What do we know about adolescent cannabis use? Prevalence, harms and interventions

Jack Wilson

Tom Freeman

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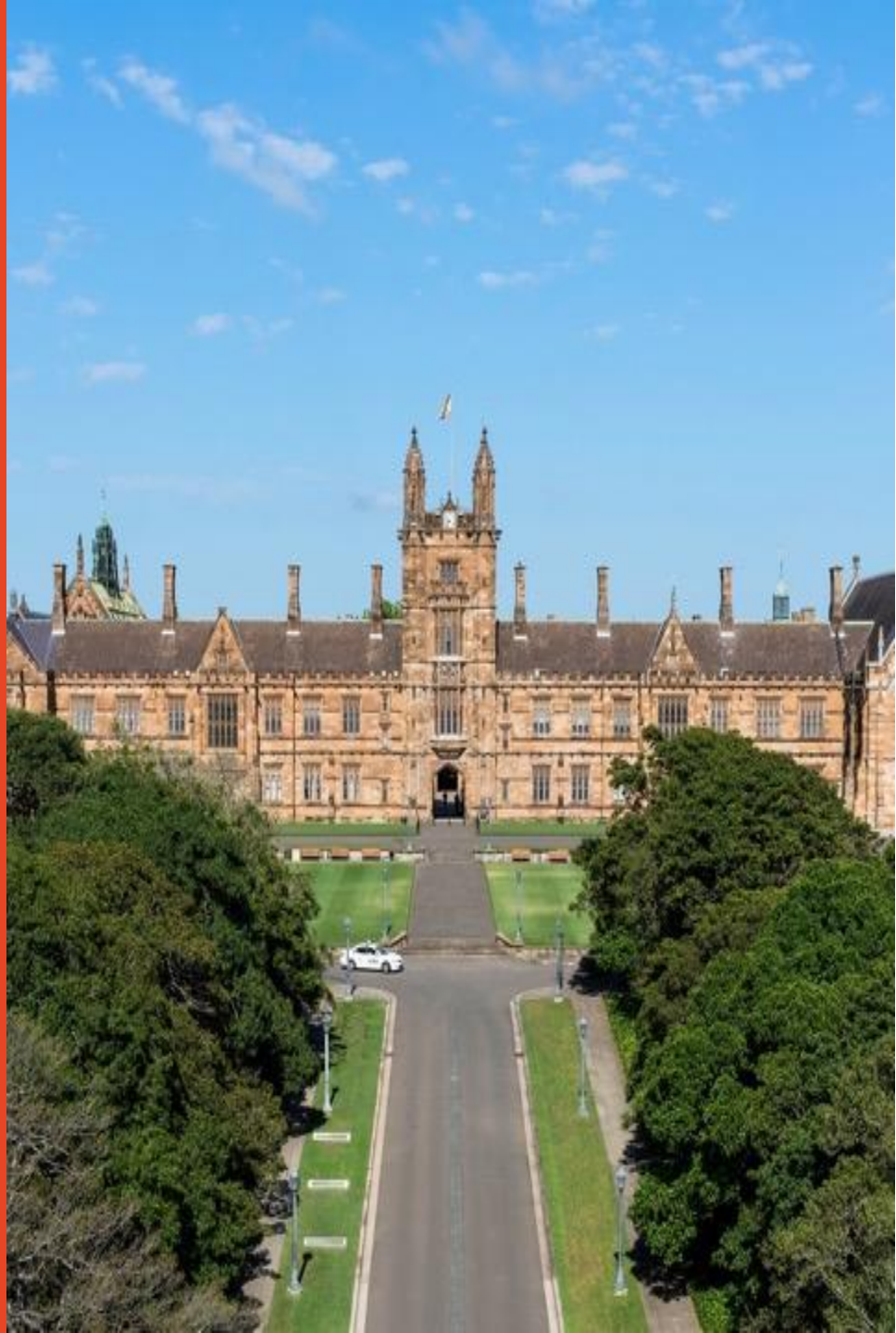

Before we begin our meeting, I would like to acknowledge the Traditional Owners of Australia and recognise their continuing connection to land, water and culture. I am currently on the land of the Gadigal people of the Eora Nation and pay my respects to their Elders, past, present and emerging. I further acknowledge the Traditional Owners of the country on which you are on and pay respects to their Elders, past, present and future

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Outline

- Characteristics and trends of adolescent cannabis use
- The effects of COVID-19 on cannabis use
- Cannabinoids, cannabis potency and different cannabis products
- The endocannabinoid system
- Harms associated with cannabis
- Evidence for prevention, treatment and harm reduction

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Background

- Approximately 188 million cannabis users worldwide in the past year *(UNODC, 2019)*
- 2.1 million Australians (>14 years) reporting past year cannabis use (10.4%) *(AIHW, 2016)*
- 17% of 12-17-year old's ever use cannabis and 5% use it weekly *(Guerrin & White, 2018)*

- Average age of first use – 18.7 *(AIHW, 2016)*
- 'Curiosity' and 'friends or family member were using it/ offered by friend or family member' *(AIHW, 2016)*

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Changes in adolescent cannabis use

- Australian data have shown both a slight decline (12.3% to 8.5% from 2004 to 2016) *(AIHW, 2016)* and increase (15% to 17% from 2011 to 2017) in ever cannabis use *(Guerrin & White, 2017)*
- Minor increase in weekly use (4% to 5%) *(AIHW, 2016)*
- US and European data report slight increase *(Johnson et al, 2018; EPSAD Group, 2015)*
- More pronounced reductions in adolescent tobacco and alcohol use

Perceptions of cannabis among young people

- Legal cannabis policies are becoming more common
- Increased support from for legalising cannabis *(AIHW, 2016)*
- Fewer people supporting penalties for illicit cannabis use *(AIHW, 2016)*
- More people approving regular adult cannabis use *(AIHW, 2016)*
- Cannabis is most commonly associated with drug problems (12-17) *(AIHW, 2016)*

