Polysubstance use is when two or more substances are used together or within a short time period, either intentionally or unintentionally. Polysubstance use involving alcohol includes drinking and using other substances such as marijuana, opioids, heroin or other illicit drugs, or medications not as prescribed. Whether intentional or not, using alcohol and other substances is unsafe because the effects may be stronger and more unpredictable than one drug alone, and even deadly.

Using alcohol and certain other substances, including other depressants like opioids or benzodiazepines, together or within a couple of hours of drinking can result in:

- Difficulty or stopping breathing.
- Damage to the brain, heart, and other organs.
- Death.

How common are overdoses involving alcohol in the United States?

- About 1 in 5 emergency department visits associated with the misuse of prescription medicines also involved alcohol in 2016.
- About 1 in 7 opioid-related deaths involved drinking alcohol within a few hours of using an opioid in 2017. The proportion of opioid overdose deaths involving alcohol varied by state, ranging from 7% to 29%.
- Opioid overdose deaths where alcohol contributed to the death increased 41% from 2019 to 2020.