Urgent and Emerging Issues in Prevention: Marijuana, Kratom, E-cigarettes

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Substance Abuse and Mental Health Services Administration
U.S. Department of Health and Human Services
Preventionists - Key to the Health and Welfare of Americans

• Opioids crisis continues, but with evidence for positive effects of government efforts in partnership with states, communities, organizations
• Ongoing work of preventionists, clinicians, peers, first responders, faith-based groups, volunteers, families
  • Major decline in heroin initiates in 2017
  • Large increases in naloxone distribution, overdose reversals
• Prevention becomes even more important as we watch the unfolding story of the impact of substance use on American communities
• Preventionists: the first line in addressing the risks presented by substance use in our communities
• Increased focus on potential harms of substances
• Raise awareness of risks with substance use
• Community outreach to youth as well as adults
Substances of Increasing Importance: Marijuana, Kratom and E-cigarettes (Nicotine)

- **Marijuana/cannabis:**
  - Increasing prevalence of use
  - Increasing understanding of risks associated with use
  - Public lack of information on these risks

- **Opioids Issues:**
  - Fentanyl-Contaminated Cocaine

- **Kratom**
  - Botanical that at low doses produce stimulation and at higher doses produce opioid effects
  - Potential for physical dependence and opioid-type effects/toxicities
  - Marketed in Western countries and increasing use/toxicities being reported

- **E-cigarettes**
  - Vaping: heating and aerosolizing nicotine for inhalation
  - Nicotine is addictive and has adverse health effects
  - In 2017 e-cigs were the most commonly used nicotine product among high (11.7%; 1.73 million) and middle (3.3%; 0.39 million) school students.
Marijuana: The Issue

- Marijuana is rapidly becoming more widely available in the U.S.
  - 33 states: allow medical marijuana with reduced penalties for possession; 9 states plus DC have legalized recreational use

- Huge and profitable industry that markets heavily with health claims that have little to no basis and which have had virtually no counter arguments put forward until the present time

- Numerous forms: smoked, edibles, oil for vaping, lotions, transdermal patches
Marijuana: The Issue

• Increasing potency of marijuana:
  • THC content: 3.8% (1990s) increased to 12.2% (2014)
  • Average MJ extract has THC levels at $\geq 50\%$
  • THC: component responsible for euphoria/intoxication
  • Can also produce anxiety, agitation, paranoia, and psychosis
  • Responsible for addiction liability with estimates that 10-20% of users will develop a use disorder (Volkow ND et al. 2016)

• Declining CBD content in currently available MJ
  • Not thought to be addictive
  • May reduce psychosis
  • Medical value: FDA approved for certain seizure disorders (Ehsoly MA et al. 2016)
Risks and Adverse Outcomes

- Downplayed by industry; ignored by states
  - Low birth weight
  - Pulmonary symptoms
  - MVAs
  - Cognitive impairment
  - Poor performance in school and at work
  - Addiction
### What Happens as State Laws Liberalize?

Past Year Marijuana Use among Persons Aged 12 or Older Residing in States with No Legalization of Marijuana, by State: Percentages and Estimated Numbers (in Thousands), Annual Averages Based on 2012-2013, 2013-2014, 2014-2015, and 2015-2016 NSDUHs

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<tr>
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<td>12.28%</td>
<td>449</td>
<td>12.79%</td>
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<td>166</td>
<td>11.33%</td>
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<td>12.56%</td>
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<td>8.97%</td>
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<td>10.77%</td>
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<td>606</td>
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<td>1,972</td>
<td>9.52%</td>
<td>2,043</td>
<td>10.10%</td>
<td>2,213</td>
<td>10.14%</td>
<td>2,264</td>
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<td>Utah</td>
<td>N/A</td>
<td>8.76%</td>
<td>196</td>
<td>9.84%</td>
<td>224</td>
<td>9.07%</td>
<td>211</td>
<td>9.62%</td>
<td>229</td>
</tr>
<tr>
<td>Virginia</td>
<td>N/A</td>
<td>12.39%</td>
<td>839</td>
<td>13.04%</td>
<td>891</td>
<td>11.54%</td>
<td>796</td>
<td>11.06%</td>
<td>768</td>
</tr>
<tr>
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<td>159</td>
<td>10.93%</td>
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<td>11.07%</td>
<td>174</td>
<td>11.45%</td>
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<td>Wisconsin</td>
<td>N/A</td>
<td>11.12%</td>
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<td>11.86%</td>
<td>572</td>
<td>12.05%</td>
<td>584</td>
<td>12.18%</td>
<td>592</td>
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<td>Wyoming</td>
<td>N/A</td>
<td>10.11%</td>
<td>48</td>
<td>10.72%</td>
<td>51</td>
<td>10.87%</td>
<td>52</td>
<td>10.62%</td>
<td>51</td>
</tr>
</tbody>
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Range: 9-13%
What Happens as State Laws Liberalize?