COVID-19 and adolescent cannabis use

- Increased nervousness and restlessness *(ABS, 2020)*
- Like alcohol, some people use cannabis as a coping strategy *(Hyman & Sinha, 2009)*
- These people may be at the greatest risk of developing CUD
- Effects of COVID-19 on cannabis use may depend on availability
- Not as much impact on the availability of locally manufactured substances, like cannabis *(Winstock et al., 2020)*

COVID-19 and adolescent cannabis use

- Initial data show that since COVID-19, cannabis use *increased* in the Netherlands (sales are tolerated) but *decreased* in UK (sales prohibited)
- Over 40% increase in cannabis use compared to before COVID-19 restrictions *(Winstock et al., 2020)*
- Australia has the second highest proportion of increased use
- Most common reasons for increase: 'I have more time to use this drug' and 'I am more bored'

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COVID-19 and adolescent cannabis use

- Cannabis often shared in joints/bongs etc: risk of COVID-19 infection
- Adolescents often engage in risky behaviours; may be more prone to break social distancing guidelines and/or risky cannabis use behaviours such as sharing joints/bongs
- Home schooling may lead to reduced access to cannabis information, prevention and treatment programs
- Reinforce the need for more digital prevention and treatment programs

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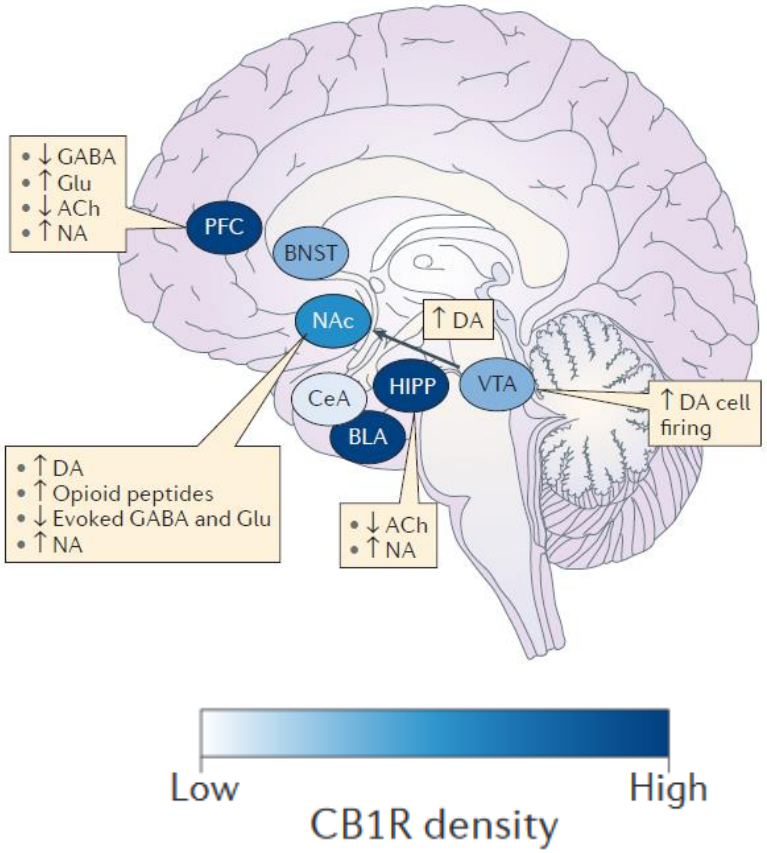
Cannabis and cannabinoids

- **THC (Δ^9-tetrahydrocannabinol)**
- Intoxicating
- ↑Anxiety & psychotic-like symptoms
- Cognitive impairment
- Addictive

- **CBD (cannabidiol)**
- Non-intoxicating
- ↓Anxiety & psychotic-like symptoms
- Pro-cognitive
- Anti-addictive



Curran et al. (2016) *Nature Reviews Neuroscience*

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Cannabis and cannabinoids

ELSEVIER

Neuroscience & Biobehavioral Reviews
Volume 107, December 2019, Pages 696-712

How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review

Abigail M. Freeman [a], Katherine Petrilli [a], Rachel Lees [a, b], Chandni Hindocha [a, d], Claire Mokrysz [a], H. Valerie Curran [a], Rob Saunders [a], Tom P. Freeman [a, b, c]

- The most common finding was that CBD reduced the acute effects of THC, however, results were mixed.
- CBD may reduce intense experiences of anxiety or psychosis-like effects of THC but this was not seen in all studies.
- CBD may blunt effects of THC on emotion and reward processing.

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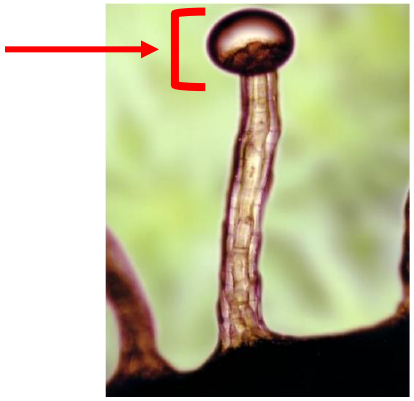
Cannabis and cannabinoids

