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Review Article

Early Cannabis Use Poses Risks to Physical and Mental Health: Delayed Use/Non Use Encouraged

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Key Points

- Early teen cannabis use correlates with higher use of mental and physical health services in young adulthood.
- Teens who use cannabis early have more injuries, poisoning, respiratory, and other problems than abstainers.
- Five years of data show that the best advice on teen use of cannabis is: Don't use. Next best: Delay use.

Introduction

Researchers compared teens who began cannabis use before vs. after age 15 to assess physical and mental health impacts. Cannabis was neither performance-enhancing nor beneficial for overall health. The findings reinforce prior warnings about adolescent use and extend them by testing whether teen cannabis exposure predicts greater medical care utilization for mental and physical conditions in young adulthood [1]. The study also addresses critiques of self-report-only designs by capturing objective clinical outcomes. Causality cannot be established, and unmeasured confounders (e.g. genetics/epigenetics) may persist.

Legalization and product availability

These health concerns have grown as legalization has brought THC vapes, gummies, and other products into neighborhoods and schools. As prevention advocate Patrick J. Kennedy cautioned in 2018 on The Last Word: "Today's THC drug products are not the marijuana of years ago. They are engineered to maximize potency and hook a new generation of high-frequency users to make huge profits for an industry that relies on addiction to succeed".

Cohort and outcomes assessed

In a JAMA cohort from Québec, Canada, 1,591 participants (51.4% female) were followed from birth to age 23 using linked health databases (Figure 1). Self-reported past-12-month cannabis use at ages 12, 13, 15, and 17 was compared with records from ages 18-23 for care related to any mental disorder, substance-related disorders, suicide-related behaviors, and physical conditions (respiratory diseases, injuries/poisoning, and other diseases) [1].

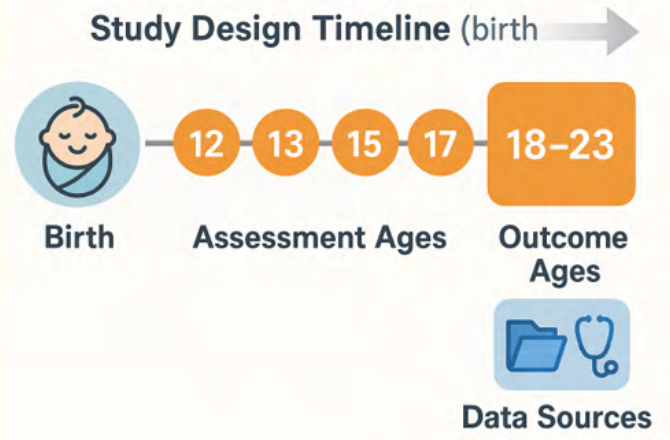

Figure 1: *Study design timeline of the Québec birth cohort. This schematic illustrates the longitudinal study design used to evaluate the effects of adolescent cannabis use on later health outcomes. Participants (N = 1,591; 51.4% female) were enrolled at birth and followed to age 23. Self-reported cannabis use was assessed at ages 12, 13, 15, and 17, while health service utilization data were collected from ages 18 to 23 through linked Canadian health databases. Outcome measures included mental disorders, substance-related disorders, suicide-related behaviors, and physical conditions such as respiratory disease and injury/poisoning [1].*

Early onset as a risk signal for health service utilization

Early adolescent use was associated with higher mental and physical health care utilization in young adulthood, consistent with prior reviews of health risks [2]. Later-onset use showed more physical, but not mental-health, signals. These results align with national recommendations to avoid cannabis during adolescence, delay initiation, and minimize exposure [3].

Moreover, the new research underscores strategies to delay initiation and reduce use intensity, aligning with public-health messaging. As co-author Pablo Martínez, PhD (McGill), noted, even after accounting for multiple pre-existing risk factors, early-onset users showed higher utilization of mental and physical health services-suggesting cannabis itself may contribute to risk [4].

Specific psychiatric or medical diagnoses were not delineated. However, among early/frequent users, emergency department visits for injuries, poisoning, and other physical problems were elevated. Cannabis-related ED visits among youths aged 10-24 years nearly quintupled from 2003 to 2017, with rising severity and admissions-an emerging public-health burden that warrants investigation into causes and consequences [5].

Mechanistic plausibility: THC pharmacology and neurodevelopment

If cannabis were treated as a medicine, it would be considered dangerous until proven safe and effective. In adolescents, use stresses the developing body and brain; early or heavy exposure increases the odds of later mental and physical morbidity requiring care.

