Davidson Resilience Scale, a latent variable was created to measure resilience. Generalized structural equation modeling was utilized to conduct the mediation analysis that estimated the effects of resilience on prescription opioid misuse associated with ACEs among respondents from a national survey. Findings suggested that resilience significantly mediated the relationship between ACEs and prescription opioid misuse. To prevent individuals with ACEs from misusing prescription pain medication, addressing the impact of ACEs should include behavioral interventions to improve resilience.

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