Cannabinoids produced in glandular trichomes

Most abundant: flowering tops of female plants

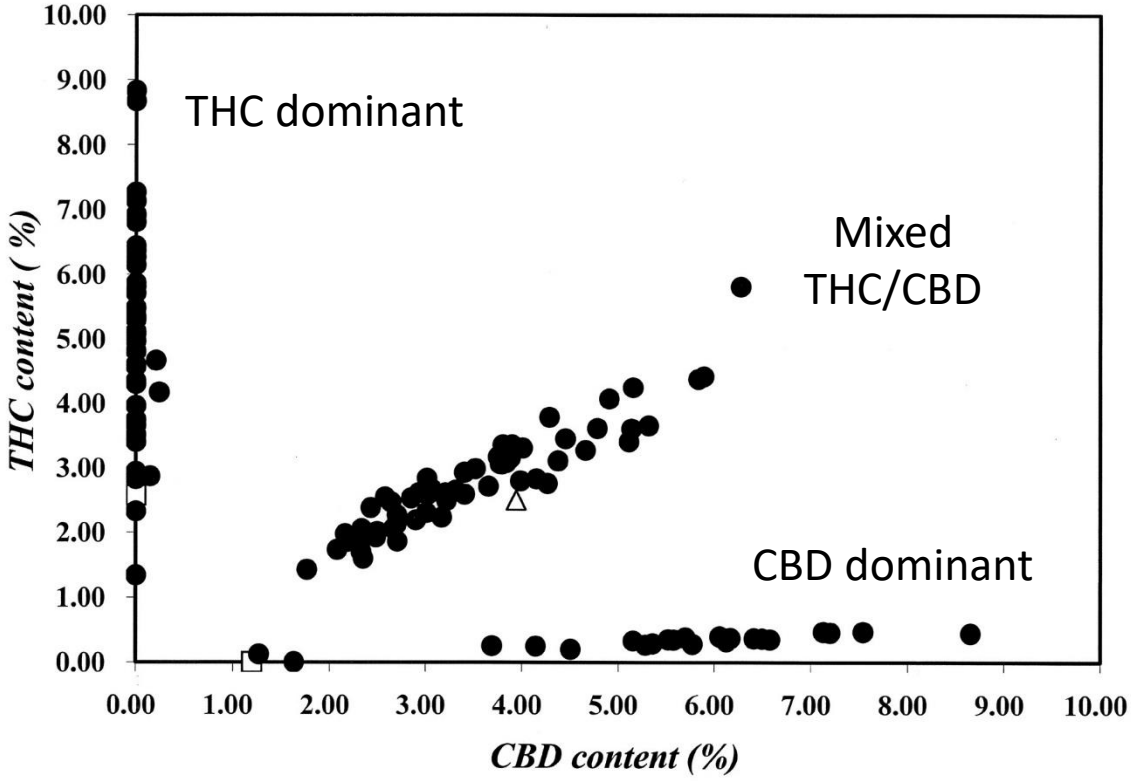
Cannabis plant produces at least 144 cannabinoids

THC (Δ^9-tetrahydrocannabinol)
CBD (Cannabidiol)



Cannabis and cannabinoids

Cannabis potency (% THC)



% CBD

de Meijer et al. (2003) *Genetics*

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Herbal cannabis

Seeded herbal cannabis

Females fertilized by males, seeded, grown outdoors:

~6% THC

Sinsemilla

Females separated from males, indoor grown, UV light:

~15% THC

Cannabis resin

Cannabis material rubbed over screen

Trichome heads detach, fall through screen

Loose trichomes: “kief”

Compressed into “resin” or “hashish” ~15% THC; ~5% CBD

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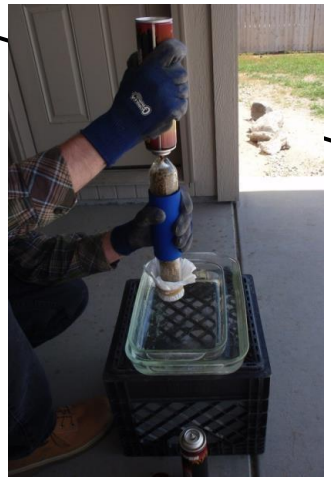
“Concentrates” - Butane Hash Oil

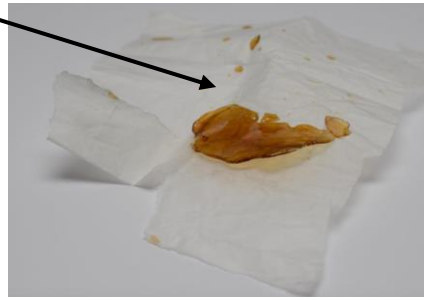
Ground cannabis in glass tube



Liquefied butane gas through tube

Extract contents
Not trichome cells or other plant material

Heat solution “purging”



“Shatter”: ~80% THC

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“Edibles”

Pop Tarts

“**Pot Tarts**” – 35mg THC

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Medicinal cannabis products

Dronabinol THC

Sativex (THC+CBD)

Epidiolex (CBD)

FIGURE 16
Medicinal cannabis in 5 g containers.

Photo © ncsm.nl.

Bedrocan (THC/CBD)

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Non-medicinal CBD products

‘Cannabis light’

CBD oil

CBD hummus

CBD dog treats

- Daily doses ~25mg CBD; clinical trials: 200-1500mg CBD
- Risk of THC content leading to positive urine screen

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Synthetic cannabinoid receptor agonists -"Spice"

- Synthetic drugs added to inert plant material
- Highly variable drug concentrations ('hot spots'); combination of drugs
- Full CB1R agonists: more severe adverse effects e.g. seizure, death