Past Year Marijuana Use among Persons Aged 12 or Older Residing in States with Legal Medical Marijuana Use Only, by State: Percentages and Estimated Numbers (in Thousands), Annual Averages Based on 2012-2013, 2013-2014, 2014-2015, and 2015-2016 NSDUHs

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<tbody>
<tr>
<td>Arizona</td>
<td>Nov 2, 2010</td>
<td>12.94%</td>
<td>699</td>
<td>13.69%</td>
<td>752</td>
<td>13.12%</td>
<td>734</td>
<td>12.22%</td>
<td>696</td>
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<tr>
<td>Arkansas</td>
<td>Nov 9, 2016</td>
<td>9.69%</td>
<td>235</td>
<td>11.37%</td>
<td>277</td>
<td>11.59%</td>
<td>284</td>
<td>11.14%</td>
<td>274</td>
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<tr>
<td>Connecticut</td>
<td>Oct 1, 2012</td>
<td>14.00%</td>
<td>425</td>
<td>14.00%</td>
<td>427</td>
<td>15.67%</td>
<td>479</td>
<td>15.08%</td>
<td>461</td>
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<tr>
<td>Delaware</td>
<td>Jul 1, 2011</td>
<td>13.97%</td>
<td>108</td>
<td>13.98%</td>
<td>109</td>
<td>13.06%</td>
<td>103</td>
<td>13.18%</td>
<td>105</td>
</tr>
<tr>
<td>Florida</td>
<td>Jan 3, 2017</td>
<td>11.43%</td>
<td>1,885</td>
<td>11.87%</td>
<td>1,990</td>
<td>12.59%</td>
<td>2,152</td>
<td>13.07%</td>
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<td>Hawaii</td>
<td>Dec 28, 2000</td>
<td>13.37%</td>
<td>151</td>
<td>12.58%</td>
<td>144</td>
<td>12.72%</td>
<td>147</td>
<td>13.05%</td>
<td>151</td>
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<tr>
<td>Illinois</td>
<td>Jan 1, 2014</td>
<td>11.66%</td>
<td>1,247</td>
<td>12.16%</td>
<td>1,305</td>
<td>12.47%</td>
<td>1,339</td>
<td>12.31%</td>
<td>1,320</td>
</tr>
<tr>
<td>Maryland</td>
<td>Jun 1, 2014</td>
<td>11.47%</td>
<td>565</td>
<td>13.48%</td>
<td>670</td>
<td>15.13%</td>
<td>757</td>
<td>15.50%</td>
<td>779</td>
</tr>
<tr>
<td>Michigan</td>
<td>Dec 4, 2008</td>
<td>15.22%</td>
<td>1,268</td>
<td>15.60%</td>
<td>1,304</td>
<td>15.10%</td>
<td>1,266</td>
<td>15.68%</td>
<td>1,317</td>
</tr>
<tr>
<td>Minnesota</td>
<td>May 30, 2014</td>
<td>11.93%</td>
<td>536</td>
<td>12.22%</td>
<td>553</td>
<td>12.69%</td>
<td>579</td>
<td>12.91%</td>
<td>592</td>
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<tr>
<td>Montana</td>
<td>Nov 2, 2004</td>
<td>15.78%</td>
<td>134</td>
<td>14.07%</td>
<td>120</td>
<td>15.38%</td>
<td>133</td>
<td>18.41%</td>
<td>160</td>
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<tr>
<td>New Hampshire</td>
<td>Jul 23, 2013</td>
<td>15.39%</td>
<td>175</td>
<td>16.95%</td>
<td>194</td>
<td>17.35%</td>
<td>199</td>
<td>17.58%</td>
<td>202</td>
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<tr>
<td>New Jersey</td>
<td>Jul 1, 2010</td>
<td>10.18%</td>
<td>759</td>
<td>11.25%</td>
<td>844</td>
<td>11.86%</td>
<td>894</td>
<td>12.01%</td>
<td>907</td>
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<tr>
<td>New Mexico</td>
<td>Jul 1, 2007</td>
<td>15.09%</td>
<td>257</td>
<td>15.61%</td>
<td>267</td>
<td>14.72%</td>
<td>253</td>
<td>15.83%</td>
<td>272</td>
</tr>
<tr>
<td>Ohio</td>
<td>Sep 8, 2016</td>
<td>12.81%</td>
<td>1,237</td>
<td>11.57%</td>
<td>1,122</td>
<td>12.13%</td>
<td>1,179</td>
<td>13.81%</td>
<td>1,344</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>May 17, 2016</td>
<td>11.33%</td>
<td>1,223</td>
<td>11.70%</td>
<td>1,265</td>
<td>12.35%</td>
<td>1,339</td>
<td>13.05%</td>
<td>1,415</td>
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<td>Rhode Island</td>
<td>Jan 3, 2006</td>
<td>20.22%</td>
<td>181</td>
<td>18.95%</td>
<td>170</td>
<td>18.81%</td>
<td>170</td>
<td>20.31%</td>
<td>184</td>
</tr>
<tr>
<td>Vermont</td>
<td>Jul 1, 2004</td>
<td>19.10%</td>
<td>104</td>
<td>19.97%</td>
<td>108</td>
<td>20.50%</td>
<td>111</td>
<td>21.79%</td>
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Range: 11-21.8%
### What Happens as State Laws Liberalize?