Over the past four decades, THC content has increased due to breeding and cultivation changes. THC mimics endocannabinoids at CB1 and CB2 receptors but functions pharmacologically as a partial agonist [6]. Emerging evidence indicates that CB1 activation by THC can reduce neuronal growth-factor production and disrupt signaling pathways essential for synapse formation. In mice, Ritchie., *et al.* observed impaired maternal spiral artery remodeling with cannabis exposure and found that CBD and THC disrupt immune-cell angiogenic factor production; oral THC or CBD caused fetal growth restriction and long-lasting, sex-specific outcomes (altered aggression and metabolism in males; impaired spatial learning in females) [7].

Adolescent brain vulnerability

Because these factors are central to brain development and neuronal maturation during puberty, THC likely affects adolescents differently than adults. In adolescent users, structural changes-including gray-matter loss in specific regions-have been observed [8]. Recent studies also show age-dependent effects of THC on brain and behavior; early use is associated with neuropsychological deficits [9].

Implications for mood disorders and research priorities

Consistent with the McGill findings, the Canadian Centre on Substance Abuse (CCSA) reports, "Early-onset cannabis use has a tremendous impact on the structure and functioning of the teenage brain and can weaken the foundation for future life success" [10]. Evidence further links cannabis use with a worsened course and functioning in bipolar disorder and major depressive disorder. Future research should more precisely measure type, dose, and frequency of use and select comparison groups that better control for shared risk factors [11].

Clinical takeaway

Take-home for parents and pediatricians: prevention is critical. Delay first use as long as possible; frequent use should trigger evaluation. Screening should explicitly assess age at first use and frequency. Beyond the harms reported in the JAMA study, cannabis use is also linked to fatal car crashes: meta-analyses and culpability studies show a small but significant increase in crash risk after acute use, with risk varying by study design, crash severity, and exposure assessment. Some studies find a correlation between high THC blood concentrations and crash risk, while most do not observe this at lower concentrations [12].

Numerous studies (2019-2025) link early and/or heavy adolescent cannabis use to higher risks of later mental-health problems, cognitive effects, and increased health service utilization (Figure 2). A major longitudinal study found that adolescent cannabis use is associated with adult depression and suicidality, with risk rising as age at first use decreases and use frequency increases-mirroring the JAMA report [13].

Mechanistic link: Working memory and academic function

Cannabis may reduce achievement-related anxiety by impairing working memory [14]. In a recent JAMA study of ~1,000 young adults, recent and heavy lifetime use correlated with reduced brain activation during working-memory tasks, a plausible mechanism for academic and functional impairment noted in the new study [15]. Adolescent use has been associated with cognitive deficits, depression, and psychosis risk; although causality is not definitive, converging evidence indicates that earlier initiation and heavier exposure carry substantial risk [16,17].

Expert consensus and practical screening questions

Prominent experts-including Nora Volkow, M.D. (NIDA), Herbert Kleber, M.D. (Yale), Kevin Hill, M.D. (Harvard), Yasmin Hurd, Ph.D. (Mt. Sinai), Surgeon General Vivek Murthy, M.D., Mark S. Gold, M.D., and Kenneth Blum, Ph.D.-warn of legalization-related harms driven by increased access, higher THC concentrations, shifts in perceived risk, and heightened vulnerability among teens who may mistakenly consider cannabis safe [18]. Precise screening is warranted: instead of "Do you use cannabis?" ask "At what age did you first try cannabis?", "What forms do you use?", and "How often do you use now (e.g. daily/near-daily)?"

Counseling priorities

We propose counseling on intoxication-related injuries (driving, sports, falls), edible-related poisoning, and respiratory toxicity from smoked products (Figure 2). "Delay initiation, reduce intensity" aligns with the evidence base, the authors' conclusions, and prevention strategies shown to curb substance-use trajectories [19-23].

Recent data warrant rethinking adolescent cannabis use given clear risks. In a birth-cohort study, early and frequent use predicted greater medical care utilization for mental and physical conditions in young adulthood, supporting strategies to delay initiation and reduce intensity [24].

Standardization and adolescent neurobiology

The evidence supports a straightforward public-health message: delay or avoid adolescent cannabis use-not for ideology, but because the drug cannot be reliably standardized or titrated. Potency, purity, and bioavailability vary across cultivars and labs; even in regulated markets, nominally identical products can deliver very different exposures. International consensus indicates that a reproducible "standard THC unit" remains elusive [25]. Such variability collides with adolescent neurobiology, when synaptic pruning and dopaminergic tuning are highly dose-sensitive. In short, the drug is most unpredictable when the brain is most vulnerable.

Policy priority #1: Delay

Each additional year before initiation lowers the odds of dependence, cognitive decline, and psychiatric comorbidity. Prevention messaging should emphasize neuroscience over moralism-the adolescent brain is still wiring itself, and today's THC is not a fixed dose-reframing "just say no" as "protect neural development".

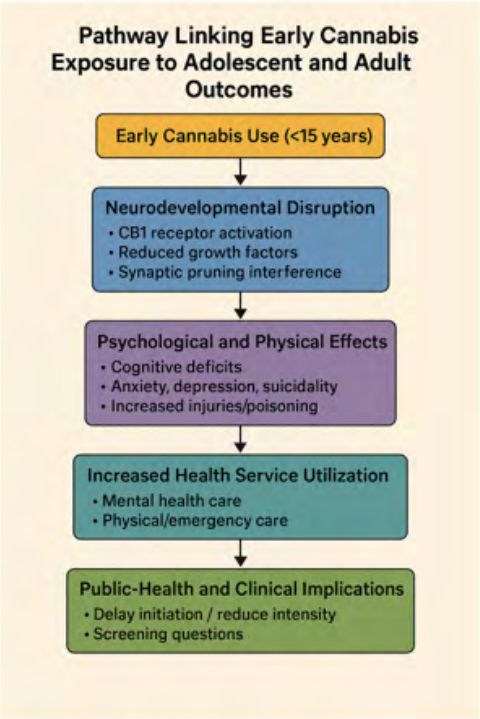

Figure 2: *Pathway linking early cannabis exposure to adolescent and adult outcomes. This conceptual flowchart illustrates the link between early cannabis use (before age 15) to later neurodevelopmental, psychological, and clinical outcomes. Early exposure may disrupt neurodevelopment through CB1 receptor activation, reduced neuronal growth factors, and interference with synaptic pruning. These alterations are associated with cognitive deficits, anxiety, depression, suicidality, and increased risk of injuries or poisoning. In young adulthood (ages 18-23), such effects translate into greater utilization of mental and physical health services. The model concludes with public-health and clinical implications emphasizing delayed initiation, reduced use intensity, targeted screening, and preventive counseling for adolescents and parents.*

Policy priority #2: Science-based Substitution (not abstinence alone)

Many adolescents use cannabis to self-manage dysphoria. Restricting access without addressing that drive ignores reward biology. Standardized pro-dopamine formulations such as KB220 exemplify a precision-nutraceutical approach aimed at homeostatic (not hedonic) modulation: manufactured under cGMP with fixed ingredient ratios and evaluated for dopaminergic normalization. Conceptually, the contrast is restoration versus intoxication.

For regulators

Psychoactive agents that cannot be standardized should not be marketed as medicines, whereas standardized, non-euphorigenic compounds should be studied under frameworks that ensure quality, reproducibility, and post-market safety. Prevention campaigns should pair education on dose variability with development of reproducible, mechanism-based interventions manufactured to pharmaceutical-grade standards. Insurance coverage for brief counseling should mirror tobacco and alcohol models, and national health metrics should track "age of first use" as a routine vital sign of prevention success. For clinicians, the policy reduces to a simple rule: when the brain is still developing and the psychoactive is unstandardized, the burden of proof for safety must rest with the substance, not the patient.

For clinicians

When the brain is still developing and the psychoactive is unstandardized, the burden of proof for safety rests with the substance, not the patient.

Finally, adolescent cannabis use introduces an unpredictable psychoactive into a system still under construction. The rational response is to delay exposure, reduce intensity, and explore standardized, homeostasis-oriented nutraceuticals as exemplars of safe, reproducible, non-euphorigenic interventions. Standardization is not bureaucratic-it is the ethical boundary between experimentation and prevention [25].

Summary

As Sarah Vinson, M.D., professor and chair of psychiatry at Morehouse School of Medicine, stated in a recent Addiction Policy Forum webcast on cannabis: "We have been warning kids and their parents that cannabis is not a medicine for them. Cannabis use during adolescence and young adulthood may directly harm and compromise the developing brain. Research shows … one in six people who start using cannabis before the age of 18 can become addicted".

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Author Contribution

The initial draft was developed by KB and MSG. All co-authors reviewed made significant comments and edits and approved the manuscript.

Conflict of Interest

KB reports owning USA and foreign patents related to both GARS and KB220.

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Bibliography

1. Martínez P., *et al*. "Health service use among young adults with a history of adolescent cannabis use: a population-based birth cohort study". *JAMA Network Open* 8.10 (2025): e2539977.
2. Hill KP., *et al*. "Risks and benefits of cannabis and cannabinoids in psychiatry". *American Journal of Psychiatry* 179.2 (2022): 98-109.
3. Gobbi G., *et al*. "Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: A systematic review and meta-analysis". *JAMA Psychiatry* 76.4 (2019): 426-434.
4. McGill University Press Release. "Study links early cannabis use and health problems". McGill University Newsroom (2025).
5. Bechard M., *et al*. "Cannabis-related emergency department visits by youths and their outcomes in Ontario: a trend analysis". *CMAJ Open* 10.1 (2022): E100-E108.
6. Dhein S. "Different effects of cannabis abuse on adolescent and adult brain". *Pharmacology* 105.11-12 (2020): 609-617.

7. Ritchie TM., *et al*. "The impact of oral cannabis consumption during pregnancy on maternal spiral artery remodeling, fetal growth and offspring behaviour in mice". *EBioMedicine* 114 (2025): 105572.

8. "How Does Marijuana Affect the Brain?". APA Monitor on Psychology. American Psychological Association (2023).

9. Li R and Tao F. "Effects of cannabis exposure on adolescent health and development: a narrative review". *Current Drug Research Reviews* 17.2 (2025): 160-169.

10. Murray CH., *et al*. "Age-related effects of cannabis and cannabinoids on brain and behavior". *Cannabis and Cannabinoid Research* (2025).

11. Tourjman SV., *et al*. "Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force Report: A Systematic Review and Recommendations of Cannabis use in Bipolar Disorder and Major Depressive Disorder". *Canadian Journal of Psychiatry* 68.5 (2023): 299-311.

12. Preuss UW., *et al*. "Cannabis use and car crashes: a review". *Frontiers in Psychiatry* 12 (2021): 643315.

13. Fontanella CA., *et al*. "Association of cannabis use with self-harm and mortality risk among youths with mood disorders". *JAMA Pediatrics* 175.5 (2021): 470-478.

14. Cuttler C., *et al*. "Acute effects of cannabigerol on anxiety, stress, and mood: a double-blind, placebo-controlled, crossover, field trial". *Scientific Reports* 14.1 (2024): 16163.

15. Gowin JL., *et al*. "Brain function outcomes of recent and lifetime cannabis use". *JAMA Network Open* 8.1 (2025): e2457069.

16. Nelson J and Nosko J. "Cannabis use in adolescence and young adulthood and its impact on brain development: A scoping review". *Frontiers in Psychiatry* 16 (2025): 1644105.

17. Churchill V., *et al*. "The association between cannabis and depression: An updated systematic review and meta-analysis". *Psychological Medicine* 55 (2025): e44.

18. Blum K., *et al*. "Cannabis-induced hypodopaminergic anhedonia and cognitive decline in humans: embracing putative induction of dopamine homeostasis". *Frontiers in Psychiatry* 12 (2021): 623403.

19. Dennen CA., *et al*. "Neurogenetic and epigenetic aspects of cannabinoids". *Epigenomes* 6.3 (2022): 27.

20. Blum K., *et al*. "Psychoactive drugs like cannabis-induce hypodopaminergic anhedonia and neuropsychological dysfunction in humans: putative induction of dopamine homeostasis via coupling of genetic addiction risk severity (GARS) testing and precision pro-dopamine regulation (KB220)". *EC Neurology* 13.4 (2021): 86-92.

21. Penman SL., *et al*. "Vaporized delta-9-tetrahydrocannabinol inhalation in female Sprague Dawley rats: a pharmacokinetic and behavioral assessment". *Current Pharmaceutical Design* 29.27 (2023): 2149-2160.

22. Bloom J., *et al*. "Cannabis use patterns and blood profiles in adolescent cannabinoid hyperemesis syndrome". *Pediatric Emergency Care* (2025).

23. Spiga F., *et al*. "Pharmacotherapies for cannabis use disorder". *Cochrane Database of Systematic Reviews* 9.9 (2025): CD008940.

24. Mari M., *et al*. "Personality-based intergenerational effects of prenatal THC exposure in an inherited mouse model of social dominance and submissiveness". *Scientific Reports* 15.1 (2025): 30624.

25. Freeman TP., *et al*. "'Standard THC units': a proposal to standardize dose across all cannabis products and methods of administration". *Addiction* 115.7 (2020): 1207-1216.

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