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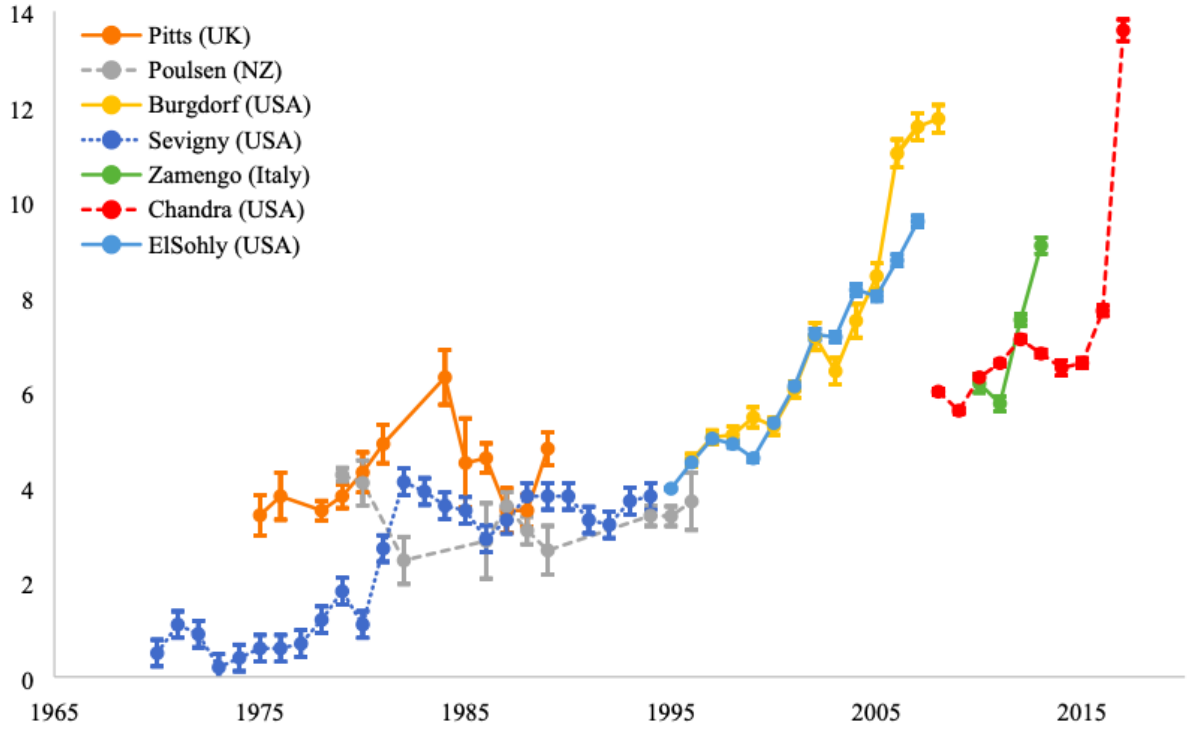
Increasing cannabis potency

- Sinsemilla/hydro cannabis dominates market in Australia, UK, US and Europe (Peacock et al., 2019; Swift et al., 2013; Smart et al., 2017; Potter, 2018; EMCDDA., 2019)

- Users only partially adapt their smoking behaviour when smoking stronger cannabis products (Freeman *et al.*, 2014, van der Pol *et al.*, 2014)

Increasing cannabis potency

Figure 2. Mean (standard error) concentrations of delta-9-tetrahydrocannabinol (THC) in all herbal cannabis



Increase in THC worldwide (Freeman et al., forthcoming)

- Annual increase of 0.3% in herbal cannabis
- Annual increase of 0.58% in hash/resin

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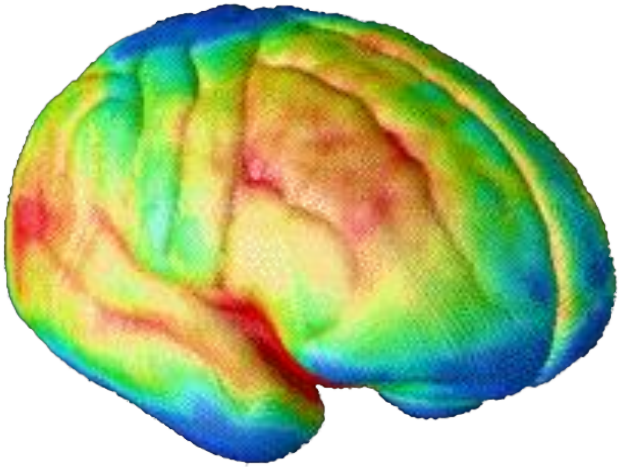
Adolescents susceptibility to the harms of greater THC content

- Period of dramatic cognitive development
- Seek reward in the face of uncertainty or potential negative outcomes *(Casey et al., 2008)*



- Adolescent cannabis users:
  - Demonstrate poor inhibition and attention
  - Require additional neural responses to do as well as non-users *(Behan et al., 2014; Norman et al., 2011; Mahmood et al., 2013; Tapert et al., 2007)*

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Cannabis and our endocannabinoid system

- The endocannabinoid system plays a critical role in human development (Curran et al., 2016)
- Exogenous cannabinoids (e.g. THC) could have a supra-physiological effect on endocannabinoid receptors, altering normal brain functioning (Keimpema et al., 2011)
- May explain why early cannabis use is associated with cognitive impairment and greater risk of mental health conditions

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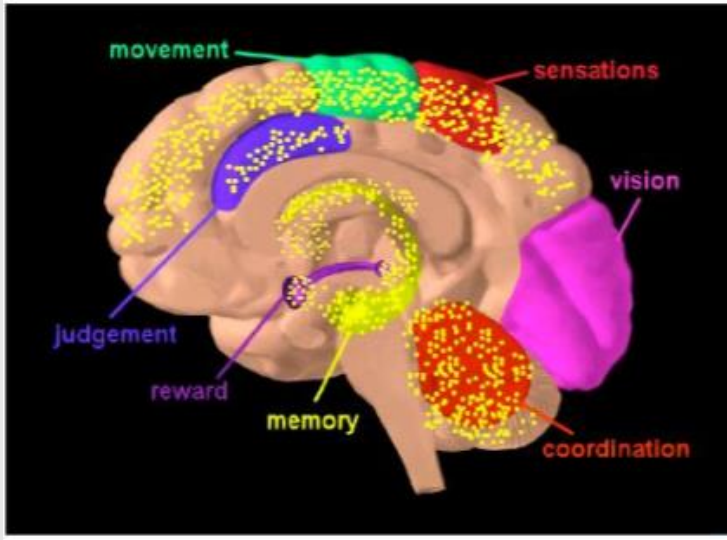

NIDA, 2014

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THE LANCET
Child & Adolescent Health

