



Effects of Opioid and Stimulant Use Disorders on COVID-19 Reinfection and Severe Outcomes

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Introduction

- In 2021, overdose deaths due to opioids, cocaine, and stimulants (e.g., amphetamine and methamphetamine) accounted for more than 90% of the total overdose fatality in the U.S.
- Persons with opioid (OUD), cocaine (CUD), and stimulant (STUD) use disorders are at increased risk of COVID-19 infection and severe complications because of immune dysregulation and impaired respiratory function from drug use.
- Despite ongoing advancements in vaccines and treatments for COVID-19, many concerns remain about reinfection and waning immunity against the SARS-CoV-2 virus and its variants, especially among people with OUD, CUD, and STUD.

Study Objectives

This study assessed the risk of COVID-19 reinfection, severe outcomes, and vaccine effectiveness among patients with opioid (OUD), cocaine (CUD), and stimulant (STUD) disorders to help clinical and public health communities improve preventive policies and treatment decisions.

Methods

This retrospective study used electronic health record (EHR) data from the TriNetX database, consisting of over 75 million patients from 55 healthcare organizations in the US. COVID-19 reinfection was defined as a new COVID-19 diagnosis reported after 45 days of the first infection.

- The study population consisted of adults (age \geq 18) infected by COVID-19 between January 2020 and May 2022, excluding individuals who had cancer diagnoses, or lived in nursing homes and palliative care facilities prior to COVID-19 infection.
- The indicative measure of COVID-19 severe outcomes included emergency department visits, hospital admissions, intensive care unit stays, and deaths within 30 days of reinfection.
- Multiple logistic regression modeling was used to assess the risk of COVID-19 reinfection and poor outcomes, controlling for baseline characteristics (age, sex, race/ethnicity, diabetes, COPD, hypertension, obesity, cardiovascular disease, and nicotine use disorder).
- Adjusted Odds ratios (aOR) and 95% confidence intervals were computed to estimate the probability of reinfection and poor outcomes.

Results

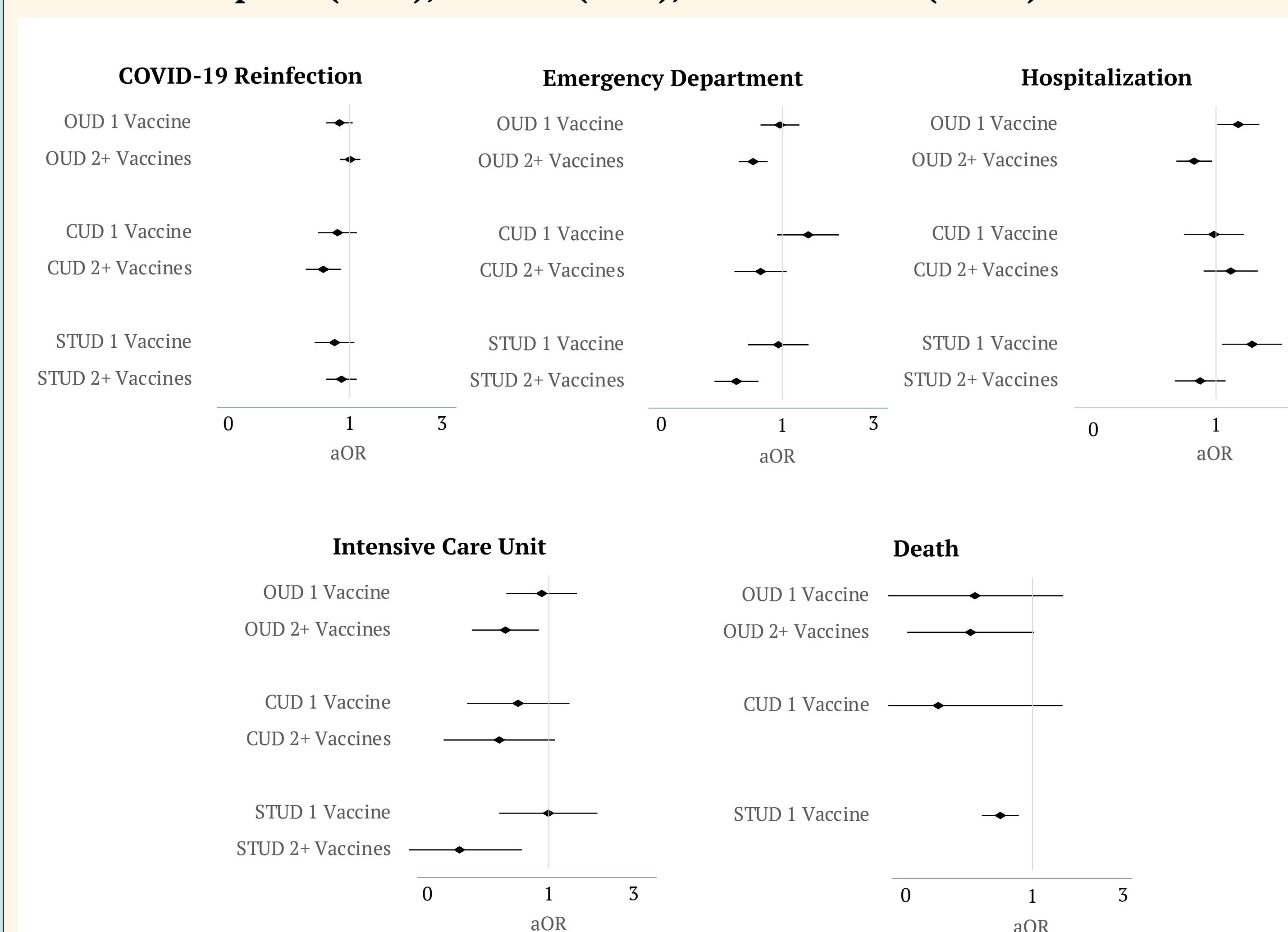
A total of 2,774,830 adults were infected by COVID-19 from January 2020-May 2022, including 904,467 (32.6%) individuals re-infected by COVID-19.