Past Year Marijuana Use among Persons Aged 12 or Older Residing in States with Legal Medical and Recreational Marijuana Use, by State: Percentages and Estimated Numbers (in Thousands), Annual Averages Based on 2012-2013, 2013-2014, 2014-2015, and 2015-2016 NSDUHs

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>Feb 24, 2015</td>
<td>19.69%</td>
<td>114</td>
<td>19.60%</td>
<td>114</td>
<td>21.92%</td>
<td>127</td>
<td>23.00%</td>
<td>134</td>
</tr>
<tr>
<td>California</td>
<td>Nov 9, 2016 (revised penalties)</td>
<td>13.89%</td>
<td>4,384</td>
<td>14.49%</td>
<td>4,633</td>
<td>15.25%</td>
<td>4,936</td>
<td>16.23%</td>
<td>5,296</td>
</tr>
<tr>
<td>Colorado</td>
<td>Dec 10, 2012 (revised penalties); Jan 1, 2014 (commercial sales)</td>
<td>18.92%</td>
<td>814</td>
<td>20.74%</td>
<td>909</td>
<td>23.09%</td>
<td>1,033</td>
<td>23.12%</td>
<td>1,057</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>Feb 26, 2015</td>
<td>21.02%</td>
<td>116</td>
<td>21.70%</td>
<td>121</td>
<td>23.51%</td>
<td>134</td>
<td>24.68%</td>
<td>143</td>
</tr>
<tr>
<td>Maine</td>
<td>Jan 30, 2017 (grow and possess)</td>
<td>16.24%</td>
<td>186</td>
<td>19.55%</td>
<td>224</td>
<td>19.69%</td>
<td>227</td>
<td>19.81%</td>
<td>228</td>
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<tr>
<td>Massachusetts</td>
<td>Dec 15, 2016</td>
<td>15.57%</td>
<td>885</td>
<td>17.23%</td>
<td>989</td>
<td>18.26%</td>
<td>1,058</td>
<td>18.64%</td>
<td>1,088</td>
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<td>Nevada</td>
<td>Jan 1, 2017</td>
<td>14.10%</td>
<td>324</td>
<td>13.01%</td>
<td>304</td>
<td>12.95%</td>
<td>309</td>
<td>13.13%</td>
<td>319</td>
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<tr>
<td>Oregon</td>
<td>Mar 29, 2016</td>
<td>19.03%</td>
<td>630</td>
<td>19.39%</td>
<td>649</td>
<td>19.42%</td>
<td>659</td>
<td>22.70%</td>
<td>783</td>
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<tr>
<td>Washington</td>
<td>Dec 6, 2012</td>
<td>17.48%</td>
<td>1,008</td>
<td>18.92%</td>
<td>1,105</td>
<td>17.49%</td>
<td>1,037</td>
<td>18.93%</td>
<td>1,140</td>
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Range: 13-25%
Illicit Drug Use Impacts Millions: Marijuana Most Widely Used Drug