REVIEW | VOLUME 3, ISSUE 2, P121-128, FEBRUARY 01, 2019

Effects of increasing cannabis potency on adolescent health

Jack Wilson • Tom P Freeman, PhD • Clare J Mackie, PhD

Published: December 17, 2018 • DOI: https://doi.org/10.1016/S2352-4642(18)30342-0 • Check for updates

- Increased risk of psychotic symptoms, anxiety, depression and possible neurological decline
- Earlier age, more frequent, greater quantity > greater risk of harms
- Few studies have investigated the effects of different cannabis products on young people

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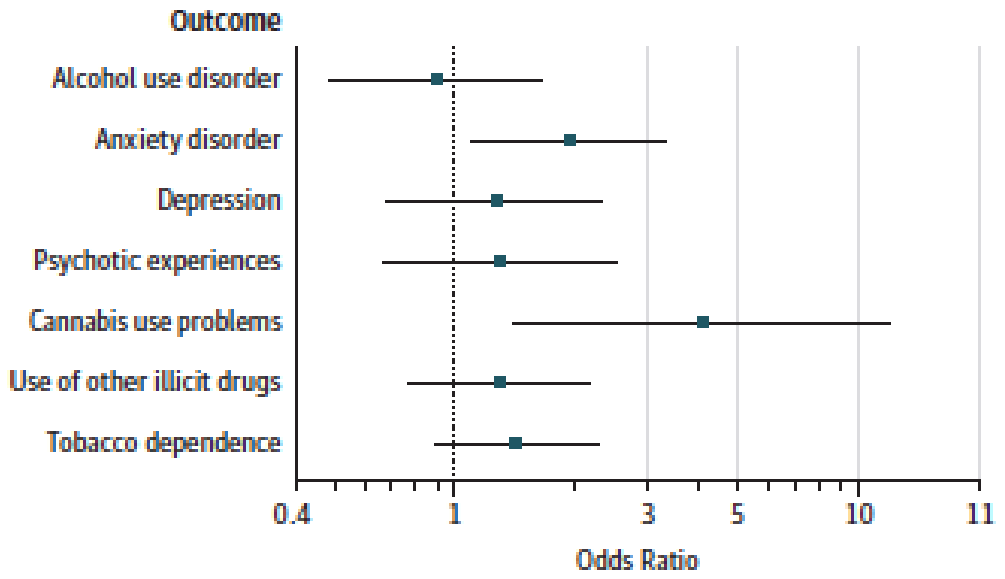
Increasing cannabis potency on adults

- Laboratory studies show dose dependent relationship between THC consumption and harms (Curran et al., 2002; D'Souza et al., 2004)

- Relationship between more potent cannabis products and:
  - Cannabis use disorder (Craft *et al.*, 2019; Freeman and Winstock, 2015; Meier, 2017)
  - Psychosis (Di Forti et al., 2015; Morgan et al., 2012)
  - Depression and anxiety (Chan et al., 2017; Morgan et al., 2012)

Effects of increasing cannabis potency on adolescents

Figure 2. Fully Adjusted Associations Between the Use of High-Potency Cannabis and Outcomes



Hines et al. (2020): General population study form the UK

When compared to low potency cannabis, use of high potency cannabis = 4 x greater risk of cannabis use problems; 2 x greater risk of anxiety disorder

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Limitations and future research

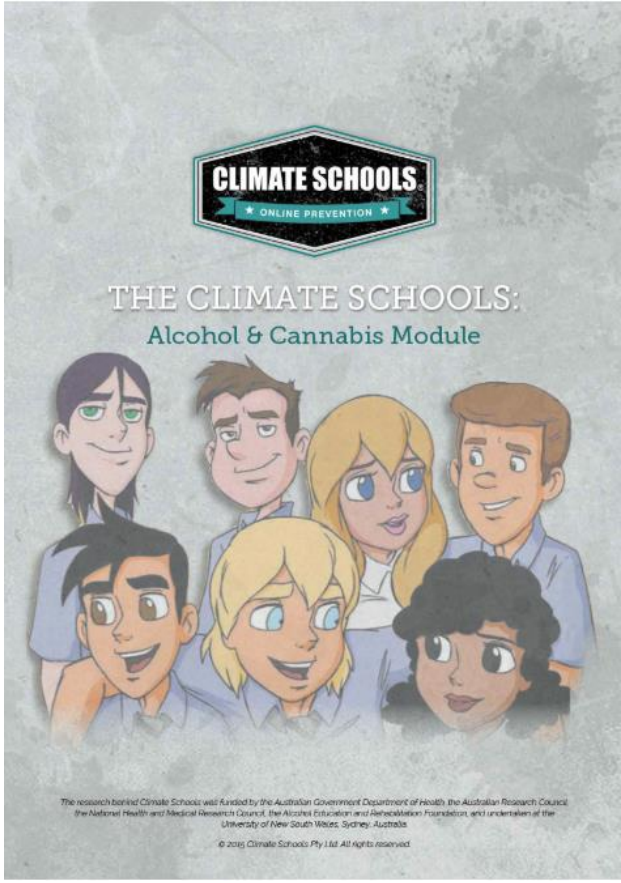
- Difficult to generalise conclusions from adult studies to adolescent populations

- Further research looking at the health effects of adolescent cannabis use must adopt measures of cannabis potency
  - Verbal descriptions
  - Pictorial aids

Prevention

Most effective:

- Interactive programs, as oppose to lecture style *(Lize et al., 2017; Faggiano et al., 2005, Foxcroft and Tsertsvadze, 2011, Norberg et al., 2013, Cuijpers, 2002)*
- Adopt a social influence approach - help develop skills to resist substance use *(Faggiano et al., 2005, Foxcroft and Tsertsvadze, 2011, Norberg et al., 2013)*
- Trained teachers or clinicians as instructors *(Lize et al, 2017)*
- Acknowledge the importance of parental relationships *(Vermeulen-Smit et al, 2015)*



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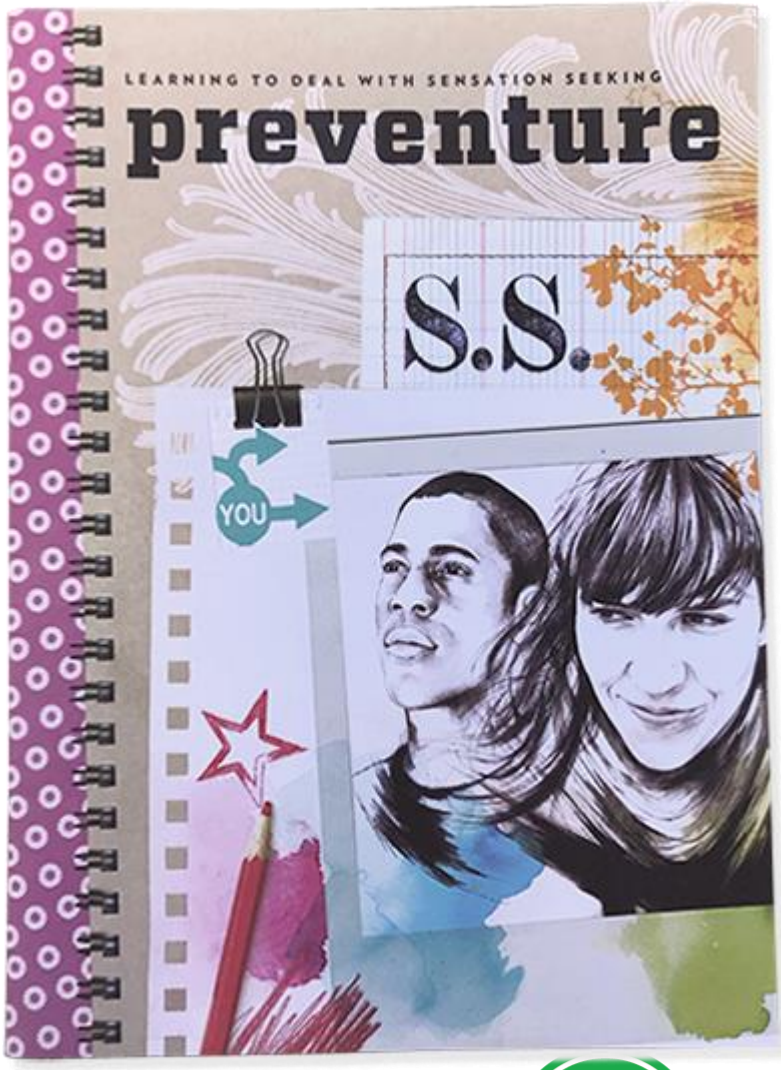
PreVenture

Personality targeted intervention towards those at greater risk of cannabis use
(Conrod, 2017)

- Focus on motivational factors for risky behaviours
- Provide coping skills
- Anxiety-sensitivity, hopelessness, impulsivity and sensation seeking
- Reduced odds of consuming cannabis over 24-month period
  (Conrod et al., 2010)



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Treatment

- Few people who use cannabis seek assistance from a health professional (Teesson et al., 2012)
- Psychosocial treatments
  - Combination of CBT, MET and CM approaches *(Gates et al., 2016)*
  - A mix of digital and clinical delivery *(Budney et al., 2015; Campbell et al., 2014)*
  - > 4 sessions and delivered for over a month *(Gates et al., 2016)*
  - Little evidence for long-term reductions in cannabis use *(Boumparis et al, 2019; Gates et al., 2016)*

Limitations to prevention and treatment

- Few programs have cannabis specific sessions
- Little discussion of different cannabis products or THC content
- Few studies have assessed the efficacy of treatments in adolescents

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Harm reduction

No recommendations based on ***quantity*** of use

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TF

Harm reduction

Australian Guidelines recommend healthy adults should drink no more than 10 standard drinks a week to cut the lifetime risk of harm from alcohol-related disease or injury

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Harm reduction

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

Addiction Opinion and Debate

'Standard THC units': a proposal to standardize dose across all cannabis products and methods of administration

Tom P. Freeman ✉, Valentina Lorenzetti

First published:12 October 2019 | https://doi.org/10.1111/add.14842

1 Standard THC Unit = 5 milligrams THC

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Harm reduction

NIH National Institute on Drug Abuse
Advancing Addiction Science

March 23, 2020 *By Dr. Nora Volkow*

Input Invited on the Establishment and Implementation of a Standard Unit Dose of Δ-9-tetrahydrocannabinol (THC) for Cannabis Research

Today, NIDA issued a Request for Information (RFI) from the research community and any other interested parties regarding the establishment of a standard unit dose of THC, the main psychoactive compound in cannabis, in order to facilitate research on cannabis.

In future, guidelines based on quantity may be available (e.g. no more than 10 THC units per week)

Standard units could offer concrete recommendations for **how much more vulnerable** adolescents are to the harmful effects of cannabis

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Summary

- Cannabis is the most common illicit drug used by young people
- COVID-19 may lead to problematic and more risky use
- Increases in THC associated with more severe adverse health outcomes

Summary

- Adolescents are particularly vulnerable to the harms associated with cannabis
- Prevention and treatment programs need to adopt evidence-based strategies
- Information and harm reduction strategies are critical

World Drug Report 2019 (United Nations publication, Sales No. E.19.XI.8)

Australian Institute of Health and Welfare 2017. National Drug Strategy Household Survey 2016: detailed findings. Drug Statistics series no. 31. Cat. no. PHE 214. Canberra: AIHW

Guerin, N. & White, V. (2018). ASSAD 2017 Statistics & Trends: Australian Secondary Students' Use of Tobacco, Alcohol, Over-the-counter Drugs, and Illicit Substances. Cancer Council Victoria.

ABS, *Household Impacts of COVID-19 Survey, 29 Apr - 4 May 2020*. 2020, Australian Bureau of Statistics.

Dietze, P. and A. Peacock, *Illicit drug use and harms in Australia in the context of COVID-19 and associated restrictions: Anticipated consequences and initial responses.* Drug and Alcohol Review, 2020

Bennett, C. (2010). *Cannabis and the soma solution*. Trine Day.

ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC (2016a) Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the United States. Biol Psychiatry 79(7):613–619

Di Forti, M., Marconi, A., Carra, E., Fraietta, S., Trotta, A., Bonomo, M., Bianconi, F., Gardner-Sood, P., O'Connor, J. & Russo, M. (2015). Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *The Lancet Psychiatry* 2, 233-238.

Morgan, C. J., Gardener, C., Schafer, G., Swan, S., Demarchi, C., Freeman, T. P., Warrington, P., Rupasinghe, I., Ramoutar, A., Tan, N., Wingham, G., Lewis, S., & Curran, H. V. (2012). Sub-chronic impact of cannabinoids in street cannabis on cognition, psychotic-like symptoms and psychological well-being. *Psychological medicine*, *42*(2), 391–400. https://doi.org/10.1017/S0033291711001322

Chan, G., Hall, W., Freeman, T. P., Ferris, J., Kelly, A. B., & Winstock, A. (2017). User characteristics and effect profile of Butane Hash Oil: An extremely high-potency cannabis concentrate. *Drug and alcohol dependence*, *178*, 32–38. https://doi.org/10.1016/j.drugalcdep.2017.04.014

Freeman, T. P., van der Pol, P., Kuijpers, W., Wisselink, J., Das, R. K., Rigter, S., van Laar, M., Griffiths, P., Swift, W. & Niesink, R. (2018). Changes in cannabis potency and first-time admissions to drug treatment: a 16-year study in the Netherlands. *Psychological medicine*, 1-7.

Englund, A., Morrison, P. D., Nottage, J., Hague, D., Kane, F., Bonaccorso, S., Stone, J. M., Reichenberg, A., Brenneisen, R., Holt, D., Feilding, A., Walker, L., Murray, R. M., & Kapur, S. (2013). Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *Journal of psychopharmacology (Oxford, England)*, *27*(1), 19–27. https://doi.org/10.1177/0269881112460109

Peacock A, Karlsson A, Uporova J, Gibbs D, Swanton R, Kelly G, Price O, Bruno R, Dietze P, Lenton S, Salom C, Degenhardt L, & Farrell, M (2019a). Australian Drug Trends 2019: Key findings from the National Ecstasy and Related Drugs Reporting System (EDRS) Interviews. Sydney, National Drug and Alcohol Research Centre, UNSW.

Swift W, Wong A, Li KM, Arnold JC, McGregor IS (2013) Analysis of Cannabis Seizures in NSW, Australia: Cannabis Potency and Cannabinoid Profile. PLoS ONE 8(7): e70052. https://doi.org/10.1371/journal.pone.0070052

EMCDDA (2019). Developments in the European cannabis market. In *EMCDDA Papers*: Publications Office of the European Union, Luxembourg.

Potter, D. J., Hammond, K., Tuffnell, S., Walker, C. & Di Forti, M. (2018). Potency of Δ9–tetrahydrocannabinol and other cannabinoids in cannabis in England in 2016: Implications for public health and pharmacology. *Drug testing and analysis* 10, 628-635.

Smart, R., Caulkins, J. P., Kilmer, B., Davenport, S., & Midgette, G. (2017). Variation in cannabis potency and prices in a newly legal market: evidence from 30 million cannabis sales in Washington state. *Addiction (Abingdon, England)*, *112*(12), 2167–2177. https://doi.org/10.1111/add.13886

Freeman, T. P., Morgan, C. J., Hindocha, C., Schafer, G., Das, R. K. & Curran, H. V. (2014). Just say 'know': how do cannabinoid concentrations Influence users' estimates of cannabis potency and the amount they roll in joints? *Addiction* 109, 1686-1694.

van der Pol, P., Liebregts, N., Brunt, T., Amsterdam, J., Graaf, R., Korf, D. J., Brink, W. & Laar, M. (2014). Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study. *Addiction* 109, 1101-1109.

Curran, H. V., Freeman, T. P., Mokrysz, C., Lewis, D. A., Morgan, C. J. & Parsons, L. H. (2016). Keep off the grass? Cannabis, cognition and addiction. *Nature Reviews Neuroscience* 17, 293.

Keimpema, E., Mackie, K., & Harkany, T. (2011). Molecular model of cannabis sensitivity in developing neuronal circuits. *Trends in pharmacological sciences*, *32*(9), 551–561. https://doi.org/10.1016/j.tips.2011.05.004

Chadwick, B., Miller, M. L., & Hurd, Y. L. (2013). Cannabis Use during Adolescent Development: Susceptibility to Psychiatric Illness. *Frontiers in psychiatry*, *4*, 129. https://doi.org/10.3389/fpsyt.2013.00129

Mahmood, O. M., Goldenberg, D., Thayer, R., Migliorini, R., Simmons, A. N., & Tapert, S. F. (2013). Adolescents' fMRI activation to a response inhibition task predicts future substance use. *Addictive behaviors*, *38*(1), 1435– 1441.https://doi.org/10.1016/j.addbeh.2012.07.012

Tapert, S. F., Schweinsburg, A. D., Drummond, S. P., Paulus, M. P., Brown, S. A., Yang, T. T., & Frank, L. R. (2007). Functional MRI of inhibitory processing in abstinent adolescent marijuana users. *Psychopharmacology*, *194*(2), 173–183. https://doi.org/10.1007/s00213-007-0823-y

Large, M., Sharma, S., Compton, M. T., Slade, T., & Nielssen, O. (2011). Cannabis use and earlier onset of psychosis: a systematic meta analysis. *Archives of general psychiatry*, *68*(6), 555–561. https://doi.org/10.1001/archgenpsychiatry.2011.5

Mackie, C. J., O'Leary-Barrett, M., Al-Khudhairy, N., Castellanos-Ryan, N., Struve, M., Topper, L., & Conrod, P. (2013). Adolescent bullying, cannabis use and emerging psychotic experiences: a longitudinal general population study. *Psychological medicine*, *43*(5), 1033–1044.https://doi.org/10.1017/S003329171200205X

Mackie, C. J., Castellanos-Ryan, N., & Conrod, P. J. (2011). Developmental trajectories of psychotic-like experiences across adolescence: impact of victimization and substance use. *Psychological medicine*, *41*(1), 47–58. https://doi.org/10.1017/S003329171000044

Kuepper, R., van Os, J., Lieb, R., Wittchen, H. U., Höfler, M., & Henquet, C. (2011). Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. *BMJ (Clinical research ed.)*, *342*, d738. https://doi.org/10.1136/bmj.d738

Henquet, C., Krabbendam, L., Spauwen, J., Kaplan, C., Lieb, R., Wittchen, H. U., & van Os, J. (2005). Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ (Clinical research ed.)*, *330*(7481), 11. https://doi.org/10.1136/bmj.38267.664086.63

Crippa, J.A., Zuardi, A.W., Martín-Santos, R., Bhattacharyya, S., Atakan, Z., McGuire, P. and Fusar-Poli, P. (2009), Cannabis and anxiety: a critical review of the evidence. Hum. Psychopharmacol. Clin. Exp., 24: 515-523.doi:10.1002/hup.1048

Lev-Ran, S., Roerecke, M., Le Foll, B., George, T. P., McKenzie, K., & Rehm, J. (2014). The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. *Psychological medicine*, *44*(4), 797–810. https://doi.org/10.1017/S0033291713001438

Gonzalez, R., Pacheco-Colón, I., Duperrouzel, J. C., & Hawes, S. W. (2017). Does Cannabis Use Cause Declines in Neuropsychological Functioning? A Review of Longitudinal Studies. *Journal of the International Neuropsychological Society : JINS*, *23*(9-10), 893–902. https://doi.org/10.1017/S1355617717000789

Lize, S. E., Iachini, A. L., Tang, W., Tucker, J., Seay, K. D., Clone, S., DeHart, D., & Browne, T. (2017). A Meta-analysis of the Effectiveness of Interactive Middle School Cannabis Prevention Programs. Prevention science : the official journal of the Society for Prevention Research, 18(1), 50–60. https://doi.org/10.1007/s11121-016-0723-7

Faggiano, F., Vigna-Taglianti, F. D., Versino, E., Zambon, A., Borraccino, A., & Lemma, P. (2005). School-based prevention for illicit drugs' use. *The Cochrane database of systematic reviews*, (2), CD003020. https://doi.org/10.1002/14651858.CD003020.pub2

Foxcroft, D. R., & Tsertsvadze, A. (2011). Universal school-based prevention programs for alcohol misuse in young people. *The Cochrane database of systematic reviews*, (5), CD009113. https://doi.org/10.1002/14651858.CD009113 Primary Prevention of Cannabis Use: A Systematic Review of Randomized Controlled Trials

Norberg MM, Kezelman S, Lim-Howe N (2013) Primary Prevention of Cannabis Use: A Systematic Review of Randomized Controlled Trials. PLOS ONE 8(1): e53187. https://doi.org/10.1371/journal.pone.0053187

Cuijpers P. (2002). Effective ingredients of school-based drug prevention programs. A systematic review. *Addictive behaviors*, *27*(6), 1009–1023. https://doi.org/10.1016/s0306-4603(02)00295-2

Vermeulen-Smit, E., Verdurmen, J. E. E., & Engels, R. C. M. E. (2015). The effectiveness of family interventions in preventing adolescent illicit drug use: A systematic review and meta-analysis of randomized controlled trials. *Clinical Child and Family Psychology Review*, *18*(3), 218-239.

Hyman, S. M., & Sinha, R. (2009). Stress-related factors in cannabis use and misuse: implications for prevention and treatment. Journal of substance abuse treatment, 36(4), 400–413. https://doi.org/10.1016/j.jsat.2008.08.005

Newton, N. C., Andrews, G., Teesson, M., & Vogl, L. E. (2009). Delivering prevention for alcohol and cannabis using the internet: A cluster randomised controlled trial. *Preventive medicine*, *48*(6), 579-584

Conrod, P. J., Castellanos-Ryan, N., & Strang, J. (2010). Brief, personality-targeted coping skills interventions and survival as a non–drug user over a 2-year period during adolescence. *Archives of general psychiatry*, *67*(1), 85-93.

Conrod, P. J. (2016). Personality-targeted interventions for substance use and misuse. *Current addiction reports*, *3*(4), 426-436.

Gates, P. J., Sabioni, P., Copeland, J., Le Foll, B., & Gowing, L. (2016). Psychosocial interventions for cannabis use disorder. *Cochrane Database of Systematic Reviews*, (5).

Teesson, M., Slade, T., Swift, W., Mills, K., Memedovic, S., Mewton, L., ... & Hall, W. (2012). Prevalence, correlates and comorbidity of DSM-IV cannabis use and cannabis use disorders in Australia. *Australian & New Zealand Journal of Psychiatry*, *46*(12), 1182-1192.

.

Budney, A. J., Stanger, C., Tilford, J. M., Scherer, E. B., Brown, P. C., Li, Z., ... & Walker, D. D. (2015). Computer-assisted behavioral therapy and contingency management for cannabis use disorder. *Psychology of Addictive Behaviors*, *29*(3), 501.

Campbell, A. N., Nunes, E. V., Matthews, A. G., Stitzer, M., Miele, G. M., Polsky, D., ... & Wahle, A. (2014). Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. *American Journal of Psychiatry*, *171*(6), 683-690.

Wilson, J., Freeman, T. P., & Mackie, C. J. (2019). Effects of increasing cannabis potency on adolescent health. *The Lancet Child & Adolescent Health*, *3*(2), 121-128.

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