Table 1. Risk of COVID-19 reinfection and outcomes within 30 days of reinfection

Characteristics	COVID-19 Reinfection	Emergency Department	Hospitalization	Intensive Care Unit	Death
Female	1.14* (1.10,1.18)	0.97 (0.95,1.02)	0.87* (0.81,0.92)	0.82** (0.74,0.91)	1.01 (0.85,1.21)
Age (ref: 18-39 years)					
40-64	0.98 (0.94,1.01)	0.92** (0.87,0.97)	1.26** (1.17,1.36)	1.44** (1.27,1.62)	2.49** (1.94,3.18)
65+	0.90** (0.85,0.96)	0.90* (0.82,0.98)	1.57** (1.41,1.75)	1.55** (1.30,1.84)	4.99** (3.73,6.67)
Hispanic/Latino	1.45** (1.37,1.54)	1.08 (0.99,1.18)	1.19** (1.06,1.34)	0.95** (0.79,1.15)	0.62* (0.43,0.90)
Race (ref: White)					
Black	1.10** (1.06,1.15)	1.52** (1.43,1.62)	1.09* (1.01,1.18)	1.06** (0.94,1.20)	0.86 (0.69,1.06)
Other	0.72** (0.68,0.75)	1.41** (1.31,1.53)	0.92 (0.83,1.02)	1.31** (1.13,1.53)	1.38* (1.06,1.78)
Chronic and mental conditions [‡]					
Diabetes	1.09** (1.04,1.14)	1.17 (1.10,1.25)	1.32** (1.23,1.43)	1.70** (1.52,1.91)	1.31** (1.09,1.59)
Obesity	1.11** (1.07,1.16)	0.96 (0.91,1.02)	0.88** (0.82,0.95)	0.76** (0.68,0.85)	0.82* (0.68,0.99)
Heart Failure	1.22** (1.14,1.30)	1.26** (1.15,1.38)	1.46** (1.32,1.62)	1.69** (1.46,1.94)	2.05** (1.64,2.51)
Nicotine dependency	0.99 (0.96,1.02)	1.45** (1.36,1.50)	1.34** (1.26,1.45)	1.37** (1.24,1.52)	1.20** (1.01,1.43)
Depression	1.22** (1.17,1.26)	1.00 (0.95,1.05)	1.03 (0.96,1.10)	0.92 (0.83,1.03)	0.91 (0.76,1.09)
Bipolar	1.15** (1.10,1.21)	1.48** (1.38,1.58)	1.26** (1.16,1.37)	0.95 (0.83,1.09)	0.94 (0.73,1.21)
Vaccine dose					
One	0.86** (0.77,0.96)	0.91 (0.77,1.07)	1.02 (0.83,1.27)	0.96 (0.69,1.35)	0.83 (0.46,1.50)
Two and more	1.00 (0.95,1.08)	0.70** (0.63,0.78)	0.68** (0.58,0.80)	0.47** (0.35,0.64)	0.46 (0.29,0.74)
Opioid Use Disorder	1.29** (1.24,1.34)	1.57** (1.48,1.66)	1.70** (1.59,1.83)	1.50** (1.34,1.67)	1.66 (1.38,2.01)
Stimulant Use Disorder	1.12** (1.06,1.17)	1.70 (1.57,1.83)	1.66** (1.52,1.81)	1.54** (1.34,1.77)	1.36* (1.05,1.76)
Cocaine Use Disorder	1.27** (1.20,1.34)	1.58** (1.28,1.48)	1.22** (1.12,1.33)	1.21** (1.06,1.38)	0.87 (0.67,1.11)

* $p < 0.05$ ** $p < 0.01$; Statistics represent adjusted odds ratios (aOR) and their 95% confidence intervals
[‡] Selected list of the chronic and mental health conditions

Figure 1. Effect of vaccine dose on COVID-19 reinfection and outcomes among those with opioid (OUD), cocaine (CUD), and stimulant (STUD) use disorders



Statistics represent adjusted odds ratios (aOR) and their 95% confidence intervals
 In the mortality analysis, the number of people with CUD and STUD receiving \geq 2 vaccines was limited so those receiving 1 and \geq 2 vaccines were merged into a single group.

Discussion

Overall, adults with substance use disorders (SUD) had higher rates of COVID-19 reinfection and severe outcomes within 30 days of reinfection.

- Individuals with OUD and STUD were consistently shown to have higher likelihood of ED visits, hospitalization, and ICU admissions, as well as death within 30 days of reinfection when compared to individuals with CUD.
- Differences in severity of risk is likely multifactorial, and may include unique pharmacologic effects of substances as well as degree of impact on respiratory depression and immune dysregulation.
- Hispanic and Black patients were more likely to experience greater risk of both reinfection and severe outcomes, highlighting health disparities of the ongoing pandemic.
- COVID-19 vaccination was associated with decreased risk. One vaccination decreased reinfection rate, while at least two vaccinations were associated with a reduction of severe outcomes.

Conclusion/Limitations

- Since individuals with SUD are more susceptible to COVID-19 reinfection and sequelae, it is essential for clinicians and public health professionals to develop strategies for risk mitigation in this vulnerable population.
- Limitations include those common to all studies using EHR data. We were unable to determine if there were uncaptured COVID-19 tests or whether SUD and other conditions were active versus inactive. The EHR data also failed to account for socioeconomic factors.

Disclosures/Acknowledgement

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