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Number of People</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Marijuana</td>
<td>40.9 MILLION</td>
<td>15.0%</td>
</tr>
<tr>
<td>Psychotherapeutic Drugs</td>
<td>18.1 MILLION</td>
<td>6.6%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>5.9 MILLION</td>
<td>2.2%</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>5.1 MILLION</td>
<td>1.9%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>1.8 MILLION</td>
<td>0.6%</td>
</tr>
<tr>
<td>Methamphetamines</td>
<td>1.6 MILLION</td>
<td>0.6%</td>
</tr>
<tr>
<td>Heroin</td>
<td>886,000</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Prescription opioids, sedatives, tranquilizers, stimulants

PAST YEAR, 2017, 12+
How did we get to where we are and what does the data tell us about ongoing risks?
Young Adult Perceptions of Great Risk of Harm From Substance Use

<table>
<thead>
<tr>
<th>Activity</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking Marijuana Once or Twice a Week</td>
<td>6.6M</td>
<td>5.9M</td>
<td>5.2M</td>
</tr>
<tr>
<td>Using Cocaine Once or Twice a Week</td>
<td>84.4%</td>
<td>83.6%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Using Heroin Once or Twice a Week</td>
<td>32.5M</td>
<td>32.0M</td>
<td>31.8M</td>
</tr>
<tr>
<td>Having 5+ Drinks of Alcohol Once or Twice a Week</td>
<td>12.7M</td>
<td>12.8M</td>
<td>12.9M</td>
</tr>
<tr>
<td>Smoking One or More Cigarettes per Day</td>
<td>23.6M</td>
<td>23.6M</td>
<td>22.7M</td>
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</table>

PAST YEAR, 2015 - 2017, 18-25

See table 3.1 in the 2016 and 2017 NSDUH detailed tables for additional information.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
Perceptions of Great Risk of Harm From Substance Use Among Adults Aged 26 or Older

See table 3.1 in the 2016 and 2017 NSDUH detailed tables for additional information.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
### Past Year Initiates, Age Group & Substance

**Past Year, 2017, 12+**

<table>
<thead>
<tr>
<th>Substance</th>
<th>12+</th>
<th>12-17</th>
<th>18-25</th>
<th>26+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette</td>
<td>1,898,000</td>
<td>604,000</td>
<td>1,151,000</td>
<td>142,000</td>
</tr>
<tr>
<td>Alcohol</td>
<td>4,914,000</td>
<td>2,332,000</td>
<td>2,440,000</td>
<td>143,000</td>
</tr>
<tr>
<td>Heroin</td>
<td>81,000</td>
<td>9,000</td>
<td>46,000</td>
<td>26,000</td>
</tr>
<tr>
<td>Rx Pain Reliever*</td>
<td>2,010,000</td>
<td>316,000</td>
<td>465,000</td>
<td>1,229,000</td>
</tr>
<tr>
<td>Marijuana</td>
<td>3,033,000</td>
<td>1,204,000</td>
<td>1,304,000</td>
<td>525,000</td>
</tr>
</tbody>
</table>

* Initiation of misuse
Since 2007, past year marijuana use has increased 37%.

Frequent marijuana use (using ≥ 200 days in the past year) increased 37% since 2002.

Nearly 1 in 3 people using marijuana in 2016 reported using ≥ 200 days in the past year.

Source: Jones CM Analysis of the NSDUH 2002-2016 Public Use Files
Marijuana Use

PAST MONTH, 2015 - 2017, 12+

See figure 13 in the 2017 NSDUH Report for additional information.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
Marijuana Use among Young Adults: Significant Increases in Women

PAST MONTH, 2015 - 2017, 18 - 25

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
Substance Use in Past Month Among Pregnant Women

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
Daily or Almost Daily Marijuana Use among Women by Pregnancy Status

PAST YEAR, 2015 - 2017, 15 - 44

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.
Marijuana and Pregnancy
May be associated with:
• Fetal growth restriction
• Stillbirth
• Preterm birth
May cause problems with neurological development:
• Hyperactivity
• Poor cognitive function  *(Metz TD and Stickrath EH, 2015)*
Co-Occurring Disorders: Youth Opioid Misuse, Heavy Alcohol Use, and Major Depressive Episode (MDE) by Marijuana Use Status

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the estimate youth with past year marijuana use is statistically significant at the .05 level.
Co-Occurring Disorders: Young Adult Opioid Misuse, Heavy Alcohol Use, and Major Depressive Episode by Marijuana Use Status

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the estimate with past year marijuana use is statistically significant at the .05 level.
Co-Occurring Disorders: Adult Opioid Misuse, Heavy Alcohol Use, and Major Depressive Episode by Marijuana Use Status

PAST YEAR/MONTH, 2017, 26+

Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the estimate with past year marijuana use is statistically significant at the .05 level.
 Intelligence: PERSISTENT CANNABIS (MARIJUANA) USE DISORDER LINKED TO SIGNIFICANT IQ DROP BETWEEN CHILDHOOD AND MIDLIFE

- Followed 1,037 individuals from birth to age 38.
- Tested marijuana use and disorders at 18, 21, 26, 32 and 38 years of age.
- Tested for IQ at ages 13 and 38

All groups started with roughly equivalent IQ scores at age 13

By age 38, those who were diagnosed with cannabis dependence in 3 study waves (the most persistent users of cannabis) had lost nearly 6 IQ points by the age of 38

There was a consistent dose-response relationship across the groups

Source: Meier MH et al., PNAS Early Edition 2012
Association of marijuana use with abuse of prescription pain medications and addiction

Risk of subsequent prescription opioid misuse and use disorder was increased among people who reported marijuana use 5 years earlier.

- Risk of incident prescription opioid misuse: 2.62
- Risk of incident prescription opioid use disorder: 2.78
Marijuana-Associated Psychosis

Risk of schizophrenia increases as marijuana use increases

Cases per 1,000

Number of times marijuana taken

0 1 2 10 <50 >50

Higher risk of schizophrenia-like psychosis with younger age of first marijuana use

Odds ratio

Cannabis users by age

15 years

18 years


Source: Arseneault et al BMJ, 2002
Drug Risks Associated with Marijuana Use Among U.S. Adults 18 and Older

- Increased Risk for Ever Using Marijuana (but no past year use) Compared to Never Using Marijuana
- Increased Risk for Past Year Marijuana Use Compared to Never Using Marijuana
- Increased Risk for Past Year Use of Marijuana 200 Days or More Compared to Never Using Marijuana

Source: Jones CM Analysis of 2015-2016 NSDUH Public Use File Data

* Result is not statistically significantly different
Mental Health and Social Risks of Marijuana Use Among U.S. Adults 18 and Older

- Increased Risk for Ever Using Marijuana (but no past year use) Compared to Never Using Marijuana
- Increased Risk for Past Year Marijuana Use Compared to Never Using Marijuana
- Increased Risk for Past Year Use of Marijuana 200 Days or More Compared to Never Using Marijuana

* Result is not statistically significantly different

Source: Jones CM Analysis of 2015-2016 NSDUH Public Use File Data
Summary: Consequences of Marijuana Use

Acute, intoxicating effects of marijuana:
- Distorts perception; poor judgment and poor decision making (e.g.: unprotected sex, driving while intoxicated)
- Impairment in balance and coordination (important to injury risk in activities such as driving, sports)
- Difficulty with attention, concentration, and problem solving
- Difficulty with learning and memory (immediate and recall)

Adverse outcomes linked to marijuana use by youth:
Poor school performance and increased drop out rates
Chronic use in adolescence has been linked to decline in IQ that may not recover with cessation (Meier et al. 2012)
Marijuana use in adolescence is associated with an increased risk for later psychotic disorder in adulthood (D’Souza, et al. 2016)
Marijuana use linked to earlier onset of psychosis in youth known to be at risk for schizophrenia (McHugh, et al. 2017)
Summary: Consequences of Marijuana Use

• Significant numbers who try marijuana will become addicted (Lopez-Quintero, et al. 2011)

• Higher overall rates of car crashes in states that have legalized (WAPO, June 2017)

• Association of marijuana use with abuse of prescription pain medications (Olfson et al. 2017)
Is There Medical Use for Marijuana?

• Evidence for some medical value of some components
  • CBD and seizure disorder (Dravet’s syndrome and Lennox-Gastaut syndrome)
  • THC products for wasting illnesses and appetite production

• Medications must have undergone substantial research to answer critical questions before getting to market and widespread use in humans:
  • Isolation of single components; manufacture processes
  • Delivery mechanism
  • Pharmacokinetics/pharmacodynamics
  • Dose-response relationships (e.g.: doubling a dose may or may not double the effect)
  • Therapeutic range
  • Adverse events: what are they and how best to avoid/address should they occur?

• These types of studies would be difficult for marijuana because there are so many components
**Where Do We Go From Here?**

- Government has a responsibility to inform Americans of the risks of marijuana use
- People need to be able to make informed choices
- States should consider short and long term issues related to marijuana
  - Tax revenue
  - Societal costs
  - Government costs

**Major Issue to Consider: Marijuana has gotten ahead of regulation**

- How do we define intoxication?
- What are the ‘legal limits’ of use (equivalent to BAC)
- How should marijuana sales centers be regulated (should we better control the opening of marijuana sales locations?)
- Should warning labels be required on marijuana products?
- How do we assure that underage sales are not occurring? (as with tobacco products, for example)
- Should people be allowed to openly use in public?
- Should people be allowed to use and operate motor vehicles?
- What are the penalties?
Cocaine laced with fentanyl:
7% of cocaine seized in New England in 2017 was contaminated with fentanyl
Connecticut: deaths involving fentanyl-laced cocaine up 420% in last 3 years
Reported increases in deaths in NYC, PA, MA, NJ, OH, CA

Why?
Poor quality control in packaging?
High Risk Groups:
Primary cocaine users
Opioid users may use cocaine to counteract sedation/intensify effect of opioid
• Underscores the need to warn the public and provide treatment for cocaine use disorders
• Epidemic is not just about opioid addiction
Cocaine users lack opioid tolerance: fentanyl overdose/death more likely
• Naloxone
• Discourage use alone

Kratom

• Kratom is a tropical tree (*Mitragyna speciose*) native to Southeast Asia, used traditionally to combat fatigue and improve work productivity among farm populations in Southeast Asia.

• Has recently become popular as a novel psychoactive substance in Western countries (*Cinosi et al, 2015*).

• FDA is concerned that kratom, which affects the same opioid brain receptors as morphine, appears to have properties that expose users to the risks of addiction, abuse, and dependence.

• Currently, there are no FDA-approved uses for kratom, and the agency has received concerning reports about its safety.
• Kratom preparations contain varying amounts of several phytochemicals, making their pharmacological and toxicological evaluation unique and difficult.

• More than 20 alkaloids in kratom have been identified in the laboratory.

• Mitragynine is classified as a kappa-opioid receptor agonist and is roughly 13 times more potent than morphine.

• Mitragynine/OH-mitragynine thought to be responsible for the opioid-like effects.

Source: Cinosi E.; Martinotti; et all. Following “the Roots” of Kratom (Mitragyna speciosa): The Evolution of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries; Biomed Res Int. 2015; 2015: 968786
Kratom: How Used

- Capsules
- Pills
- Extract
- Leaves
  - Chewed
  - Brewed as tea
  - Smoked
The effects of kratom in humans are dose-dependent:

- Small doses produce stimulatory effects resembling the stimulant effect of drugs such as cocaine or amphetamines.
- Larger dosages associated with sedative-narcotic, pain reducing effects that resemble drugs such as opiates.
- Regular kratom use is associated with addictive disorders, as evidenced by craving and compulsive use. Opioid withdrawal symptoms upon cessation.

Use of Kratom in the US

• An anonymous online survey was conducted in October 2016 of 10,000 current kratom users through available social media and from the American Kratom Association (https://speciosa.org/home/).

• 8,049 respondents completed the survey.

• Findings:
  • Kratom was primarily used by a middle-aged (31-50 years) males (56.91%) with income $35,000 or higher with private insurance (61.31%).
  • Kratom was used to self-treat pain (68%) and emotional or mental conditions (66%) and for withdrawal symptoms associated with prescription opioid use.
  • Subjects reported dose-dependent nausea and constipation with high doses (5g) and with and frequent dosing (Q22 doses/wk).

SOURCE: Grundmann O.; Patterns of kratom use and health impact in the USVresults from an online survey. Drug Alcohol Depend. 2017; 175(5):63-70.
Number of Kratom-related Reported Exposure Calls to Poison Centers in the US

National Poison Data System - United States and Puerto Rico
January 2010–December 2015

## Fatal Overdoses Involving Kratom

From July 2016 to June 2017, 25 fatal overdoses involving kratom across 8 CDC SUDORS states were identified.

<table>
<thead>
<tr>
<th>States</th>
<th>ME</th>
<th>NH</th>
<th>NM</th>
<th>OH</th>
<th>PA</th>
<th>RI</th>
<th>WV</th>
<th>WI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid overdose deaths</td>
<td>301</td>
<td>402</td>
<td>322</td>
<td>4,534</td>
<td>3,231</td>
<td>265</td>
<td>844</td>
<td>825</td>
<td>10,724</td>
</tr>
<tr>
<td>Deaths involving kratom</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Percent involving kratom</td>
<td>1.3%</td>
<td>0.5%</td>
<td>0.3%</td>
<td>0.07%</td>
<td>0.25%</td>
<td>0.4%</td>
<td>0.6%</td>
<td>0.1%</td>
<td>0.23%</td>
</tr>
</tbody>
</table>

Caution: testing of kratom is not uniform thus these numbers are underestimates.

In 2017, the Food and Drug Administration (FDA) began issuing a series of warnings about kratom and has now identified at least 44 deaths related to its use.

Most kratom associated deaths appeared to have resulted from adulterated products or taking kratom along with other potent substances.

Source: CDC SUDORS Overdose Death Data
Kratom Concerns

• Kratom has gained popularity for its euphoric effects and is being popularized as a safe herbal product capable of giving a “legal” high (Swogger et al., 2015), and as an alternative to other sedative and stimulant type drugs (Warner et al., 2016).

• Reports of physical dependence on kratom in Western nations emerge from case reports from the UK (Boyer et al., 2008, McWhirter and Morris, 2010), Germany (Kapp et al., 2011) and the US (Dorman et al., 2014, Nelsen et al., 2010, Forrester, 2013, Sheleg and Collins, 2011).

• It can be surmised that given the large and growing number of internet purchase sites for kratom (cited in Cinosi et al., 2015), addiction to kratom is also likely to be growing in the Western countries.

• No treatment specific for kratom addiction available

• One case of NAS in an infant whose mother was a kratom user and who responded to opioid treatment.
International Status of Kratom

Kratom is restricted or illegal in:

- Australia
- Lithuania
- Romania
- Denmark
- Myanmar
- South Korea
- Finland
- Malaysia
- Sweden
- Israel
- Poland
- Thailand
- United Kingdom

Scheduling under consideration in U.S.

On November 14, 2017, the FDA issued a public health advisory related to mounting concerns regarding the risks associated with kratom and reported deaths with use.
Conclusions

- Kratom is a recognized emerging public health threat ([MMWR. July 29, 2016;65(29):748Y749](https://mmwr.cdc.gov/mmwr/))
- People need to understand that “legal” and “available” are not the same as “safe.”
- In the West, kratom has been valued for its analgesic effects and to aid in managing opioid withdrawal. However, some of these individual attempts have resulted in cases of toxicity and fatalities.
- Physicians should be aware of these herbal supplements and potential toxicity or withdrawal effects in patients including in newborns which cannot be picked up by the standard toxicology screen ([Davidson et al, 2018](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5997268/)).
- Preventionists should be aware of this drug and work with their communities raising awareness, providing education about effects and risks.
E-cigarettes
Vaping in the US: Trends and Effects
Cigarette Smoking Continues to Decline

Source: Adult cigarette smoking prevalence data are from the National Health Interview Survey (NHIS). High school cigarette smoking prevalence data are from the National Youth Risk Behavior Survey.

15.5% of adults are current smokers
7.6% of youth are current smokers

Source: CDC. Styles Survey. 2010-2017
Cigarette Smoking Status Among Current Adult E-Cigarette Users, by Age Group

Current e-cigarette users: Persons who reported using e-cigarettes or some other electronic “vaping” product “some days” or “every day”
Youth E-cigarette Use: Infographic from CDC’s MMWR

Current Use of E-cigarettes and Any Tobacco Product Among Middle and High School Students—NYTS, US, 2011–2018

Adverse Health Effects of Nicotine

• Nicotine exposure during adolescence can result in addiction.
• Nicotine can harm the developing adolescent brain.
• Nicotine delivered by e-cigarettes during pregnancy can result in multiple adverse consequences, including sudden infant death syndrome, and could result in altered corpus callosum, deficits in auditory processing, and obesity.
• Ingestion of e-cigarette liquids containing nicotine can cause acute toxicity and possibly death if the contents of refill cartridges or bottles containing nicotine are consumed.

E-cigarette Adverse Health Effects

• E-cigarettes expose users to several chemicals, in addition to nicotine: heavy metals (chromium, lead, manganese, nickel and zinc), arsenic, volatile organic compounds (propylene glycol or glycerol), all known to have adverse health effects.

• The health effects and potentially harmful effects of doses of heated and aerosolized constituents of e-cigarette liquids, including solvents, flavorants, and toxicants, are not completely understood.

• E-cigarettes can also be used to deliver other drugs, including marijuana. In 2016, one-third of U.S. middle and high school students who ever used e-cigarettes had used marijuana in e-cigarettes.


SAMHSA Actions in coming year

**Marijuana:**
- Continue NSDUH and DAWN data collection related to marijuana
- Provide education/training materials oriented to providers and to the public related to marijuana risks
- Specific materials aimed at special populations e.g.: pregnant women, youth
- Assist in identification of hazardous use and use disorders with SBIRT
- Fund prevention, treatment and recovery services in states/communities

**Kratom**
- Education for healthcare providers and the public on kratom properties/adverse effects
- PSAs

**E-cigarettes/vaping**
- Add NSDUH questions to better understand epidemiology
- Education for healthcare professionals and public, PSAs
- Continue to speak out on known risks and accumulating evidence for adverse effects of marijuana, kratom, and e-cigarettes/nicotine
Thank you!

Elinore.McCance-Katz@samhsa.hhs.gov
Kratom:
Cinosi E.; Martinotti; et al. Following “the Roots” of Kratom (Mitragyna speciosa): The Evolution of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries; Biomed Res Int. 2015; 2015: 968786.
https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm584952.htm
The Surgeon General's Warning on Marijuana

The Surgeon General of the Public Health Service has issued the following warning on marijuana:

Marijuana use is a major public health problem in the United States. In the past 20 years, its' use has increased 30-fold; it estimated that more than a quarter of the American population has used it. The age at which persons first use marijuana has decreased gradually to the junior high school years. Until recently, nearly 11% of high school seniors used it, and although that figure has declined to 7%, its daily use still exceeds that of alcohol; more high school seniors use marijuana than smoke cigarettes. In a recent study, 32% of those surveyed had used marijuana during the previous 30 days, while 25% had smoked tobacco.

On March 24, 1982, the Department of Health and Human Services submitted to Congress a report reviewing the consequences of marijuana use. Marijuana and Health, 1982, ninth in a series, is primarily based on two recently conducted, comprehensive, scientific reviews by the Institute of Medicine of the National Academy of Sciences, the Canadian Addiction Research Foundation, and the World Health Organization (WHO).

Both independent reviews corroborate the Public Health Service's findings of health hazards associated with marijuana use: Acute intoxication with marijuana interferes with many aspects of mental functioning and has serious, acute effects on perception and skilled performance, such as driving and other complex tasks involving judgement or fine motor skills.

Among the known or suspected chronic effects of marijuana are:

- short-term memory impairment and slowness of learning.
- impaired lung function similar to that found in cigarette smokers. Indications are that more serious effects, such as cancer and other lung disease, follow extended use.
- decreased sperm count and sperm motility.
- interference with ovulation and pre-natal development.
- impaired immune response.
- possible adverse effects on heart function.
- by-products of marijuana remaining in body fat for several weeks, with unknown consequences. The storage of these by-products increases the possibilities for chronic, as well as residual, effects on performance, even after the acute reaction to the drug has worn off. Of special concern are the long-term developmental effects in children and adolescents, who are particularly vulnerable to the drug's behavioral and psychological effects. The "amotivational syndrome," characterized by a pattern of energy loss, diminished school performance, harmed parental relationships, and other behavioral disruptions, has been associated with prolonged marijuana use by young persons. Although more research is required, recent national surveys report that 40% of heavy users experience some or all of those symptoms.

The Public Health Service concludes that marijuana has a broad range of psychological and biological effects, many of which are dangerous and harmful to health, and it supports the major conclusion of the National Academy of Sciences' Institute of Medicine.