Marijuana is the Most Commonly Used Illicit Drug In the U.S.

• Over 114 million Americans have tried it at least once

• An estimated 2.4 million Americans used it for the first time in 2013

Tetrahydrocannabinol (THC)
Active Ingredient in Marijuana

Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol

Average Past Month Use by 12 to 17-Year-Olds, 2013

- Non-Medical Marijuana States: 6.1%
- Medical Marijuana States: 8.9%
- Recreational/Medical Marijuana States: 10.5%

SOURCE: SAMHSA.gov, National Survey on Drug Use and Health 2012 and 2013

Youth (Ages 12 to 17 Years) Past Month Marijuana Use National vs. Colorado

- National Average: 6.74, 6.67, 6.67, 7.03, 7.38, 7.64, 7.55, 7.15
- Colorado Average: 7.60, 8.15, 9.13, 10.17, 9.91, 10.72, 10.47, 11.16

Commercialization and Legalization highlighted.
Natural and Drug Reinforcers Increase Dopamine in NAc

Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptions that result in addiction.

Di Chiara et al.
Constituents of MJ and the Cannabinoid System

Delta-9-tetrahydrocannabinol (Δ⁹-THC)
Delta-9-tetrahydrocannabinol varin (Δ⁹-THCV)
Delta-8-tetrahydrocannabinol (Δ⁸-THC)
Cannabigerol (CBG)
Cannabichromene (CBC)
Cannabinol (CBN)
Cannabidiol (CBD)
Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

- Brain Development
- Memory & Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia
Cannabinoid Receptors Are Also Located Throughout the Body

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of 11C-MePPEP)

PET images of [11C]-NE40 (CB2R radioligand)

Terry et al., Eur J Nucl Med Mol Imaging. 2010
Ahmad et al., Mol Imaging Biol. 2013 A
Cannabinoid CB1 Receptors in Human Brain are Downregulated in Marijuana Abusers

Does Marijuana Use negatively affect the developing brain and an individual’s personal trajectory into adulthood?
Long Term Effects of Marijuana Addiction:
About 9% of users may become dependent, 1 in 6 who start use in adolescence, 25-50% of daily users

Estimated Prevalence of Dependence Among Users

* Nonmedical Use
Source: Anthony JC et al., 1994

Drug Use Outcomes in Twin Pairs (n = 234) Discordant for Cannabis Use Before Age 17

Consistent and dose-response association were found between frequency of adolescent cannabis use and adverse outcomes.

Silins E et al., The Lancet September 2014.
Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife

Dunedin prospective study of 1037 Ss born 1972/73,

Tested for IQ at age 13 and 38y.

Tested THC use ages 18, 21, 26, 32 and 38y

Early (<18y) Long-Term Cannabis Use Decreases Axonal Fiber Connectivity

Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33). Zalesky et al Brain 2012.
Effects of THC on Mental Illness
Brain abnormalities associated with long-term heavy cannabis use

Hippocampus and amygdala volumes are smaller in cannabis users than controls and this has been linked with impaired memory performance.

Yucel et al., Arch Gen Psychiatry. 2008

Lorenzeti et al., Biological Psychiatry 2015
Schizophrenics have Smaller Hippocampus and Amygdala

Areas in Hippocampus and Amygdala where volumes were smaller in schizophrenics than controls

Hippocampus/Amygdala volumes correlated with psychosis in schizophrenics (closed) and bipolar patients (open)

Prestia et al., Am J Geriatr Psychiatry 2015.

Watson et al., Brain Imaging Behav. 2012.
Cannabis-Associated Psychosis


Study of Swedish Conscripts (n=45570)

Risk of schizophrenia-like psychosis at age 26 years

Arseneault et al. BMJ 2002

Regular Cannabis Use Increases Schizophrenia Risk in those with AKT1

Di Forti et al., Biological Psychiatry, 2012.

Effect of High Potency Cannabis on Risk of Psychosis

Di Forti M et al., The Lancet published online February 18, 2015.
12th Graders’ Past Year Marijuana Use vs. Perceived Risk of REGULAR Marijuana Use

Source: The Monitoring the Future study,

SOURCE: University of Michigan, 2013 Monitoring the Future Study
### EXAMPLES OF RISK AND PROTECTIVE FACTORS

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**Prevention Programs Should**

**Enhance Protective Factors & Reduce Risk Factors**
Adolescent Brain Cognitive Development
National Longitudinal Study
NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OBSSR, ORWH

Ten year longitudinal study of 10,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories