



CO Tox: Fentanyl, Edibles and Mushrooms...
oh my


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Objectives:

1. Discuss fentanyl epidemic, and risk mitigation strategies
2. Trends in cannabis edible ingestions
3. Hallucinogenic mushrooms, and recent legislation



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Illicitly Manufactured Fentanyl (IMF)



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Contaminated with Fentanyl

- Illicitly manufactured pharmaceuticals
 - Benzodiazepines (Alprazolam/Xanax)
 - Oxycodone
- Recreational drugs
 - Methamphetamine
 - Heroin
 - Cocaine

Fentanyl overdose deaths spike, Denver Police seize 3x more this year

"When you're selling fentanyl, you're selling a time bomb. It's only a matter of time before it goes off in that person's life."

Children's Hospital Colorado
 Affiliated with University of Colorado Anschutz Medical Campus
<https://www.brow.com/video/news/health/fentanyl-overdose-deaths-spike73-28f0915-0cd-4437-8808-649d268325f4>

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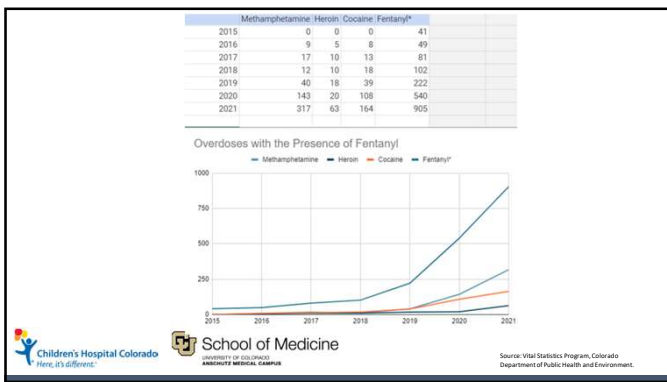
Fentanyl contaminated "M30" pill overdoses in pediatric patients

Patrick Y. Joynt, MD ^a, George Sam Wang, MD

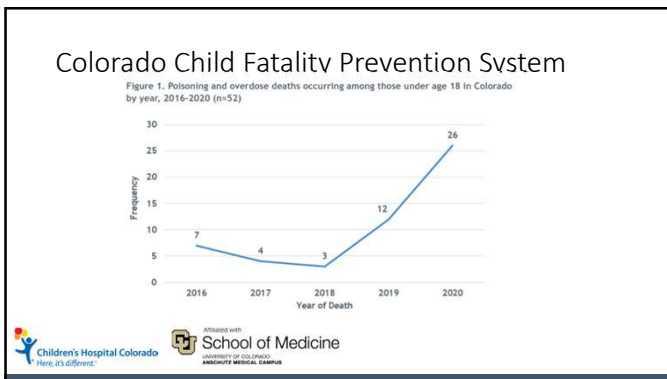
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Joynt PMID 34030905

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Fentanyl

- Opioid agonist
- 50-100x potency of morphine
- Therapeutic: Sublingual (SL), intravenous (IV), transdermal (TD)
- Peaks in 0.5-1.5 hours SL/IV

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Isotonitazene

Report on a novel emerging class of highly potent benzimidazole NPS opioids: Chemical and in vitro functional characterization of isotonitazene


Peter Blankaert¹ | Annelies Cannoot² | Katrien Van Luyfange² | Fabian Hulpia² | Eric Deconinck⁴ | Serge Van Calenberg³ | Christophe Stove²

- Benzimidazole Derivatives
- Etonitazene
- Clonitazene
- Nitazene

- Highly potent synthetic opioid

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Morbidity and Mortality Weekly Report (MMWR)

Notes from the Field: Nitazene-Related Deaths — Tennessee, 2019–2021

Weekly / September 16, 2022 / 71(37):1196–1197

Allison Roberts, PhD¹; Jessica Korona-Bailey, MPH¹; Sutapa Mukhopadhyay, PhD¹ (VIEW AUTHOR AFFILIATIONS)

Roberts PMID 36107790

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Xylazine


- Veterinary tranquilizer
- Similar to alpha-2 agonists (clonidine)
- Primary misuse
- Adulterant in illicit opioids

TABLE. Characteristics of drug overdose decedents with xylazine detected on postmortem toxicology (xylazine positive) or listed as a cause of death (xylazine involved) — State Unintentional Drug Overdose Reporting System, 38 states and the District of Columbia, 2019

Characteristic	Classification of deaths, no. (%)	
	Xylazine positive ^a (n = 826)	Xylazine involved ^b (n = 333)
Sex		
Male	402 (72.9)	388 (73.1)
Female	224 (27.1)	143 (26.9)
Race^c		
White, non-Hispanic	404 (74.8)	396 (75.4)
Black, non-Hispanic	106 (13.1)	68 (13.0)
Hispanic	90 (11.3)	— ^d
Other	11 (1.4)	— ^d
Age group, yrs		
15-24	60 (7.3)	41 (7.7)
25-34	265 (32.1)	181 (34.1)
35-44	227 (27.9)	138 (26.1)
45-54	147 (17.8)	91 (17.3)
55-64	109 (13.2)	— ^d
≥65	18 (2.2)	— ^d
U.S. Census region^e		
Northeast	568 (68.8)	356 (67.0)
Midwest	144 (17.4)	91 (17.3)
South	104 (12.6)	— ^d
West	10 (1.2)	— ^d
Co-occurring drugs listed as a cause of death^{f,g}		
Any Antipsy ^h	815 (98.7)	526 (99.1)
Including antipsy ⁱ		
Haloperidol ^h	215 (26.0)	151 (28.4)
Risperidone ^h	141 (17.3)	105 (19.8)
Prescription opioids ^h	94 (11.4)	71 (13.4)
Cocaine	265 (32.1)	157 (29.6)
Heroin	98 (11.9)	62 (11.6)
Morphine/oxycodone	102 (12.4)	62 (11.7)


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Naloxone Nasal Spray



1. **Remove** Nasal Spray from the kit. Peel back the tab with the circle to open the nasal spray.
2. **Hold** the nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.
3. **Gently insert the tip of the nozzle into either nostril.** Tilt the person's head back and provide support under the neck. Gently insert the tip of the nozzle into one nostril, until your fingers are on either side.
4. **Press the plunger firmly** to give the dose of nasal spray. Remove from the nostril after giving the dose.

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Colorado Naloxone Project


Our Goal:

All Colorado hospitals and emergency departments distribute naloxone to at-risk patients, placing naloxone — a lifesaving medication — in patients' hands prior to their departure from the hospital.

Background:



The Colorado Naloxone Project is a collaborative effort between multiple organizations. The project's initial sponsorship and continued financial oversight will be provided by the Foundation for a Safer Colorado, a nonprofit organization that supports statewide efforts to decrease the misuse of prescription pain medication, prevent addiction, and support victims and their families, implementation, technical expertise, and leadership is provided by Orsler Opilco Consultants LLC, a Colorado-based consulting firm with a long history of innovative initiatives and project management across the country. As the Colorado Naloxone Project continues to evolve, we hope that you and your organization will strongly consider a leading role in our efforts.





<http://naloxoneproject.com/about/>

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Harm Reduction and Legislation- CDPHE

- Syringe Exchange Programs
- Drug Paraphernalia Law Exemption
- Good Samaritan Law
- Third Party Naloxone
- Naloxone Standing Order
- Needle-stick Prevention
- Coverage for Opiate Antagonists Provided by a Hospital

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Opioid Use Disorder and Adolescents

- Behavioral Psychotherapy
- Medications for Opioid Use Disorders
 - Methadone
 - Buprenorphine
 - Opioid antagonists (Naltrexone)
- Outpatient Clinics (selected)
 - ENCOMPASS (UCH)
 - ARTS SYNERGY (UCH)
 - STEP CLINIC (DENVER HEALTH)
 - STRIDE

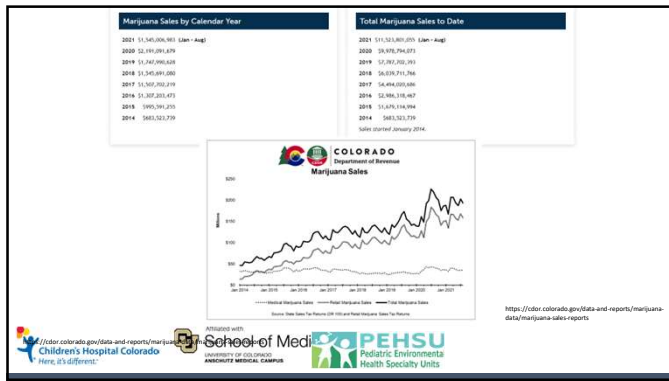



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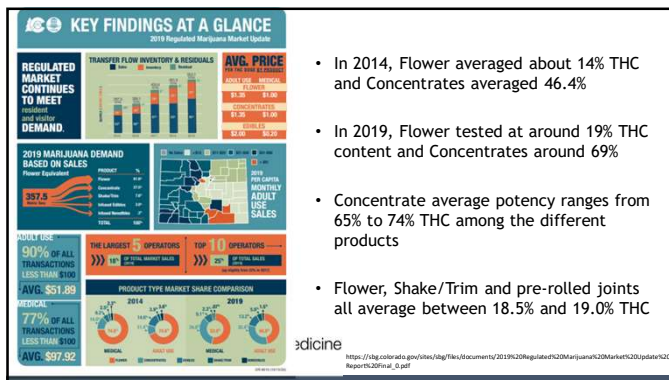
Cannabis Edibles

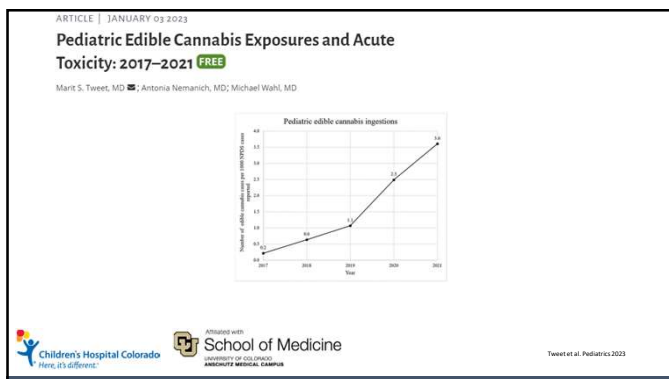
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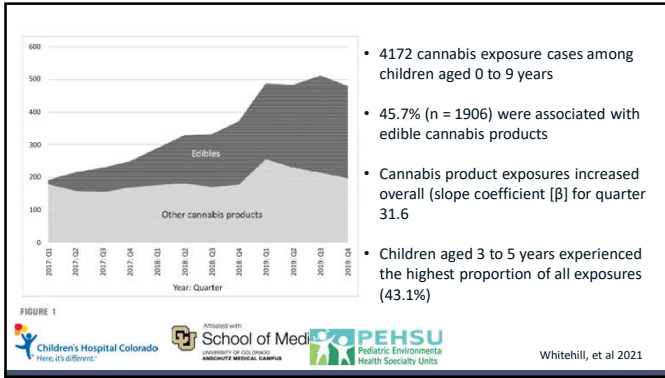


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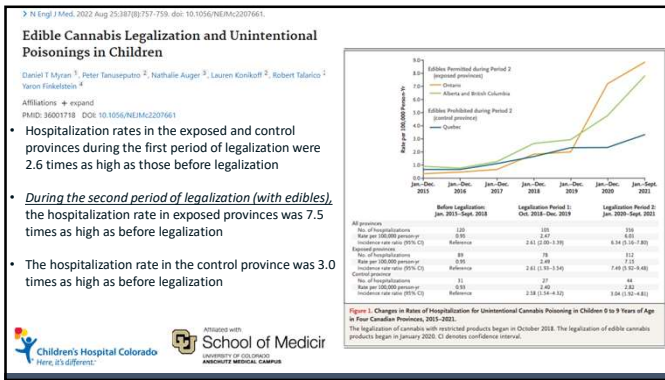


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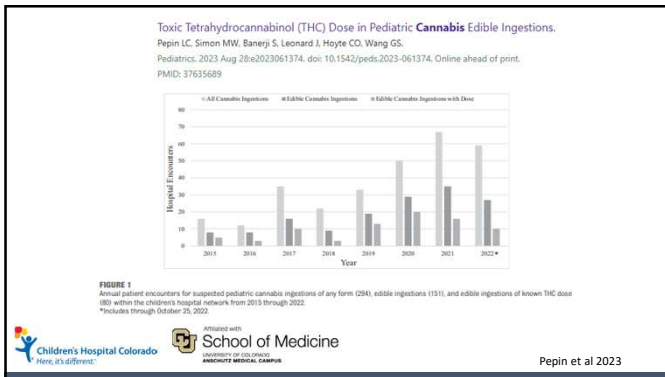




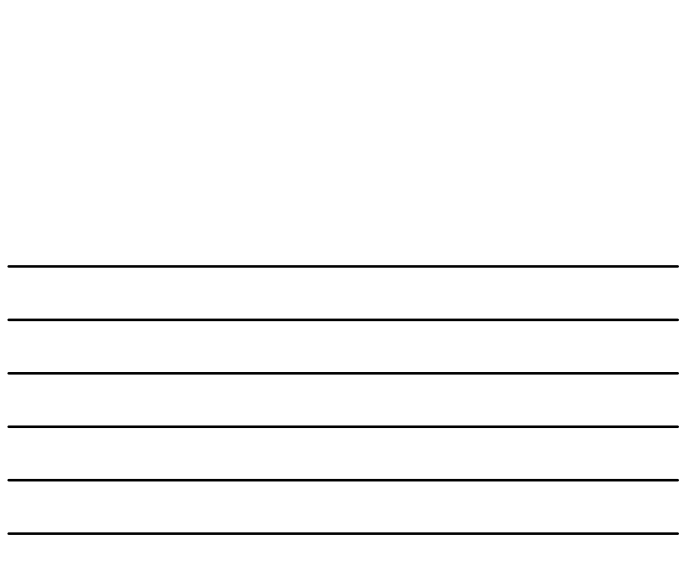
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Subst Use Misuse. 2022;57(8):1215-1219. doi: 10.1080/10826084.2022.2069268. Epub 2022 May 2.

Presence of Content Appealing to Youth on Cannabis-Infused Edibles Packaging

Andy S L Tan^{1,2}, Erica Weinreich³, Alisa Padon⁴, Mirsala Sanchez⁵, Kyle M Snyder², Anna Vasilyeva⁵, Simon Sandh⁵, Emily Goldmann^{5,6}, Melody Goodman⁵, Danielle C Ompad^{5,6}

Affiliations: [expand](#)
 PMID: 35491732 DOI: 10.1080/10826084.2022.2069268

- Analyzed 256 photos of cannabis-infused edible packaging in the US
- 15% of packages resembled product knockoffs
- 23% contained human/non-human creatures
- 35% contained flavor images
- 91% contained flavor text
- Median number of colors was 5 (range from 1 to 10+)










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CO REGULATIONS

- Recreational
 - Each individual packaged edible retail product, even if comprised of multiple servings ≤ 100 mg THC
 - May not be designed to appeal to children (specifically targets individuals < 21 yo, including but not limited to cartoon or similar images)
 - Statement whether the container is child-resistant
 - Must leave with exit package that is child-resistant (meet PPPA/CPCS standards)
 - Warnings: "keep out of reach of children"
 - No mass market campaigns
- Medical
 - Legislation matches recreational regulations
 - Exception is THC amount

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Hallucinogenic Mushrooms




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Colorado Proposition 122 – Nov 2022

- Decriminalize the personal possession, growing, sharing, and use, but not the sale, of five natural psychedelic substances by individuals aged 21 and over
- Including two substances found in psychedelic mushrooms — psilocybin and psilocin
- Three plant-based psychedelic substances — dimethyltryptamine, ibogaine, and mescaline



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Colorado Proposition 122 – Nov 2022

- Late 2024, allow the supervised use of psychedelic mushrooms by individuals aged 21 and over at licensed facilities and require the state to create a regulatory structure for the operation of these licensed facilities.
- Allow the state to expand the types of substances that may be used in licensed facilities to include the use of additional plant-based psychedelic substances — dimethyltryptamine (DMT), ibogaine, or mescaline — starting in 2026.



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Colorado Proposition 122 – Nov 2022



- Prohibit local governments from banning licensed facilities, services, and use of natural psychedelic substances as permitted by the measure, while allowing local governments to regulate the time, place, and manner of operation of these facilities.
- Establish penalties for individuals under the age of 21 for possessing, using, or transporting natural psychedelic substances and for individuals aged 21 and over who allow underage access to these substances.



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History

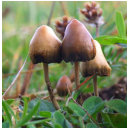
- Studies using LSD since 1940's as a coadjuvant in psychotherapy
- 1960's increased recreational use
- 1970: DEA scheduled 1
- 1975: NIMH withdrew research funding
- 2000's: Resumed research



Rivera-Garcia et al. Rev Invest Clin. 2023;75(3):369-378

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Hallucinogenic Mushrooms

- Psilocybin-containing mushrooms
- Structure similar to serotonin (and LSD)
 - 1:100 potency
- Rapid produce symptoms
 - Ataxia, hyperkinesia
 - Visual illusions and hallucinations
- 20-30 min, peak 2-3 hours, last 4-6 hours



CC1=CN(C=C1C2=CC=C(C=C2)C3=CC(=O)C=C3OP(=O)(O)O)CCN(C)C



Psilocybin

CC1=CN(C=C1C2=CC=C(C=C2)C3=CC(=O)C=C3O)CCN(C)C

Psilocin

CC1=CN(C=C1C2=CC=C(C=C2)C3=CC(=O)C=C3O)CCN


Serotonin





Stevens et al. 2011. https://commons.wikimedia.org/wiki/File:2009-03-13bufo_ajuaru007.jpg

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Other "Natural" Hallucinogens

- Dimethyltryptamine (DMT)
 - N,N-dimethyltryptamine, 5-methoxydimethyl tryptamine (Bufo Toad)
 - Serotonin agonist
 - Yakee (*Virola calophylla*) plant
 - Ayahuasca hallucinogenic tea
 - Take with plants with harmine alkaloids
 - Inhibit MAO in gut to increase bioavailability
 - 30-60 min onset, max 1-2 hours, 4 hour duration








Stevens et al. 2011. https://commons.wikimedia.org/wiki/File:2009-03-13bufo_ajuaru007.jpg

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Other "Natural" Hallucinogens

- Ibogaine
 - Psychoactive indole alkaloid
 - African rainforest shrub *Tabernaemthe Iboga*
 - CYP 2C9 metabolism
 - NMDA (antagonist), mu-opioid receptor, acetylcholine, serotonin, dopamine
 - Role in SUD?
 - alcohol, psychostimulants and opioids









Ugens et al 2016
https://commons.wikimedia.org/wiki/File:Tabernaemthe_Iboga-Jardin_botanique_Mexico_3287x29.jpg

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Other "Natural" Hallucinogens

- Mescaline
 - Morning glory seeds (*Ipomoea* spp)
 - Peyote cactus (*Lophophora williamsii*)
 - Phenylethylamine – stimulant effects like amphetamine
 - Serotonin receptor agonist
 - Slow onset of action, 2-4 h, and its effects last from 10 to 14 h








https://commons.wikimedia.org/wiki/File:Flowering_peyote_cactus.jpg
https://commons.wikimedia.org/wiki/File:Wild_Morning_Glory_-_Ipomoea_cordatoribba_328x29.jpg

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Why Hallucinogens?

- In 2006, a double-blind, randomized, and controlled study conducted on healthy subjects described that a high dose of psilocybin (30 mg) significantly improved psychological well-being over 2 months
- Anxiety, depression, OCD, psychiatric stress (ie cancer)
- Alcohol and nicotine dependence
- Lack of proper control conditions, discrepancies in dose, difficulties in double-blind studies.



Rivers-García et al. Rev Invest Clin. 2023;75(8):169-178

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Future

- Research using rigorous and validated methodology
- Safety and efficacy profile
- Long term impacts of use
- Unintended consequences
- Non-medical use, or use with minimal/lack of evidence



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Thanks for your attention

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